Advanced Concepts in Lumbar Degenerative Disk Disease

João Luiz Pinheiro-Franco
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Editors

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The Work was first published in 2010 by Dilivros Editora Ltda., Rua Dr. Satamini 55, Tijuca, Rio de Janeiro, RJ, Brazil with the following title: Conceitos Avançados em Doença Degenerativa Discal Lombar.

ISBN 978-3-662-47755-7 ISBN 978-3-662-47756-4 (eBook)
DOI 10.1007/978-3-662-47756-4

Library of Congress Control Number: 2015952115

Springer Heidelberg New York Dordrecht London

Printed on acid-free paper

Springer-Verlag GmbH Berlin Heidelberg is part of Springer Science+Business Media (www.springer.com)

This book is dedicated to the neurosurgeon who inspired my career: my father, Luiz Fernando Pinheiro-Franco, who is fond of saying Natura non facit saltus (Latin for "Nature (Life) *makes no leap").*

João Luiz Pinheiro-Franco

We also dedicate this book to our patients and our colleagues. Without all of them, this book would not have been possible.

João Luiz Pinheiro-Franco
Alexander R. Vaccaro
Edward C. Benzel
H. Michael Mayer

Preface

After my graduation in neurosurgery, I had the unexpected privilege to immerse myself in 4 years of clinical and research fellowships, working with or simply observing the clinical and surgical techniques of several world-renowned experts in treating spinal diseases. Being far from my native country, I had at times longed for family, friends, and colleagues, yet at the same time, the experience thrust me into the emerging field of globalized spinal surgery. It was during this time that I first came in direct contact with incredibly interesting people, all of us breaking the barriers of language to make sense of many different concepts, with different ideas bubbling forth from so many gifted minds. Although there was tremendous diversity in our avenues of thought, everyone was driven by the common pursuit of great results.

These were my earliest impressions as a "global spinal surgeon." Reflecting on that time, I can say undoubtedly that the single unifying element of that great diversity in talent and ideas was an underlying modus operandi dedicated to the common goal of serving the well-being of patients suffering from lower back ailments. It was during this period when I conceived the notion of a "puzzle theory" of knowledge: different pieces of a puzzle falling into place. At first, only a few scattered pieces seemed to make sense, others less so or not at all. However, gradually, as more pieces came together, a clear image steadily emerged, more tangible, more solid, and more understandable.

I share this experience with you to offer insight into the origin of this book. In some respects, it is a tribute to the people from around the world who contributed with total mind and dedication to what had once seemed the serendipity of solving the "puzzle" of what today we call *lumbar degenerative disk disease*. This is the wellspring we present to you as *Advanced Concepts in Lumbar Degenerative Disk Disease*.

It is a great honor to share with you the insights and rigor of my coeditors, Dr. Alexander R. Vaccaro, Dr. Edward C. Benzel, and Dr. H. Michael Mayer. They are perhaps the three greatest minds I have ever had the opportunity to work with. Above all, they each possess a particular magnetism and charisma that electrify audiences with their knowledge in a way that influences people to make a difference in the world. They themselves have made many great differences, yet they are modest and sincere in their relationships with both colleagues and patients. I thank them dearly for the time invested and the enormous knowledge shared in the chapters of this book.

Similarly, I extend my thanks to everyone who participated in the production of the various chapters in this book. This dedicated group of men and

women from all over the world helped gather a variety of concepts into an extensive knowledge base for our field. These contributors include internationally recognized thinkers of new concepts, creators of innovative techniques and novel instruments, and courageous voices of provocative new philosophies—all at the vanguard of lumbar degenerative disk disease.

Advanced Concepts in Lumbar Degenerative Disk Disease was written and designed for spinal surgeons, neurosurgeons, and orthopedic surgeons: those who are new to the field as well as those who are more seasoned professionals.

Part I of the book begins by laying out the foundations of bipedalism and the importance of the verticalization of the spine, that is, the alignment of the intervertebral disks to bear the weight and function of the upper body. The opening chapter was written by the internationally award-winning French paleoanthropologist Yves Coppens, who also gave his name to the asteroid. Then, Gusmão et al., in fine detail, take the reader through the evolution of the concept of sciatica to what is known today as lumbar disk degeneration. Part I continues with an award-winning German scientist's discussion of the pathophysiologic fundamentals of disk degeneration and the degenerative cascade. Epidemiology is treated by the late Pierre Kehrli, with the section on genetics perhaps deserving the most attention. This subject is examined further in the chapter by Cheung et al.

Part II opens with contemporary advancements in spinal imaging, with a subsequent chapter by Dr. Michael Modic. An experienced team of experts then takes on the controversial theme of diskography.

Part III examines the day-to-day issues faced by surgeons in practice: psychosocial aspects in patient care, work-related issues, costs, outcome measures, and conservative treatments. This section also includes a comprehensive chapter dedicated to facet pain.

Part IV deals with lumbar disk herniation, once disregarded by many surgeons as "just an herniated disk." Here, the subject receives the attention it deserves. This section closes with chapters on scientific considerations, technical operation, and revision surgeries.

Part V focuses on the surgeon's decision-making process in providing individualized care. In detail, it examines when to operate, when to fuse or not to fuse, adjacent disease, biomechanics, techniques to increase lordosis, bone substitutes, the osteoporotic spine, and the advantages of different accesses: frontal, posterior, lateral, transpsoas, and oblique.

Part VI consists of several engaging discussions regarding studies on minimally invasive techniques: intradiscal therapy, endoscopy, spinal injections, use of tubes, disk cell transplantation, and robotic spinal surgery, as well as a comprehensive chapter on the use of spinal injections after spine surgery.

Part VII addresses nonfusion technologies such as disk arthroplasty and dynamic techniques based on pedicle screws and interspinous devices.

Part VIII includes discussions on degenerative scoliosis, the modern concept of sagittal balance of the spine, compensatory mechanisms of sagittal imbalance, and osteotomy techniques.

Finally, in part IX, “Lessons from a Life,” some of the most experienced spine surgeons today share their personal clinical experiences. This is a valuable resource for all surgeons.

This is just a glimpse of what we have included in *Advanced Concepts in Lumbar Degenerative Disk Disease*. I hope you enjoy reading it as much as I have enjoyed bringing it together for you.

São Paulo, Brazil João Luiz Pinheiro-Franco

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Part I

Essentials in Lumbar Degenerative Disk Disease

We've Been Standing Up for 10 Million Years

1

Yves Coppens

1.1 Introduction

Editor's Note In this chapter, Professor Yves Coppens provides an enlightening perspective regarding a field of science that he pioneered. His account, in conversation form, is unique from historical and scientific perspectives.

Dr. João Luiz Pinheiro-Franco has invited me to contribute to this important work on advanced concepts of degenerative lumbar disk disease. As this subject is undoubtedly beyond my field of expertise, he proposed that I elaborate on the developmental factors involved during the human transition from locomoting in quadruped position to the biped upright standing position, which comfortably fits within my academic considerations.

Thusly framed, I have decided to address the history of our human-primate "kinship," that period when Homininae separated themselves from the Paninae, probably for environmental reasons, somewhere in tropical Africa, 10 million years ago.

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Human beings are, obviously, living beings and as such have their place in a taxonomy of their presumed natural relationships: a chronologically ascending and integrative classification, we are all at once a eukaryote, metazoon, chordate, vertebrate, gnathostomata, sarcopterygian, tetrapod, amniote, synapsid, mammal, and primate. And among primates the taxonomy continues: haplorrhine, simiiform, catarrhinian, hominoid, and hominid. At present, in most scientific classifications, Hominidae include Paninae, which are in common terms the pre-chimpanzees and

Editor's Note Professor Yves Coppens, along with Donald Johanson and Maurice Taïeb, discovered the now famous "Lucy," at that time, the oldest bipedal hominid skeleton. The name Lucy was given as reference to the Beatles song, "Lucy in the sky with diamonds," which was popular at the time of their excavations and research. Prof. Coppens was the Chairman of Anthropological Biology in the Natural History Museum (Paris, France, 1969-1983). For 22 years (1983–2005), he served as Chair of Paleoanthropology and Prehistory at the prestigious Collège de France. He is also member of the "Académie des Sciences de l'Institut de France" (since 1983) and member of the National Academy of Medicine (France) since 1991. From 2005, Professor Coppens serves as Emeritus Professor of Paleoanthropology and Prehistory in the Collège de France. The Collège de France was founded in 1530. Its alumni include renowned scientists such as André-Marie Ampère (1824–1836) and Charles-Édward Brown-Séquard (1878–1894), among others. He has discovered tons of fossils of vertebrates and signed or cosigned six new Hominidae. He was nominated Grand Officier de la Légion D'Honneur of France. His name was given to an asteroid (172850 Coppens).

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_1

chimpanzees, and equally include the Homininae, which are the prehumans and humans of today. This leads to the assumption that Paninae and Homininae share a common ancestry.

As it is known that all primates have tropical origin and Paninae stem from African origin, there is the significant probability that this common ancestry and at least their first descendants were tropical and African.

And, in fact, it is only tropical Africa that provided the necessary conditions.

Furthermore, analyses of the great morphological, anatomical, physiological, genetic, molecular, and ethological distances between our "cousins" Paninae and ourselves have allowed us to calculate our last common ancestry to have happened in the upper Miocene, around 10 million years ago, the birth date of our taxonomic subfamily. The location: tropical Africa.

Today, there are three candidates with such an origin and age for this ancestry: *Chororapithecus abyssinicus*, from Ethiopia, 10.7 to 10.1 million years ago; *Nakalipithecus nakayamai*, from Kenya, 9.88 to 9.89 million years ago; and *Samburupithecus kiptalami*, also from Kenya, 9.6 million years ago.

Fossils of these candidates provide an idea of our common ancestor's appearance, but not clear enough to place them before or after the divergence of Paninae/Homininae, raising the dilemma if they were already Paninae (pre-chimpanzee) or Homininae (prehuman) or existing side by side. What is known is that the location was unequivocably a tropical and forestal biotope and that it was at this time that the separation occurred for environmental reasons. This was the departure point for our evolution as a Homininae, our exclusive developmental path.

Over the course of 10 million years, this path has been recorded by genus and species, primarily prehumans from 10 to 1 million years ago and then humans, from 3 million years ago until today and into the future. This trajectory, therefore, implies that the last prehumans were contemporaries of the first humans.

The prehumans are numerous and differentiate widely into 7 genera and 14 species, discovered in South Africa, Malawi, Tanzania, Kenya, Ethiopia, and Chad, and all share tropical origins that are solely African. These specimens also all possessed a static, permanent upright position with a biped and arboreal locomotion initially, then transitioning to be exclusively bipedal. These prehumans also demonstrate a brain in mild expansion and facial feature undergoing a mild reduction with teeth at times under reduction and at other periods under expansion.

1.2 How Did We Become Upright?

The acquisition of an upright posture – the underlying contingency which made it possible for early humans to extend the trunk, pelvis, thigh, and legs – combined with the resulting bipedal locomotion, represents the key transformation point in the history of Homininae, one that gradually and mechanically induced other transformations, in particular changes in the hands and brain, which facilitated consecutively the emergence of tools and consciousness, culture, and society.

In successive order, from an anatomic and as functional as possible perspective, I shall lay out the underlying factors concerning the acquisition of an upright posture in a static condition and the ability to walk upon the hind feet. The following considerations are based upon observations gleaned from different parts of the skeleton of the *Australopithecus afarensis* species.

Observations for body size and body displacement movements were made from a fragmentary skeleton excavated from a field in Ethiopia, AL288,[1] a separate group of bones related to the same species from the same excavation field and 34 footprints from a field in Tanzania; indeed AL288 is the most complete archeological sample set known concerning erect posture acquisition and hind feet locomotion.

[1] AL288 is "Lucy," discovered in 1974 by Yves Coppens. It was, at that time, the oldest bipedal hominid ever discovered, over more than 3 million years old.

1.2.1 Vertebral Column

There are ten artifacts to describe the vertebral column, all from skeleton AL288: seven thoracic vertebrae, two lumbar vertebrae, and one sacrum.

The seven thoracic vertebrae – T2, T6, T7, T8, T10, T11, and T12 – are very similar to their human homologues. On initial observation, they differ only for two main features, moreover without any relationship between them: *Australopithecus afarensis* (*AL288*) vertebrae are significantly smaller in all linear dimensions. However, there is one exception: the sagittal diameter is proportionally very large as it is artificially increased due to a bony arch on the ventral surface of vertebral bodies.

The two lumbar vertebrae – L3 and L4 – are also small in size. Their morphology and the orientation of their different parts make one surmise that the thoracic kyphosis had extended until them. Therefore, it had been more akin to a thoracolumbar kyphosis with a large radius curvature.

Finally, the sacrum, formed by its five fused parts, appears strikingly human, albeit obviously smaller in measurement and proportion. Besides being shallow, it is proportionately extended at its frontal dimension.

Although extremely fragmentary as evidence, this spinal column clearly represents an upright and erect being. Cervical lordosis was highly likely, while thoracic kyphosis was clearly undeniable, appearing only slightly more stretched downward into the lumbar region than ours today. It is appropriate to consider the human variability in this matter: the sagittal angle of its curvature can be estimated to be between 30° and 40°. Lumbosacral lordosis is also present but, however, clearly reduced due to the thoracolumbar stretch. In addition, lordosis is slight, with a curvature of between 40° and 55°. Furthermore, it is quite probable that the spinal cord had had a lower cervical dilation and lower lumbar component (transversal diameter of T2 triangular and large; sagittotransversal index of the L4 vertebral hole quite high).

1.2.2 Pelvis

Half of the pelvis of the AL288 skeleton is very well preserved. The proportions of this pelvis are human-like; however, its anatomy differs in a certain number of particularly interesting features and in their functional consequences, which we shall touch upon briefly.

Firstly, the iliac bones are oriented in a much more frontal coronal plane than in the human pelvis and are clearly wider than human counterparts. Of the ilium, there is a very slight indentation in the internal iliac fossa and is also very wide. The pelvic cavity is broad and also extended thankfully to the important development of the acetabular diameter and the length of the pubis cranial ramus, with its ventrocaudal inclination. The sacrum is, as previously mentioned, also very wide, though short and slightly curved. The sciatic notch is barely marked, and finally, the coxofemoral joints are seemingly undersized. The length of the caudal segment and the short size of the cranial segment confer the ilium-specific longitudinal proportions: a narrow sacral plane and excessively broad iliac plane attenuating to a slender lower extremity.

Furthermore, the ilium presents an iliac crest almost straight in line between the ventrocranial iliac spine (anterior superior iliac spine) and dorsocranial iliac spine (posterior superior iliac spine). The ventrocranial iliac spine is, indeed, distinctively beak shaped, which at this level results in the superposition of the iliac pillar above the iliac spine.

The following discussion involves other segments of the inferior member that cannot be dissociated with the pelvis. The femur is short with a slim and elongated neck. It is obliquely oriented relative to the pelvis, but almost perpendicular to the diaphysis, which is also oblique. The large trochanter is flattened, while the intercondylar fossa is broad and deep. The tibia is short with compact and poorly developed spines possessing asymmetric cavities and a slightly convex external aspect. The foot is short, broad, and flat, with a splayed first radius and stepping onto external support.

Vertebrae morphology and the projected curves of the column represent a weight-bearing pelvis, with a distinctively extra large width and small height proportions. Coupled with the obliquity of the femur to the pelvis, all these aspects are evidence that the AL288 skeleton is an incontestable example of a being endowed with an upright erect posture with bipedal locomotion.

Also confirming these conclusions are the extraordinary fossilized footprints found in Tanzania dating back to the time period of 3.7 million years ago.

The reconstitution of balance to accommodate a static upright posture and bipedal gait was evidently accompanied by the adaptation of the muscles, in particular, the gluteal and ischiotibial complex. Consequently, as in many other aspects of anatomy, the Australopithecus appears similar to its ancestors, which are also the common ancestors of the Paninae, and appears similar to their descendants: humans. However, on closer examination of the gluteal muscles of the current representatives of the two lineages, that is, chimpanzees and humans, they are clearly quite different from each other. Schematically, while the chimpanzee possesses, at the superficial level, a thin *tensor fasciae latae* and a thin *gluteus maximus*; a thick *ischio-femoralis* and a thick *gluteus medius* at the mid-tissue level; and finally, at a deep tissue level, a modest *gluteus minimus*, human beings, while also endowed with a *tensor fasciae latae*, *gluteus medius*, and *gluteus minimus*, have however a very generous, thick, and fasciculated *gluteus maximus*, extending from the dorsal part of the ilium and the lateral border of the sacrum to the proximal femoral diaphysis, and do not posses in any form an *ischio-femoralis*. Another fundamental difference is the diminutive insertion size of the *gluteus maximus* to that of the Australopithecus pelvis. This conjures the hypothesis that the Australopithecus gluteal muscles were more representative of Paninae. This is also supported by the presence of a biacetabular enlargement of the pelvis, the orientation of the iliac wings, the smallness of the coxofemoral joints, as well as the length and orientation of the femoral neck. These clearly indicate a more efficient Paninae-like biomechanics with a greater importance on the ischio-femoralis: especially a tight external rotator, extensor (with the *biceps femoris caput longum*), and hip adductor (with *pectineus* and *magnus* adductor); and a powerful *gluteus minimus*, flexor, which does not occur in humans, and hip abductor, and also internal thigh rotator (with the *gluteus medius*, *which represents the* external rotator in humans). According to the fossilized footprints cited above, the surface contact position of the feet was in varus the surface contact position of the feet was in varus and corresponds exactly to the axis of the previous step, the axis of the previous step, sometimes intersecting. From this data, for Australopithecus, it is clear that while walking or in a static upright position, the lower members were extended and adducted, while the pelvis was rotated around the vertebral column.

The sum of these direct and indirect anatomical data, as well as the reconstructions obtained from these data, leads to the academic conclusion that Australopithecus was capable of an upright static balance with inferior quality than that of humans and a bipedal locomotion that considerably consumed more energy. The instability of the hip joint, that was just discussed, and the inherent weakness of the knees and ankles, to be elaborated on below, in all likelihood did not allow Australopithecus to support weight-bearing pressure or static motionlessness for extended periods of time. The extensor muscles were, as already noted, efficient, however probably utilized more to rotate the pelvis than to stabilize it during extension. The Australopithecus gait, although aided by powerful flexors and extensors, was most likely to have been relatively unstable, quickly thrown out of balance, and therefore briskly executed, more like a trot, with extended lower limbs (enabled by the small, dorsally oriented ischial tuberosities and farther spaced from femoral diaphysis than in humans); the knee buckled slightly inward causing the tibial plateau to slope outward and downward. In order to ensure some stability to the lower support members and shift the center of gravity toward the knee, Australopithecus would have had to generate an exaggerated rotation of the pelvis and

shoulders around the vertebral axis, a rotational movement obtained through an exceptionally demanding balance of the forelimbs while framing a broad and heavy thorax. This rotation has been estimated to be between 50° and 60° instead of 4° found in humans.

Considering parturition, it must be assumed that the skull of the fetus passes sagittally between the farthest point of the sacrum and the lower edge of the pubic symphysis, and the maximum length for *Australopithecus afarensis* is estimated to be between 85 and 90 mm. Given the particularly flattened shape of the pelvic brim, the orientation of the fetal skull into the narrow pelvic outlet must have been oblique or transverse, and consequently the head would not have been able to pass through the pelvic outlet as easily as that in human parturition. Also, the fetus would have had to rotate just as humans do. Bipedalism, in fact, initiated the processes that significantly reduced the distance between the sacroiliac and coxofemoral joints due to the inherent limitation of ponderal pressure on the pelvic walls and hip. It also determined a better suspension of the abdominal organs and especially the fetus during pregnancy. However, at the same time, bipedalism triggered a reduction in the pelvic cavity giving rise to new proportions between the fetal head dimensions and pelvic outlet and an increase in pressure exerted by the pelvic walls upon the fetus, hence a complex set of obstetric mechanics consisting of a double dorsal flexion movement, deflection, and twist of the baby itself. Despite the biacetabular extension and elongation of the cranial pubis ramus aligned with the ilium ventral edge (whereas in humans the same ramus is perpendicular to it), the shape of the pelvic outlet forced the evolution toward a curved trajectory and parturition forward of ischial tuberosities, as seen in women today.

If, instead, there were a rectilinear trajectory and retrosciatic parturition, as in the great apes, the fetus would have had to exit in a transversal position into the pelvic outlet, which would have forced the ischial tuberosities to exert a dangerous amount of pressure on fetal frontal and occipital skull walls, walls incapable of compressing as the parietals. And the absence of fetal rotation during parturition would have entirely impeded passage of the shoulders.

In all, this is a pelvis and spinal column of a female being with an undeniably upright orientation, able to walk on its two hind limbs and give birth as a woman. It is apparent however that the upright, standing posture was difficult to maintain and that prolonged bipedal locomotion probably proved exceedingly wearisome.

1.2.3 Lower Limbs

For analysis there are a femur, a tibia, and a talus from the AL288 skeleton and also a femur, tibia, three calcanei, a first cuneiform, the first three metatarsals, and some phalanges from the same archeological site and 34 footprints from a site in Tanzania.

The femur, like the tibia, is short, 28 cm for the reconstituted femur and 23 cm for the tibia, also reconstituted. The neck of the femur, as noted previously, is elongated and thin, while the trochlea is wide. This femur clearly demonstrates the three traditional traits of bipedalism: femoral diaphysis obliquity, an anterior prominence, and an exaggerated external trochlea labium height. Associated with the former two, there is an elliptical profile of the external condyle. Although the obliquity of the femoral diaphysis is particularly elevated and the anterior prominence especially small (possessing a slightly sharp trochlear groove), the side profile of the external condyle is undeniably elliptical.

On even deeper examination, it can be observed that the distal femoral epiphysis is predominantly asymmetrical regarding the parasagittal plane, passing through the middle of the trochlea, with an obvious preponderance in size on the internal aspect compared to the external side. This epiphysis can be inscribed schematically inside a rectangle, and it can be noted, finally, that the intercondylar fossa is disproportionately wider than higher. These three characteristics are exclusively shared among the chimpanzee.

The tibial plateau, when examined, reveals an exceptional proximity between the tibial spines, a

convexity of the lateral condyle and a cleft marking the single insertion of an external meniscus, also all homologous traits of Paninae.

Thus, the knee joint differs remarkably from that of human beings. Considering the gap between the very narrow pivot of the tibial spine and the width of the intercondylar notch, this can be assumed a poor fit for articular surfaces to have such a large rotational amplitude in knee motion. The only mode of insertion of the meniscus, which determines the type of mobility, in turn influences rotational amplitude. Mediolateral enlargement of the femur and tibia epiphyses suggests a more measured amplitude in the flexion-extension movement and a shorter stride.

The slight protrusion of the femoral trochlea and the convexity of the external tibial plateau, also associated to femoral obliquity, do not seem to fully allow for the adducted position of the knees, like those present in humans. The asymmetry of tibial epiphysis and the rectangular contour of the intercondylar femoral notch support the assertion, finally, that full extension of the knee was probably not the normal use. Taken together, these data reveal the probable active practice of arboreal locomotion where freedom of the knee joint was necessary than its solidity.

The *Australopithecus afarensis* foot had an estimated total length of 18.5 cm. The talus, while having the size of a chimpanzee although with human proportions, possesses an original morphology, suggesting a unique relationship between the foot and the leg. The calcaneus has a large curved axis with medial concavity instead of being straight as in humans, and its lateral side is equipped with a large fibular tubercle, which when present in humans has only the appearance of a modest button. Its dorsal surface is egg shaped with its major axis tilted toward the lateral side and has a lone medial tubercle. With this heel bone morphology, one can deduce that movement was unstable, in varus, i.e., rotating over the external side.

The first cuneiform, instead of being flat as in humans, has a highly rounded articulate surface with the corresponding metatarsus. This contact flexibility suggests that the first metatarsus might have rotated around the first cuneiform and as consequence a gap in the first commissure. The first metatarsus does in fact confirm this articular property with a characteristic posterior surface that is a hollow, bilobular set between two distinctive edges. The phalanges are long. They represent up to thirty percent (30 %) of the foot length, while in humans the proportion is just twenty-three percent (23 %). They are wider at the level of the diaphysis, flattened dorsoventrally, and curved with a ventral cavity.

The footprints have each from 17 to 20.5 cm in length and 46 cm distance between three consecutive footprints that track of the smaller feet (G1) and each with a length from 30.5 to 33 cm with the track of the larger feet (G2) and a distance of 47.5 cm between two consecutive footprints (sizes of the steps are measured between points that correspond to the heel).

These footprint sample sets have a number of common characteristics that confirm and compliment the anatomical data. Firstly, all both foot tracks have a pointed narrow heel whose axis is slightly toward the medial side, with a clear medial expansion, rectilinear lateral depression, and separation between the first ray and lateral rays, which are often represented by small round cavities. Secondly, the depression of the heel corresponds to a tuberosity of the calcaneus. The medial prominence indicates the existence of an abductor hallucis longus muscle, as observed in chimpanzees, and the lateral depressions indicate external support and varus; separation between the first ray and the others indicates hallux abduction, and small rounded cavities indicate the toes bent in on themselves. A cross-sectional flexion over the tarsus, observed in some of the footprints, indicates a certain foot flexibility; however, it is difficult to compare it to a true plantar arch. It begs to be noted that the human footprint has broad heel, hallux, and laterally adduced toes; five short, thin, and straight toes; and, usually, a very marked plantar arch. From these footprints, a line can be drawn (for G2) and a thin band of just 1 cm wide (to G1), tangentially to the medial edge of the footprints, which indicates that the steps had been placed consistently one in front of the other, which is reminiscent of pelvis rotation described above. The axis of these footprints is a thirty (30) degree angle from the centerline of the whole track.

1.2.4 Upper Limbs

This sample is comprised of one scapula, two humeri, two ulnas, and a radius bone from the AL288 skeleton and six other humerus fragments and two ulna fragments from the same archeological site.

The glenoid fossa of the scapula has a more cranial than lateral orientation, as observed in the large apes. Moreover, it presents a large supraglenoid tubercle and an elongated infraglenoid tubercle, also as in the large apes. Inserted into the former was, in fact, the *biceps brachii caput longum* muscle, and into the later, *triceps muscle brachii caput longum*, both flexors used for suspension. The coracoid process, curved when observed laterally, is strikingly Paninae and developmentally very important and different than the shape of the coracoid process observed in humans. It is particular to Paninae in that it is, literally, triangular, and as it has insertions bored into it by the *coracobrachialis*, the flexor of the humerus over the scapula and by the *biceps brachii caput breve*, the flexor of the radius over the humerus. From these observations it can be hypothesized that Australopithecines used this structure of the upper limbs for the arboreal part of its locomotor repertoire.

The humerus is not long, measuring about a mere 23 cm. Its head is rounded, like a "half ball," and slightly elongated vertically; its anatomical neck is very pronounced, almost as much as that in a chimpanzee; its very long *tuberculum minus* is prominent above the bicipital groove, and as it bears an important insertion of the *subscapularis* muscle, it can be presumed that the internal arm rotational movements and humerus adduction over the scapula were developed. The *tuberculum majus*, significant here, is similar to its Paninae counterpart, especially with the elongation of one of its two facets, which is nearest to the groove, over which inserts the *supraspinatus* muscle, the abductor of the arm over the scapula. These muscles, at the same time, reinforce the humeral head joint within the glenoid cavity. The bicipital groove is notoriously narrow and deep as in Homininae, which uses its upper limbs in a certain form of suspension. The two crests, *crista tuberculi minoris* and *crista tuberculi majoris*, are highly differentiated. The insertion on *teres major* and *pectoralis major* firmly suggests an ample arm adduction and a significant humerus internal rotation over the scapula. The morphology of distal articular extremity of the humerus is a double trochlea, as in Paninae. Indeed, a bony lateral prominence inserts itself between the trochlea and capitulum, reinforcing elbow joint stability, extremely valuable in suspension movements. Known in great apes, the *epicondylus lateralis* clearly carves out a lateral prominence; however, here its projection is skewed upward in relation to the *capitulum humeri* in a position somewhere between the great apes and human beings. Yet interposed between these two beings' morphologies is the extension to the back of *capitulum humeri*. The morphology of the *fossa olecrani* is, on the other hand, exactly to that of human beings, devoid of the strong lateral crest that exists in Paninae, a crest which reinforces stabilization of the elbow in Paninae. The *incisura trochlearis* of the proximal extremity of the ulna is equally devoid of a lateral facet, which supports in the existence of this ridge in Paninae. Finally, the extremely well-developed *epicondylus medialis* lends merit to the assumption that the flexor muscles were also, as a whole, very well developed.

The ulna presents, at its proximal extremity, a very slight development of an *incisura trochlearis* and a very modest expression of the fossa adjacent to the olecranon, as in humans, but with a pronounced reentrance of the *incisura radialis*, both lateral and rounded, as in the chimpanzee. This last incisura suggests the importance of prone and supine movements of the upper extremities. As to radius proximal extremity, the tuberosity and the long and narrow neck, and the joint circumference highlighted by a crest in the middle, all these elements are reminiscent of the morphology observed in chimpanzees, indicating a more stable suspension and better supination.

The wrist joint demonstrates stabilization marks comparable to those observed in the shoulder and elbow joints. These characteristics suggest the usage of the upper limb at least partially for arboreal locomotion.

As for the hand, there are long and curved phalanges, resembling the development as the

foot, probably indicating the same interpretation of the morphology.

Hence, this is the description of a small living being that had an active and arboreal locomotion, not quadrupedal, not even in the use of its arms, but rather a mixture of climbing trees and suspending itself from its arms.

1.3 Final Considerations

The vertebral column, pelvis, and limbs described also belong to the same small being: still arboreal and already biped.

Contrary to what has often been written, bipedalism is not, since the early history of our evolution, the same as today. Bipedal locomotion has its own history, its own evolution. Most importantly, contrary to what has often been claimed, bipedalism was not initiated through the transformation of feet. The transition to walking exclusively upright on two feet undoubtedly began through adaptations within the pelvis, that is, from the pelvis downward to the feet. *Australopithecus afarensis* is, thus, the first species that clearly demonstrates the adaptations wrought upon a skeleton by the simultaneous use of these two very different locomotion practices. The recent discovery of a young individual skeleton of the same species, a female, 3–4 years old, called Selam, by its discoverer, Alemseghed Zeresenay at a site near Hadar (AL288 site), and of comparable age, brilliantly confirmed the association between static erect position, bipedalism (mainly lower limbs), and tree climbing (using mainly the upper limbs).

Early Homininae, those related to other genera and other species, *Orrorin tugenensis*, 6 million years ago, from Kenya, and *Ardipithecus ramidus*, 4.4 million years old, from Ethiopia, that were discovered after Lucy (AL288), were also endowed with this double locomotive movement, although slightly different from that described here in *Australopithecus afarensis*, which opens the possibility that this locomotive state was a pattern among all first prehumans and perhaps even among "second-generation" prehumans such as Lucy.

As for exclusive bipedal locomotion, it has been estimated to have begun 4 million years ago with another Homininae, genera *Australopithecus*, which has been named *Australopithecus anamensis*. This genus was a contemporary of Lucy, *Australopithecus afarensis*, having lived for 4 and 3 million years ago and in the same regions, Kenya and Ethiopia, but most probably not in the same niche. *Australopithecus anamensis* by comparison possessed typically modern lower limbs, i.e., extremely stable, and upper limbs that were much less solid, literally the opposite of *Australopithecus afarensis* with unstable lower limbs and very solid upper limbs.

Worth mention are the ecological changes that were also taking place 4 million years ago, a landscape opening to glades and widening grasslands that may have favored the transition to exclusive bipedalism. Humans, the genus *Homo*, appear precisely after that second "step" of prehumans, around 3 million years ago, ostensibly from a prehuman ancestor that we have not as yet identified. This means that whoever this ancestor may be, mankind also has tropical Africa as its evolutionary cradle, but with a geological age of 3 million years.

What was taking place 3 and 2 million years ago in tropical Africa? The climate was changing and evolving from a humid one to one much drier. As a result, flora and fauna archeology specimens demonstrate grandly this climate change, especially in the generous and extensive sites of the lower Omo Valley in Ethiopia, where these geologic levels are well represented and organic remnants are especially numerous today. Among these are prehuman remnants dating before this change, i.e., *Australopithecus afarensis*, *Australopithecus anamensis*, and *Kenyanthropus platyops*, and human remnants from after the change, *Homo habilis* and *Homo rudolfensis*. The emergence of human beings, as with many other mammals of that geological era, arises as the result to the necessary evolution of prehumans which were forced to adapt to a new and pervasive environment. This adaptation was dependent upon a much better performing brain and improved dentition to accommodate an

opportunistic feeding regime, becoming omnivore. Homininae, therefore, came to have an upright posture some 10 million years ago while being exclusively bipedal for 4 million years. The new environmental circumstances also offered the emergence of a reflective consciousness.

In my writings, I gave name to this climatic and historical event as the (H)Omo event, combining words Homo and Omo to remind all that it was in the Ethiopian Omo valley where I was able to link, for the first time, the appearance of human beings to climate change (1975).

It was through this change that for the first time a living being, human in its being, would carve stone, as an act through its own will and be used upon its environment in order to form circumstances to its advantage. This is reflective consciousness, for example, deliberately hitting one stone against another in order to change the shape of the first stone and obtain a new form for the function that it was consciously intended.

For 10 million years, that's how this somewhat funny small mammal standing on its hind legs has evolved as a result of a changed environment, the only mammal that 3 million years ago was able to develop a cultural environment like no other. Paradoxically, within this new environment, two somewhat opposite distinguishing human hallmarks have emerged: freedom and responsibility on the one hand and arrogance and guilt on the other hand.

A Historical Overview of Sciatica

2

Sebastião Gusmão, Aluizio Arantes,
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2.1 Introduction

The currently well-established concept of sciatica due to lumbar intervertebral disk degeneration is the result of a long historical evolution whose various stages in thinking and exploration are the focus of this brief historical review.

2.2 Sciatica: Historical Overview

The first neurological reference to this ailment is credited to Imhotep, a few thousand years ago in Egypt. Imhotep, astronomer, physician, and architect to Pharaoh Djoser (2686–2613 BC), is thought to be the author of precious medical papyrus, studied by Brested in 1930, which through various case studies differentiated lesions with or without neurological signs. Most striking is Case 48 in which he describes a clinical examination of the leg identical to the Lasègue maneuver commonly used today.

By the time of Jacob, the father of the 12 tribes of Israel, the debilitating condition of sciatica had already reached biblical proportions. In fact, in ancient Hebrew medicine, Jacob lost his well-known wrestling match against an angel because of an injury to his sciatic nerve, as reported in Genesis 32: 24–32:

> And Jacob was left alone. And then a man wrestled with him until daybreak. When the man saw that he could not overcome him, he touched the sinew of his thigh, and forthwith it shrank while they were wrestling … and he was limping on a leg.

This is the reason why until this day, children of Israel do not eat the sinew of the thigh, remembering the one from Jacob's thigh that was touched and lost the movement.

In fact, with regard to Jacob's injury, the sciatic nerves of animals were declared unsuitable for human consumption. To better regulate this recommendation, the Talmud provided specific instructions for the removal of the sciatic

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Editor's Note In this chapter, Gusmão et al. retrace, in conversational style, the evolution of medical thought and practice that ultimately led to the field of sciatica in the context of lumbar degenerative disk disease. This fascinating account is unique in both historical and clinical perspectives.

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_2

nerve from the flesh of slaughtered animals. This Bible passage is shown in the painting "Jacob wrestling with the angel" (1850–1861, Chapelle des Saints-Anges – the Chapel of the Guardian Angels- at the Church of Saint-Sulpice, Paris, France) by Ferdinand Victor Eugène Delacroix (1798–1863). This painting shows the angel touching the back of Jacob's left thigh.

Not until the Greek and Roman times does sciatica move from iconography to a form of medical description of disease. Hippocrates was the first physician to use the term "sciatica" taken from the Greek ischios meaning hip. The earliest Greek and Roman references are reports of pain in the area of the sciatic nerve, which was always referenced as a disease of the hip joint. The concomitant pain in the pelvis and leg was diagnosed as sciatica and attributed to a subluxated hip or a hip disease. Hippocrates (Fifth Century BC), in his Treatise of Predictions, described the natural history of patients with "cramps and colds at the loin and the legs."

Galen (130–200 AD), another Roman from Pergamum in Asia Minor and one of the greatest physicians of antiquity, reported several cases of sciatica with specific descriptions of abnormal spinal posture. He coined the labels for conditions that still stand today: lordosis, kyphosis, and scoliosis. It was at this same time that other Greek and Roman authors have described sciatica without distinguishing between pain arising in the hip joint and spine.

Despite Andreas Vesalius, the undisputed father of modern anatomy (1514–1564) (Fig. 2.1) and his landmark description of the intervertebral disk, the Medieval and Renaissance periods contributed very little or nothing to the concept of the mechanism and etiology of sciatica. But the word sciatica was widespread. The words "Thou cold sciatica" were placed into the mouth of Timon of Athens by William Shakespeare.

A significant step forward in the field occurred in 1764, when Domenico Cotugno (1736–1822) (Fig. 2.2), anatomist and professor of surgery in Naples, published *De ischiade nervosa commentarius* ("Remarks on nervous ischialgia") (Fig. 2.3), which defined sciatica as a clinical entity and related the pain in the leg to disease of

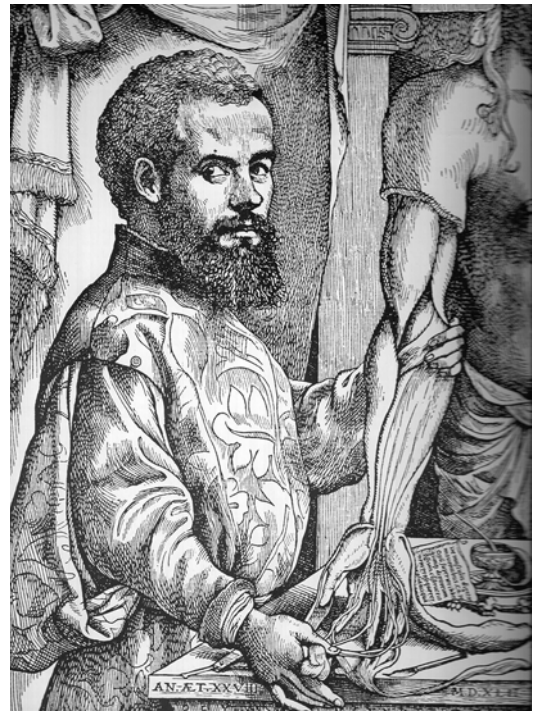

Fig. 2.1 Andreas Vesalius (1514–1564). This portrait is from his book *De humani corporis fabrica libri septem*, or *on the fabric of the human body* (Basel: Johannes Oporinus; June 1543), and is attributed to Ján Stephan van Calcar

Fig. 2.2 Domenico Cotugno (1736–1822)

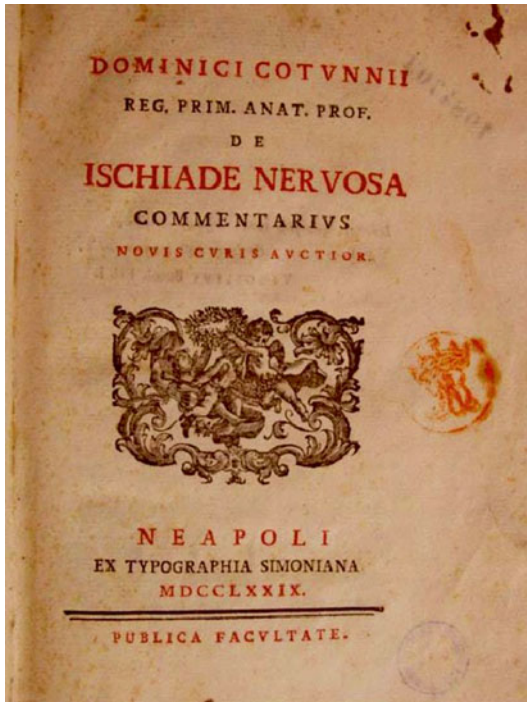

Fig. 2.3 Domenico Cotugno (1736–1822). Cover from *De Ischiade Nervosa Commentarius* (Ed. Typograph. Naples: Simoniaca; 1779)

the sciatic nerve. He distinguished pain of the lower limb of "arthritic" origin, or "arthritic sciatica," identified as hip pain, from pain of "nervous" origin or "nervous sciatica," which was classified as "postica" (posterior) or "antica" (anterior). He accurately differentiated sciatic nerve pain from arthritis of the hip with a precise description of the clinical status and by indicating the relationship of pain to the sciatic nerve [1]:

> If the pain indicated by the patient's finger runs from the foot to the sacrum, as competent anatomists we must evaluate this patient by tracing the precise course of the sciatic nerve. The patient's pain is felt in this nerve, and we should look for the cause of their limping in this nerve, and for the origin of paresis and impairment in this disease.

It is thus how the eponym "Cotugno's syndrome" found its way into medical vernacular to indicate a unilateral sciatic neuralgia. Cotugno attributed these symptoms to the accumulation of an acrid matter within the sheath of the sciatic nerve that had derived from the vessels irrigating the sheaths of the nerve or from the brain itself. In order to prove the existence of free circulation between the cranial and spinal dura, he propped cadavers upright on their feet and then decapitated them so as to observe the flow of cerebrospinal fluid. Twenty headless cadavers stood in for the cause which established the existence of this free circulation of the "Liquor Cottunnii," the first known reference to cerebrospinal fluid.

His description of this "Liquor Cottunnii," or cerebrospinal fluid as we know it today, included a precise indication as to its formation and absorption from the vessels. From this, Cotugno postulated its relationship with sciatica [1]:

> The cerebrospinal liquor is in *perenni statu renovationis*, through exudation by minimal arteries and reabsorption through minimal veins. It penetrates into the dural sleeves of the nerve roots; hence, it is apt to accumulate in the sheaths of the sciatic nerve and as so promote pain along its course. The sciatic pain, weakness and limping may be cured, if necessary, by the use of vesicants and caustics in order to leech out the hydrops.

Within the folds of the history of sciatica, there were intermittent parallel investigations into the intervertebral disk; however, such findings were not correlated with sciatica. Nearly a hundred years after Cotugno's landmark work, Rudolf Virchow (1821–1902) (Fig. 2.4) described the first case of traumatic rupture of the intervertebral disk. This rupture, known as "Virchow's tumor," was discovered during the necropsy of a trauma victim [2].

In 1896 Swiss surgeon Kocher documented the first case of a disk displacement leading to paraplegia; however, its clinical correlation to sciatica remained moot [3]. The patient developed paraplegia after a fall and subsequently succumbed to injury to the internal organs. During necropsy, Kocher identified dorsally displaced disk at L1–L2. Sciatica and the lumbar region would remain dissociated until the beginning of the twentieth century. Until the late nineteenth century, sciatica was interpreted as a sciatic nerve pain, a neuralgia, or neuritis. The cause remained unknown, and the authors were limited to describing symptoms.

French neurologist, Lasègue (1816–1883) (Fig. 2.5) called attention to a pain provoked by lifting the leg in patients with sciatica. He later demonstrated that this phenomenon was due to the stretching of the sciatic nerve roots (1864) [4]. Although his medical writings do not mention this sign, it was his former pupil, Forst, who published the findings of his master and illustrated the "Lasègue maneuver" for the first time (Fig. 2.6) [6].

Fig. 2.4 Rudolf Virchow (1821–1902) (Image from the History of Medicine, US National Library of Medicine)

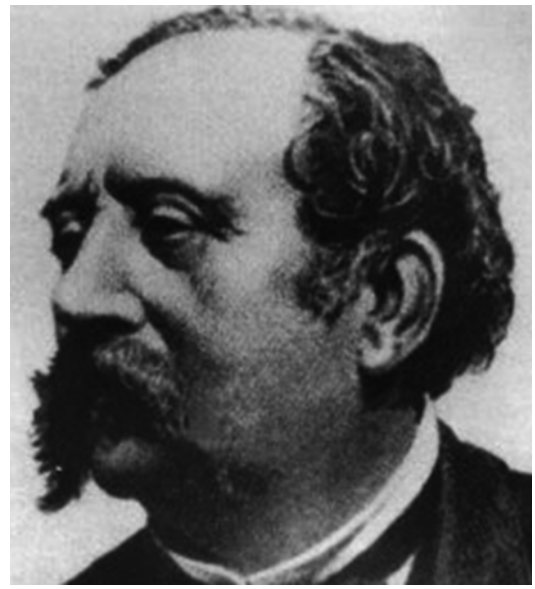

Fig. 2.5 Ernest Lasègue (1816–1883)

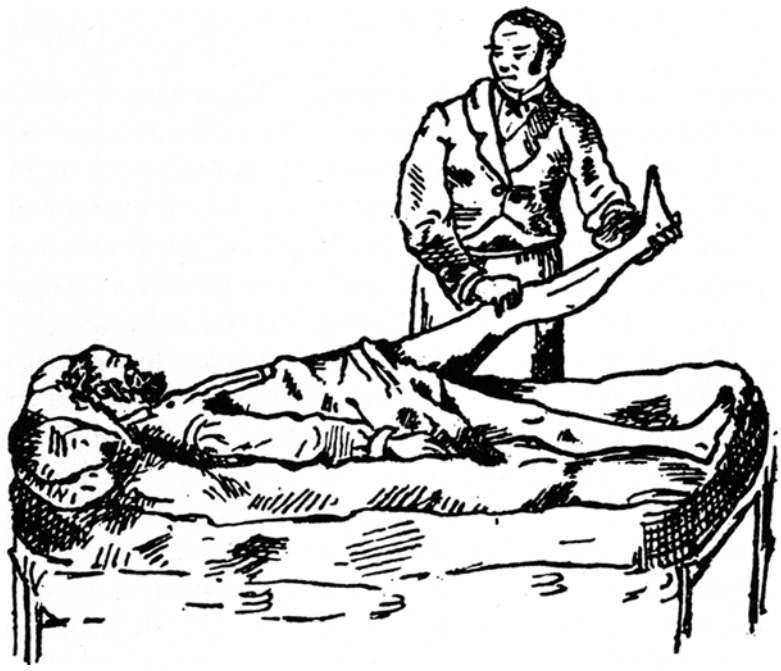

Fig. 2.6 Lasègue Forst sign, 1881 (From de Castro et al. [5]; licensed under a Creative Commons Attribution License)

Concurrently, another French physician, François Valleix (1807–1855), identified specific sensitive points within the course of the sciatic nerve. These anatomic points, known today as Valleix's points, are points at which pain is experienced upon pressure in cases of neuralgia. Valleix's points are in fact segments of the sciatic nerve that are accessible to palpation in patients with sciatic pain. Along the sciatic nerve these segments lie in the buttocks, thigh, leg, and foot [7].

It were Charcot and Brissaud who in 1888 described "sciatica scoliosis," abnormal postures that were in fact caused by severe sciatica. They accurately distinguished crossed and ipsilateral scoliosis. In crossed scoliosis, the trunk is inclined laterally toward the side not affected by sciatica. In direct or ipsilateral scoliosis, the lateral inflection of the spine always tilts toward the side affected by sciatica [7].

For sciatica, the early twentieth century opened to the phenomena of "sensorimotor radiculitis." Dejerine demonstrated that sciatica is a root condition and not a truncal condition. He noted that some cases of sciatica are accompanied by areas of hypesthesia or cutaneous anesthesia, and the distribution of the insensitive areas did not correspond to the areas of the sciatic nerve branches but rather to the areas of the nerve roots. These cases of cutaneous anesthesia corresponded more precisely to the areas of the fifth lumbar nerve root and first sacral nerve root. He defined the phenomenon as a sensorimotor radiculitis caused by "partial lumbar meningitis," following the then-current interpretation of the impairment of the nerves and roots by inflammation caused by syphilis [7].

At the transition between the height of inductive reasoning and the dawn of evidence-based medicine, the French medical establishment reigned supreme. Continuing in that fine tradition, Jean-Anselme Sicard (1872–1929), a neurologist, presented sciatica in 1918, as a condition caused by spinal conditions. He advanced the hypothesis that compromise of the roots that form the sciatic nerve does not occur within the dural sac but outside the dura mater, at its exit of the intervertebral foramen. Furthermore, he postulated that the cause of this impairment in the roots could be due to bony and ligamentous elements surrounding the root within the intervertebral foramen. He was of course inferring to the fact that the thick sciatic nerve roots, especially the L5 root, pass within a particularly narrow osteoligamentous canal [7].

So it seems that by the start of the twentieth century, the road map into the scientific understanding had been laid. Social circumstances of the new century such as the progression of modern thought with its exchange of ideas and technology, particularly the invention of anesthesia conspired to favor the advancement of surgical technique and subsequently to what was once all-encompassing sciatica, would now become the consequence of lumbar intervertebral disk degeneration.

First of these advancements was the hypothesis that sciatica might be associated with herniated lumbar disk. There was then a small but growing body of surgical reports of uncommon benign tumors, chondromas on patients undergoing surgical treatment for sciatica. Mixter and Barr were at the vanguard of these advancements demonstrating that such lesions corresponded to a herniated disk.

Victor Horsley, in 1887, is credited to be the first surgeon to remove such a tumor; however, the association to sciatica was not recognized. In fact, the first successful removal of a herniated disk took place in 1901 via laminectomy under the hands of Fedor Krause (1857–1937) (Fig. 2.7) and Hermann Oppenheim. They removed what they had thought was an "enchondroma" [8].

And the evidence continued to mount. It wasn't until 1911 when Joel Goldthwaite (1866–1961), building upon Middleton and Teacher's work of the same year, conceived the hypothesis that there existed a precise correlation between herniated disk and sciatic pain. Middleton and Teacher described two cases of intervertebral rupture observed during necropsy. Similar to Virchow and Kocher, they failed to postulate a correlation with lower back pain or sciatic pain [9]. Joel Goldthwaite did however.

Goldthwaite discussed a case of a patient with recurrent sciatica in the absence of any apparent

Fig. 2.7 Fedor Krause (1857–1937) (Courtesy of the US National Library of Medicine)

Fig. 2.8 William J. Mixter (1880–1958) (Courtesy of the Mixter Library Collection)

lesion who had been operated on by Harvey Cushing. He concluded that the pain resulted from recurrent disk dislocation into the vertebral canal. He went on to explain the negative exploration by the fact that the disk had consistently slipped back into place. He hypothesized, "Such a condition could produce the symptom of sciatica, low back pain" [10]. At last, the foggy vagueness surrounding the causality of sciatic had begun to lift. And even though it was proved a correlation, however not precise correlation between herniated disk and radiculopathy in Goldthwaite's landmark work, his assertion that herniated disk and sciatic pain were related failed to arouse interest in the medical establishment at that time.

Soon exciting new enabling technologies began to filter into the modern medical armory: radiology. The first gas myelography was performed by Jacobus and Ackerland in 1921, soon to be followed by the first lipiodol myelography in 1922 by Sicard and Forestier [11].

Although not recognized for its value until a review article by Barr, an orthopedist at Massachusetts General Hospital in 1932, Schmörl and Junghanns of the Dresden Pathology Institute in 1925, took on a mammoth radiological and pathological study of 5,000 human spines that conclusively documented the posterior prolapse and degeneration of the nucleus pulposus. However, no correlation to sciatica could ever be made as the study failed to include anatomoclinical correlations [12].

As visualizing and surgical techniques advanced, so too did the understanding of the intervertebral disk. In two cases where patients underwent surgery for cauda equina syndrome, Walter Dandy, in 1929, found cartilaginous fragments within the spinal canal. He described these fragments as being "loose cartilage from the intervertebral disk," simulating in their agglomeration, a spinal tumor [13]. He was the first to consider that intervertebral disk disease could be added to the list of indications for decompressive laminectomy.

Alas! 1932: the Holy Grail sciatica was with reach. The landmark breakthrough was to happen in the United States by William Mixter (1880–1958) (Fig. 2.8) and Joseph S. Barr. These two orthopedists from the Massachusetts General Hospital proved beyond all reason of doubt, the relationship between alterations in the

intervertebral disk caused by trauma or degeneration and sciatica. From this point on, sciatica would never be vaguely associated with interstitial neuritis related to emotion, fatigue, or infection.

A patient suffering from sciatic pain came to Barr in 1932. Barr subsequently consulted Mixter who recommended a myelogram which later revealed a defect in the dural sac. Mixter performed the surgery, removing a "tumor" via laminectomy. Barr conducted the postoperative study of the tumor and performed microscopic comparisons with those in Schmörl's study of which Barr had previously published a comprehensive review. He recognized the specimen from the index patient to be of the nucleus pulposus.

Together with Mallory, a pathologist, Mixter and Barr reassessed all the cases at the Massachusetts General Hospital that had previously been "diagnosed" as having chondromas. Retrospectively, they diagnosed nineteen patients with reported sciatic pain due to disk prolapse, more specifically, disk herniation compressing the nerve root. This landmark study was published in 1934 in the New England Journal of Medicine. It heralded in a pioneering era that encouraged intervertebral disk intervention as the standard treatment for sciatic pain.

Soon after its publication, Mixter and Barr's diagnosis and laminectomy technique for lumbar disk herniations became the most frequently surgery performed by neurosurgeons [14]. Widespread acceptance of laminectomies to remove the intervertebral disk spurned the emergence of newer surgical techniques. And entire new body of literature dedicated to the association of sciatic pain due to herniated disk appeared. The scientific discussion moved off the strict analysis of symptoms and fostered new areas of endeavor such as contrast examinations, surgical techniques, and the careful cataloging of postoperative statistics. In less than 10 years after the first laminectomies by Mixter and Barr, the removal of the herniated disk by fenestration, a technique developed by Love from the Mayo Clinic in 1939, had become universally widespread [15, 16].

Subsequently, advances in lumbar intervertebral disk degeneration diagnosis and surgical treatment followed.

First in the list of outstanding accomplishments was the "diagnostic puncture of intervertebral discs in sciatica" by Lindblom from the Karolinska Institute in 1948. This first study on diskography used 15 diskographies in 13 patients.

In 1969, Fischgold and Gonsette proposed radiculography with Dimer X. Then in the early 1970s computer tomography and magnetic resonance were introduced and dramatically improved diagnosis of disk injuries.

Then there was the advent of microscope-assisted surgery in 1977. M. Gazi Yasargil reported on 105 cases of lumbar disk surgeries using microscopes [17]. That same year, Caspar published a report on 102 patients undergoing microdiskectomy and then later adding a medial facetectomy to the procedure [18]. By the end of the 1970s, Robert Williams popularized microsurgery, which became the standard procedure for the treatment of herniated lumbar disks [19].

Advancements continued relentlessly until the close of the twentieth century. Advancements came from abled scientists and surgeons from around the world. Microsurgery spawned the quest for progressively less invasive surgical techniques in the treatment of herniated lumbar disks. New techniques were developed: the percutaneous diskectomy and the direct approach to the disk using a percutaneous technique (chemonucleolysis). Hijikata pioneered the development of instrumentation for the percutaneous removal of a herniated lumbar disk [20]. Others perfected upon Hijikata's instrumentation. Lyman Smith introduced chemical nucleolysis, with the injection of an enzyme into the nucleus pulposus to chemically destroy the disk [21].

Spinal fusion had become a reality and even more so recognized as being useful treatment option for lumbar degenerative disk disease associated or not with sciatica. The principles of spinal fusion evolved over the course of several decades during the twentieth century. Its evolution was discreet and separate from that of sciatica-lumbar degenerative disease. So many authors contributed to the surgical innovations of spinal fusion. Among them are Lange [22] for the stabilization of the lumbar spine with plastic bars, followed on by the use of steel bars attached

to wires, Campbell [23] pioneering the use of the iliac crest bone graft in spinal fusion, Briggs and Milligan [24] perfecting the posterior lumbar interbody fusion along with Cloward [25], Boucher [26] who advanced the use of pedicle screws, and Roy-Camille [27] who perfected osteosynthesis of the spine using metal plates with pedicle screws: such a rich retrospective tribute and not by any means comprehensive.

A recent chapter in the history of the surgical treatment of lumbar degenerative disk disease has been the search to replace the lumbar disk, starting in the late 1950s. The concepts of lumbar arthroplasty began in the 1950s with isolated attempts to replace the nucleus pulposus with artificial implants to relieve pain and restore function of the degenerated spinal motor segment.

One of the first such artificial implants was the stainless steel ball. In 1964, Fernström implanted steel balls and published the clinical results in a 30-month follow-up. The results suggested that arthroplasty with stainless steel balls was better than results of diskectomy alone or spinal fusion. While primary goal of these implants is preservation of disk height and segment mobility, an unexpected negative outcome, the premature subsidence into the vertebral bodies, led to the failure of the use of the instrumentation [28].

Alternative to the arthroplasty approach was the search for substitutes for the nucleus pulposus. Some substitutes were developed, as the Raymedica Prosthetic Disk Nucleus (PDN) (Raymedica, Minneapolis, MN) and the Aquarelle (Stryker Howmedica Osteonics, Allendale, NJ). Common to both disk substitutes is the use of a hydrogel core.

Total lumbar disk replacement, commonly known as an artificial disk, represents an evolution in lumbar disk arthroplasty. Current study and limited clinical use is tug-of-war between several competing patent holders. There exist different models of these implants on the market now, all with similar implantation techniques with minor differences in design and mechanical function.

And while the industry of our profession vies for market space, the role of lumbar disk arthroplasty among researchers remains unclear. Two of its major advantages over fusion are preservation of motion and prevention of adjacent segment degeneration.

2.2.1 Final Considerations

From Jacob to lumbar arthroplasty is a story of the evolution of knowledge on the pathophysiology of lumbar degenerative disk disease and sciatica. Even as current research seems pinned in a balance over the uncertainty of arthroplasty technology, the story of sciatica is a testament to the persistence of disease in humankind and the physician's endless commitment to do battle with condemning angels.

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Lumbar Intervertebral Disk Injury, Herniation and Degeneration

3

Michael A. Adams and Patricia Dolan

3.1 Introduction

3.1.1 Intervertebral Disks

Intervertebral disks are pads of fibrocartilage which lie between the vertebral bodies of the spine. A soft nucleus pulposus is surrounded by concentric layers ('lamellae') of the annulus fibrosus (Fig. 3.1). Human lumbar disks are the largest avascular structures in the body, and the consequent metabolite transport problems ensure that cell density is barely sufficient to maintain the disk in health and quite insufficient to repair it when injured or diseased.

The disk nucleus contains a high concentration of proteoglycans, which attract water into the tissue and ensure that it behaves like a pressurised fluid, distributing load evenly on the adjacent vertebral bodies. The annulus is mostly comprised of coarse collagen type I fibres which run obliquely between the vertebrae (Fig. 3.1). Annulus tissue is sufficiently soft to allow small intervertebral movements and yet strong enough to prevent excessive movements and to restrain the nucleus. Disks are too stiff to act as efficient shock absorbers.

3.1.2 Disk Injury or Degeneration?

Disks must distribute forces evenly on the vertebral bodies, even when the spine is heavily loaded in flexed or extended postures. This is a physically demanding role, especially in the lower lumbar spine of humans, and disks often show signs of structural damage even by the age of 20 years [1]. The traditional orthopaedic view of intervertebral disk pathology emphasised structural lesions [2] and physical causes [3, 4]. More recently, however, this common-sense approach has been overshadowed by the 'disk degeneration' paradigm, which considers that some biological process related to genetics and disk nutrition can be held responsible for all aspects of disk pathology and pain. Mechanisms of disk injury, either by wear and tear ('fatigue') or by trauma, have been overlooked on the grounds that they represent an outmoded 'injury model', with some advocates of degeneration appearing to deny the possibility that intervertebral disks can be injured at all!

And yet, there is increasing evidence that intervertebral disks often are injured and that injury leads directly to altered biology, including nerve ingrowth and pain. Animal experiments show that

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_3

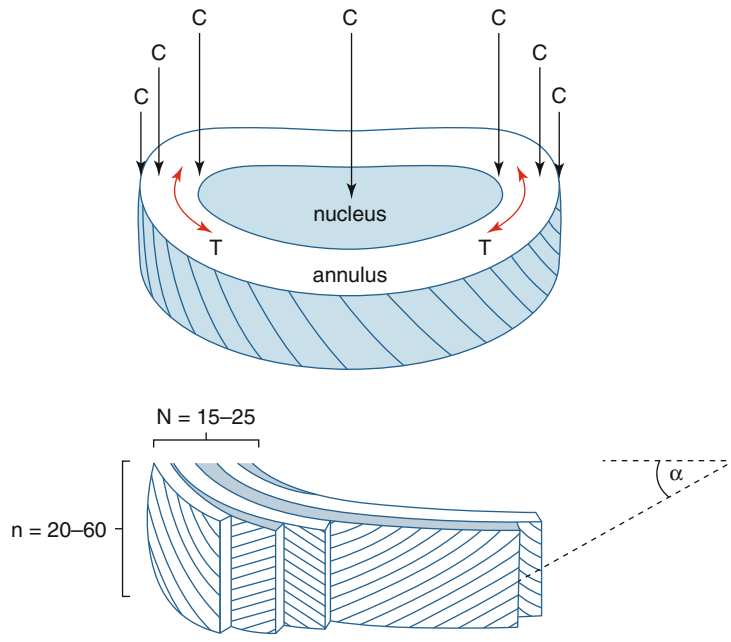

Fig. 3.1 (*Upper*): oblique diagram of an intervertebral disk. The nucleus behaves like a pressurised fluid and is restrained by tensile stresses (*T*) in the surrounding annulus. Compressive loading (*C*) is evenly distributed across most of the disk. (*Lower*): expanded detail of annulus, showing the alternating collagen fibre direction (α) in adjacent lamellae. Typically, $\alpha = 30°$. Also shown are the number of lamellae (*N*) and the number of collagen fibre bundles that cross a typical vertical section (*n*) [116]. Adapted from Adams et al. [15] with permission

disk injury leads inevitably to degeneration [5–7], and longitudinal studies on humans confirm that disk degeneration usually follows an injury to a disk or vertebral body [8, 9]. Epidemiological studies show that *excessive* mechanical loading is associated with disk degeneration and prolapse [10–12], although we now suspect that moderate mechanical loading actually strengthens spinal tissues by the process of adaptive remodelling [13, 14]. All of the structural features of disk degeneration (such as annulus fissures, nucleus herniation, endplate defects and internal disk disruption) can be reproduced by excessive mechanical loading applied to cadaveric spines, and the failure mechanisms have been explained by mathematical models [15]. No 'disk degeneration gene' has been found, only a range of gene variants (alleles) which appear to exert their influence by weakening the extracellular matrix of the disk [16, 17] or bony endplates [18]. Finally, we now know that metabolite transport into the disk *increases* with advancing age and degeneration, as the vertebral endplates become more porous and permeable [19], suggesting that inadequate disk nutrition is unlikely to be a direct cause of disk degeneration.

3.1.3 Purpose and Scope of This Chapter

The purpose of this chapter is not to revive some old 'injury' model of intervertebral disk failure, but to integrate old and new evidence concerning disk injury with that concerning disk biology, pathology and pain. Essentially, the following sections will show how some intervertebral disks can be so weakened by genetic inheritance and by advancing age that they fail mechanically in response to specific types of everyday mechanical loading. Attempts at healing are frustrated by low cell density and the harsh mechanical environment, so that disk cell metabolism becomes increasingly abnormal ('degeneration') and structural disruption increases. Eventually, blood vessels and nerves are able to grow into the disrupted tissue, and the disk becomes painful.

The chapter begins with an account of forces acting on the spine, because many clinicians consider only gravitational forces and overlook the much greater forces that arise from muscle tension and from accelerations. This is followed by a detailed account of how excessive forces can

cause specific types of structural damage to lumbar disks and their adjacent vertebrae, including disk herniation. Damage can be caused by injury or by fatigue ('wear and tear') loading, and forces need not be high if the tissues are weak. Subsequent sections compare disk ageing and degeneration, because they are not the same thing: ageing is only one of several risk factors for degeneration, which is not inevitable, not even in old age.

3.2 Forces Acting on the Lumbar Spine

3.2.1 Compression, Shear, Bending and Torsion

The nature of these forces can be appreciated from Fig. 3.2a. The compressive force denotes the force acting down the long axis of the spine, perpendicular to the mid-plane of each intervertebral

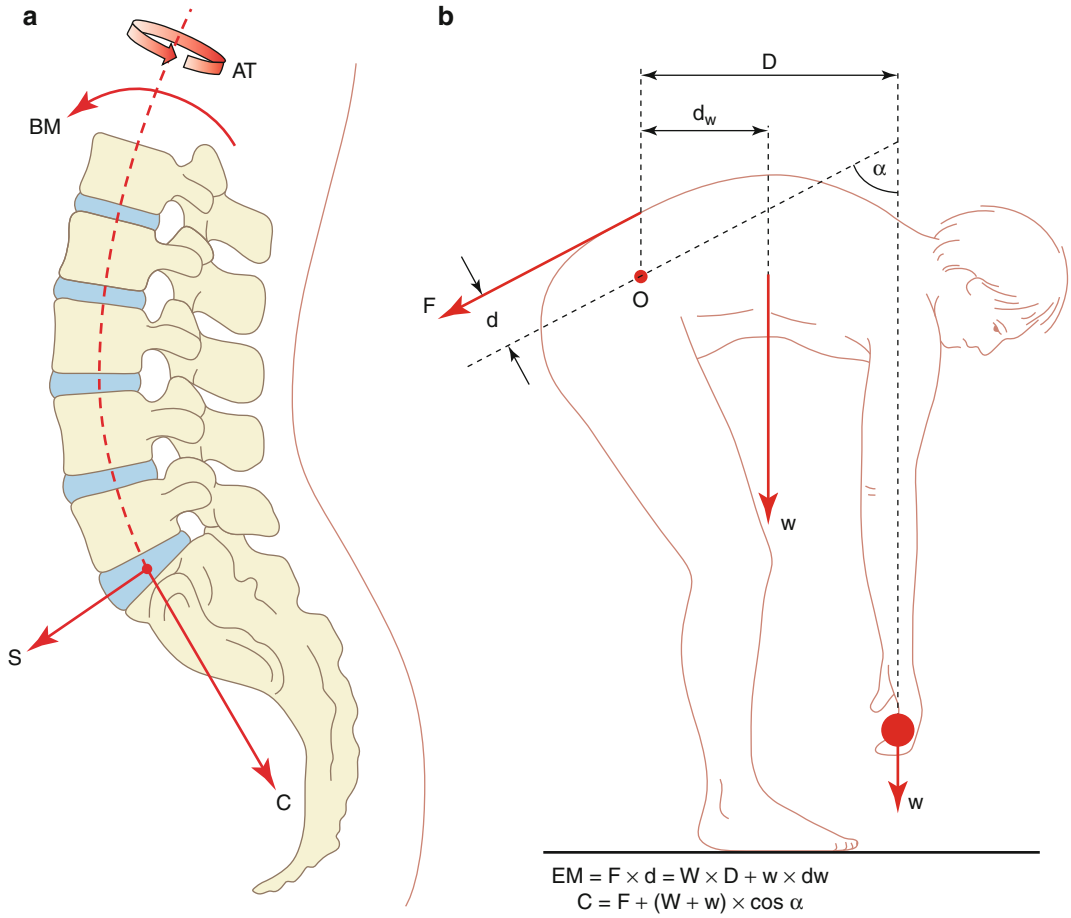

Fig. 3.2 (**a**) Human lumbar spine showing the direction of the spinal compressive force (*C*) and shear force (*S*) acting on the L5–S1 disk. A bending moment (*BM*) causes the spine to flex, extend or bend laterally, and an axial torque (*AT*) twists the spine about its long axis. (**b**) Analysis of forces during manual handling. A high tensile force (*F*) must be generated by the back muscles in order to lift up the weight (*W*), as well as upper body weight (*w*). The back muscles act on a short lever arm (**d**) relative to the centre of rotation (*O*), whereas *W* and *w* act on much longer lever arms (*D* and d_w). Therefore F must be much greater than *W*. The equations show how to calculate the spinal compressive force (**c**) in a static analysis. F and C would increase greatly if the weight was lifted quickly. Reproduced from Adams et al. [15] with permission

disk. Note that its direction varies with spinal level and with posture. Compression is resisted mostly by the intervertebral disks and vertebral bodies [20]. The shear force acts parallel to the mid-plane of each disk and is steeply inclined to the horizontal in the lower lumbar spine. Forward shear is resisted by the articular surfaces of the apophyseal joints as well as by the disk [21]. A 'bending moment' (force X distance) causes the spine to bend forwards, backwards or laterally. Forward and backward bending are resisted primarily by spinal ligaments [22] and the neural arch [23], respectively. Torsion (axial rotation) twists the spine about its long axis and in the lumbar spine is resisted primarily by the neural arch [24].

3.2.2 Gravitational Loading

Superincumbent body weight exerts a vertical force of approximately 60 % of body weight on the lumbosacral joint. In upright postures, the gravitational force mostly compresses the spine, but also exerts a forward shear force on the lower lumbar vertebrae (Fig. 3.2a).

3.2.3 Inertial Forces During Rapid Movements and Falls

High forces are required to move the body quickly, in accordance with Newton's 2nd Law of motion which states that

$$\text{Force} = \text{mass} \times \text{acceleration} \qquad (3.1)$$

When a pilot ejects from an aircraft, the vertical force on his lumbar spine is equal to his upper body mass multiplied by the vertical acceleration (rate of change of velocity) of his seat. This acceleration can be sufficient to crush one or more vertebrae. More commonly, high inertial forces are generated by a fall on the buttocks, when the deceleration on impact magnifies the effect of upper body weight. Peak deceleration increases with the length of the persons' legs and with the hardness of the landing.

3.2.4 Forces Arising from Muscle Tension

Muscle contractions pull their bony attachments towards each other, often compressing the joint that lies between them. Standing or sitting erect requires considerable 'antagonistic' muscle tension to stabilise the spine, in a similar manner to cables that stabilise a radio mast, so that the compressive force on the lumbar spine is typically 80–100 kg [25]. Muscle forces rise to high levels when objects are lifted on outstretched arms (Fig. 3.2b) because the external moment of the weight being lifted must be balanced by an internal moment, generated by muscle tension acting on a short lever arm, close to the centre of rotation. Internal muscle forces increase when movements are performed quickly [26, 27] because fast movements require high accelerations, which in turn require high forces (Eq. 3.1). It follows that maximum muscle forces are required to move the body as quickly as possible. Evidence from people suffering from epilepsy indicates that, when neural inhibitory controls are deficient, muscle tension can be high enough to crush a vertebra [28].

Confusion occasionally arises in medicolegal disputes (see final section, below) when an otherwise expert witness is unaware that forces generated by muscle tension and by falls can be *much* greater than the weight of the external object being handled and that the external object often weighs a good deal less than upper body weight, which must also be lifted against gravity by muscle tension (Fig. 3.2b).

3.3 Mechanisms of Disk Injury and Prolapse

3.3.1 Compressive Injury Causes Endplate Fracture

Excessive compressive loading, in the direction of the spine's long axis, always damages a vertebral endplate before the adjacent disk. This fact has been demonstrated in many experiments on cadaveric spines [29] and probably

contributed to the myth that healthy disks can degenerate but not become injured. The problem appears to have arisen historically when calculations first showed how great the compressive force on the spine can be (see Fig. 3.2b). Spinal loading became synonymous with spinal *compressive* loading, and the harmful effects of torsion and bending (see below) were overlooked.

Compressive failure occurs by fracture of the bony endplate, as the incompressible fluidlike disk nucleus causes it to bulge into the vertebral body [30]. Various types of endplate fracture have been described [29, 31], and later work showed how a wider range of vertebral body fracture patterns can occur, depending on posture (flexion or extension) and on the degree of disk degeneration [32]. If compressive loading is applied in a repetitive cyclic manner, in order to simulate manual labour, then similar fracture types are observed to those caused by sudden injury, but the peak compressive force can be up to 50 % lower [33]. Generally, it is the central region of the superior endplate (relative to the vertebra) that is damaged first, because it is the thinnest and supported by less dense trabecular bone [34]. Thickness and strength of the central endplate evidently have a very low margin of safety, probably because thickness is minimised to allow adequate metabolite transport into the disk nucleus [35].

3.3.2 Torsion and Bending Injuries Tear the Annulus

Axial rotation ('torsion') of the lumbar spine (Fig. 3.2a) occurs about a centre of rotation in the posterior quadrant of the disk [24]. The movement is resisted primarily by the anterior annulus and by the articular facets of the apophyseal joints. Damage probably occurs first in the apophyseal joint that is compressed, at a rotation angle of 1–3°, although this is not certain [24]. If the neural arch is removed, then unprotected lumbar disks can be rotated to much greater angles [36, 37], and failure occurs in the annulus, by a mechanism that involves delamination and rim tears [36]. However, torsion has not been shown to cause radial fissures or disk prolapse.

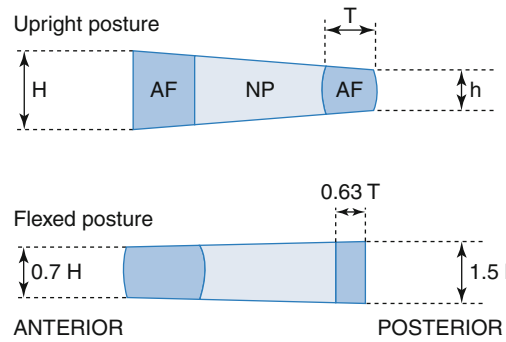

Fig. 3.3 The mechanism of disk prolapse depends on how the lumbar disks are deformed in flexed posture (such as that shown in Fig. 3.2b). The upper diagram shows typical dimensions of a lumbar disk in upright posture (*AF* annulus fibrosus, *NP* nucleus pulposus, *H* anterior height, *h* posterior height, *T* thickness of posterior annulus). Full flexion then deforms the annulus as shown in the lower diagram. Note that the posterior annulus typically is stretched vertically by 50 % and so must be thinned by 37 % to maintain constant volume. The stretched and thinned posterior annulus is then vulnerable to high pressures in the disk nucleus

3.3.3 Complex Loading Can Cause Disk Herniation

Bending of the spine causes the intervertebral disks to be compressed on one side and stretched on the other (Fig. 3.3). In the case of forward bending (flexion), the posterior annulus is typically stretched by 50 % in a full range movement [38]. There is a corresponding decrease in annulus thickness in the radial (inner to outer) direction because the wet tissue must maintain constant volume, at least initially. Thinning of the posterior annulus in flexion has been confirmed in a radioactive tracer study [39], and it leaves this region of annulus vulnerable to injury from a high nucleus pressure. Consequently, if a cadaveric spine specimen is first positioned in full flexion or hyperflexion, and then compressed vigorously, the most common mode of failure is for the nucleus to herniate through the stretched posterior annulus [38, 40]. The herniated tissue

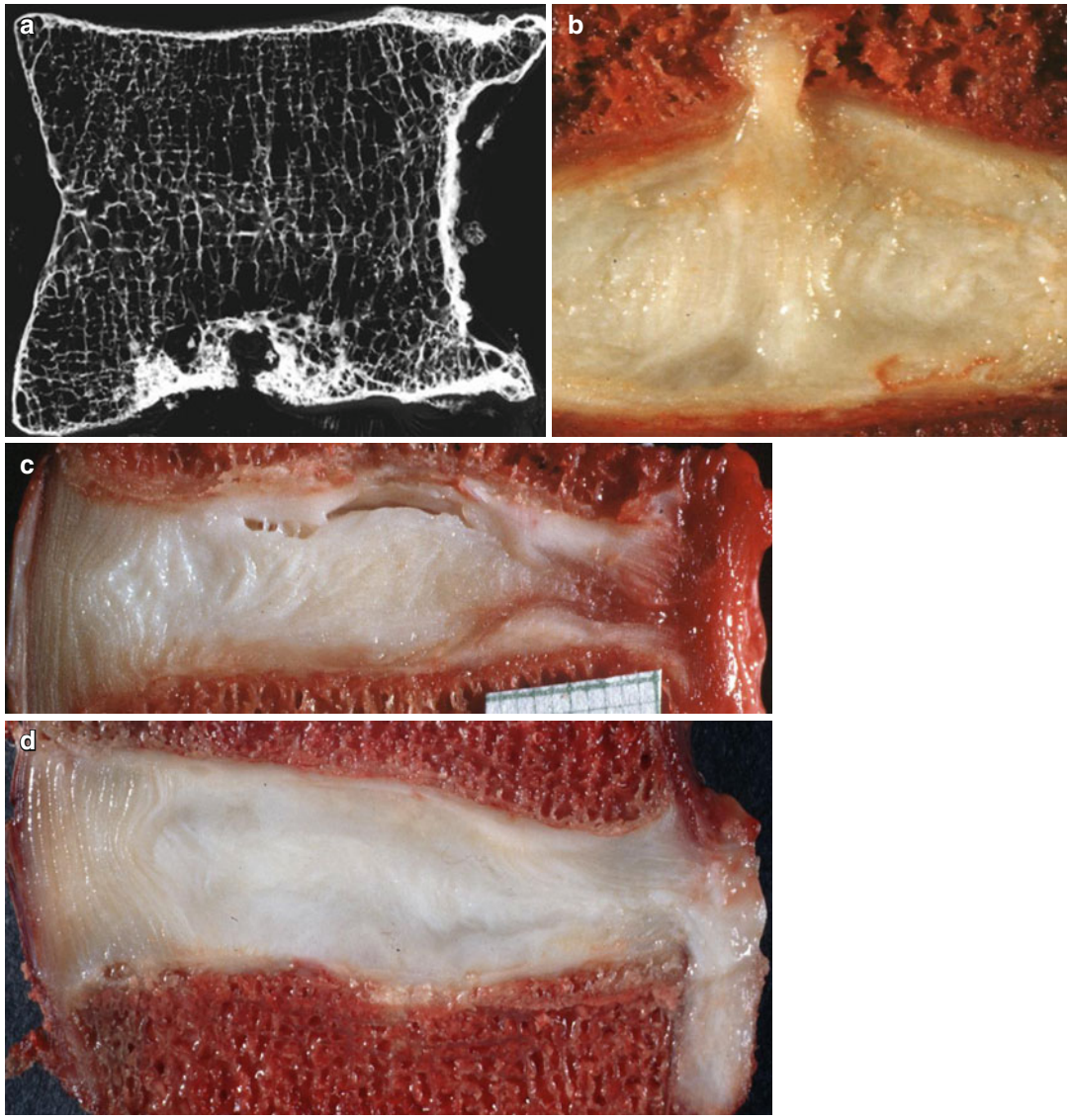

Fig. 3.4 Structural defects in degenerated and herniated lumbar disks. Anterior is on the left in all figures. (**a**) Microradiograph of a midsagittal slice of a cadaveric vertebral body, showing a large Schmorl's node resulting from an endplate fracture that was followed by vertical disk herniation. (**b**) Photograph of a cadaveric disk that has herniated vertically through the endplate in response to compressive loading. Lamellae of the inner annulus are collapsing into the decompressed nucleus. (**c**) Midsagittal section of a cadaveric intervertebral disk showing a complete radial fissure in the posterior annulus. (**d**) Similar to (**c**), except that in this specimen, high loading in bending and compression has caused the nucleus to herniate through the annulus. The disk was intact before loading. Images adapted from Adams et al. [15] with permission

(Figs. 3.4d and 3.5) emerges in a fraction of a second, sometimes with an audible 'pop'. Spinal bending is crucial to the disk herniation mechanism, and no cadaveric experiment has created disk herniation in the absence of a high bending moment.

The mechanism occurs most readily in spines aged 40–49 years [38] at which age there is a demonstrable fluid pressure in the nucleus [41], and yet the annulus is normally showing some signs of age-related weakening, most notably in the proliferation of concentric tears or clefts [1]. It is

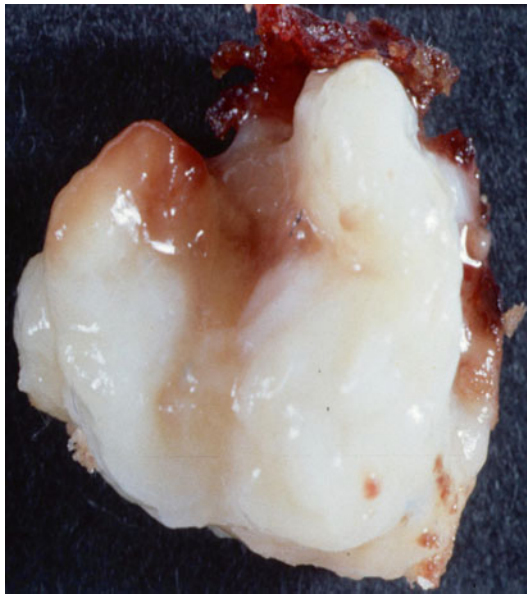

Fig. 3.5 Large disk prolapse created by mechanical loading of a cadaveric spine in bending and compression (bar = 5 mm). The herniated tissue is mostly nucleus and inner annulus, but there is also some hyaline cartilage and bone from the adjacent endplate. Adapted from Adams et al. [15] with permission

not easy to create disk herniation in this way if the disk is already degenerated [38] or if its nucleus has been dehydrated artificially by prior creep loading [42], indicating that high nucleus pressure plays an important role. Lower lumbar disks are more likely to herniate in this way [38], presumably because they have a thin posterior annulus which can be stretched substantially when the spine is flexed.

The underlying mechanism of herniation – pressurised nucleus pulposus bursting through a stretched and weakened annulus – has been clearly demonstrated by artificially raising the pressure inside animal disks and tracking the pattern of annulus disruption from inner to outer lamellae [43]. Later work emphasised the importance of flexion in causing a radial fissure to track through the posterior annulus, often close to its junction with the vertebral endplate [44]. Anterolateral bending (forwards and to one side) is closely related to disk prolapse in life [10], possibly because it causes maximum stretching of one posterolateral corner of the annulus, which lies further from the axis of bending than does the midline posterior annulus.

If the same combination of bending and compression is applied in a repetitive fashion, to simulate heavy manual labour, then a radial fissure (Fig. 3.4c) can be formed in a gradual progressive manner [45]. Only a small quantity of nucleus pulposus can then be extruded though the annulus, presumably because even a small loss of nucleus volume causes a relatively large drop in nucleus pressure [46] so that no more material is forced down the fissure. Experiments on young porcine disks confirm that this mechanism of progressive radial fissure formation in the posterior annulus does not require any prior degenerative changes in the disk [47, 48].

3.3.4 Endplate Involvement in Disk Prolapse

Disk herniations are mostly comprised of displaced annulus fibrosus and nucleus pulposus tissues [49], with the annulus/nucleus ratio increasing in patients aged over 30 years [50]. In addition, almost half of all herniations also contain some hyaline cartilage from the vertebral endplate [49, 51]. The relatively hard and smooth hyaline cartilage has a three-dimensional network of fine collagen type II fibrils which prevent it from swelling much, even when physically disrupted [52]. Consequently, hyaline cartilage fragments lose little of their proteoglycan content, so that they are relatively resistant to revascularisation, reinnervation and resorption [51]. This probably explains why their presence in a herniation is associated with more severe and prolonged clinical symptoms [50]. The cartilage endplate is mechanically integrated with the collagen network of the disk [53, 54], and yet it can easily be peeled off the underlying bone if the annulus is stretched vertically [51], so spinal bending is likely to play an important role in cartilaginous herniations. They are most frequent in patients aged 50–60 years, and relatively large cartilage fragments are most commonly found in herniations of L5–S1 disks [50].

Bone fragments also occur in some disk herniations [49], including those created in the laboratory [38]: see Fig. 3.5. The reported frequency

in patients varies from 6 % [50] to 58 % [55], with the latter figure including any abnormality (including avulsion fracture) of the vertebral rim that could be visualised by CT. Close association between hyaline cartilage and bone fragments (Fig. 3.5) suggests that herniating annulus sometimes pulls away a small fragment of cartilage and bone endplate together. In other cases, displaced outer annulus appears to pull some bone off the posterior vertebral margin, without the inclusion of any hyaline cartilage. Detailed study of cadaveric bony endplates has shown that 'erosions' are common in the posterolateral margins of lower lumbar vertebrae [56]. Their appearance, location in the spine and association with patients' symptoms are all consistent with them representing the stripping of cartilage off the underlying bone during disk herniation.

Defects in the human bony endplate are densely innervated [57], so it is no surprise that disk herniations involving the endplate are of particular clinical significance. As well as the above-mentioned link with prolonged sciatica, it appears that they are also associated with inflammatory ('Modic') changes in the endplate and with severe and painful disk infections [58, 59]. One possible explanation for these findings is that focal loss of hyaline cartilage endplate exposes the subchondral bone, which has much greater porosity and permeability than the cartilage [19]. Hence, focal cartilage loss increases focal endplate permeability, allowing anaerobic bacteria to enter the nucleus from the vertebral body and for inflammatory cytokines from disk cells to leave the nucleus and sensitise nerves in the bony endplate.

3.3.5 Mechanical Consequences of Disk Injury and Herniation

Endplate fracture creates more space for the disk nucleus (Fig. 3.4a, b), causing the pressure within it to fall immediately, often by more than 50 % [40, 60, 61]. Consequently, compressive load bearing is shifted from the nucleus to annulus and also from the disk overall to the neural arch [60], with effects being the greatest in older spines and at upper lumbar levels [61]. High stresses in the inner annulus can cause it to collapse into the decompressed nucleus, as shown in Fig. 3.4b [40]. Localised tears in the outer annulus have much less immediate effect on nucleus pressure [62], although animal experiments suggest that peripheral annulus tears can propagate inwards over several months until they reach the nucleus [5].

Another immediate mechanical consequence concerns the tissue displaced in a disk herniation: once removed from the pressurised confines of the disk, it can swell rapidly in tissue fluid. Cadaver experiments suggest that herniated tissue can more than double its weight in just 4 h and then shrink again during the following few days as it loses both proteoglycans and water [63]. These physico-chemical events could explain why some patients report a gradual onset of sciatica several hours after some recalled incident. Disk herniation also reduces nucleus pressure and volume, probably by an amount that is proportional to the herniated mass [64].

Over a longer timescale, nucleus decompression arising from either endplate fracture or disk herniation allows the annulus to bulge radially outwards, and also inwards, so that the disk loses height [65, 66]. Disk narrowing can result in the transfer of more than 50 % of the spinal compressive load on to the neural arch [20], where it appears to lead to osteoarthritis in the apophyseal joints [67–69]. Reduced separation of adjacent vertebrae creates slack in the intervertebral ligaments, so that they resist bending less [42], and the motion segment is then able to 'wobble' freely [70]. This 'segmental instability' can subsequently be reversed by the growth of vertebral body osteophytes [71].

3.4 Lumbar Disk Ageing and Degeneration

These processes are considered in detail elsewhere in this book, but they are mentioned briefly here in order to differentiate them from each other and to integrate them with the evidence concerning disk injury.

3.4.1 Inevitable Age-Related Changes in Human Lumbar Disks

All old intervertebral disks become dehydrated, discoloured and fibrous. Progressive age-related fragmentation and loss of proteoglycans explain why disk water content falls, especially in the nucleus [72]. Concurrent replacement of collagen type II with type I explains the increased fibrous texture of the nucleus and inner annulus [73], and increased collagen cross-linking involving sugars explains the yellowish discoloration [74]. These biochemical changes can, in turn, be attributed to an increasing proportion of disk cells becoming senescent [75] so that continuing repair ('turnover') of matrix macromolecules becomes slower with advancing age [76]. After growth is complete, age-related changes in disk composition make them stiffer, less able to distribute loading evenly on the adjacent vertebrae and more easily injured. Hence, minor structural defects tend to accumulate in the disk after the second decade [1]. In addition, the bony endplate becomes thinner and more porous with increasing age [77] reflecting systemic osteopaenia in many older people. However, most old disks do not become grossly disrupted or narrowed [78], and their internal mechanical functioning is little affected [41]. Generally, there is no blood vessel or nerve ingrowth in most old disks [79].

3.4.2 Features of Intervertebral Disk Degeneration

Disk 'degeneration' has traditionally been graded on numerical scales (e.g. 1–4) according to the presence or absence of specific features [80–82]. Features associated with 'degeneration' include accelerated age-related changes in composition, radial and circumferential fissures in the annulus, rim tears in the outer annulus, bulging or damaged endplates, annulus bulging radially outwards or collapsing inwards, disk space narrowing, marginal osteophytes on adjacent vertebral bodies and ingrowing blood vessels and nerves. Disk degeneration scales are exercises in pattern recognition and do not seek to define or explain what is going on. However, they can be used to establish statistical associations between disk degeneration and back pain [83, 84] and with aspects of abnormal disk function such as a decompressed nucleus [41], high stress gradients in the annulus [85] and decreasing spinal mobility [86].

3.4.3 What Is 'Disk Degeneration'?

If all age-related changes in intervertebral disks are considered to represent 'degeneration', then it becomes difficult for epidemiologists to identify risk factors for the condition (because all disks age) or to assess the efficacy of disease-modifying treatments (reversing ageing may prove difficult!). Evidently, specific age-related changes that are closely related to pain need to be distinguished from 'normal' ageing.

The most widely cited definitions were suggested in 2006 [87]. *Intervertebral disk degeneration* is proposed to be 'an aberrant, cell-mediated response to progressive structural failure', and a *degenerate disk* is the one with 'structural failure combined with accelerated or advanced signs of ageing'. *Degenerative disk disease* is 'a degenerated disk which is also painful'.

The rationale behind these definitions is that some disks degenerate because they are so weakened by genetic inheritance, age and loading history that they can be injured during normal everyday activity. Disk injuries create regions of abnormally high and low matrix compressive stress [40], both of which inhibit matrix synthesis [88, 89] and create abnormal cell signalling [90], elevated enzyme activity [72, 91] and cell clustering [92] as the injured tissue attempts to repair itself. Unfortunately, repair is frustrated by the disk's low cell density, so that degeneration often progresses to complete structural failure, as suggested in Fig. 3.6. The emphasis on structural failure is justified by the close association between structural defects and pain and by the fact that all of the structural features of disk degeneration can be created in cadaveric specimens by mechanical loading.

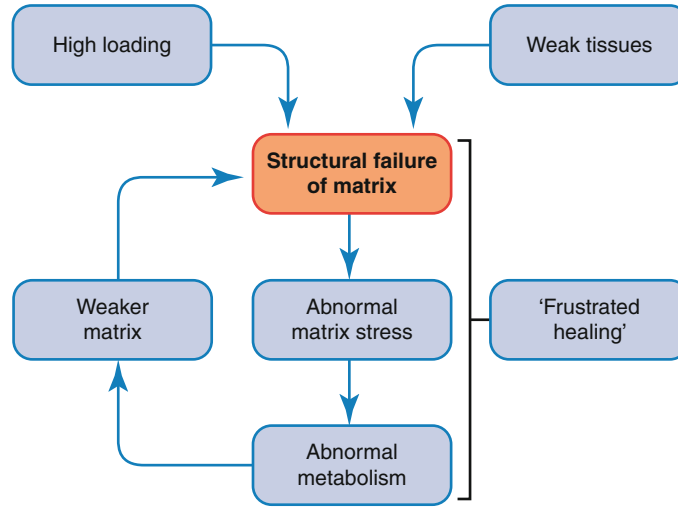

Fig. 3.6 Diagram depicting the aetiology of intervertebral disk degeneration. The definitive step is structural failure of the matrix, which may take one of the forms shown in Fig. 3.4 and which is caused either by high mechanical loading or by abnormally weak tissues. Structural failure creates abnormal stress distributions in the disk matrix, which impair disk cell metabolism and further weaken the matrix. Repeated minor injuries, and inadequate attempts at repair, lead to a vicious circle of weakening and further damage. This process can be likened to frustrated healing. Reproduced from Adams et al. [15] with permission

It is sometimes implied that disks degenerate *because of* altered cell signalling or *because of* impaired regulation of matrix-degrading enzymes, but there is no evidence to support this conjecture, and it merely begs the question: what caused the abnormal signalling or impaired enzyme regulation in the first place?

3.4.4 Two Disk Degeneration 'Phenotypes'?

Disk herniation can be considered as one specific feature of degeneration or as a separate pathological entity. But whichever convention is used, it should be realised that disk herniation is much more closely related to mechanical loading, and to pain, than are other features of degeneration such as MRI signal intensity, which is primarily related to water loss. It is instructive to consider distinct 'phenotypes' of lumbar disk degeneration, which have different characteristics, risk factors and consequences. In a recent review, we proposed that there are two such phenotypes [93].

'Endplate-driven' degeneration is initiated by endplate fracture, involves internal annulus disruption, mostly affects the upper lumbar and thoracic disks, has relatively high heritability and can start early in life, but has a lower association with pain. In contrast, 'annulus-driven' degeneration involves a radial fissure and/or a disk herniation, mostly affects the lower lumbar spine, has relatively low heritability, develops progressively in middle age and often leads to severe back pain and sciatica. The structural defects which initiate the two processes both act to decompress the disk nucleus, making it less likely that the other defect could occur subsequently, and in this sense the two disk degeneration phenotypes can be viewed as distinct. It remains to be seen just how useful this concept is in identifying risk factors and in devising treatments [93].

3.4.5 A 'Final Common Pathway' for Disk Degeneration?

The annulus of a decompressed degenerating disk tends to bulge like a flat tyre and typically loses 3 % of its height per year [94]. The degeneration process may therefore take many years before the disk space is obliterated and the adjacent vertebrae fuse. Loss of disk height transfers compressive loading on to the neural arch and probably precipitates a degenerative cascade of segmental instability, apophyseal joint osteoarthritis, vertebral osteophytosis and spinal stenosis [15].

3.4.6 Disk Degeneration, Back Pain and Sciatica

Injuries play an important role in the genesis of diskogenic back pain and sciatica. A disk

herniation can compress a spinal nerve root or ganglion, and chemicals leaching out from the swollen and displaced tissue [63] may sensitise the affected neurons [95]. Fissures within the annulus encourage ingrowth of blood vessels and nerves [96] because they are focal regions of low pressure [97] in which hollow blood vessels would be less likely to collapse. The disrupted edges of annulus fissures are able to swell and lose proteoglycans, leaving a collagenous scaffold [97] that would not inhibit nerve and blood vessel ingrowth as much as a proteoglycan-rich matrix would [98, 99]. Similar events probably occur in a disrupted endplate, because endplate defects have been shown to have an increased nerve density [100]. In both annulus and endplate, the sequence of events leading to chronic pain is likely to be injury, reinnervation, sensitisation by inflammation or infection and provocation of sensitised nerves by focal stress concentrations within the disrupted tissue.

3.5 When Do Disk Injuries Occur In Vivo?

3.5.1 Moderate Mechanical Loading Strengthens the Spine

The small cell population of adult human disks does not normally decline after skeletal maturity [101] and appears well adapted to the anaerobic conditions that arise from poor metabolite transport [102]. Slow matrix turnover is measurable [76], and comparisons between the mechanical properties of human disk tissues and their adjacent vertebrae suggest that disks are capable of limited adaptation to mechanical demands [103], at least in the outer annulus where cell density is highest [104]. This could explain why effective healing is observed in the outer annulus of sheep disks following surgical injury [5] and why increased body mass appears to have positive effects on disk hydration and health [14]. Other fibrous connective tissues are known to strengthen in response to moderate mechanical loading [105], as of course is bone [106].

3.5.2 'Injury' Occurs When Loading In *Excessive*

An 'injury' denotes damage to a living tissue. If the cause is mechanical, then injury starts at the elastic limit, when resistance to loading first becomes impaired. Beyond this limit, nonreversible deformation starts and is probably accompanied by pain [107]. In brittle tissues such as bone, injury is accompanied by visual and audible signs. However, in tough fibrous and cartilaginous tissues, injury begins with collagen fibres sliding imperceptibly past each other [108], and 'injury' can be identified in vitro only from subtle changes in a force-deformation graph [109].

In living people, soft tissue injuries must be inferred from patients' symptoms and from MRI scans, and often there is no objective confirmation that an injury has occurred. This disparity in the ability to detect hard and soft tissue injuries can lead to the latter being overlooked or dismissed as unimportant. It is true that some well-vascularised soft tissues heal quickly and are not as serious as bone fractures. But injuries to intervertebral disks, cartilage and tendon can be *more* serious than bone fractures, because their low healing potential often results in progressive and painful degenerative conditions [87].

The word 'injury' should not be used synonymously with 'trauma', which implies very high loading associated with collisions and falls. Injury simply requires the mechanical loading to exceed tissue strength, and if the tissue has been severely weakened by the combined influences of an unfavourable genetic inheritance, ageing and prior 'fatigue' loading, then injury can occur during the activities of everyday living. This is widely accepted in the case of osteoporotic vertebral fracture, which can be caused simply by opening a window [110].

3.5.3 Repetitive Loading and 'Fatigue Failure'

Mechanical injury may represent a single excessive loading cycle or a large number of more moderate loading cycles which cause microscopic damage to propagate within the material

until gross 'fatigue failure' occurs. This is the process by which metal fatigue can propagate in aeroplane wings. For example, fatigue failure is likely to occur in human vertebrae following 5,000 loading cycles at only 40–50 % of the normal failure load [33]. Similar weakening occurs if annulus fibrosus is subjected to repetitive loading [111]. Intervertebral disks are particularly vulnerable to accumulating fatigue damage because they have so few cells to turnover and repair their matrix.

3.5.4 Why Are Some Intervertebral Disks so Weak?

Genetic inheritance explains approximately 30 % of the variance in disk degeneration in the lower lumbar spine and 50 % of variance in the upper lumbar spine [112]. The difference is probably explained by greater environmental (especially mechanical) influences at L4–S1. Heritability can rise as high as 70 % in middle-aged women [113], who are less likely to be 'discordant' for mechanical loading. There is no single 'disk degeneration gene': rather, many gene variants exert small influences on matrix strength and metabolism. Evidently, genes and environmental influences are both important in disk degeneration. Age-related increases in disk degeneration [83, 114] are probably attributable to the matrix becoming weaker and more vulnerable to injury.

3.5.5 Medicolegal Considerations

The following section is an abridged account of a recent review [115].

3.5.5.1 Disk Degeneration vs Herniation

These two terms should not be used synonymously. Disk herniation could be viewed as a distinct pathological entity or as an advanced stage of 'annulus-driven' disk degeneration, as described above. Certainly, both of these disk degeneration phenotypes should be distinguished from disks that are merely growing old, perhaps with a little 'middle-aged spread'. Unfortunately, there is still no scientific consensus on what 'disk degeneration' actually means, with scientists placing varying emphasis on the role of disk nutrition, or genetic inheritance, or abnormal cell signalling or mechanical loading. Disk herniation is better understood than disk degeneration, and there is no doubt that it can be a mechanical injury, but there is still disagreement over the relative influences of age and genetic inheritance.

3.5.5.2 Must a Disk Degenerate Before It Can Herniate?

No, this much is now certain. A high proportion of middle-aged lower lumbar cadaveric disks will herniate if loaded severely enough [38], and most of the 'degenerative' changes found in herniated disk material removed at surgery probably occur after the herniation takes place, as a result of tissue swelling, leaching of proteoglycans and revascularisation [92]. It is important to avoid circular arguments such as 'This disk herniated because it was degenerated. We know it was degenerated because it herniated'.

3.5.5.3 Mechanical 'Acceleration' of Disk Degeneration?

It is sometimes proposed that an injury or work practise has 'accelerated' disk degeneration, so that pain and disability develop earlier than might be expected. The problem with this concept is that excessive mechanical loading does not influence the musculoskeletal system by accelerating metabolic ageing effects. Rather, it diverts the disk from its normal 'ageing' pathway to a separate 'degeneration' pathway, which involves structural disruption, altered biomechanics and metabolism, revascularisation and reinnervation. It is the diverging 'degeneration' pathway rather than the ageing pathway that leads to pain and disability.

3.5.5.4 Who Is Prone to Injury?

The evidence presented in this chapter may appear to blame mechanical loading for diskogenic back pain, by diverting an ageing disk on to a 'degeneration pathway'. However, even

moderate mechanical loading can disrupt a very weak disk, and tissue weakening depends on genetic inheritance and ageing. If pain and disability arise in the absence of any substantial mechanical provocation, then it can mostly be attributed to constitutional factors (ageing and genetic inheritance) that weaken the disk and *predispose* it to injury and degeneration. Alternatively, if there is a substantial mechanical provocation, then pain and disability can mostly be blamed on the injury or work practise which *precipitated* the disk injury and degeneration. Liability should be apportioned according to the perceived relative importance of these predisposing and precipitating causes.

3.5.5.5 Summary of Recent Scientific Advances

The following statements would be difficult to refute on the basis of current evidence:

- Injury to the annulus or endplate can cause intervertebral disks to degenerate.
- Excessive mechanical loading can cause many lower lumbar intervertebral disks to herniate, even if they appear 'normal' for their age.
- Disk herniations are often injuries, but few are traumatic, and prior tissue weakening (arising from genetic inheritance, age and prior 'wear and tear') will often contribute to the herniation.
- Most degenerative changes in surgically removed disk herniations are consistent with them occurring *after* herniation.
- It should not be assumed that a herniated disk must have been degenerated before it herniated, unless there is independent evidence of this prior degeneration.

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Advances in Lumbar Degenerative Disk Disease Pathophysiology Comprehension

4

Andreas G. Nerlich and Norbert Boos

4.1 Chronic Back Pain and Disk Degeneration: Physiology and Pathophysiology of the Ageing Spine

Nowadays, low back pain faces two important issues:

1. Chronic low back pain is still one of the most frequent diseases in Western industrialised countries. Estimates count approx. 70 % of all adults in those countries to suffer from chronic or recurrent back pain during their lives, and figures are still increasing. Accordingly, this disease is the second most frequent cause for short or long-term absence from work.
2. Despite its extensive clinical significance and increasing scientific research efforts, aetiology and pathogenesis of this disease are still a matter of great debate and differing concepts.

A major obstacle in understanding disk degeneration is the problem of defining "degeneration" from (normal) "ageing". Currently, it is the concept to identify disk degeneration as a clinically symptomatic process that frequently, but not exclusively, is linked to premature or pathologic ageing. The concept allows us to combine the most recent findings that initial degenerative alterations even occur in early infantile disks [1, 2] and the observation that various disk levels within one individual are morphologically "degenerated" to a similar level, while there exists significant interindividual variation in occurrence and extent of degeneration [3]. Taking these preliminary issues together, both age and individual (extrinsic and intrinsic) factors seem to affect disk degeneration.

The human spine – and in particular the disk – is subjected to an age-related disarrangement which proceeds with increasing age leading to "degeneration". The extent of degenerated disk disease (DDD) depends on age and affects various anatomic structures differently [1, 2]. Therefore, substantial individual differences can be observed in the sense that young individuals exhibit the disk of an elderly person and vice versa. Because of the extensive destructive changes that ultimately lead to an osseous transformed (ankylosed) motion segment, many clinicians and researchers believe that the intervertebral disk is a predominant source of low back pain. From a clinical point of view, differentiating "normal" age-related (i.e. asymptomatic) from "pathologic" degenerative (i.e. painful) changes would be sensible. However,

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_4

this task is extremely difficult due to the lacking reference standard for painful disk degeneration. So far, the best reference standard is provocative diskography. However, the role and potential benefit of this diagnostic procedure are controversially discussed in the literature.

While it is becoming more and more clear that the degenerated disk suffers from a progressive disease, the cartilaginous end plates that frame the nucleus pulposus and major parts of the annulus fibrosus come into focus for the pathophysiology of DDD. In consequence, the changes in the structure and the biochemical composition of the end plates – in combination with alterations of the anterior/posterior annulus fibrosus (AF) and the nucleus pulposus (NP) – are of utmost significance for the development and understanding of DDD. In order to understand the potential pathomechanism, we will be evaluating both the "normal" age-related changes in the disk with particular reference to the end plate and also the "premature" pathological changes that may end up in degenerated disk structures.

4.2 Structure and Function of the Normal Disk

The intervertebral disk is composed of three major components which are intimately linked to each others, but also to several adjacent structures, underlining the complexity of the disk (Fig. 4.1). In order to understand the function – and to evaluate any pathological condition – a concise analysis of the normal disk structure is necessary. Only recently, several extensive studies have been performed on the morphological changes in autopsy and surgical material which define the following disk components (see also Fig. 4.1):

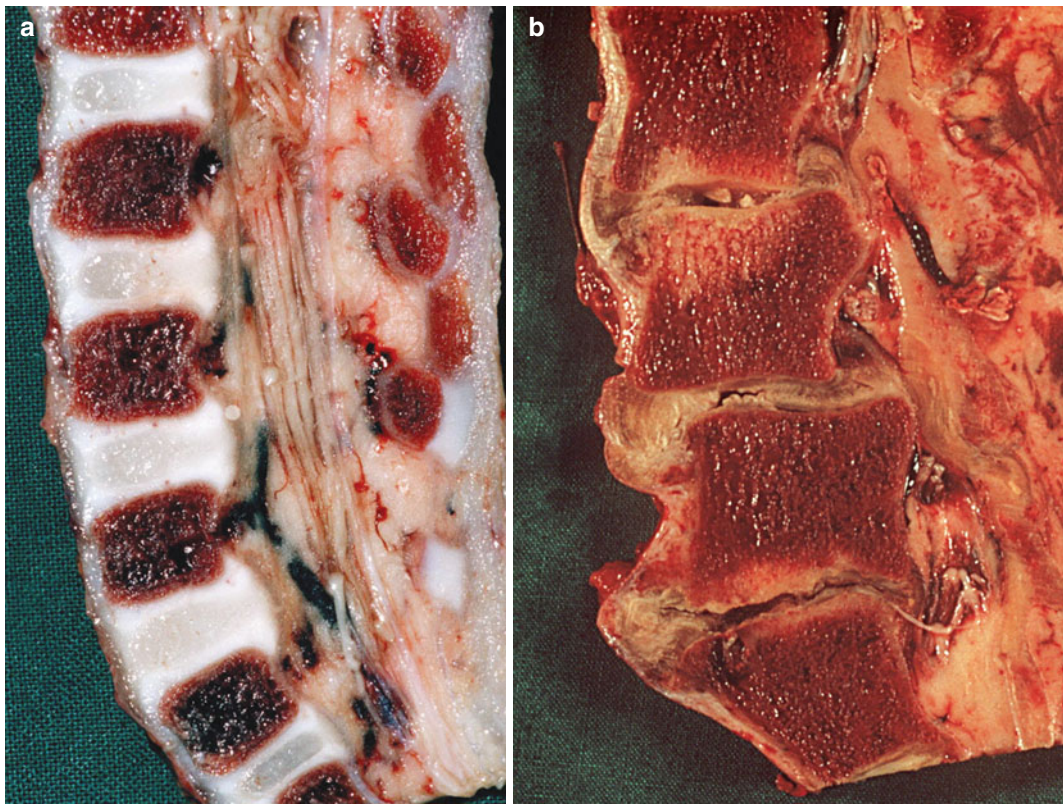

Fig. 4.1 From foetal to old-age disk – macroscopy of the intervertebral disk. (**a**) Foetal lumbar spine (36th week of gestation) vs. (**b**) old-aged spine (86 years) showing the tremendous changes of the disk structure during age

- The nucleus pulposus (NP) is a gelatinous mass filling a central "core" of the disk between the two end plates and the ring-like fibres of the annulus fibrosus (AF). It is made up of a particular type of cartilage which contains relatively few chondrocytic cells and an abundant matrix mainly of proteoglycans (aggrecan) along with moderate amounts of collagen molecules (mainly collagen type II). The high concentration of proteoglycans leads to significant binding of water and swelling of the highly hydrated NP the extension of which is limited by the adjacent structures. Therefore, the NP has the main function of a "shock absorber", a cushion compression, providing both stiffness and flexibility of the motion segment.
- The annulus fibrosus (AF) is comprised of dense sheets of highly oriented collagen fibres in concentric lamellae running obliquely between adjacent vertebral bodies. The angle relative to the vertebral bodies alternates from one lamella to the next resulting in a cross-woven network. The AF can be subdivided into an inner and outer part. The inner AF represents a structure close to that of the NP, while the outer AF is composed of a densely organised structure with thick bundles of collagen as the main constituent. The fibre network allows some relative movement between the bundles, thereby providing a certain degree of disk deformation during flexion and extension of the vertebral column. The main structural component of the AF is collagen (mainly made of collagen types I and III, with some type II collagen in the inner AF, but no collagen II in the outer AF). The content of proteoglycans is significantly lower than in the NP and does not serve mainly as a water adsorbent, but these proteoglycans are important for a proper interaction of the collagen lamellae and therefore for a regular function of the AF fibre network.
- The normal disk is framed by two end plates (EP) forming each a sheet of hyaline cartilage adjacent to the upper and lower vertebral body which is very similar to articular hyaline cartilage. This layer of cartilage separates both the NP and the AF from the vertebral bones providing a firm attachment of AF fibres to the bone structures. Therefore, the end plate is essential for the rigidity of the motion segment. In addition, the end plate is of significance for the nutrition of discal structures, as the major part of the disk is nourished via diffusion of oxygen and nutrients from the bone marrow spaces of the vertebral bones (in "normal" adult disks, there exists only minor vascularisation of the outer AF from small capillary vessels). Structurally, the EP is composed of a fine collagenous network mainly made up by collagen type II fibrils along with proteoglycans. The orientation of the collagen fibres as horizontal layers provides significant rigidity of the motion segment. At birth, the human cartilage end plates make up approximately 50 % of the intervertebral space (compared with approximately 5 % in the adult) and have large vascular channels running through them. Soon after birth, the vascular channels of the cartilage end plate fill in with extracellular matrix such that no channels remain by the end of the first life decade.

Besides the NP, the AF and the EP, the disk is surrounded by various other structural elements that contribute to the function of the motion segment. This holds particularly true for the anterior and posterior longitudinal ligaments which provide further stiffness, but also some flexibility of the spine and which delineate important adjacent structures such as the spinal canal. The ligament zone is important not only with respect to the vascular supply but also with regard to a significant innervation which may be relevant during the induction of disk pain.

The vertebral bodies are further functional elements of the spine which intimately interact with the disks. These osseous bodies significantly stabilise the vertebral column, but they are also important with respect to the nutrition of the various disk structures since the bone marrow cavity is filled with blood with low perfusion velocity.

Under physiological circumstances, these various structures interact properly with each others. There exist, however, significant influences of structure and thus function with different stages of age. Therefore, age-related changes have to be taken into account when differentiated from pathological alterations.

4.3 The Morphology of the Disk During Development and Ageing

The disk and its various substructures undergo significant macro- and micromorphological changes with advancing age which are important for the evaluation of DDD. Again, the disk has to be considered as a whole, but alterations of the end plates seem to be particularly important.

4.3.1 Embryonal and Foetal Development

The vertebral column is already determined during very early embryogenesis (Fig. 4.2). At about 4 weeks gestational age, the human spine can be identified as a typical series of vertebral bodies. These form under the combined influence of the notochord and neuronal tube. The disk grows initially in an environment with only few blood vessels and is surrounded by a perichondrial layer which forms the future longitudinal ligaments. Between the vertebrae, the notochord expands as local aggregations of cells, the notochordal cells, within a proteoglycan-rich matrix, forming the gelatinous centre which results in the NP (Fig. 4.2). The circularly arranged fibres surrounding the NP finally form the AF which is derived from the perichordal mesenchyme. With ongoing development, the notochordal cells are

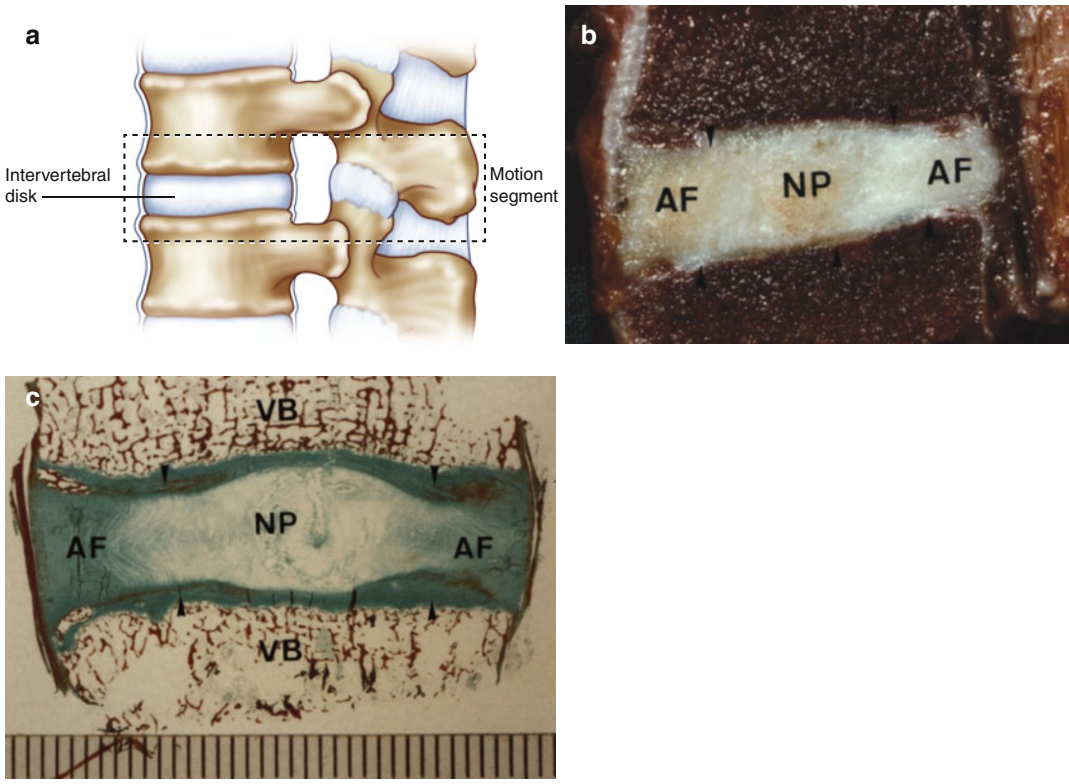

Fig. 4.2 Anatomy of the intervertebral disk. (**a**) Schematic presentation of the motion segment and the disk. (**b**) Macroscopically the central nucleus pulposus (*NP*) is surrounded by the annulus fibrosus (*AF*). (**c**) Histologically the very different fibre structure of the various structures is evident

replaced by chondrocytic cells, while the cells of the AF region have a more fibroblastic phenotype. As yet, the exact role and interaction of notochordal, chondrocytic and fibroblastic cells within the developing disk remains unclear. Recent studies suggest, however, that there exists a significant communication between those cells leading to the final disk structure [4]. This synergy may be of importance in maintaining a normal, "non-degenerated" disk. Interestingly, the notochordal cells disappear from the human disk during early infancy. This is in contrast to various species, such as cat, pig, mouse, rat, rabbit and others where notochordal cells persist in the nucleus pulposus into adulthood. As yet, it remains speculative whether those animals with persisting notochordal cells have a much lesser degree of disk degeneration or if other factors may be the cause therefore. In summary, the loss of notochordal cells may be seen as an important, initial step towards ageing of the disk.

A further significant structural peculiarity of foetal (and early infantile; see below) disks is the presence of blood vessels within the disk (Fig. 4.3). These are mainly formed by large vessel "loops" which originate from bone marrow vessels, perforate the EP and extend into the inner AF close to the NP. These vessels have thin walls such as seen in venules. Due to the dimension, it can be assumed that they provide a major blood supply to all disk structures. Only to a significantly fewer part, small vessels of the capillary type extend from the longitudinal ligaments into the AF, but not into more distant structures. Accordingly, they are restricted to the outer AF.

During the postnatal development, three major time periods can be separated with respect to morphological age-related changes. These are infancy and early adolescence (c. 0–17 years), young and medium adulthood (c. 18–60 years) and advanced age (more than 60 years). These time periods are characterised by significant structural changes affecting the various anatomic sub-settings differently but leading to a progressive loss of "normal" structure and thus function (Fig. 4.4). Any distinction between "physiological" ageing and "pathological" degeneration is highly problematic and should be oriented at the clinical situation, i.e. at the presence/absence of pain and/or disabling loss of function.

4.3.2 The Disk of Infants and Adolescents

Besides the loss of notochordal cells which gradually is seen between the prenatal period to an age of approx. 4 years, the most important structural change is a complete loss of disk vascularisation (see above, also Fig. 4.3). This is closely related to changes in the EP structure and is seen in infants of few months of age presenting with regressively obliterated vessel residues. In a series of autopsy cases of lumbar spines, we did not find intradiscal vessels originating from the bone marrow space as early as 4 years of age [1]. Coincidently with these two features, even the infantile and early adolescent lumbar disk provided focal, minor and very initial morphological changes which suggest initial "degeneration". Likewise, we observed foci of granular matrix alteration, beginning clonal chondrocyte proliferation and initial small disruptions of the matrix even in this age group, mostly restricted to the NP without alterations of the AF. In the EP mainly those areas with presumably obliterated blood vessels show a disturbance of the EP structure. The extent of all these changes correlated well with the increasing age [1].

4.3.3 The Disks of Young and Medium-Aged Adults

With further proceeding age, the extent and degree of the aforementioned changes increases (Figs. 4.4 and 4.5). The most dramatic rise in morphological signs for tissue degeneration is seen at the end of puberty when the rapid growth process has led to a significant increase of diffusion distances within the disk. This impairment of the disk nutrition has previously been made responsible for most degeneration-associated morphological changes. However, more recent concepts – that will have to be discussed below

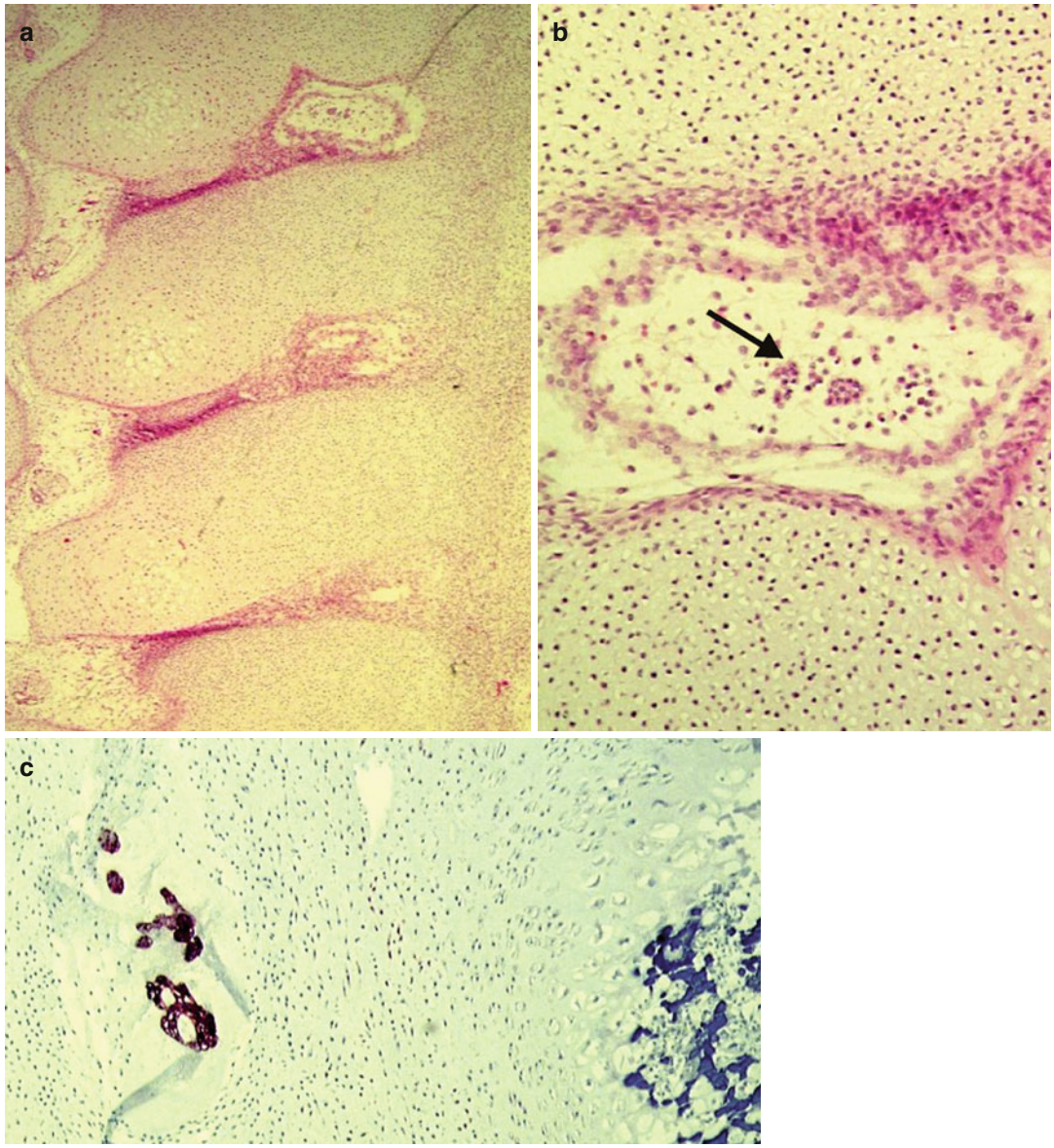

Fig. 4.3 Embryonal vertebra (11th week of gestation). (**a**) The overview shows the typical segmentation; in the centre (**b**) islands of notochordal cells are visible (*arrow*) which can selectively be labelled by immunohistochemistry (*brown* reaction product, cytokeratin 8, **c**)

more in detail – suggest that several other factors seem to play an essential deleterious role during DDD. As the most typical morphological signs for disk degeneration, we previously identified significant tears and clefts of the disk matrix, an increasing amount of clonally growing "proliferating" chondrocytes, granular and mucoid matrix changes and the occurrence of decaying cells (Fig. 4.6) [1]. The changes are seen first in the NP, but frequently extend to the inner AF and to lesser extent to the outer AF. Then the outer AF provides focal clefts which – when in connection with similar tears and clefts of the inner AF and the NP – may lead to protrusions and even prolapse of the disk into the spinal canal. Those changes are then often associated with an

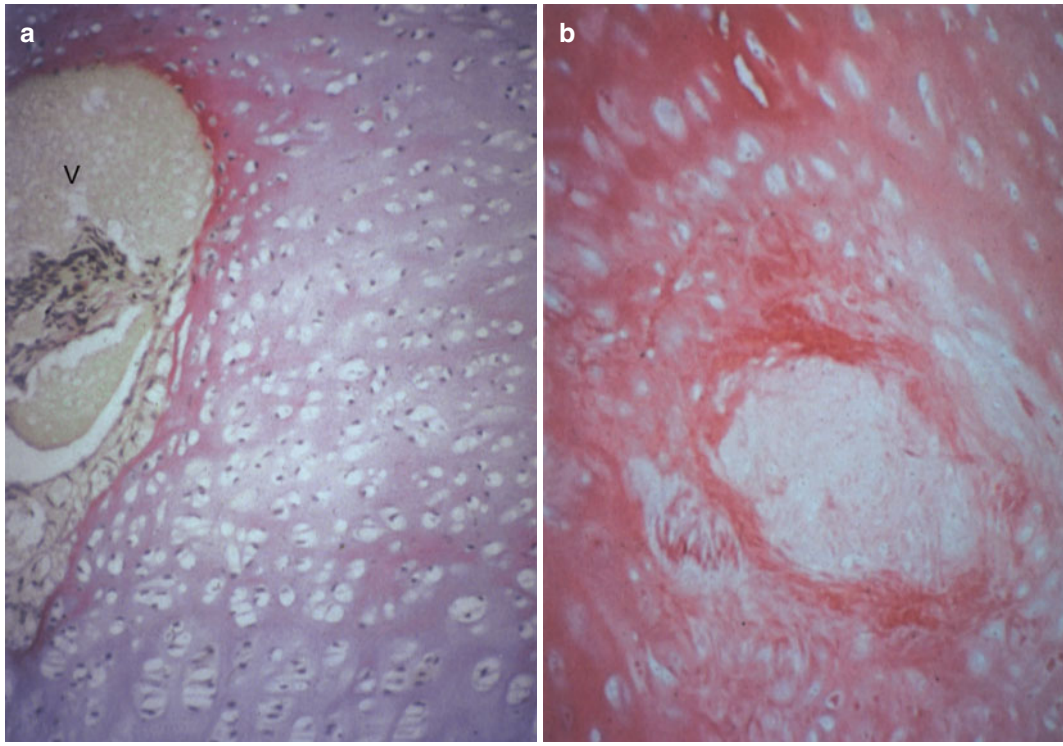

Fig. 4.4 Changes in disk vascularisation. The foetal end plate contains large blood vessels (**a**) which are obliterated during the first postnatal months (**b**). There, small islands of irregular cartilage indicate the residues of the previous vasculature

"inflammatory" reaction as seen by the in-growth of capillary blood vessels and histiocytic cells into the affected AF areas.

4.3.4 The Disks of Adults of Advanced Age

Finally, the age-related changes in the old-age group are characterised by even more pronounced morphological signs of disk degeneration. While part of those cases that have been investigated as yet have shown extensive clefts, a loss of disk height, chondrocytic proliferation and extensive mucoid matrix degeneration (Fig. 4.6b, c), we identified individuals with a transition into a scar-like morphology with loss of the chondroid matrix and replacement by a more or less "fibrous" tissue. Those disks frequently reveal a complete loss of the disk tissue structure and can be termed as a "burnt-out" appearance.

4.3.5 Particular Morphologic Changes of the End Plate

Since the end plates form a very unique structure, in the context of this chapter, a particular view on its anatomic and developmental structure might be presented.

Within the thin cartilage end plates, collagen fibres run horizontal and parallel to the vertebral bodies along with the fibres continuing into the disk. This separates both the NP and the AF from the vertebral bones and provides a firm attachment of AF fibres to the bone structures. Therefore, the end plate is essential for the rigidity of the motion segment. At birth, the human cartilage end plates make up approximately 50 % of the complete intervertebral space (compared with approximately 5 % in the adult). They have large vascular channels running through them. Soon after birth, the vascular channels of the cartilage end plate fill in with extracellular matrix

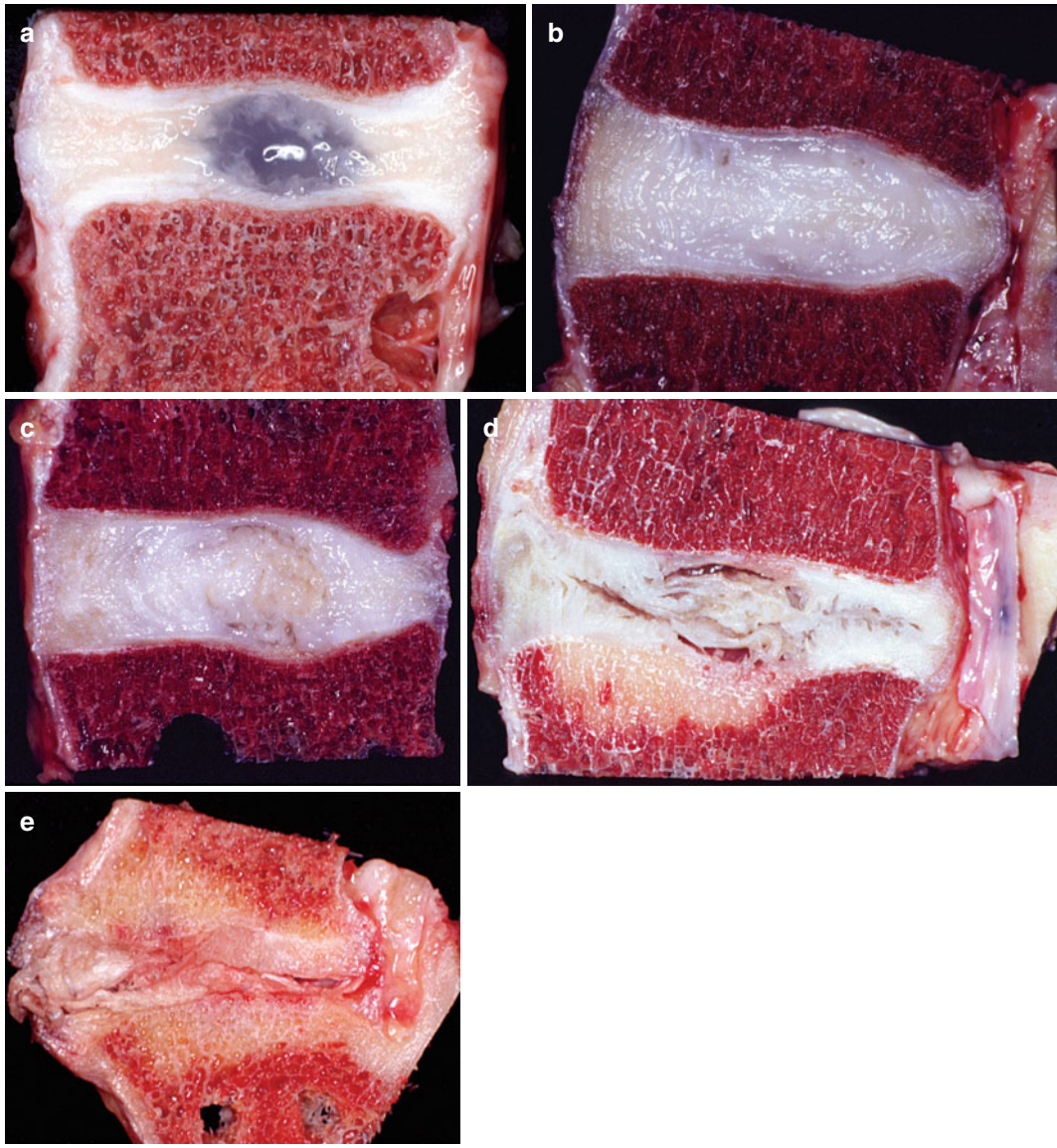

Fig. 4.5 Macroscopic aspects of the intervertebral disk with increasing age. This figure shows typical macroscopic examples of age-related changes of the disk. The alterations with increasing age are used in the classification by Thompson in five grades: I (**a**), II (**b**), III (**c**), IV (**d**) and V (**e**)

such that no channels remain by the end of the first life decade. This change gains even more significance as the disk grows strongly in size during puberty, and therefore, the distances between the vascular supply and the disk cells elongate substantially (see below).

The cartilage end plate in humans functions in early life as a growth plate for the adjacent vertebral body; its structure is typical of that seen in the epiphyseal growth plates of long bones. This structure is lost during skeletal maturity. By adulthood, the cartilage end plate is a layer of hyaline cartilage (approximately 0.6 mm thick) with calcified cartilage adjoining the bone. In adults, the end plate occupies the central 90 % of the interface between the disk

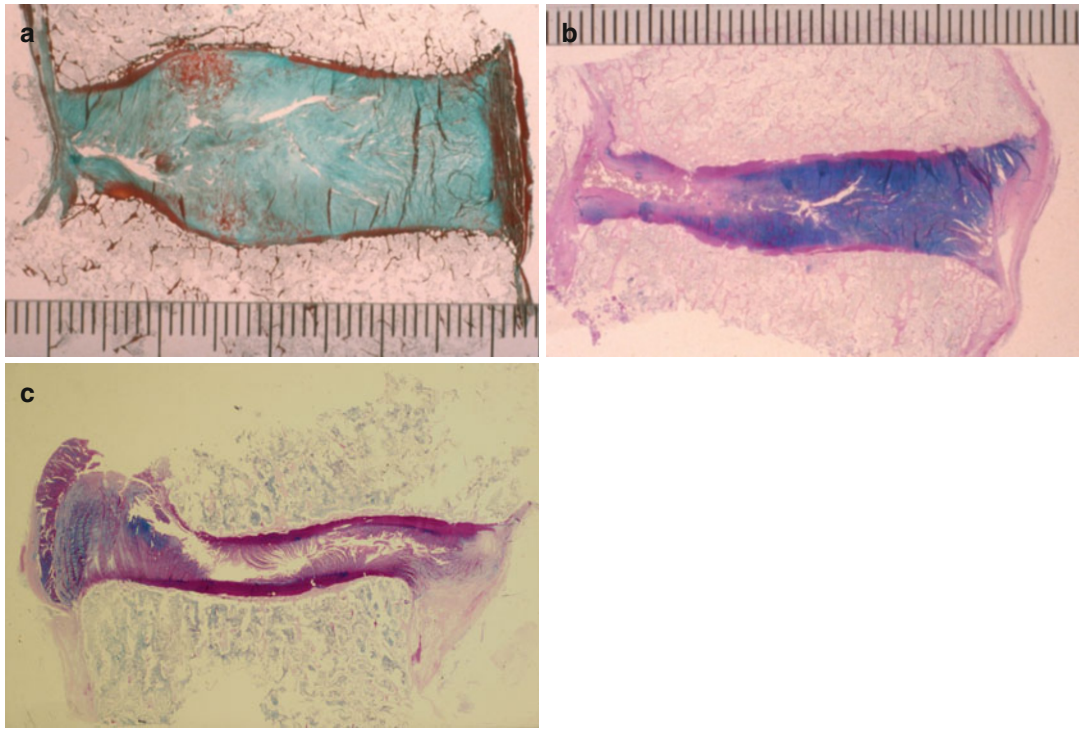

Fig. 4.6 Histology of complete motion segments of intervertebral disks with various age. (**a**) The section through the complete disk of a young adult individual shows regular features of disk morphology. However, despite the young age, the disk reveals already some clefts within the nucleus pulposus. (**b**) The disk of a 62-year-old individual in contrast demonstrates a much more irregular shape of the disk with extensive clefts and tears of NP and AF. Furthermore, the disk shows reduced height and a lack of anatomical distinction between AF and NP. (**c**) The disk of a 77-year-old individual with very extensive alterations (when compared to **b**) with highly significant reduction in disk height and loss of disk tissues (**a** Masson's trichrome; **b**, **c** alcian blue-PAS)

and the vertebral body, encompassed by a ring of bone that forms via the epiphysis fusing with the vertebral body in the rim region. The end plate is totally avascular and aneural in all healthy adults.

Within the cartilage end plates, typical lacunar cartilage cells are surrounded by a small territorial matrix (thereby forming the typical functional unit of cartilage called "chondron") which in turn is enveloped by the inter-territorial matrix. The latter is somewhat more "compact" than the territorial matrix which is reflected on the molecular level by differences in the collagen type distribution. The biomechanical properties of the end plate are defined by its extracellular matrix composition which includes collagen types II, III, V, VI, IX and X and major proteoglycans and glycoproteins. The composition of those constituents alters by age [5].

Functionally, the end plate is involved in two important mechanical functions [6]:

I. Preventing the nucleus pulposus from bulging into the vertebral bodies
II. Partially absorbing the hydrostatic pressure dissipated by the nucleus pulposus under loading. Similar to the disk, the ability of the end plate to withstand mechanical forces depends on the structural integrity of the matrix. In addition, the end plate is of significance for the nutrition of discal structures, as the major part of the disk is nourished via diffusion of oxygen and nutrients from the bone marrow spaces of the vertebral bones.

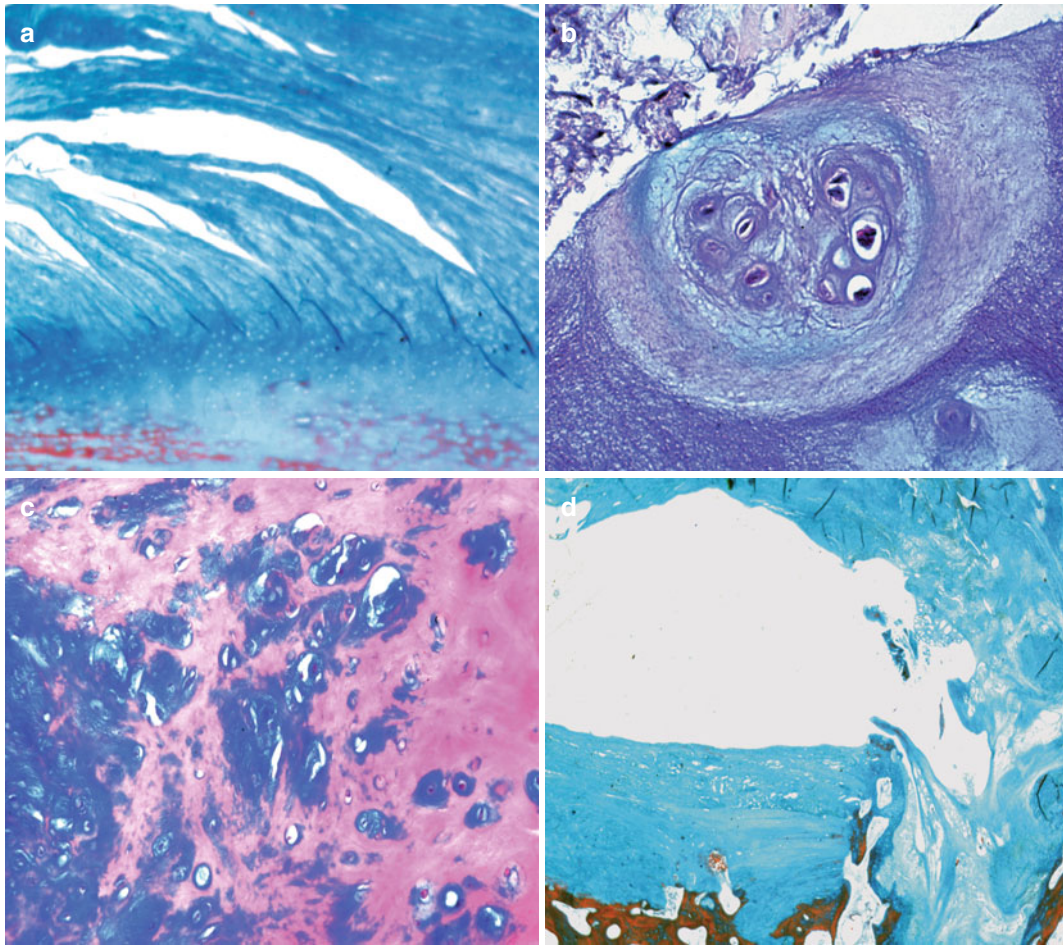

Fig. 4.7 Typical microscopic alterations of disk degeneration. This figure shows characteristic microscopic features of disk degeneration: (**a**) Extensive clefting, originating in the NP, extends with ongoing degeneration to the AF. (**b**) Focal, "cluster"-like cell proliferation. (**c**) Small areas with typical mucoid matrix indicate substantial changes in the matrix composition; this can selectively be made visible in the alcian blue-PAS staining. (**d**) In late-stage degeneration tissue defects occur (**a**, **c** alcian blue-PAS; **b** H **d** Masson's trichrome)

Age-related changes of the EP have been identified to comprise [7] fissure formation, fractures of calcified cartilage, horizontal cleft formation, death of chondrocytes (apoptosis), increased vascular penetration, extension of calcification and ossification. These changes start to occur in the third decade of life. A study of cadaveric human vertebrae demonstrated that the number of vascular channels perforating the osseous vertebral end plate diminishes drastically between 6 and 30 months of age [8]. Analyses on the microscopic level revealed that the abundance of obliterated blood vessels in the end plate gradually increases between 1 month and 16 years of age. The decrease in blood vessels is paralleled by an increase of cartilage disorganisation, end plate cell density, cartilage cracks and microfractures (Fig. 4.7).

These changes, especially the loss of blood vessels, can cause nutritional consequences for the intervertebral disk (Fig. 4.8). With advanced degeneration and markedly reduced disk height, further changes of the end plate are induced resulting in complete end plate disarrangement and dense sclerosis of the adjacent vertebral bodies.

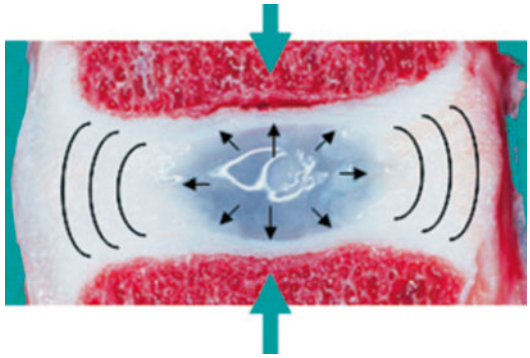

Fig. 4.8 Biomechanical and nutritional conditions of the intervertebral disk. While the nucleus pulpous has high water-binding properties resulting in a cushion-like structure, the annulus fibrosus and the end plates frame the nucleus. However, the avascular disk structure requires long distance diffusion of oxygen and nutritional substances from the bone marrow to the central portions of the disk

4.4 Aetiology of Disk Degeneration and Obvious Factors Influencing Disk Degeneration

Although the aetiology of disk degeneration is far from being completely understood, there is consensus that not a single factor can be held responsible for the complex phenomenon of disk degeneration. Extensive studies suggest a complex cascade of events, factors, transmitters, etc. that seem to induce, promote and enhance disk degeneration. Both exogenous and endogenous factors, each contributing individually, might influence the progress of degenerative changes of the disks. In consequence, we can divide the process of DDD into an initiation, propagation, (abortive) healing and burn-out stage.

4.4.1 Genetic Predisposition of DDD

To our knowledge, DDD has its origin very early in life. Likewise, the methodical analyses of infantile disks indicate that as early as 2 years of age, initial morphological evidence disk alteration is present [1] predominantly related to the blood supply of the intervertebral disk through the end plates. These alterations mimic the later typical features of (clinically relevant) degeneration. This suggests that three main causes may have to be associated with this process: genetic predisposition, biomechanical load and altered disk metabolism/nutrition.

The very first evidence for the influence of genetic predisposition came from twin studies that had demonstrated an overall heritability between 52 and 74 % for disk disease of the lumbar spine [9, 10]. These studies furthermore suggested that the influence of genetic factors is much higher than environmental, behavioural and anthropometric factors, such as gender, obesity, height, occupational activities and exogenic influences by food or smoking habits [9].

Association studies of genes encoding for structural and functional disk components have highlighted the participation of polymorphisms in DDD with a major focus on structural proteins, mainly collagen types I, IX and XI; proteoglycans such as aggrecan or the cartilage intermediate layer protein (CILP); and also on matrix-degrading enzymes and their inhibitors, such as MMP-3, MMP-9 and TIMP-2. Finally, a genetic association with inflammatory cytokines, such as interleukin-1α and interleukin-1β (IL-1α/β), IL-6 and TNF-α, has been described. Cell receptors, such as the vitamin D-receptor (VDR) were also identified such as thrombospondin-2 (THBS2) [11].

Within the focus of the genetic investigation is the role of molecularly modified proteins, such as the aggrecan gene which was demonstrated with shorter variable numbers of tandem repeat length of the gene, leading to a shorter aggrecan core protein [12] which in turn might lead to a lower water content similar to what is seen in degenerated disks. Polymorphisms affecting collagens have mostly been found in collagen type IX genes. The mutations were located in *COL9A2* and *COL9A3*, thus belonging to the so-called cartilage "minor" collagen chain genes. Meanwhile, genetic studies confirmed an association of DDD and other structural proteins, mainly collagen types I [13] and XI [14]. Among the non-collagenous matrix proteins, polymorphisms in the gene encoding

the cartilage intermediate layer protein (CILP) have been recently identified to enhance the susceptibility to lumbar disk disease [15]. All these studies suggest that minor genetic modifications of structural proteins, as in aggrecan, or altered production capacity of the disk cells to produce those proteins may strongly predispose to the development of DDD.

Besides the association between a genetic diversity of disk structural proteins and DDD, similar studies found a comparable association with matrix-degrading enzymes and their inhibitors. Likewise, the major collagen-degrading enzymes MMP-3 and MMP-9 and the metalloproteinase inhibitor TIMP-2 [16] were associated with DDD. Here again, structural changes and/or changes in the amount or activity of those enzymes may be involved in an altered matrix metabolism that may lead more rapidly to degenerative alteration. In particular, polymorphisms in the promoter responsible for the expression of the matrix-degrading enzyme matrix metalloproteinase-3 (MMP-3) were found to accelerate degenerative changes in the lumbar disks in the elderly [16]. As an example, the authors identified a mutation in the MMP-3 promoter that resulted in an increased expression of the matrix-degrading enzyme, which together with environmental conditions might lead to enhanced disk degeneration.

But not only polymorphisms in genes encoding for matrix proteins have been associated with disk degeneration. Recently, mutations in various genes intimately involved in DDD propagation have been identified. Likewise, genes encoding the pro-inflammatory cytokine interleukin-1β (IL-1β) have been associated with disk degeneration and low back pain [17]. The authors suggest that the mutation in the IL-1 gene cluster modifies the effect of occupation on disk bulges and joint occurrence of degenerative changes. Similarly, genetic variability of the IL-1 receptor, interleukin-1α (IL-1α) and IL-6 and IL-10 have statistically been linked with the process of developing DDD [18]. These findings suggest that mutations in these gene clusters contribute to the pathogenesis of lumbar disk degeneration possibly via enhancement of inflammation within the disks of predisposed individuals.

4.4.2 Biomechanical Load

For a long period of time, it was the main theory that higher than normal loads during any physical activities were the main contributors to DDD. These observations were mainly nourished from the observations that the lumbar spine is affected more often and to higher degree than any other spinal zone, a region of the vertebral column that has to carry more mechanical load that any other spine region. Meanwhile, more sophisticated studies confirmed an association between mechanical load and DDD [11] with the main speculation that overload-induced alterations mainly affect the end plates, since it has not clearly been shown that the disk itself is directly suffering from abnormal loads [19], but the adjacent system of vertebral bodies and the cartilage frame work of the end plates. Further support for a more "indirect" role of direct mechanical influences on developing DDD comes from the histological observations that indicate early signs of disk degeneration even in early infantile disks when mechanical load normally does not play any major role and the recent systemic analysis of disks of various disk heights (cervical, thoracal and lumbar) that showed major interindividual differences in the extent of morphological disk degeneration, but not within the individuals analysed.

To investigate the influence of mechanical stress on disk degeneration uncoupled from psycho-social factors and work perception and to be able to tightly control the load impacting the intervertebral disk, animal experiments have been carried out. By applying dynamic load forces to the intervertebral disks of various experimental animals, changes indicating the onset of degeneration were found when the disks were analysed macro-morphologically or histologically [20]. Recently it has also been shown that not only compressive forces induce changes in the intervertebral disk related to degenerative changes but also particularly the application of vibrational

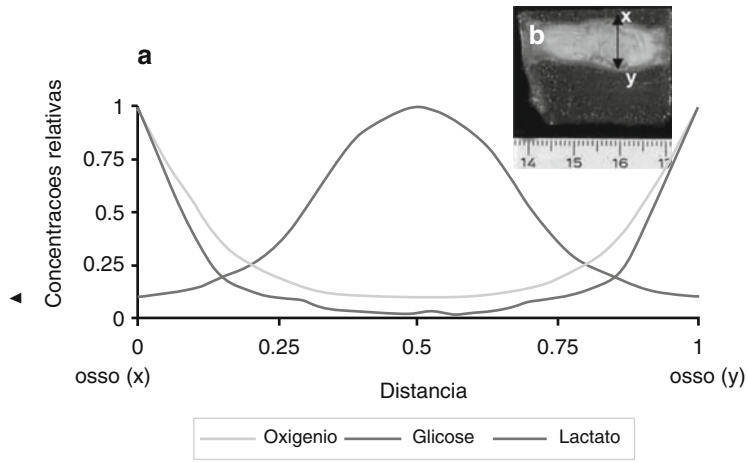

Fig. 4.9 Oxygen, glucose and lactate levels in the lumbar disks (**a**) – in relation to the distance from the vertebral bone (**b**) (Adapted from Holm et al. [23])

forces revealed signs of degenerative changes. Although the majority of the animal studies might suggest that certain forms of mechanical loads suffice to induce disk degeneration, several studies in humans did not provide a strong causal link between occupational exposures and disk degeneration, suggesting a more complex aetiology of disk degeneration.

4.4.3 Metabolic and Nutritional Effects

Insufficient nutritional supply of the disk cells is thought to be a major problem contributing to disk degeneration. Since the intervertebral disk is the largest avascular tissue in the human body, its cells are facing the precarious situation of having to maintain a huge extracellular matrix with a "fragile" supply of nutrients that is easily disturbed.

Although some vascularisation of the disk exists during the foetal and early infantile stage of life (see above), there is consensus that the tissue becomes avascular during the juvenile age and that it remains normally avascular throughout further life. The blood vessels originally extending into the disk then terminate before reaching the cartilage end plate. Whereas the cells in the outer annulus fibrosus may be supplied with nutrients from blood vessels in the adjacent longitudinal ligaments, the supply of the nucleus pulposus cells is almost completely dependent on the capillary network and the sinus of the vertebral bone marrow [21] and the concomitantly long diffusion distances into the disk. With the originally cartilaginous end plates becoming calcified when degeneration progresses, the supply with nutrients becomes even more restricted [22]. Not only the supply with nutrients like glucose and oxygen is restricted due to diffusion distances, also the removal of metabolic waste becomes critical [23]. In vitro experiments have shown that low oxygen concentrations and acidic pH significantly affect the synthetic activity of disk cells (Fig. 4.9). Especially proteoglycan synthesis rates were observed to be particularly sensitive to a decrease of the extracellular pH. The reduced proteoglycan synthesis rates might then lead to a fall in proteoglycan content and therefore to disk degeneration. This combination of restrictive nutrient supply and metabolite environment may lead to increased cell death and therefore reduced cell numbers in the disk.

Beyond the mere physical influence of e.g. diffusion distances, several other indirect factors may also play an important role. Recent studies evaluated the role of a systemic reduction of perfusion, such as by arteriosclerosis (particularly arteriolosclerosis in diabetic microangiopathy), chronic smoking habits and systemic vascular diseases, such as lipidaemia, hyperuricaemia and others, as risk factors to develop more rapidly DDD [24]. Likewise, it has been hypothesised that the low metabolic activity of disk cells hinders adaptation of the disk to abrupt increases in physical activity.

4.5 Presumed Molecular Mechanisms of Degeneration

As described in the chapter before, a whole series of endogenous and exogenous factors induce and promote DDD. These factors act via various molecular mechanisms that have meanwhile been identified. Induction of the degeneration process requires the translation of adverse impacts like nutritional restrictions to the disk cells and mechanical stress into molecular mechanisms. None of the adverse conditions seem to be sufficient to induce degeneration on its own, thereby leading to a concomitant induction of degeneration and low-back pain. In this regard the disk cells play a central regulatory role in the translation of the various impacts into molecular mechanisms. This holds, e.g. true for the expression of an array of matrix-degrading enzymes, changes of the disk cell phenotype or initiation of signal transduction cascades.

4.5.1 Matrix-Degrading Enzymes

Disorganisation of the disk matrix is one of the prevalent features of disk degeneration. This is seen in very "early" stages of disk degeneration and is present very consistently until a burnt-out stage has been reached. Several studies indicate an enhanced presence/activity of major matrix-degrading enzymes [25]. The most important and best-characterised group of degrading enzymes are the matrix metalloproteinases (MMPs) which are responsible for degradation of the various types of collagens. According to their specificity, MMPs can be divided into four groups. Activation of MMPs during degenerative disk disease might be of ambiguous benefit. Whereas MMP activation in intact disks might contribute to the degeneration of matrix molecules and therefore be unfavourable, it might be beneficial in herniation by supporting the resorption of the prolapsed/extruded tissue.

The expression of major MMPs is accordingly enhanced around clefts and tears in the matrix of degenerated disks providing a co-localisation between enzymatic activity of MMPs and formation of clefts and tears. Evidence for an influence of infiltrating macrophages on MMP production by disk cells from herniated disk material was mostly provided by in vitro studies showing that co-incubation of herniated disk material with homologous peripheral blood mononuclear cells induced production of MMP-1 and MMP-3 by the disk cells. Additional strong evidence shows that the disk cells themselves also produce matrix-degrading MMPs during disk degeneration (Figs. 4.10 and 4.11) [26].

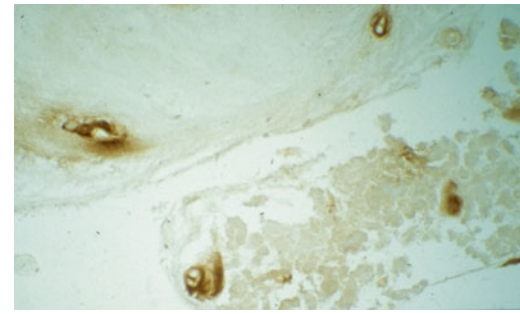

Fig. 4.10 Immunohistochemical staining for MMP-1. The immunostainings for MMP-1 shows a highly specific and selective localisation of this matrix-degrading enzyme (*brown* reaction product). This indicates focal enzyme action resulting in matrix disruption

Collagens, however, are not the only matrix components that are degraded during degeneration. Aggrecan, a large proteoglycan that forms macromolecular aggregates with hyaluronic acid via link protein, is also degraded during degeneration. Recently, the number of cells expressing aggrecanase-1 (ADAMTS4), a member of the ADAMTS (*a d*isintegrin *a*nd *m*etalloproteinase with *t*hrombo*s*pondin motifs) gene family, has been found to increase with increasing degeneration [27]. This finding suggests that ADAMTS4 might play an important role in tissue degradation during disk degeneration.

4.5.2 Pro-inflammatory Mediators

Disk cells do not only produce matrix-degrading enzymes but also have the ability to initiate or propagate signal transduction cascades to

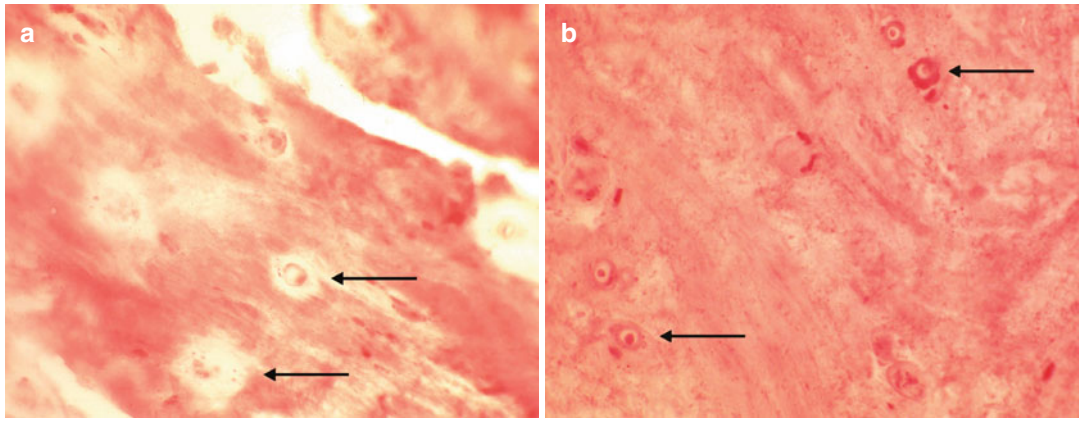

Fig. 4.11 Enzymatic degradation of disk tissue by MMPs. In a special detection technique (in situ zymography), the local activity of specific MMPs can be localised. While in degenerated disk tissue (**a**) a loss of staining around disk cells (*arrows*) indicates enzymatic activity of MMPs, in non-degenerated disk tissue (**b**) cells remain unstained (*arrows*)

manipulate their own environment. Production and secretion of cytokines, growth factors and the respective receptors by disk cells has been investigated extensively. The knowledge gained so far mostly originates from studies on herniated disks (protruded, extruded or sequestrated disks), in vitro experiments or the use of animal models [18].

Studies using protruded but contained disk material show that disk cells do have the possibility to produce an array of pro-inflammatory factors. There, chondrocytes were found to produce significant levels of IL-1α, IL-1β, IL-6, TNF-α and granulocyte-macrophage colony-stimulating factor (GM-CSF). Consistently, strongly increased levels of prostaglandin E2, a key modulator of inflammation, were found in in vitro experiments. Since prostaglandin E2 is also involved in pain induction, the authors suggest that the inflammatory cytokines IL-1α and TNF-α produced by disk cells might contribute to pain induction [16]. This hypothesis has been further evidenced by detection of IL-1α, TNF-β and COX-2, an enzyme essential for the synthesis of prostaglandin E2, in vivo and in vitro. In addition a positive feedback loop of IL-1α has been identified in vitro, upregulating its own production and also the production of IL-6 and COX-2. Recently, it has been demonstrated that TNF-α is substantially more expressed in disk material from symptomatic patients compared to samples taken at autopsy. Accordingly, one can assume that disk cells do have the potential to produce the inflammatory cytokines necessary to mediate and propagate an inflammatory reaction. In addition, the expression of cytokine receptors suggests that these cells are able to not only initiate signal transduction cascades but also endue the requirements to react to pro-inflammatory mediators. Several studies provide strong evidence that the chondrocyte-like cells of the nucleus pulposus are the origin of the observed mediators in contained, degenerated disks.

4.5.3 Growth Factors

Growth factors are usually low-molecular-weight proteins that have the potential to increase mitogenesis, cyto-differentiation and also matrix synthesis. This combination of proliferative and biosynthetic effects on target cells and tissues promoted the investigation of growth factors and their effects on disk tissue. The first "research targets" were the transforming growth factor-β (TGF-β) and epidermal growth factor (EGF) which revealed a strongly significant increase of collagen and proteoglycan synthesis in disk cells in vitro and in experimental models. Additionally,

TGF-β has not only positively affected the extracellular matrix by increasing proteoglycan synthesis but also reduced tissue resorption by decreasing the levels of MMP-2. Human disk cells do not only respond to exogenous TGF-β but are also able to produce this growth factor. TGF-β was generally found in tissue specimens from human herniated disks and was mainly associated with disk cells.

In a series of animal experiments using so-called senescence accelerated mice (SAM), it has been shown that the disks of young mice contain all members of the TGF-β family and the respective receptors type I and type II were expressed. During ageing, the expression of TGF-βs and receptors was found to decrease consistently in all mice used in this study, indicating a role of TGF-βs in this type of rapid disk degeneration [28].

As a further target, insulin-like growth factor-1 (IGF-1) has also been studied in detail. Originally known for its ability to stimulate growth of bone and cartilage, IGF-1 has also been described to increase proteoglycan synthesis in the nucleus pulposus along with a reduction of tissue resorption in disks by lowering the level of active MMP-2 in nucleus pulposus cells. Previous work has suggested that apoptosis substantially contributes to this loss of viable cells. The ability of IGF-1 to significantly reduce the number of apoptotic cells in vitro after serum withdrawal from cultured human intervertebral disk cells might hint the importance of IGF-1. Expression of IGF-1 was found in disk cells from human, cattle, canines and rats and the positive effect on proteoglycan synthesis seen in human disks was verified in vitro using cultured bovine and rat disk cells.

4.5.4 The NF-κB Pathway and Disk Degeneration

Recent molecular investigations identified the so-called NF-κB pathway as one of the central control mechanisms that may also be involved in disk degeneration [29]. This family of transcription factors plays a central role in the mediation of cellular responses to damage, stress and inflammation. Enhanced or chronic activation leads to degenerative diseases of various organs and organ systems and recent data include DDD into this list of diseases.

First evidence for the activation for this transcription factor pathway came from the aforementioned observations of major interleukins and matrix metalloproteinases which are mainly regulated through this pathway. Very recent in vitro experiments provide substantial support to this idea since it has been shown that the application of NF-κB pathway inhibitors blocked major cellular response of nucleus pulposus cells to stress factors in terms of inhibition of cytokine and MMP production and activation. These observations – albeit still in an experimental format – offer new opportunities for a therapeutical intervention on one of the obviously most important regulatory pathways during early disk degeneration. It is important to note that natural regulators of the NF-κB pathway, such as by the natural substance curcumin [30], may provide novel options in the prevention of (preclinical) early stage disk disease [31].

4.6 Pathophysiologic Role of the End Plate in DDD

As outlined before, DDD results from various alterations of the complex structures of the intervertebral disk. Within the current concepts of disk pathophysiology, the end plate plays a pivotal role that is, however, mainly restricted to the biomechanical and nutritional/metabolic part of disk degeneration and that does not seem to play a major (direct) role in pain induction/transmission:

- It seems to control the nutritional influx of metabolic substances, as well as the efflux of waste products from the disk cells.
- The structural and molecular composition of the end plate is, therefore, crucial for the

preservation of the phenotype of disk cells (mainly those of the NP).
- The biomechanical integrity of the disk is based on the structure of the end plates.

Taking the aforementioned pathophysiologic features of DDD into account, the end plates seem to be the main player in the initiation and promotion of disk degeneration, but they do not seem to be involved in the transmission of diskogenic signalling, such as pain induction. The latter may be promoted by the clefting of the NP and AP and the subsequently much more rapid translocation of pain-inducing (pro-inflammatory) cytokines to the peridiscal space with its neuroceptive structures.

In general, the currently most favoured hypothesis for DDD comprises:

- Genetic predisposition renders individuals more or less susceptible to develop disk degeneration.
- Changes in the biomechanical and or nutritional/metabolic conditions of the disk, e.g. by overload, associated with an enhanced "weakness" of the disk tissue by genetic conditions and metabolic "stress" (including alterations of nutrition and metabolism by arteriosclerosis, chronic nicotine and other drug application, etc.).
- Alteration in the composition and structure of the end plate leading to disturbed supply of nutrients and oxygen and accumulation of waste products within the disk
- Change in the disk cell metabolism with the upregulation of pro-inflammatory cytokines and growth factors.
- Altered composition of the pericellular/interstitial matrix of the disks (change in collagen type and proteoglycan production, enhanced synthesis of matrix-degrading enzymes such as MMPs).
- Disruption of the disk structure and cleft and tear formation of NP and subsequently of the AF.
- Liberation of pro-inflammatory messenger substances (such as Tumor-necrosis-factor α, etc.) from the altered disk cells and rapid transport via the tissue clefts to the peridiscal space.
- Induction of pain sensation in the peridiscal space (i.e. diskogenic low back pain).

Besides this hypothesis, it must be clear that several other mechanisms and pathways may also play a role in the process of disk ageing and degeneration, such as facet joint arthrosis, production of oxygen radicals and NO, etc. The exact role and contribution of those factors to the degeneration process is still being unclear.

4.7 Conclusions and Clinical Implications

The past decades have provided us with considerable insights into the mechanisms of DDD. The identification of major pathways that are disturbed and the elucidation of factors such as distinct cytokines and their pathways not only provided us with an understanding of DDD but also may offer us novel therapeutic approaches in the future. The application of specific drugs/substances that interfere with cytokine pathways and their regulation may offer new options to block pain induction mechanisms. The identification of phenotypic changes of the disk cells helps us to design strategies for gene therapy of disk cell cure. The investigation of matrix changes let us understand which environment is needed to successfully implant cells into the disk during disk repair.

Finally, all these studies make clear that the prevention of disk degeneration is one of the most desired (and obviously most effective) therapeutic means. We have also learned that this prevention must start early before secondary changes of the facet joints, ligaments and muscles occur. Early intervention must include not only the control of intrinsic metabolic factors (e.g. diabetes) but also the avoidance of deleterious exogenic influences (e.g. smoking). From a clinical perspective, however, there is still a long way to bring the intriguing research results of the past two decades from the bench to the bedside.

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Epidemiology of Lumbar Degenerative Disk Disease

5

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It is of the highest interest for surgeons to study the epidemiology of symptomatic lumbar degenerative disk disease: A basic question to pose is "What is DDD?"

In the recent literature, DDD covers a wide spectrum of symptoms and radiological findings, from low back pain to acquired spinal canal stenosis and symptomatic herniated disk-related symptoms. Symptoms at first glance appear to result from the cumulative exposure of the spinal elements to excessive loading, sports, and principally work. However, this simple theory is not consistent with our contemporary understanding of developmental biology and genetics. A fundamental question arises too: Are we studying radiological aspects or real illness?

5.1 Disk Degeneration: A Spectrum of Definitions

It is not always clear if the term "disk degeneration" is routinely employed for normal or pathological states, reflecting the most difficult challenge in treatment: In a given case, are the symptoms related to what is seen on even the most sophisticated radiological images?

For example, the definition taken from Battié and Videman's paper [1] includes the paradox of simultaneous occurrences of normal and abnormal states: "disk degeneration is a product of lifelong degradation of the intervertebral disk with synchronized remodeling of the disk and neighboring vertebrae, including simultaneous adaptation of the discal structures to changes in physical loading and responses to occasional injury."

In this definition, the word "injury" is referring to trauma, reflecting an acute event, but may also include the concept of cumulative stresses from the environment, i.e., way of life, history of accidents, heavy work, etc.

This cumulative load may reflect chronic injury to the spine, a sort of premature aging.

✠ Author was deceased at the time of publication
Dr. Pierre Kehrli, Chairman of Neurosurgery of the Strasbourg University, France, tragically died before completing this chapter. He died suddenly, in May 2014, at the age of 50, from an aortic aneurysm. His legacy to the privileged people who worked with him included his extreme technical ability as a neurosurgeon and his gentle character. The coauthors pay a small tribute to this fantastic human being with this chapter to the book.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_5

The term "disk degeneration" is an ambiguous term which covers the spectrum of radiographic images not always correlated to pain. This findings on images such as plain X-ray films, CT, and MRI include disk height narrowing, osteophytes, bulging disk, disk herniation, low-signal appearance on T2-weighted MRI, end plate changes, fatty marrow degeneration, posterior facet changes, etc. [2].

5.2 Traditional Epidemiological Studies

5.2.1 Age and Sex

"Normal aging" presupposes proportional "normal disk alterations or changes" over time; however, the findings of advanced early disk degeneration are well known in certain individuals [3].

Similar disk degenerative changes occur in women as in men, but with a delay usually of 10 years [4, 5]. Females may report low back pain associated with hormonal changes related to changes in systemic exposure to progesterone treatment common in pregnancy. A confusing clinical scenario is a woman with an ovarian cyst in mid-menstrual cycle with concomitant lumbar DDD and symptomatic low back pain. In this situation, the spinal surgeon has to be very careful in proposing surgery, even if radiological findings demonstrate significant DDD.

It is quite common in the elderly to see impressive DDD on radiological films in the absence of symptoms.

5.2.2 Postural Factors

Postural factor has often been cited as a cause for low back pain. This has not been fully supported by the peer review literature. For example, there is no relationship between retrolisthesis in patients with L5-S1 disk degeneration and baseline pain or function [6].

A comparison of lumbar degenerative changes between primates and humans demonstrated similar aging DDD patterns species nonspecific. This suggests "that the bipedal posture may not be the singular, or even the most important, biomechanical factor in the development of human DDD" [7].

5.2.3 Weight

In symptomatic patients with sciatica, excessive weight has often been cited as a causative factor for sciatica [8]. Studies indicated that overweight and obesity could increase the risk of chronic or severe low back pain [9, 10]. However, a definitive association between sciatica and excessive weight is just suggested, not widely proven in the literature.

5.2.4 Loading Efforts

Lifting heavy loads, torsional stress, and motor vehicle driving are among the best-identified environmental risk factors associated with symptomatic DDD. A definitive association between loads carried and symptomatic lumbar degenerative disease has also not been proven. Routine heavy physical loading demands at work or at leisure explain only a minor portion of the overall variance in lumbar disk degeneration in Battié's study of twins [11, 12].

5.2.5 Work/Sports

Excessive loading due to repetitive work activities was shown in one study to be second to inheritance as a causative factor in symptomatic disk degeneration [13]. A study by Ong et al. [14] in athletes found that elite athletes have a greater prevalence and degree of lumbar disk degeneration than the normal population. This may also vary with the type of sport.

5.2.6 Vibrations

There was no clear correlation in a study of 45 pairs of monozygotic twins, highly discordant for exposure to motorized vehicles and associated

whole-body vibration, between lumbar disk degeneration on MRI and extensive lifetime driving histories [15].

However, the study of Weber found that after a long duration to whole-body vibration exposure, an increased degree of spondylotic changes was noted at the thoracolumbar junction and mid-lumbar spine [16].

5.2.7 Cigarette Smoking

Results from twins studies are inconclusive on the influence of cigarette use and symptomatic lumbar DDD. An association with cigarette use and heavy work style has been associated with vertebral inflammatory disease [17]. If this finding can be reproduced in other studies, it may have consequences in relation to both primary and secondary prevention measures for low back pain.

5.2.8 Genetic Factors

The recent literature on DDD has been enriched with genetic studies which have given us new insight on the influence of inheritance and symptomatic DDD [18]. In 1991, Varlotta et al. [19] found that 32 % of adolescent patients with a symptomatic disk herniation had a family history.

As Ala-Kokko in 2002 concluded a study, "Even though several environmental and constitutional risk factors have been implicated in this disease, their effects are relatively minor. And recent family and twin studies have suggested that sciatica, disk herniation and disk degeneration may be explained to a large degree by genetic factors" [20].

In 1992, Matsui et al. [21] reported that there is familial clustering of symptomatic lumbar disk herniation among the young (18-year-old or younger). In 1997, Matsui et al. [22] surveyed 3,042 Japanese factory workers regarding a history of acute low back pain. The authors found that the average age of initial symptoms in workers whose parents also suffered from the same condition was significantly younger than that in workers with no familial history.

Sambrook et al. [23] conducted a classic twin study using the Australian and British twin registries to examine the hypothesis that disk degeneration has a major genetic component. Spine MRIs were obtained on 86 pairs of monozygotic twins and 154 pairs of dizygotic twins, 80 % of whom were female. A substantial genetic influence on disk degeneration was found. A summary score of disk degenerative changes were compiled which included disk height, signal intensity changes, bulging of the intervertebral disk, and anterior osteophyte formation. This revealed that heritability estimates were very high, 74 % (95 % confidence interval, 64–81 %) for the lumbar spine and 73 % (95 % confidence interval, 64–80 %) for the cervical spine, after adjusting for age, weight, smoking, occupation, and physical activity. An analysis on individual MRI findings suggested that disk bulging and height were influenced primarily through genetic influences. A genetic influence on intervertebral signal intensity was not apparent. A comprehensive chapter in this book will discuss in great detail genetics and lumbar DDD.

5.2.9 Twin Studies

A series of studies on exposure-discordant monozygotic twins revealed only modest, if any, effects of various environmental exposures on the acceleration of disk degeneration [18].

Results from studies conducted on male monozygotic twin pairs demonstrated substantial familial aggregation in terms of the extent and location of disk degeneration: in 1995, Battie et al. [12] assessed lumbar MRIs of 115 pairs of male monozygotic twins in order to investigate the relative effects of environmental risk factors, age, and familial aggregation on disk degeneration. Disk bulging, height narrowing, and disk desiccation as indicated through signal intensity changes were used as phenotypic clinical markers. In a multivariate analysis of the thoracic 12–lumbar 4 vertebral region, physical loading exposures explained 7 % of the variance in disk degeneration scores, with this percentage climbing to 16 % due to age and 77 % when familial aggregation was considered. In the lumbar 4–5

vertebrae and lumbar 5–sacral 1 vertebrae region, physical loading explained only 2 % of the variance in disk degeneration summary scores in multivariate analysis. The variance score in the lower lumbar region due to age was approximately 9 % which increased to 43 % when considering familial aggregation. This study provided the first estimate of the relative importance of specific environmental agents and overall familial influences including genetic factors on the presence of symptomatic DDD.

Chromosomal loci particular to the presence of DDD have been evaluated in several studies: The 21q locus was identified in a finish population (based on clinical and radiological findings) when evaluating for imaging presence of lumbar DDD [24]. Another study found that chromosome 19 (study based on MRI findings), near a locus associated with hand osteoarthritis [25], was associated with imaging evidence of lumbar DDD. In the latter twin series, a significant correlation on gene loci and imaging presence of DDD was noted only in the lumbar spine and not the cervical spine. In this study the majority of the twins did not have pain.

In terms of molecular biology, Zhang noted that collagen IX, a structural component of the nucleus pulposus and annulus fibrosus of the intervertebral disk, is considered to serve as a bridge between collagenous and non-collagenous proteins within the intervertebral disk [26]. Collagen IX is a heterotrimer of three alpha chains, 1(IX), 2(IX), and 3(IX), encoded by the genes *COL9A1*, *COL9A2*, and *COL9A3*, respectively. Tryptophan alleles of COL9A2 and COL9A3 have been shown to be associated with lumbar disk disease in the Finnish population [27].

Sox genes appear to encode transcription factors with diverse roles in differentiation and development. *Sox9* is expressed in mesenchymal condensations prior to and during chondrogenesis and has been shown to activate Col2a1, the gene encoding type II collagen, the major component of cartilage matrix. Gruber et al. considered that the loss of expression of *Sox9* in some of the annulus cell population may play a role in disk aging and degeneration, possibly through decreased modulation of the expression and production of type II collagen within the disk cells [28].

Polymorphisms in the vitamin D receptor gene, the matrix metalloproteinase-3 gene (MMP-3), and the aggrecan gene (AGC1) VNTR have been reported to be associated with disk degeneration [2].

Inflammatory cytokines have a well-recognized contribution to the generation of back pain. Interleukin-1, in particular, has been shown to contribute to disk degeneration by inducing enzymes that destroy proteoglycan.

5.2.10 Psychological Factors

Anxiety, depression, and somatization have been suggested as risk factors for chronic low back pain in several prospective studies [29, 30].

Conclusion

Epidemiological studies have now shed light on the important influence of molecular biology and genetics on asymptomatic and symptomatic DDD, derailing the long-held beliefs of the strong association of environmental factors and axial spine pain. Multiple comorbid factors including lifestyle and physical, psychological, and social factors influence overall prevalence and outcomes.

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Genetics of Lumbar Disk Degeneration

6

Kenneth M.C. Cheung, Yan Li, Pak Chung Sham, and Danny Chan

6.1 Introduction

The field of genetics is playing an increasingly important role in clinical medicine. As the fundamental "blueprint" of any organism, genes now are considered a central component of most common diseases. The aim of genetic research is to determine which genes and environmental factors contribute to traits of interest (called phenotypes) and, of most interest to clinicians, to identify mutations that contribute to diseases. The application of such knowledge might lead to early detection, better treatment, and, ultimately, prevention of disease. Low back pain (LBP) is one of the most common disorders for which patients seek medical consultation. The severity of the pain ranges from mild discomfort to severe, disabling pain. The etiology of LBP is complex and involves multiple factors, with disk degeneration of the lumbar spine being a major contributor [1]. This chapter aims to equip readers with a basic understanding of genetics and introduce the principles and findings of genetic studies in lumbar disk degeneration (LDD), following a general framework for genetic studies of all complex diseases (Fig. 6.1).

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6.2 Basic Concept of Genetics

6.2.1 Structure and Function of Genes and Chromosomes

The gene is the basic unit of heredity of living organisms. It stores the instructions for diverse protein molecules that control development, survival, and reproduction. The whole human genome encodes 20,000–30,000 genes. Deoxyribonucleic acid (DNA) is the molecular component of a gene. The molecular unit of DNA is the nucleotide, which has three basic components: a pentose sugar, a phosphate group, and a nitrogenous base. There are four types of nitrogenous bases: cytosine, thymine, adenine, and guanine. They commonly are represented by their first letters: C, T, A, and G. Nucleotides attach to one another in a certain order to form a polynucleotide chain. Two complementary polynucleotide chains, G pairing with C and T pairing with G, held together by weak thermodynamic

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_6

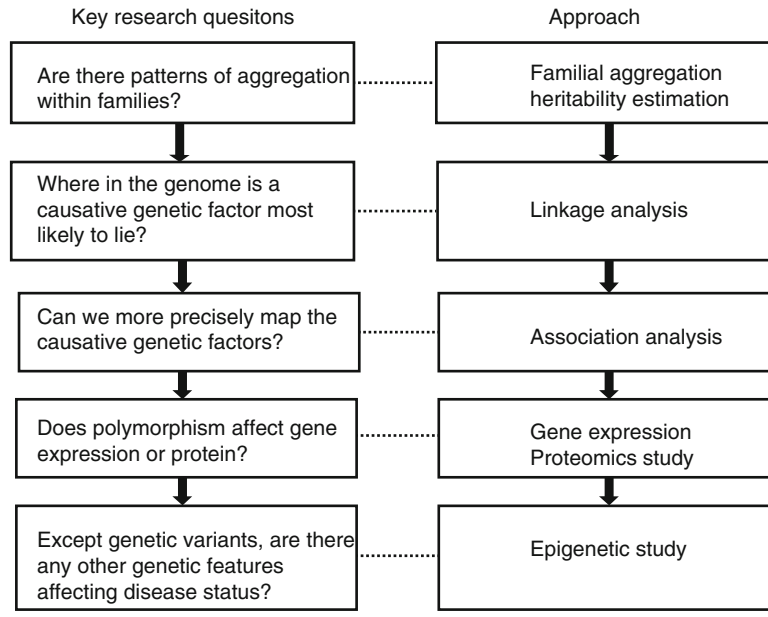

Fig. 6.1 Basic approaches to genetic studies of complex diseases

forces, form a DNA molecule. Different sequences of nucleotides represent different proteins or different regulatory functions. To encode all the information of the human body, each cell contains approximately three billion nucleotide pairs. To package all this DNA into a tiny cell nucleus, DNA coils around histones in an organized manner and loops into a helical line, thereby forming chromosomes (Fig. 6.2).

For diploid organisms, chromosomes exist in pairs. One member of each pair originates from the father and the other originates from the mother. Each human somatic cell contains 23 pairs of chromosomes, including 22 homologous pairs of autosomes and one pair of sex chromosomes. In normal males, the sex chromosomes are a Y chromosome inherited from the father and an X chromosome inherited from the mother. Two X chromosomes are found in normal females, each inherited from one parent. Two homologues have similar sequences; only a small fraction of positions have sequencing variations that can be used to distinguish the chromosomes. The variants on the same position of paired chromosomes are defined as alleles. The two alleles at a certain position may be the same (homozygous) or different (heterozygous).

The functions of genes may be classified into two general categories: protein-coding and nonprotein-coding genes. The coding sequences of protein-coding genes (exons) are separated from each other by noncoding intervening sequences (introns) (Fig. 6.3). They encode proteins through two major steps: transcription and translation. First, the DNA is transcribed pre-messenger ribonucleic acid (pre-mRNA). Introns then are spliced out, and exons join to form mature messenger RNAs (mRNAs). Second, mRNAs are translated to protein. Every three nucleotides (codons) in mRNA represent an amino acid. Nonprotein-coding genes are transcribed into noncoding RNAs, which are not translated to protein, but form secondary structures to mediate gene expression or mRNA degradation (microRNAs).

6.2.2 Genetic Variations and Genetic Markers

Any two human genomes differ at millions of different positions. There are small variations in the individual nucleotides of the genomes, as well as many larger variations, such as microsatellites, insertions, deletions, and copy number variations. Any of these may cause alterations of protein structure or gene expression profile, altering the risk of disease.

One important type of genetic variant is the single-nucleotide polymorphism (SNP). SNPs

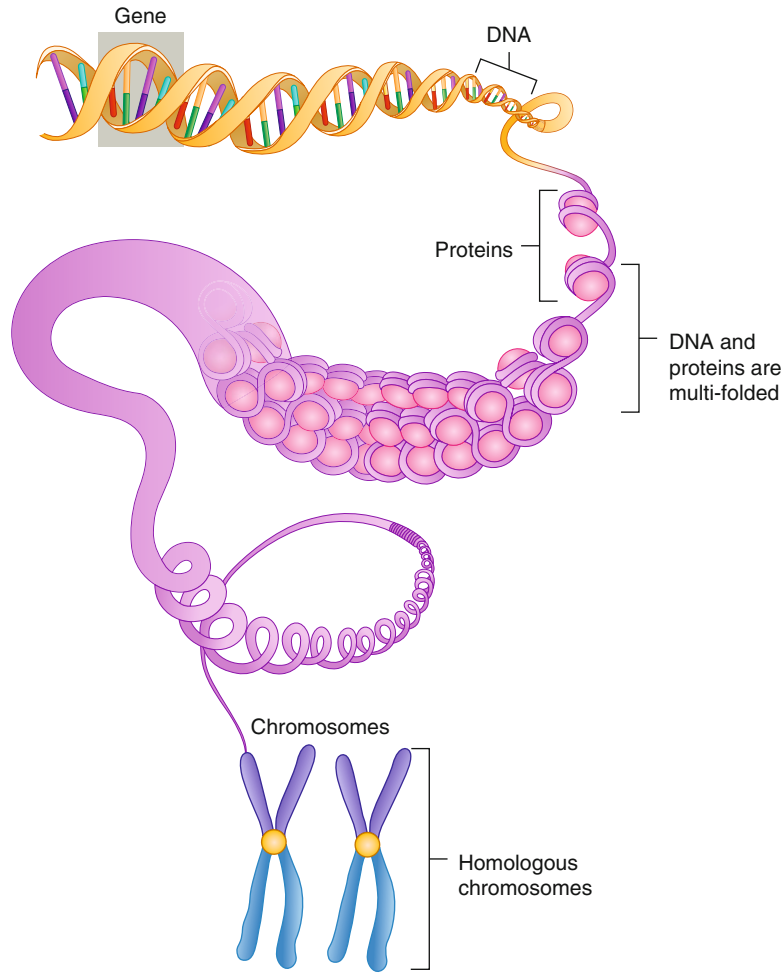

Fig. 6.2 Structures of DNA, genes, and chromosomes

are a 1 bp substitution of DNA sequences that may be found in any position of the genome. In the human genome, on average, an SNP occurs every 300 nucleotides. Approximately 90 % of the genetic variants in the genome are SNPs, which means there are roughly ten million SNPs in the human genome.

A second major type of variation is the microsatellite, also called a variable number of tandem repeats (VNTR). This term refers to a short nucleotide sequence that occurs as a repeating sequence. The number of repeats differs among different chromosomes in different people, enabling VNTR to be a marker for personal identification.

Another type of genetic variant is the insertion or deletion (indel) of one or more bases in DNA sequences. For protein-coding genes, these changes may result in extra or missing amino acids in a protein if the inserted or deleted sequence is 3 bp long or in a complete change of the protein sequence beyond the indel if the inserted or deleted sequence is not a multiple of 3 (the so-called frameshift). Changes in amino acid sequences may have profound consequences, and many serious genetic diseases are caused by such changes.

On a larger scale, recent studies also focused on many large structural variations in DNA sequences. For example, duplications of large chromosome segments containing one or more genes have been studied widely. The number of duplicates is defined as the *copy number*, and variation in the number of duplicates among people is termed *copy number variation* (CNV). Another type of large structure variation is an inversion, a segment of chromosomes reversed end to end. Inversions also have been associated with complex diseases.

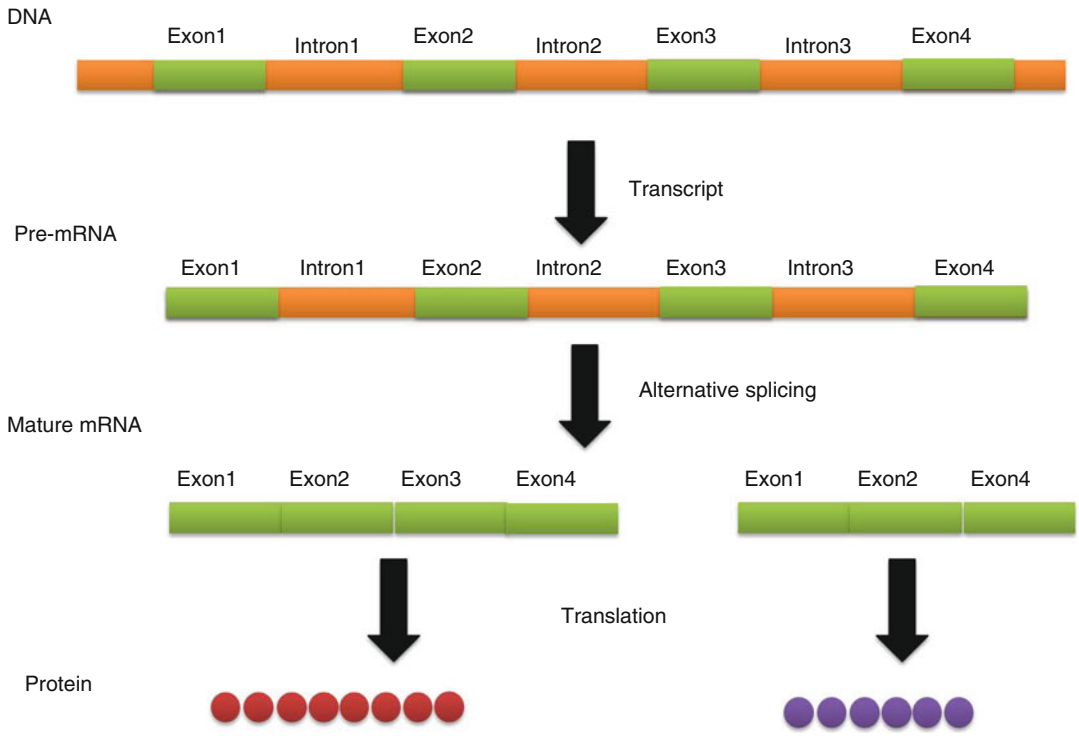

Fig. 6.3 Gene structure, transcript, and translation

A genetic marker is a variable DNA sequence at a known location in the genome. All genetic variants may be used as genetic markers once their locations are confirmed. One of the most important objectives of the HapMap Project is to identify the positions of genetic variants [2]. Genetic markers may be used to study the relationship between an inherited disease and its genetic causes (see details later).

6.2.3 Mutations and Polymorphisms

A mutation is a change in DNA sequence caused by unrepaired damage to DNA or replication errors. Mutations lead to new genetic variants, and their effects range from fatal to mildly detrimental or even beneficial. If a mutation is not fatal, the individual carrying it can reproduce, thereby allowing the mutation to be passed to the next generations and to increase in frequency. For a seriously detrimental mutation, the individual is less likely to survive and reproduce, so the mutation very likely would become extinct over a few generations. Therefore, such deleterious mutations usually are rare in the general population. Genetic variants with a minor allele frequency (MAF) of less than 1 % are classified as rare variants. If the MAF is greater than 1 %, the variant is termed a polymorphism. Among polymorphisms, variants with an MAF greater than 5 % are called common variants; variants with an MAF from 1 % to 5 % are called low-frequency variants. In genetic studies, different methods and technologies are used to assay genetic variants with different frequencies (see later).

6.2.4 Mendelian Genetics and Complex Disease

A genetic disease is a disorder caused by an abnormality in an individual's DNA. Abnormalities range from a small mutation in a single gene to the addition or subtraction of a subset of chromosomes or even an entire chromosome. There are two major categories of genetic diseases: Mendelian and complex diseases. With regard to Mendelian

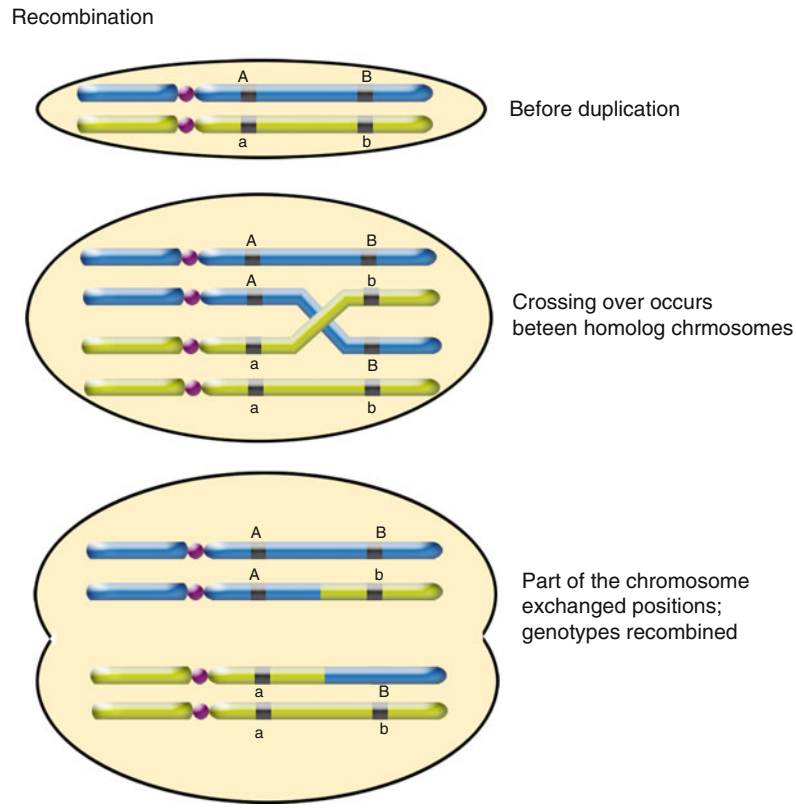

Fig. 6.4 Concepts of recombination

disorders, mutations in a single gene are sufficient to cause disease. Mendelian disorders are relatively rare and often are first recognized clinically by their predictable patterns of inheritance in families. Common Mendelian modes of inheritance include dominant inheritance, recessive inheritance, and X-linked and Y-linked dominant or recessive modes. More than 4,000 human diseases are caused by single-gene defects. Several skeletal abnormalities follow Mendelian inheritance; classic examples include osteogenesis imperfecta (OI) and spondyloepiphyseal dysplasia.

Mendelian disorders account for only a small proportion of the total burden of human genetic diseases. A much larger component is composed of congenital malformations and common adult diseases. These diseases have significant genetic components and also are influenced by multiple environmental factors. They commonly are called complex diseases or polygenic diseases. Complex disorders are caused by variant forms of genes and environmental factors; they may act independently or modify the effects of one another through gene–gene and/or gene–environment interactions.

LDD is an example of a complex disease. In earlier studies, age, gender, occupation, cigarette smoking, height, and weight were found to be associated with LDD [3]. Later studies suggested a large degree of genetic influences [4]. Recently, many susceptible genes were found to be associated with LDD [5].

6.2.5 Recombination, Linkage, and Linkage Disequilibrium

With regard to the relationship between two genetic variants in a population, some alleles located near each other on the same chromosome are transmitted together, rather than independently during reproduction. Such co-segregated behavior is termed *linkage*. However, not all genes on the same chromosome are linked, because recombination occurs during meiosis. When homologous chromosomes are paired, crossover occurs between non-sister chromosomes that are part of the chromosome exchanged (Fig. 6.4). As a result

of exchange, new combinations of alleles can be formed on a chromosome. The probability of crossover events varies among the different regions of a chromosome. The nearer two positions are, the less chance recombination will occur. The recombination rate is an indication of the distance between two genetic markers, because the further away the markers are, the greater the likelihood of recombination. The distance between two markers may be expressed in centimorgans; 1 cM corresponds to 1 % of recombination and to about one billion bases.

In the human population, crossover positions vary; therefore, the allelic combinations of two markers differ among individuals. Normally, the frequency of non-recombined and recombined alleles is not equal to the randomized frequency. This nonrandom association between markers is called *linkage disequilibrium* (LD) and is measured by r^2. The greater the r^2, the more likely co-segregation will occur between two markers. Thus, the presence of one allele of a marker provides information indicating the allele of the nearer markers by the degree of LD. Recombination and LD are the theoretical basis of the linkage and association studies introduced later.

6.3 Identify the Genetic Cause of Disease

6.3.1 Estimate the Genetic Contribution of LDD

The first step in studies to identify disease genes is to estimate the heritability or the genetic contribution to the disease. This estimation involves observation and statistical analysis of the patterns of phenotypes with various genetic or environmental backgrounds in close kin, such as parent–offspring, siblings, and twins [6]. Familial aggregation and twin studies are two widely used methods for estimating heritability. Familial aggregation estimates the likelihood of a phenotype in close relatives compared with that in controls. On the other hand, studies of twins are useful in estimating the contribution to a phenotype by comparing monozygotic (MZ) pairs (in which all genes are shared) with dizygotic (DZ) pairs (in which half the genes are shared). If the similarity between MZ pairs is greater than that between DZ pairs, the greater part of similarity must be caused by genetics.

Traditionally, disk degeneration was thought to be caused by aging and "wear and tear" from mechanical changes and injuries; however, after familial aggregation and twin studies were conducted, there was a dramatic change in our knowledge of what causes disk degeneration. Several familial aggregation studies conducted in LDD found that young patients with disk herniation had a family history of the disease [7, 8].

The first systematic evaluation of lumbar degenerative changes blinded to twinship was conducted in 1995. Twenty MZ twin pairs from Finland were studied in a pilot investigation of disk degeneration, disk height narrowing, and disk bulging or herniation detected by MRI. A high degree of similarity (26–72 %) was observed between identical twin pairs [4]. Subsequently, a larger and more comprehensive investigation was conducted in 115 pairs of MZ twins. The result showed that 61 % of the variance in disk degeneration was explained by familial aggregation; beyond that, age and occupations requiring heavy lifting together explained 16 % [9]. A 1999 study of female twins in the United Kingdom and Australia enrolled 86 pairs of MZ twins and 77 pairs of DZ twins. The investigators reported 74 % heritability of LDD after adjusting for age, body weight, body height, smoking, occupation, and exercise [10].

6.3.2 Identify the Specific Genes Involved in the Degeneration of Disks

The high heritability estimates for LDD motivated researchers to identify the specific genes responsible. Accurate mapping of the genetic architecture of LDD provides clues to its etiology and pathogenesis. Moreover, those genes might

be targets for drug discovery or markers for diagnosis. For Mendelian and complex diseases, the methods for identifying causal genes are different because of the different genetic architectures of these disorders. In Mendelian diseases, causal genes usually are rare and might be identified by studying affected families. Accurate analysis of the mode of disease inheritance might lead to the direct location of the causal variant on the genome. As for complex diseases, the involvement of multiple genes, as well as interactions between genes and the environment, makes it more difficult to identify the causal genetic factors. Two study designs for mapping disease genes are used commonly, namely, family-based design and population-based design; the statistical methods are linkage and association analysis, respectively. A study approach may be classified further as a candidate gene or genome-wide approach depending on whether prior biologic and etiologic knowledge is applied.

6.3.2.1 Linkage Studies

Linkage analysis determines whether the marker segregates with the disease in families with multiple affected individuals, according to a Mendelian mode of inheritance. If a marker is passed down through generations of a family, it may be used as a surrogate for locating adjacent genes. Based on the characteristics of recombination, a linkage study maps disease-causing genes by tracking how alleles of a genetic marker have combined with different members of a family to identify possible crossover regions, thereby indicating shared regions in cases and controls, respectively. Regions shared in cases but not in controls are the candidate positions of disease association genes (Fig. 6.5). Because the crossover event occurs at different positions in different families, a linkage study in multiple families with the same phenotype will narrow down the candidate regions further by overlapping the candidate regions. Microsatellites and SNPs commonly are used as DNA markers in linkage studies.

Regarding LDD, a two-stage linkage study in 18 families of southern Chinese descent with early-onset LDD was reported in 2013 [11]. A novel susceptible variant in carbohydrate sulfotransferase 3 (*CHST3*) was found to be associated with LDD. In the first stage of the study, 400 microsatellites of 89 individuals from 10 families were genotyped. Regions on chromosomes 1, 5, 8, 10, and 20 were identified as candidate regions. In the second stage, 37 individuals from 8 families were added, and another candidate in chromosome 10 was identified. The following association study detected the variant in *CHST3* associated with LDD. Additionally, expression of *CHST3* mRNA decreased significantly in the intervertebral disk cells of individuals carrying the A allele of SNP rs4148941.

Linkage studies in OI also have been conducted. In one of these studies, an autosomal recessive cause of OI was found in five Turkish families. Linkage mapping demonstrated that all affected individuals shared a 0.83 Mb region on chromosome 17. Further sequencing of this region revealed that the OI phenotype resulted from homozygosity for an in-frame deletion in *FKBP10* [12]. A frameshift mutation in transcription factor Osterix, which causes recessive OI, was detected in an Egyptian child [13]. Also found was a missense change, causing autosomal recessive OI [14].

6.3.2.2 Association Studies

Genetic association studies look for a correlation between disease status and genetic variations to identify candidate genes or genome regions that contribute to a specific disease. A genetic association exists if a particular allele is more frequent in the affected group than in the nonaffected group. The greater frequency of this allele in the affected group may indicate that it increases the risk of the disease in question. Statistical analysis usually is performed to determine the significance of the frequency differences. SNPs are the most widely tested genetic markers in association studies, although microsatellite markers, indels, and CNVs also may be used.

A genetic association study usually is conducted in a population-based sample of affected

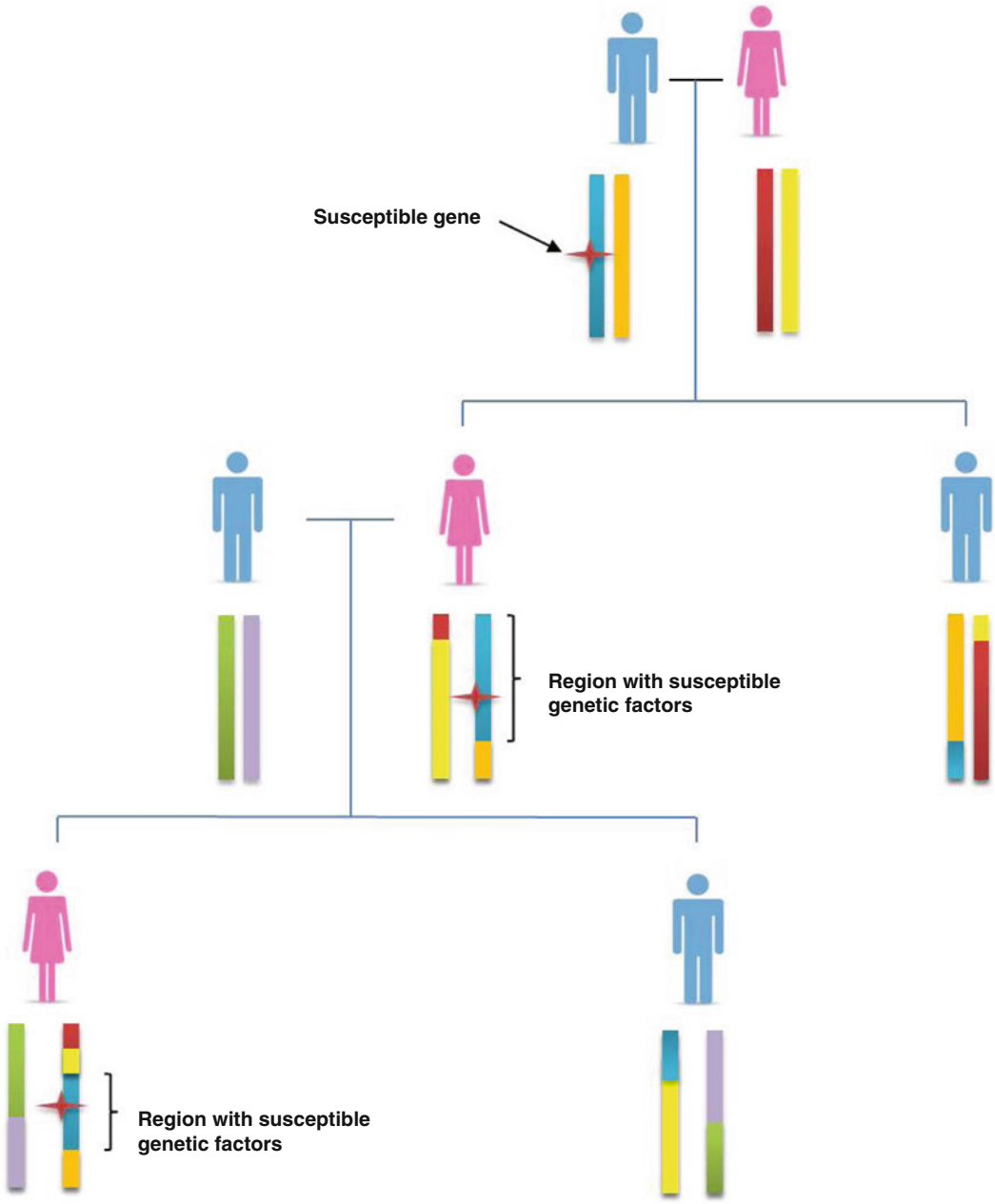

Fig. 6.5 Linkage analysis

and unaffected individuals (case–control study). After genotyping is performed (Box 6.1), the genotype distributions of each marker are compared between the case and control groups (Fig. 6.6). Statistical measurements of frequency differences then are calculated. A marker that is significantly more frequent in the case versus the control group is identified as a possible disease-causing variant.

Association studies may be performed in one of two ways: (i) direct testing of an exposure SNP with known variable phenotypes,

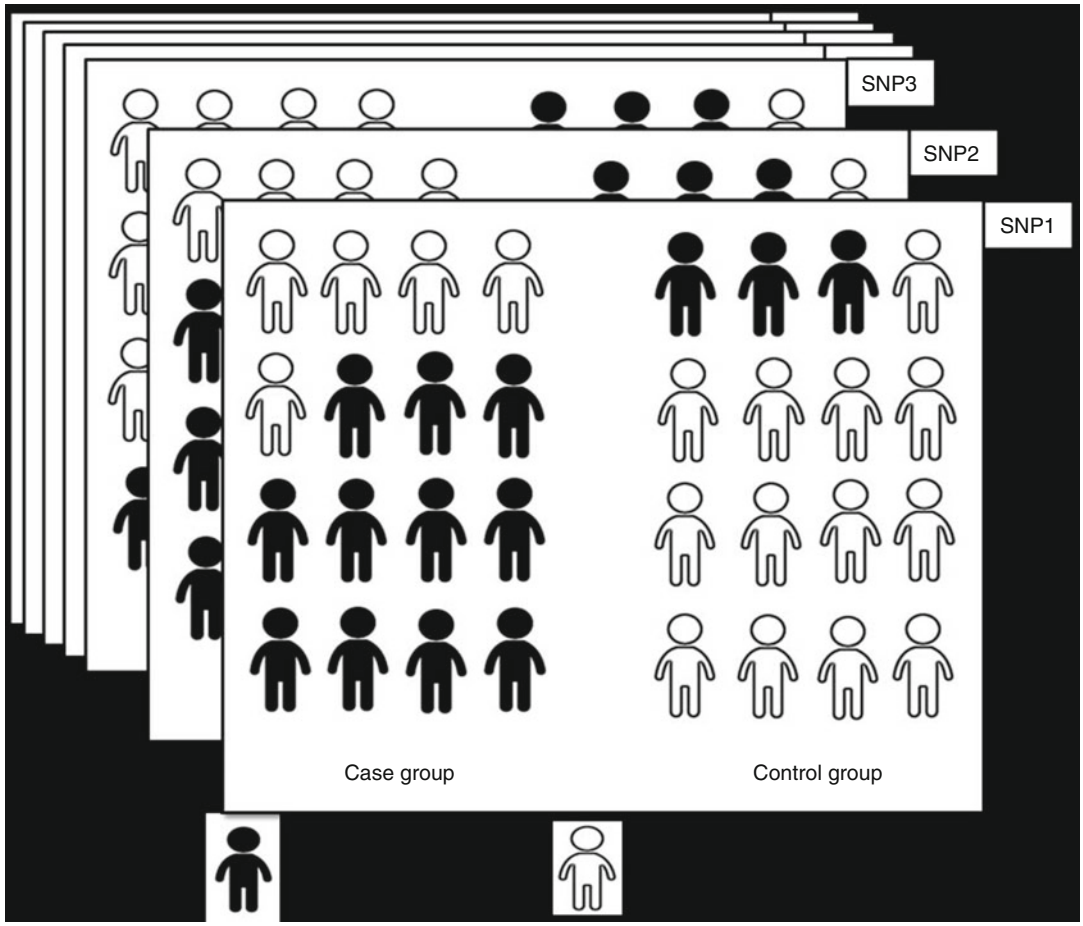

Fig. 6.6 Case–control association studies

such as altered protein structure, and (ii) indirect testing of an SNP, which is a surrogate marker for locating adjacent functional genes that contribute to disease status. The first method requires identification of all variants in the coding and regulatory regions of genes. Although the cost of genotyping continues to decrease, genotyping all ten million SNPs of the whole genome is still expensive. The latter method eliminates the need to catalog all potential susceptibility variants by relying instead on the LD between a genetic marker and susceptible polymorphisms; only a subset of SNPs is genotyped. The genetic constitution of SNPs that are not genotyped may be inferred based on r^2, which is provided by the HapMap Project [2] (Box 6.1).

Box 6.1. Technologies of SNP Genotyping

The International HapMap Project has enabled researchers to identify most of the common variants across the whole genome [2]. The project also generated allele frequencies and correlations (r^2) of the SNPs in different populations. From these data, the LD map was generated as a reference, recording the co-inheritance of the SNPs. The recently launched 1000 Genomes Project aims to provide a more profound characterization of genetic variations in multiple populations [15]. The use of high-throughput sequencing technologies has provided an opportunity to detect not

only common variants but also rare variants in different populations. Based on the data generated from these two projects, commercial genotyping microarrays were designed. The genotyping microarray is a solid surface on which artificial microscopic DNA spots of known variants may be attached. The attached DNA spots can capture corresponding sequences marked with an optical signal for identifying genotypes. The Illumina Omni array can detect more than 4.3 million markers, whereas the Affymetrix SNP array can assess 1.8 million markers. Furthermore, the multiplexing Sequenom MassARRAY system and Illumina VeraCode technology have enabled us to genotype a specific region with many SNPs efficiently and cost-effectively. Thanks to these microarrays, a two-step cost-effective approach has been used widely by researchers. The first step is to select a subset of SNPs as a marker for genotyping and to perform an association scan to identify candidate regions. The second step is to genotype a denser set of SNPs within potential regions to look for the exact functional genetic variants.

Candidate Gene Approach

In recent years, the cost of genotyping has dropped dramatically, but the cost of customized genotyping platforms remains high, and limited budgets prevent studies from genotyping a dense set of SNPs across the whole genome. The statistical significance and power of a study are directly affected by the number of individuals tested and by the number of SNPs genotyped. The more SNPs that are genotyped, the more information is obtained and the greater the chance a causal SNP will be identified. To balance cost with study power, investigators select and type the number of SNPs that will maximize the power of the association study. Usually, they do this by choosing a subset of SNPs from candidate genes whose number is commonly determined by the available resources.

The candidate gene approach focuses on selecting genes according to the biological knowledge and etiology of the disease. It takes advantage of our biological understanding of the phenotype, tissues, genes, and proteins that likely are involved in the disease. With regard to disk degeneration, for example, collagen and aggrecan, together with other structural proteins, form the basis of the extracellular matrix, which is an integral part of the disk. These proteins are essential for normal disk function in terms of tensile strength and osmotic pressure. Therefore, the extracellular matrix genes have been prime candidates for genetic study. In addition, gene expression studies are another important way to identify candidate genes. Several tissue homeostasis genes, such as matrix metalloproteinases (*MMPs*), have elevated expression levels, as well as increased enzymatic activity, during disk degeneration [16]. Moreover, genes identified from other skeletal disorders also may be candidates for LDD. For example, growth differentiation factor 5 (*GDF5*) is one of the promising candidate genes of osteoarthritis (OA), as it has been reported in multiple populations and has shown high significance [17]. *GDF5* was studied as a candidate gene of LDD in northern European women. An SNP (rs143383) was found to be significantly associated with the combination of disk space narrowing and osteophytes [18]. One major drawback of the candidate gene approach, however, is that a priori knowledge of the pathogenesis of the disease is required. If the molecular mechanism is poorly understood, the wrong genes might be selected. Therefore, candidate gene studies are more successful when used as a follow-up to linkage studies [11].

Genome-Wide Association and Meta-Analysis

An advantage of a genome-wide association study (GWAS) is that it requires no prior knowledge of the structure or function of susceptibility genes. A GWAS examines common genetic variants across the whole genome in different individuals to determine whether any variant is associated with disease status. Therefore, this approach makes it possible to identify novel

suspected genes. Typically, the power of a GWAS relies on the sample size, definition of the phenotypes, and control of environmental factors. A large sample size, a well-defined phenotype, and proper control of environmental factors might lead to a successful GWAS.

Although GWASs have identified many variants associated with complex diseases, these variants currently explain little about the heritability of most diseases. Normally, the effect sizes of common variants are small, and detection of such small effects requires large sample sizes. Although individual GWASs are underpowered, meta-analyses increase power and reduce false-positive findings. In a meta-analysis, results from several independent studies are contrasted and combined in the hope of identifying the same patterns among study results, sources of disagreement among those results, or other interesting relationships that might come to light in the context of multiple studies.

6.3.2.3 Interpreting the Results

A significant genetic association may be interpreted as (1) a direct association, in which the genotyped SNP is the true causal variant conferring disease susceptibility; (2) an indirect association, in which an SNP in LD with the true causal variant is genotyped; or (3) a false-positive result, in which there is either chance or systematic confounding, such as population stratification. Population stratification is the presence of a systematic difference in allele frequency between subpopulations of the same population, possibly as the result of different ancestry, especially in the context of association studies.

In recent years, the number of genetic studies of LDD has been increasing. It is important to interpret and integrate the results from these studies to improve our overall understanding of LDD, especially with regard to phenotype definitions, statistical significance, and the effects of suspected genes.

Phenotype Definitions

A precise phenotype definition is essential for genetic studies in that the phenotype should be a distinguishable trait and preferably quantifiable. Generally, a trait may be classified as qualitative or quantitative; a qualitative trait can fit into distinct phenotypic categories (case or control), whereas a quantitative trait is measurable as a continuous variable.

With regard to LDD, for example, current assessments of disk degeneration rely on imaging, including radiography and magnetic resonance imaging (MRI). Radiographs may provide information on disk height and osteophyte formation, whereas MRI may show hydration status and disk bulging and herniation, as well as endplate irregularities. From these images, the presence or absence, or even the severity, of disk degeneration can be defined.

There are several ways to evaluate the degenerative changes in the intervertebral disk. The first is to make a diagnosis based on the presence or absence of disk degeneration, which is an example of a qualitative trait; it is simple and commonly used clinically. However, a disadvantage is that it provides no information about the progressive changes that take place during the degenerative process. Another method is to classify the severity of degeneration based on some well-defined criteria. This method is the one used most widely in genetic studies, and several scoring systems have been developed. For radiographic studies, the Kellgren scale combines the features of osteophytes and joint space narrowing to generate a score ranging from 1, indicating no or very small osteophytes, to 4, representing large osteophytes and pronounced disk space narrowing [19]. For MRI, two scoring systems were developed: the Schneiderman and Pfirrmann scales. Schneiderman's system focuses on the signal intensity of the nucleus pulposus on MRI, classifying it into four grades, with 0 indicating normal disk with a hyperintense signal (bright disk) and 3 illustrating a hypointense signal with disk space narrowing (black disk) [20]. Pfirrmann's classification uses MRI images to evaluate the homogeneity of disk structure, signal intensity, and distinction between the nucleus pulposus and annulus fibrosus, as well as disk height. This information is converted into one of five grades, the lowest of which is applied to homogeneous disk structure,

Risk	Disease status	
	Present	Absent
Allele 1	a	b
Allele 2	c	d

a

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} = \frac{a*(c+d)}{c*(a+b)}$$

b

$$OR = \frac{\frac{\frac{a}{a+b}}{1-\frac{a}{a+b}}}{\frac{\frac{c}{c+d}}{1-\frac{c}{c+d}}} = \frac{a*d}{b*c}$$

Fig. 6.7 Relative risk and odds ratio

hyperintense signal, and normal disk height and the highest to inhomogeneous disk structure, hypointense signal, and loss of distinction between the nucleus pulposus and annulus fibrosus, as well as collapsed disk space [21]. These grading systems provide a semiquantitative evaluation of degenerative status, reflecting the severity of disk degeneration. Interpreting the images from MRI is subjective and thus requires multiple experienced radiologists to perform the grading. The third method for assessing disk degeneration is computational evaluation, which avoids personal errors and saves human resources. Both semiautomated [22] and automated [23] frameworks have been developed for the diagnosis of degenerative disks. The output of computational evaluation is quantitative measurement.

Statistical Significance

The most conspicuous information from a genetic study is whether a genetic variant or gene is associated with a certain disease and may be derived from the test statistics and their corresponding *P* values. The *P* value represents the possibility of no association, indicating there is no difference in genotypic distribution between cases and controls. Generally, if $P<0.05$, the hypothesis of no association is rejected, meaning there is an association between a genotype and the disease status. In candidate gene studies or GWASs, every genetic variant is tested. If the number of hypotheses being tested increases, the false-positive rate also might increase; therefore, several methods were developed to address this possibility, with the Bonferroni correction being one of the most widely used approaches [24]. The corrected statistical significance level is $1/n$ times what it would be if only one hypothesis were tested. Thus, the significance threshold of association studies should be 0.05/number of markers being tested.

Effects of Suspect Genes

In epidemiology, relative risk (RR) is the ratio of the probability of a disease occurring in an exposed group to the probability of it occurring in a comparative, nonexposed group (Fig. 6.7a). An RR of *N* means that the affected group has a risk *N* times greater than that of the nonaffected group. In genetic association studies, the fundamental unit for reporting effect sizes of suspect genes is the odds ratio (OR). The OR represents the ratio between two proportions: the proportion of individuals in the case group with a specific allele and the proportion of individuals in the control group having the same allele (Fig. 6.7b). An OR >1 demonstrates that individuals carrying the allele are more susceptible to the disease; an OR <1 indicates less susceptibility. The OR is

similar to the RR when the disease prevalence is low (in Fig. 6.7, when *a* and *c* are small). ORs usually are reported together with 95 % confidence intervals, which show the possible range of a gene's effect.

6.3.3 Genes Associated with LDD

So far, more than 20 genes have been associated with LDD (Table 6.1), although only a few of them can be replicated, and the results of these studies should be scrutinized closely. In 2008, a Human Genome Epidemiology Network (HuGENet) working group developed a scoring system to provide a reasonable assessment based on three criteria: amount of evidence, replication, and protection from bias. For each criterion, a classification of strong (A), moderate (B), or weak (C) is assigned to the gene study or studies [53]. Eskola et al. [5] used the HuGENet criteria in their systematic review of genetic association studies in LDD. According to their results, most of the associations presented with a weak level of evidence; only five genes showed moderate evidence. None of the studies of disk degeneration genes reached the level of strong credibility. In this chapter, some specific genes are introduced to enhance our understanding of the genetics of LDD.

Vitamin D receptor (*VDR*) is the best replicated gene and has been verified in three different populations. Identified in a Finnish twin study, it was the first gene reported to be associated with LDD [25]. In this study, a reduction in signal intensity on MRI was associated with the *TaqI* and *FokI* polymorphisms. The association of *TaqI* was replicated later in a Japanese study [26], with genotype Tt occurring more frequently in individuals with disk degeneration and severe disk degeneration. *TaqI* was replicated further in a Chinese population-based study [27]. The replication of the *TaqI* polymorphism of *VDR* in three different ethnic populations indicates that *VDR* is the most robust gene associated with LDD. Although no functional validation has been performed, it is hypothesized that the variation in *VDR* leads to changes in the structural characteristic of the extracellular matrix in the vertebral disks [54].

Aggrecan, encoded by the gene *ACAN*, is the major proteoglycan component of cartilage and the nucleus pulpous of the intervertebral disk and is responsible for maintaining hydration of the disk structure. Thus, *ACAN* is considered a good candidate for genetic association studies. A variable number of tandem repeats (VNTR) in *ACAN* were first associated with LDD in a group of 64 young Japanese women aged 20–29 years [28]. The study found that the shorter allele (<25 repeats) carried a higher risk of disk degeneration. This association was replicated in Han Chinese [29], Korean [30], and Turkish [31] populations. The Han Chinese study also showed that the shorter allele carried an even higher risk (OR, 4.5) for symptomatic disk degeneration in smokers, suggesting there might be a link between the risk allele and smoking. However, a Finnish study found that the allele with 26 repeats was significantly associated with a dark nucleus pulposus [32]. These conflicting findings might be the result of ethnic differences. Nevertheless, the Finnish study still showed that *ACAN* is a risk factor for LDD.

An association between the asporin gene (*ASPN*) and LDD was found in two independent Asian cohorts, one Japanese ($N=1{,}353$) and the other Chinese ($N=1{,}055$) [33]. *ASPN* became a candidate gene of LDD susceptibility because asporin is an extracellular matrix protein shown to be associated with OA of the knees. In the Japanese cases, the presence of at least one D14 allele was found to be significantly associated with lumbar disk herniation (LDH) characterized by sciatica, whereas in the Chinese population, the presence of at least one D14 repeat was associated with LDD. A meta-analysis using the aforementioned phenotypes showed that individuals carrying the D14 allele had a higher risk of LDH or disk degeneration, with an OR of 1.58.

Several types of collagen have been studied widely in LDD, with type XI collagen, encoded by *COL11A1*, providing the most reliable evidence. A Japanese study found an association between the *COL11A1* rs1676486 T allele and LDH characterized by sciatica. This study consisted of three stages ($N=367$, $N=645$, $N=710$), each of which showed a significant association. When the populations were combined for meta-analysis (823 cases and 838 controls), the individuals with minor

Table 6.1 Genetic risk factors of lumbar disk degeneration

Gene	Cohort	N	Variant	OR	Phenotype	Reference
VDR	Finnish	85 MZ pairs	TagI and FokI		LDD	Videman et al. [25]
	Japanese	205	TaqI		LDD, LDH	Kawaguchi et al. [26]
	Southern Chinese	804	TaqI	2.61	LDD, LDH	Cheung et al. [27]
ACAN	Japanese	64	VNTR		*Aggrecan* protein size	Doege et al. [28]
	Han Chinese	132	VNTR	1.03–4.5	LDD	Cong et al. [29]
	Korean	104	VNTR		LDD	Kim et al. [30]
	Turkish	100	VNTR		LDD radiographic	Eser et al. [31]
	Finnish	132	VNTR		LDD	Solovieva et al. [32]
ASPN	Japanese	1,353	D14 allele	1.69	LDD	Song et al. [33]
	Chinese	1,055	D14 allele	1.49	LDD	Song et al. [33]
COL11A1	Japanese	1,722	rs1676486	1.34–1.55	LDD, LDH	Mio et al. [34]
COL9A2	Finnish	157	TRP2		Lumbar spinal stenosis, sciatica	Annunen et al. [35]
	Southern Chinese	804	TRP2	2.4, 4	Annular tears, DDD, and end-plate herniations	Jim et al. [36]
COL9A3	Finnish	164	TRP3	3	DDD	Paassilta et al. [37]
COL1A1, COL1A2	Dutch	517	rs1800012	3.6	Osteophytes and articular joint space narrowing radiographs	Pluijm et al. [38]
	Greek	40	rs1800012		LDD	Tilkeridis et al. [39]
GDF5	Northern European	5,259	rs143383	1.72	Disk space narrowing and osteophytes	Williams et al. [18]
SKT	Japanese	1,758	rs16924573	1.34	LDD	Karasugi et al. [40]
	Finnish	506	rs16924573	1.34	LDD	Karasugi et al. [40]
	Finnish	538	rs16924573	0.27	LDD	Kelempisioti et al. [41]
MMP1	Southern Chinese	691	Indel in promoter, −1607G/D	1.5	LDD	Song et al. [42]
MMP2	Chinese	480	SNP in promoter, −1306C->T	3.08	LDD	Dong et al. [43]
MMP3	Japanese	49	SNP in promoter, 5A/6A		LDD	Takahashi et al. [44]
MMP9	Han Chinese	859	SNP in promoter, −1562C->T	1.29	LDD	Sun et al. [45]
THBS2	Japanese	1,743	rs9406328	1.38	LDH	Hirose et al. [46]
PARK2	Northern European	4,600	rs926849		LDD	Williams et al. [47]
CASP9	Han Chinese	799	SNP Ex5+32 G/A	1.91	LDH	Sun et al. [48]

CILP	Japanese	1,121	SNP 1184 T –>C	1.61	LDD	Seki et al. [49]
FAS	Chinese	563	rs2234767	1.88	LDD	Zhu et al. [50]
FASL	Chinese	563	rs763110	2.34	LDD	Zhu et al. [50]
IL1RN	Korean	281	VNTR A1, A3	0.45, 3.86	LDH	Kim et al. [51]
IL10	Chinese	589	–592 A/C		LDD	Lin et al. [52]

allele T had a higher risk of LDH. In addition, the study suggested the SNP rs167486 affected mRNA stability [34].

A rare mutation (Trp2 allele) of the type IX collagen gene (*COL9A2*) was first identified in 6 of 157 Finnish patients with sciatica, with no evidence of this mutation in any of the controls. Furthermore, a family linkage study indicated that this mutation causes disease [35]. The allele frequency of this mutation is much higher in the Chinese population, and this association was found to be age related, with the greatest effect observed in the 40–49 age group [36]. Another variant (Trp3 allele) also was found in the Finnish study [37] but not in the Chinese population [36], and it had no replications in southern Europeans [55]. A subsequent functional study suggested that the Trp2 and Trp3 variants in type IX collagen are associated with degenerative lumbar spinal stenosis.

Type I collagen, encoded by *COL1A1* and *COL1A2*, was first studied in patients with reduced bone mineral density [56]; an SNP (rs1800012) was reported to be associated. Later, a study in 517 Dutch cohorts reported that those with genotype TT of this SNP have a higher risk of disk degeneration; however, the disk degeneration phenotype was defined by the presence of osteophytes and articular joint space narrowing based on radiographs [38]. The only investigation using an MRI definition of disk degeneration was a Greek study with 40 young army recruits, which was not a large enough sample [39]. Therefore, how this SNP increases the risk of LDD remains unknown.

A recent collaborative study with northern European subjects investigated the SNP (rs143383) of the growth differentiation factor (*GDF5*) gene. Of the total population ($N=5,259$), one cohort ($N=613$) underwent MRI. Among women, the meta-analysis revealed a significant association between rs143383 and the combined phenotype of disk space narrowing and osteophytes. When only the MRI cohort was investigated, however, the association was not statistically significant, thus generating some inconsistency regarding this association [18]. *GDF5* is required for joint formation [57] but also associated with OA [17].

The polymorphisms of the sickle tail (*SKT*) gene were analyzed in a Japanese population, in which an SNP (rs16924573) was strongly associated with LDH ($N=1,758$), and this finding was replicated among Finnish subjects ($N=506$) [40]. Although the allele frequencies were different between the Finnish and Japanese populations, the meta-analysis of more than 2,200 subjects supported the association. A replication study between decreased disk signal intensity and *SKT* rs16924573 in a Finnish population has been published (OR, 0.27; 95 % CI, 0.07–0.96; $P=0.024$) [41]. The G allele was more frequent in the case group in both studies, thus indicating an increased risk. The function of *SKT* is unknown and further studies are needed.

Matrix metalloproteinases (MMPs) are a large protein family expressed in disks, and the genes *MMP1*, *MMP2*, *MMP3*, and *MMP9* are reported to be associated with disk degeneration. Interestingly, all the susceptible polymorphisms of *MMP*s are located in the promoter region. In a study of *MMP1* in a southern Chinese cohort of 691 individuals, significant signal was found only among individuals aged 40 or older [42]. An SNP on the promoter region of *MMP2* was found to be associated with severe disk degeneration in another Chinese cohort [43]. *MMP3* was reported to have a polymorphism on its promoter associated with both the onset and progression of disk degeneration in 49 elderly Japanese patients [44]; however, this association was not replicated in young subjects. Regarding *MMP9*, an SNP in the promoter region was associated with disk degeneration in a northern Chinese cohort ($N=859$) [45].

The thrombospondin 2 (*THBS2*) gene was examined in two independent Japanese populations ($N=1,089$ and $N=654$) as a candidate gene for LDH. The SNP (rs9406328) showed significant association in each population independently as well as in the meta-analysis [46]. These studies also suggest that *THBS2* might be involved in regulating *MMP* expression in the disk, in turn participating in the pathogenesis of disk herniation. Moreover, the authors also examined the combined effects of *THBS2* and *MMP9*; the OR of 3.3 for the combination indicates a potential gene–gene interaction [46].

The first GWAS of LDD, a meta-analysis of a northern European cohort, involved 4,600 samples from four populations. This study identified an association between an SNP (rs926849) in the parkin gene *PARK2* ($P = 2.8 \times 10{-}8$) and LDD [47].

6.3.4 Moving from Common Variants to Rare Variants

Disk degeneration provides an overall, subjective impression of the spine's condition. It may include signal intensity loss, bulging, herniation, end-plate irregularities, osteophytes, and narrowing of the disk space. A wide range of symptoms and degrees of severity are associated with LDD. Nearly everyone shows some signs of wear and tear on the lumbar disks as they age; however, not everyone will have symptoms such as back pain or sciatica. Severe disk degeneration sometimes is observed in the very young, whereas relatively normal disks may be found in older individuals, although these situations are rare and different from commonly seen cases. On the other hand, according to estimates from twin studies, LDD has up to 74 % heritability, although very few common variants for LDD have been functionally validated. Considering the genetic variants currently associated with LDD, as well as their effect size, a substantial number of cases remain unexplained, suggesting that there are several genetic factors waiting to be identified.

So far, most genetic studies have focused on common SNPs in candidate genes, whereas the human genome contains many more variations, including rare SNPs, indels, CNVs, inversions, and others. Evidence is accumulating that rare variants do play a role in common complex disease; for example, three rare deletions were found to be associated with schizophrenia, one of which had an OR of 14.8 [58]. Four rare SNPs in *IFIH1* independently reduced the risk of type 1 diabetes, with one of the SNPs having an OR of 0.5 [59], and 36 very rare non-synonymous variants were associated with type 2 diabetes with an OR of 3.3 [60]. These findings suggest that rare variants contributing to susceptibility of common diseases is not an unusual event. Therefore, a more complete understanding of LDD requires genome-wide studies that fully examine both common and noncommon variants in populations.

To identify rare variants, it will be necessary to sequence entire genomes of cases, instead of genotyping a catalog of variants. Although the best method is to sequence the whole genome, this approach is expensive, especially if there is a large cohort to be sequenced for a complex disease. To reduce the cost, whole-exome sequencing has been used widely to detect variants located in exons. A targeted sequencing method also has been used to sequence regions where potential associations have been indicated through linkage or GWASs (Box 6.2).

Box 6.2. DNA Sequencing Technologies

DNA sequencing is the process used to determine the precise order of nucleotides within a DNA molecule. The first DNA sequencing methods were developed in the 1970s. Frederick Sanger and colleagues [61] developed rapid DNA sequencing methods with chain-terminating inhibitors, whereas Walter Gilbert and Allan Maxam [62] developed sequencing methods by using chemical degradation. These two methods commonly are referred to as *first-generation sequencing*. Since then, the demand for reducing cost and increasing throughput has driven the development of DNA sequencing technology. By the 1990s, new technologies paralleled the sequencing process, greatly improving throughput; thus, DNA sequencing entered the next generation and several second-generation sequencing technologies were developed. The major commercial entities that came into existence include 454 Life Sciences, Solexa/Illumina, SOLiD, and the Polonator. With the availability of a multitude of platforms, dramatically lower costs, and a higher throughput of sequencing, second-generation sequencing technologies have been used widely in studying genetic diseases.

6.4 Epigenetics

Epigenetics refers to heritable, functionally relevant changes to the genome that do not involve a change in the nucleotide sequence. Packaging genes into chromatin and dynamic chromatin remodeling processes are required for the initial step in gene expression (transcription). Epigenetic factors are responsible for this regulatory process, the major components of which are DNA methylation, histone modifications, and the action of noncoding RNAs. Unlike the DNA sequence, which largely is fixed throughout a person's lifetime, epigenetic patterns not only vary from tissue to tissue but become altered with advancing age and are sensitive to environmental exposures.

Recent studies provide evidence that DNA methylation, a biochemical process whereby a methyl group is added to the cytosine or adenine DNA nucleotides, is involved in the development of complex disease. Hypermethylation at one CpG island of the *PARK2* promoter was associated with MRI-determined LDD [47]. DNA methylation changes also were reported in other complex diseases: in schizophrenia and bipolar disorder, substantial differences in genome-wide DNA methylation patterns were found between monozygotic twins discordant for these diseases [63]. Epigenetic variation also might help explain the late onset and progressive nature of most common diseases, the quantitative nature of complex traits, and the role of environment in disease development [64]. Evidence exists that epigenetic patterns are altered by environmental factors known to be associated with disease risk (e.g., diet, smoking, alcohol intake, environmental toxicants, and stress) [65]. These observations suggest that complex diseases are the product of the integration of epigenetic and genetic factors.

Currently, arrays and sequencing technologies both are available for identifying genome-wide methylation variations [66]. Similar to the GWAS, an association scan that uses methylation variations is referred to as an *epigenome-wide association study* [66].

Besides DNA methylation, noncoding RNAs, functional RNA molecules that are not translated into a protein, are integral components of biological networks with a fundamental role in regulating gene expression. Significantly different expressions of microRNAs have been detected between patients with intervertebral disk degeneration and those with an intervertebral disk injury [67]. Differential expressions of microRNA also have been reported in OA [68].

6.5 The Way Forward

Genetic studies of LDD have been carried out for nearly two decades. With the continuous advancement of genotyping and DNA sequencing technologies, as well as improvements in imaging and statistical methods, our knowledge about the natural history of degenerative disk disease is constantly improving [69]. However, the complexity of the degenerative process still is not fully understood [5]. One serious problem is that very few susceptible genes can be replicated [5]. In addition, there still is a large proportion of missing heritability that cannot be explained by current findings. According to our experience, there are several approaches that might be able to maximize the chance of identifying new LDD risk factors. For a complex trait, a larger sample size may provide a more accurate evaluation of variants. In OA, a recent GWAS from the United Kingdom enrolled up to 70,000 subjects and found several promising loci [70]. For LDD, which is more prevalent than OA, the largest association study enrolled only 4,600 subjects [47]. In a study of body height and lipids, a very large sample size enabled researchers to find many reliable genetic factors [71]. Therefore, to identify reliable and relevant variants associated with LDD, larger-scale multiethnic genetic studies and interethnic comparisons through international collaborations inevitably are necessary. Nevertheless, there is a wide variation in phenotype definitions among research groups, with differences in sample selection strategies and image features used to represent disk degeneration. Therefore, to ensure the same group of genetic factors is identified, a unified phenotypic definition is required. Moreover, based on the

hypothesis that disk degeneration is the product of genetic, epigenetic, and environmental factors, as well as their interactions, more information should be considered in future genetic studies, such as gene–environment interaction, gene regulation, and so on. Also, instead of looking at one genetic variant at a time, all factors should be studied systematically, because the overall picture may provide a better understanding of the genetic architecture and etiology of degenerative disk disease.

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Part II

Imaging

Imaging of Degenerative Disk Disease

7

Guillaume Bierry and Jean-Louis Dietemann

7.1 Introduction

Degenerative disk disease (DDD) results in alterations of both the intervertebral disk and vertebral end plates and has three common sequelae: disk herniation, stenosis, and instability [1]. The progressive dehydration of the nucleus pulposus secondary to degradation of proteoglycans and the development of clefts within the anulus fibrosus lead to loss of height of the intervertebral space and bulging of anulus outer fibers. Besides, cartilaginous end plate thinning and focal anular rupture occur, associated with alterations of subchondral bone properties. DDD is usually associated with apophyseal joint osteoarthritis which contributes to central, radicular, and/or foraminal stenosis. Instability secondary to the loss of normal spinal biomechanics may be identified on static or dynamic radiographs and manifest potentially as spondylolisthesis or retrolisthesis.

Plain radiographs are able to demonstrate disk space loss of height; however, CT is more accurate in the morphological evaluation of spinal bony structures, and MRI is the modality of choice for the evaluation of soft tissues including disks, ligaments, neural structures, and bone marrow. In postsurgical conditions with spinal hardware, myelography might be useful to detect nerve root compression. In rare cases, DDD may be difficult to differentiate from infectious diskitis or rheumatoid arthritis; PET-CT or biopsy under fluoroscopic or CT control may be required to assist in the diagnosis.

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7.2 Radiographs

The major signs of DDD on radiographs are disk space narrowing, sclerosis of the vertebral end plates, and osteophytes.

In nondegenerative conditions, the disk progressively increases in height from T12/L1 to L4/L5 with the L5/S1 level being generally equal in height to L4/L5 [2] (Fig. 7.1). Decreased disk height is correlated with dehydration on T2-weighted MRI [3].

Osteophytes are bony projections that develop along vertebral end plates, classically in the axial plane, and are mostly anterior and lateral in the lumbar and thoracic spine and anterior and posterior with uncovertebral osteoarthritis in the cervical spine (Figs. 7.2, 7.3, and 7.4). Osteophytes differ from traction spurs located 2–4 mm above or below the anterior vertebral body edge, indicative of instability [4].

As DDD progresses, a vacuum disk phenomenon which represents the accumulation of gas

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_7

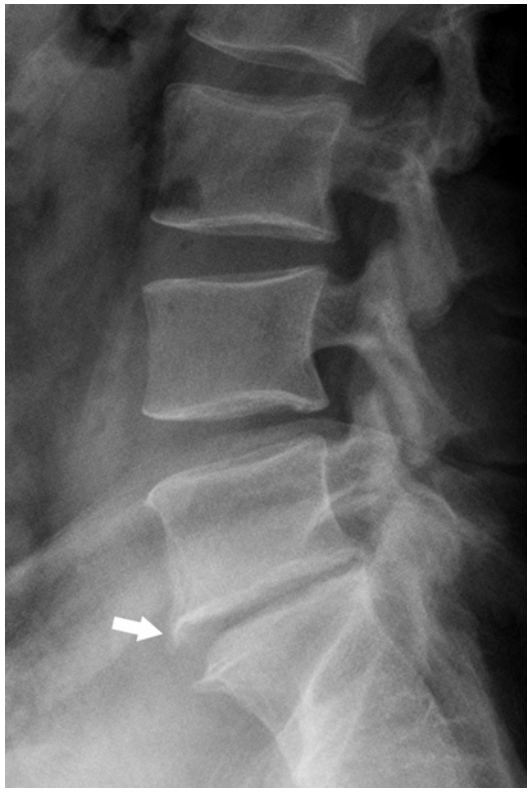

Fig. 7.1 Focal degenerative disk disease at L5-S1 level. Lateral radiograph shows isolated height loss of L5-S1 disk with anterior osteophytes (*arrow*)

within disk can appear (Fig. 7.2). Intradiscal gas is identified in 20 % of elderly patients and is related to negative intradiscal pressure and may be accentuated during spinal extension and decreased during spinal flexion [5]. The vacuum phenomenon may be related to lower back pain in the morning and when standing up and may be influenced by changes in weather and barometric pressure (atmosphere depression) [6, 7]. Identification of a vacuum phenomenon may be difficult on conventional spin-echo MR sequences; however, gradient-echo MR appears more sensitive [8, 9].

As in peripheral skeleton osteoarthrosis, subchondral sclerosis of the end plates may be seen with advanced disk space loss (Fig. 7.4).

Facet arthrosis is present in 50 % of adults younger than 30, the most common level involved being L4-L5 [10, 11]. Facet joint osteophytes with foraminal stenosis are often seen on lateral radiographs (Fig. 7.5).

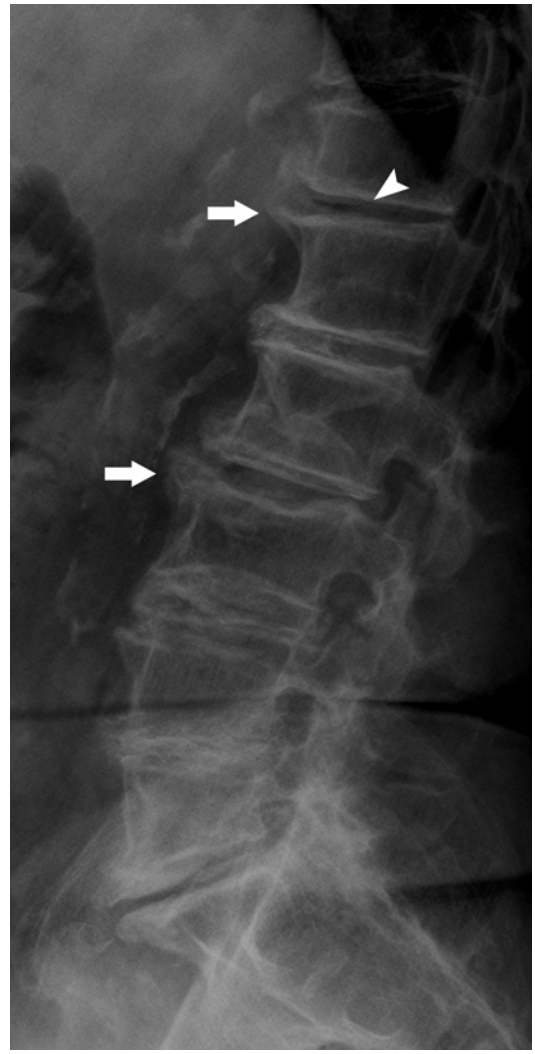

Fig. 7.2 Degenerative disk disease at multiple levels. Lateral radiograph shows disks narrowing with osteophytes (*arrows*) and vacuum phenomenon (*arrowhead*)

Other plain radiographic signs include Schmorl nodes and disk calcification which is most frequent in the lower thoracic and upper lumbar spine [12]. Weakening of the end plate and subchondral bone related to osteochondrosis may predispose to cartilaginous Schmorl nodes, which appear as a round radiolucent lesion that could have various depths within the vertebral body. Intervertebral disk calcifications involving the anulus fibrosus are common in elderly patients in the lower thoracic spine (60 %) [13].

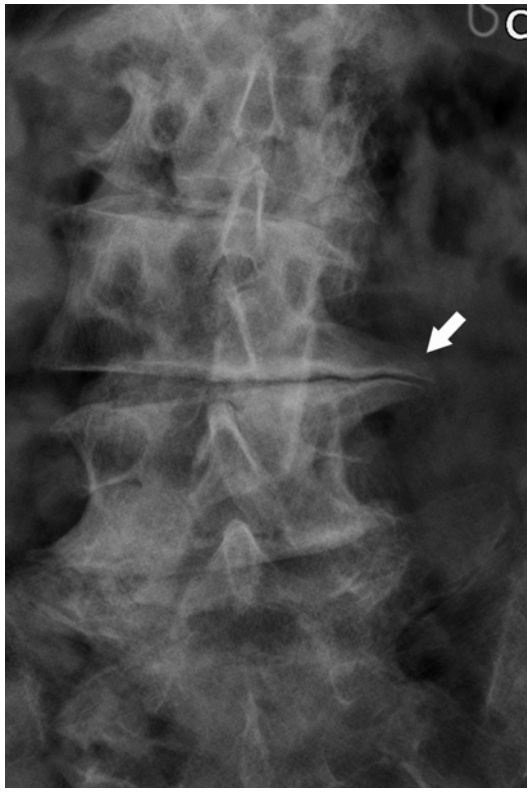

Fig. 7.3 Lateral radiograph shows asymmetrical disk space narrowing and massive osteophytes with typical "parrot beak" aspect (*arrow*)

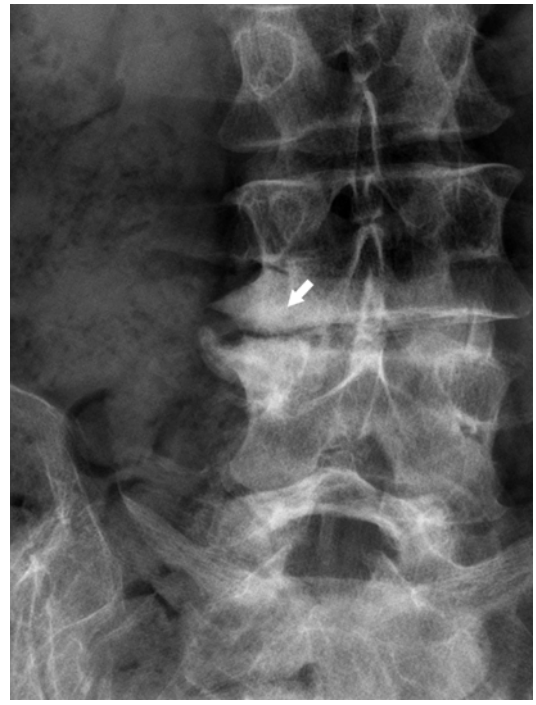

Fig. 7.4 Radiograph (AP view) shows L4/L5 disk space narrowing with osteophytes and subchondral sclerosis of end plates (*arrow*)

7.3 Computed Tomography

High-resolution multislice CT is more sensitive for demonstrating a vacuum phenomenon, disk calcification, subchondral osteosclerosis, and associated bony changes, particularly on sagittal, para-axial, and coronal reformations (Fig. 7.6). Herniations including diffuse bulging disk are clearly demonstrated on axial scans and sagittal reformations (Fig. 7.7).

Anterior and lateral osteophytes do not compress nerve roots in the lumbar spine; large lateral osteophytes may be associated with lumbar scoliosis (Fig. 7.6). Axial reformats demonstrate accurately facet joint osteoarthrosis with disk space narrowing, sclerosis, and osteophyte formation (Fig. 7.8).

Spondylosis deformans with degenerative lumbar scoliosis leads to transverse vertebral displacement, spondylolisthesis, retrolisthesis, and anterior and anterolateral protrusion of disk material and osteophytes (Fig. 7.9).

Disk calcifications of degenerative origin are mainly located within the anulus fibrosus. Lumbar intervertebral disk calcifications are noted in 50 % of elderly patients [14].

Schmorl nodes appear as a round radiolucent lesion, sometimes containing gas, with a rim of bony sclerosis on CT (Fig. 7.10).

7.4 Magnetic Resonance Imaging (MRI)

MRI is the modality of choice for the evaluation of the degenerative spine, as it allows an analysis of the disk, bone marrow, and facet changes as well as structures that might be injured secondary to degenerative changes such as nerve roots and muscles. Routine MRI of the spine includes sagittal spin-echo T1 and fast-spin-echo T2-weighted

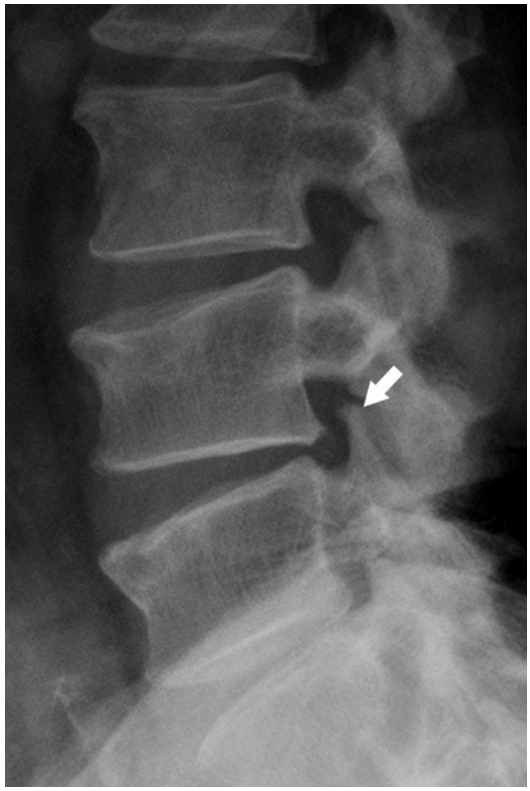

Fig. 7.5 Posterior articulation degenerative disease. Lateral radiograph shows posterior articulation arthrosis with osteophytes narrowing intervertebral foramen (*arrow*)

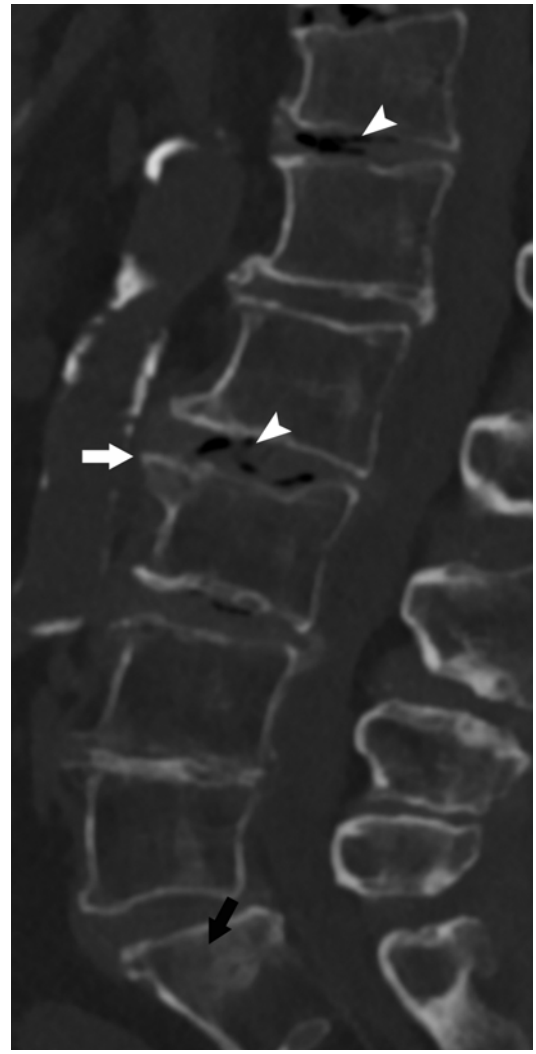

Fig. 7.6 Multilevel degenerative disk disease. CT sagittal reformat shows multiple disk space narrowing with intradiscal gas (*arrowheads*) and osteophytes (*arrow*)

imaging. T2 (sagittal and/or coronal) sequences with fat saturation (STIR, fatsat) are useful for the visualization of bone marrow edema. Axial T1- and T2-weighted images are useful for visualization of nerve root compression in patients with radicular pain. The use of intravenous gadolinium may demonstrate enhancement related to neovascularization involving the intervertebral disk and/or subchondral bone.

On T1- and T2-weighted MRI, the signal of the normal intervertebral disk is, respectively, lower and higher than that of the vertebral body; the high signal is related to bounded water by the proteoglycans of the nucleus pulposus. According to Pfirrmann et al. [15], five grades can be described for lumbar disk degeneration on T2-weighted MRI (Fig. 7.11). In normal young patients, the high signal on T2-weighted images appears homogeneous in the central area of the disk; the peripheral anulus may demonstrate a low signal (grade 1) (Figs. 7.11, 7.12, 7.13, and 7.14). Loss of signal intensity in the nucleus pulposus on T2-weighted MRI closely correlates with disk dehydration related to alteration of proteoglycans. During the second decade of life, a horizontal linear hypointense band appears within the nucleus pulposus on T2-weighted images as a result of the development of collagen fibers within the nucleus pulposus (grade 2).

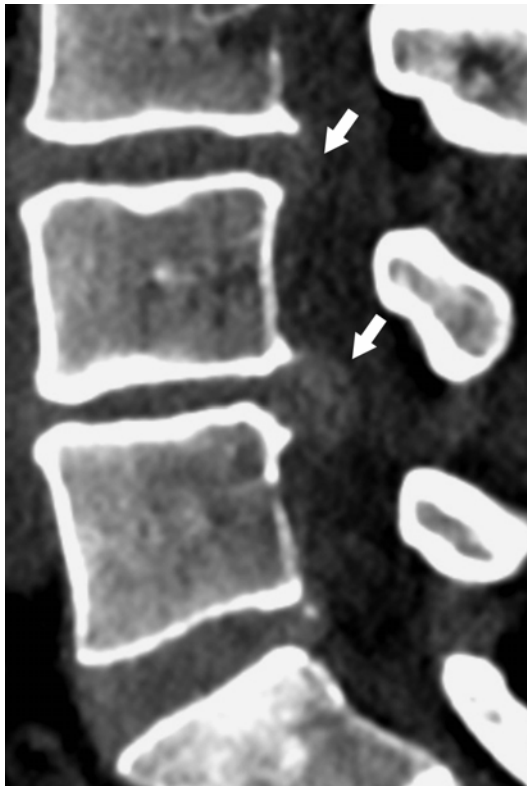

Fig. 7.7 Disk herniations. CT sagittal reformat shows posterior disk bulge on L3/L4 level and larger herniation on L4/L5 level

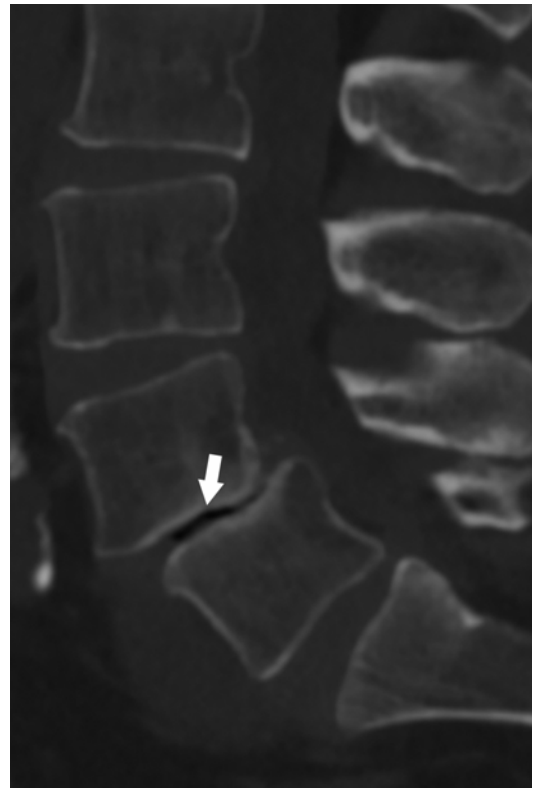

Fig. 7.9 Spondylolisthesis. Sagittal CT reformat shows L4/L5 degenerative spondylolisthesis with major disk space narrowing and intradiscal gas (*arrow*)

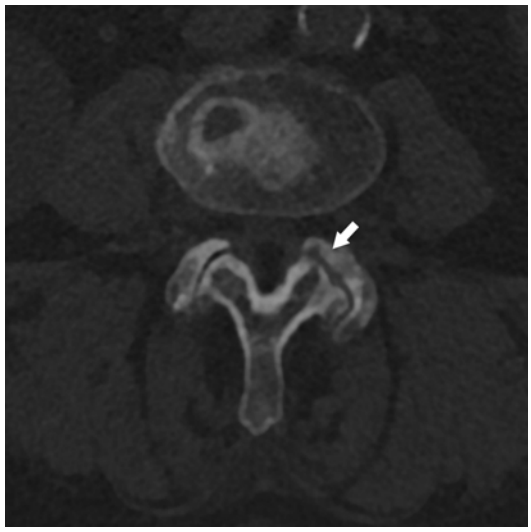

Fig. 7.8 Posterior articulation degenerative disease. Axial CT reformat shows sclerosis of articular facets with osteophytes (*arrow*)

Later, a diffuse signal loss is noted on T2-weighted images and is associated with mild narrowing of the intervertebral space (grade 3) (Figs. 7.11, 7.12, 7.13, and 7.14). At this stage, posterior radial tears may be detected as an area of high signal intensity on T2-weighted images (sometimes described as a HIZ or high-intensity zone lesion) in the posterior and peripheral anulus; enhancement is possible after intravenous administration of gadolinium (Fig. 7.13). A black disk with significant narrowing of the space (grade 4) or with a collapsed disk space (grade 5) corresponds to severe disk degeneration.

Neovascularization is often observed within the degenerative intervertebral disk and leads to a band-like enhancement parallel to the end plates or, less commonly, in the center of the disk. Such findings are associated with local back pain [16] (Fig. 7.14).

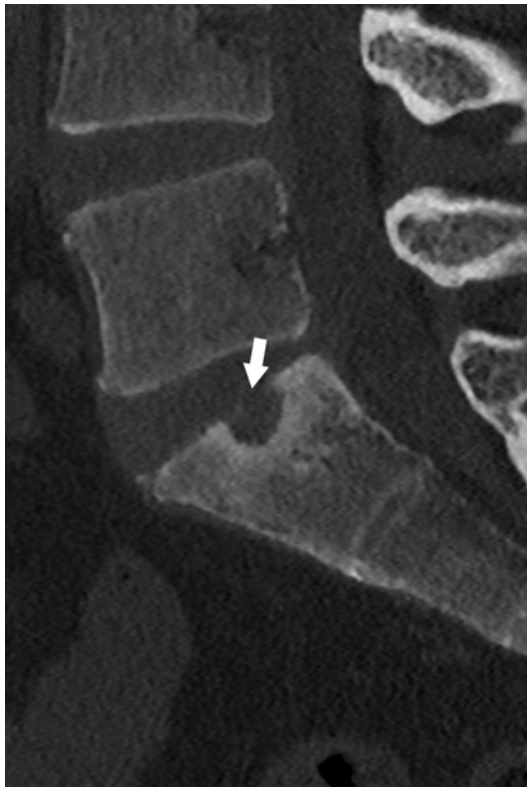

Fig. 7.10 Schmorl node. Sagittal CT reformat shows hypodense lesion within the end plate with peripheral sclerosis (*arrow*)

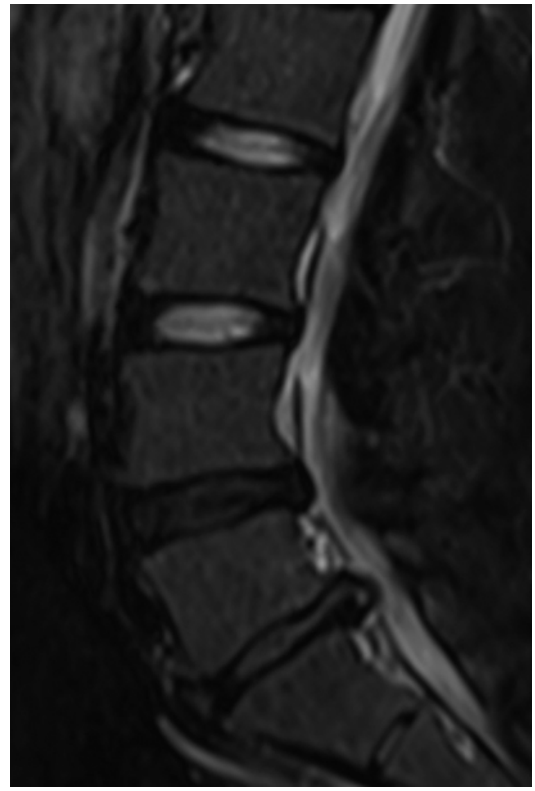

Fig. 7.11 Different grades of disk degeneration on sagittal MR T2w images with disk bulge at L4/L5 level and herniation at L5/S1 level

Intradiscal gas appears hypointense on all sequences, and the vacuum phenomenon is therefore more effectively detected on radiographs and CT. Intradiscal calcifications can have various presentations on MRI: they may appear hypointense on T1- and T2-weighted images or hyperintense on T1-weighted images due to the presence of fatty marrow within ossification of the disk [17, 18].

End plate bone marrow is frequently abnormal on MRI in the setting of DDD. According to Modic et al. [19, 20], two types of signal intensity changes involving the bone marrow of the adjacent vertebral body may be associated with DDD. Type 1 changes are visualized as low signal intensity on T1-weighted images and high signal intensity on T2-weighted images with enhancement after administration of gadolinium (Fig. 7.15). This results from the replacement of normal bone marrow with fibrovascular marrow with an increase in free water and hypervascularity responsible for enhancement after gadolinium injection [19]. Modic type 1 changes are noted in 4 % of patients with back pain and are closely correlated with painful disk derangement [15, 21, 22]. A positive pain provocation test is not clearly correlated with Modic type 1 end plate changes [21, 22]. Similar changes are observed after surgery or percutaneous treatment of a disk herniation.

Modic type 1 end plate changes may at times simulate infectious diskitis and should be correlated with patients' symptoms, clinical history, and laboratory data. In difficult cases, differentiation of degenerative and infectious end plate abnormalities may require a biopsy, MRI follow-

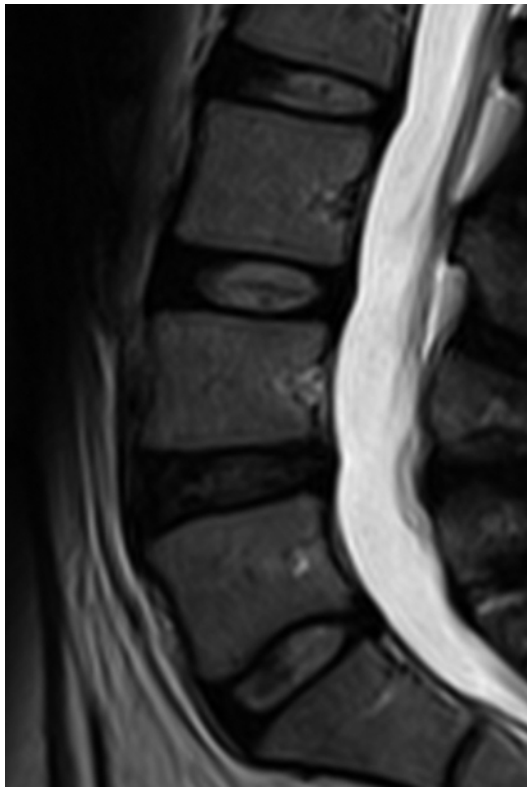

Fig. 7.12 Isolated degeneration of L4/L5 disk on sagittal T2w MR image

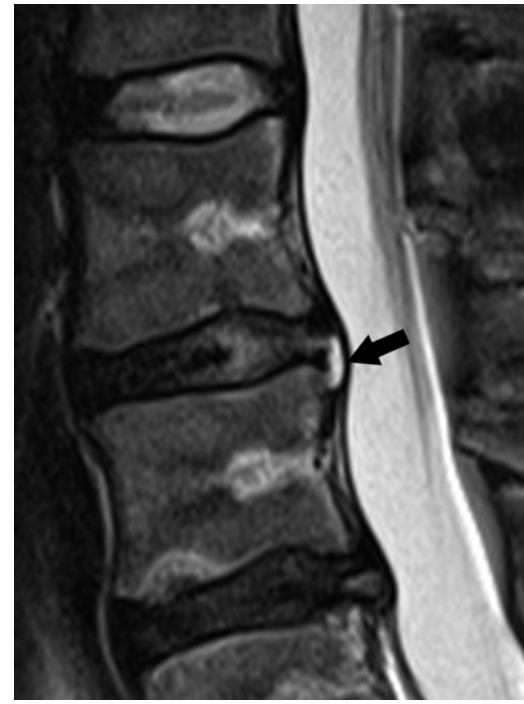

Fig. 7.13 Multilevel disk degeneration with L2/L3 posterior hyperintense zone (HIZ) on sagittal T2w MR image (*arrow*). L3/L4 level demonstrates posterior disk bulge

up, or fluorodeoxyglucose (FDG) positron emission tomography (PET) [23]. Modic type 1 end plate changes may also simulate erosive diskitis associated with rheumatoid arthritis, gout, or chronic hemodialysis [24–27].

Modic type 2 end plate changes are visualized as high-signal-intensity lesions on T1- and T2-weighted images without enhancement; type 2 changes represent fatty marrow and are observed in 16 % of patients presenting with back pain [28] (Figs. 7.16 and 7.17).

Modic type 1 changes represent a dynamic process that often converts to Modic type 2 changes over time (Fig. 7.13). Modic type 2 end plate changes rarely progress [29]. Conversion of Modic type 1 changes to Modic type 2 changes is a very slow process (only 50 % conversion over an observation interval ranging from 1 to 6 years); regression of back pain is noted in two thirds of patients that fully convert from Modic type 1 changes to Modic type 2 changes; associated factors (apophyseal joint osteoarthritis, instability) may explain the absence or partial regression of symptoms [29]. Rapid conversion from Modic 1 to 2 changes is seen after a lumbar posterior arthrodesis [30]. Reverse transformation of Modic type 2 changes to Modic type 1 changes occurs rarely and is probably related to superimposed disease [31, 32].

Modic type 3 changes represent sclerosis of the end plates at the end stage of DDD and appear as a low signal intensity on T1- and T2-weighted images without enhancement (Fig. 7.18).

The signal appearance of recent cartilaginous Schmorl node formation is similar to that of the corresponding intervertebral disk on T1-weighted images and appears slightly hyperintense on T2-weighted images; enhancement is possible

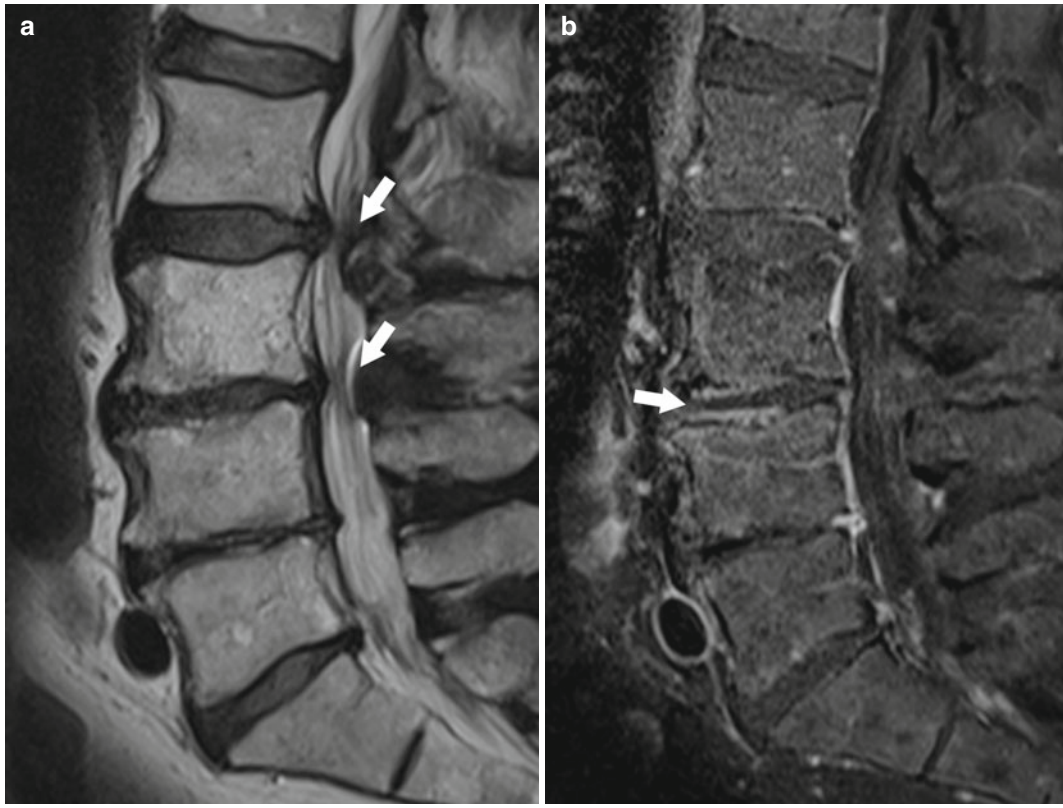

Fig. 7.14 Canal stenosis (*arrows*) secondary to posterior disk bulge and posterior facet hypertrophy on sagittal T2w MR image (**a**); degenerative disk demonstrates linear enhancement on sagittal fat-saturated gadolinium-enhanced T1w MR image (**b**) (*arrow*)

and may remain in the chronic stages. During acute and subacute stages, edema and inflammatory changes involving the surrounding bone marrow are noted as a low signal intensity on T1-weighted images, high signal intensity on T2-weighted images, and postcontrast enhancement and may be correlated with acute or subacute back pain (Fig. 7.19).

Reactive edematous changes can be observed in osteoarthritis involving apophyseal joints (facet joint effusion, inflammation involving articular processes) especially on axial and coronal STIR or T2-weighted images with fat saturation. Facet joint edema (seen in 14 % of patients with low back pain) and intra-articular fluid can also be seen [10, 33].

MRI is the modality of choice for the evaluation of ligament morphology. DDD is associated with hypertrophy and/or degeneration of the ligamentum flavum that, associated with discal bulging and osseous changes, might be responsible for central or foraminal stenosis (Figs. 7.11, 7.13, 7.14, 7.19, 7.20, 7.21, 7.22, and 7.23). Axial T1- or T2-weighted images can clearly depict ligament hypertrophy and neural compression. In addition, modifications in interspinous changes such as bursitis (Baastrup disease) are easily identified on sagittal T2 or STIR images [33–36] (Fig. 7.24).

Paraspinal muscles can be involved in DDD: progressive atrophy can be observed due to reduced activity of the patient. Acute myositis can be seen in cases of nerve root injuries secondary to spinal instability. While axial T1 images are best suited for the evaluation of muscular atrophy, muscular inflammation is best explored on coronal STIR images (Fig. 7.25) [37–39].

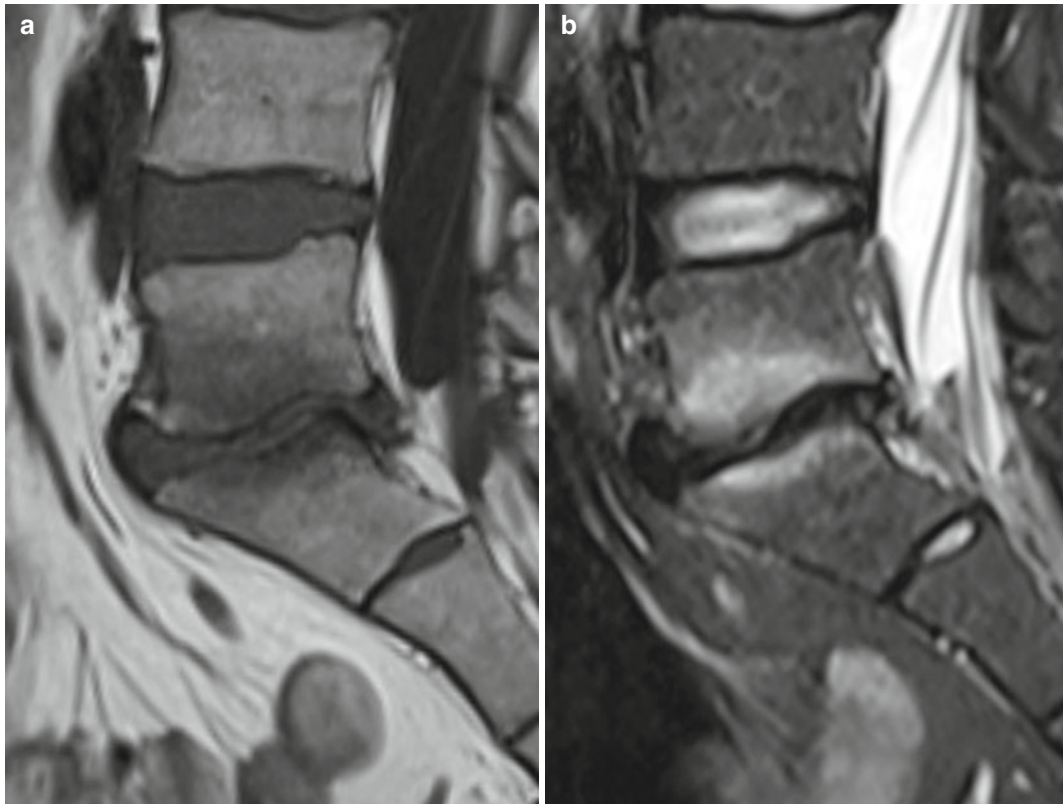

Fig. 7.15 Modic type 1 L4-L5 end plate changes, hypointense on T1 (**a**) and hyperintense on T2 (**b**) sagittal MR scans. Signal abnormalities are located on the portion of the end plates next to the disk

7.5 Postoperative Imaging

In postoperative follow-up, imaging is used to check the integrity of the neurologic structures (foramina, spinal cord, nerve roots) and adjacent elements (vessels, muscles, soft tissues) [40].

If instrumentation is present, CT is the best modality to evaluate hardware-related complications. Correct position and integrity of implants, screws, and rods as well as progress of bone fusion can be assessed (Figs. 7.26 and 7.27).

Complications involving nerves and soft tissue are best visualized by MRI. The most sensitive finding is a collection along the surgical bed with intense rim enhancement. The identification of disk hernia recurrence requires the injection of contrast media in order to discriminate recurrence versus epidural fibrosis: fibrosis enhances, while the absence of enhancement confirms hernia recurrence (Figs. 7.28 and 7.29).

Muscles can be injured during spinal surgery, either directly during rod and screw implantation or secondary to posterior nerve root sectioning. Involved muscles present with diffuse high signal imaging. The extent of injury is best assessed using coronal fat saturation T2-weighted images (Fig. 7.30).

7.6 Perspectives in Spinal Imaging

Nerves can be morphologically evaluated using routine MR protocols. More specific sequences might nevertheless be used such as MR neurography that allows for more precise evaluation of nerve entrapment.

Apparent diffusion coefficient (ADC) has been widely evaluated in nondegenerative and degenerative disk disease. Most studies report

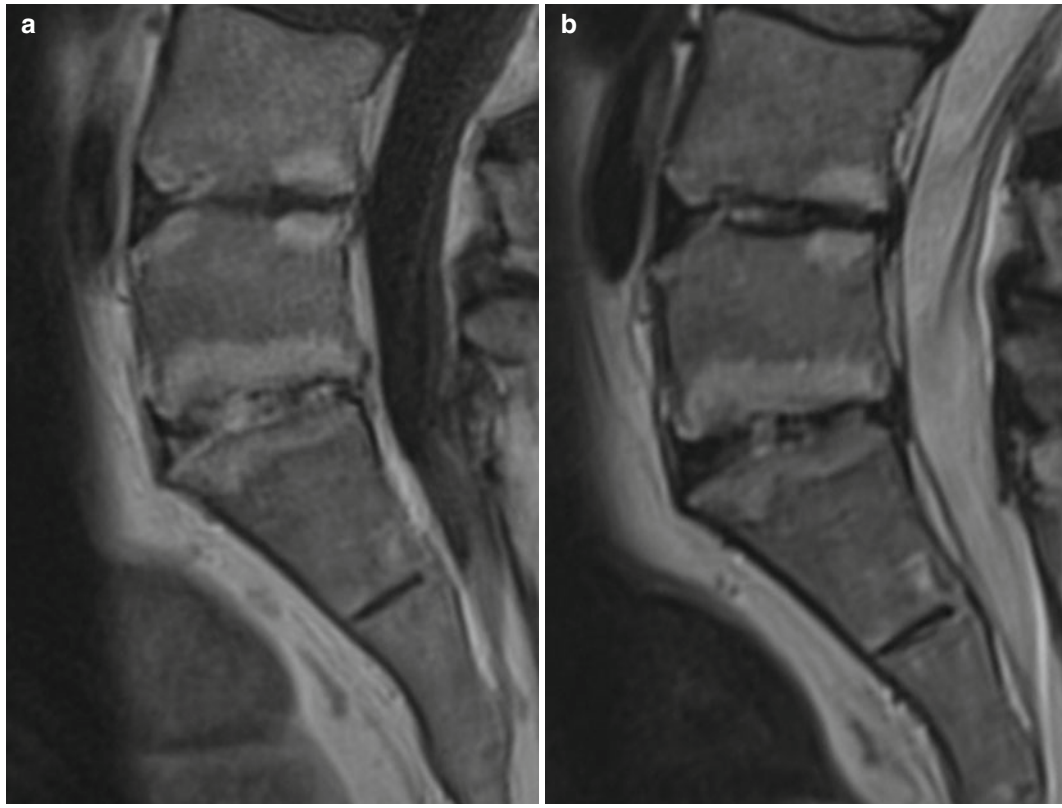

Fig. 7.16 L4-L5 and L5-S1 Modic type 2 end plate changes hyperintense on T1 (**a**) and hyperintense on T2 (**b**) sagittal MR images

that ADC tends to decrease with disk degeneration [41, 42]. Sequencing with ultrashort TE (UTE) time allows the identification of the different components (calcified and uncalcified) of the vertebral end plate and might enable the identification of early degenerative changes [43, 44]. Nevertheless, the role of diffusion and UTE imaging in routine practice remains to be defined. Similar sensitivity is being investigated with glycosaminoglycan-dependent chemical exchange saturation transfer (gagCEST) imaging, 3-T MRI for quantification of glycosaminoglycan (GAG) content in the intervertebral disk [45], and in vivo magnetic resonance spectroscopy [46].

Besides static MR examination, dynamic evaluation with upright positional MRI of the lumbar spine may enhance the presence of a mobile disk herniation or vertebral translation. Supine MRI with the legs straightened seems to be comparable to vertical MRI for evaluation of spinal canal morphology [47, 48]. In addition, imaging of lumbar spine in the prone position with axial loading may reveal significant changes in canal dimension as compared to non-loaded examinations [49].

EOS imaging is increasingly used in the evaluation of spinal disorders, notably in scoliosis-related degenerative changes. EOS imaging is based on the simultaneous detection of X-rays by two orthogonal innovative Nobel-awarded detectors, resulting in the acquisition of biplanar images with the possibility of generating 3D reformat images [50]. EOS imaging enables the production of high-quality full-body images in the weight-bearing position, using low irradiation. The potential use of EOS imaging includes scoliosis evaluation in children or in the evaluation of spinal balance in elderly with degenerative disk disease [51].

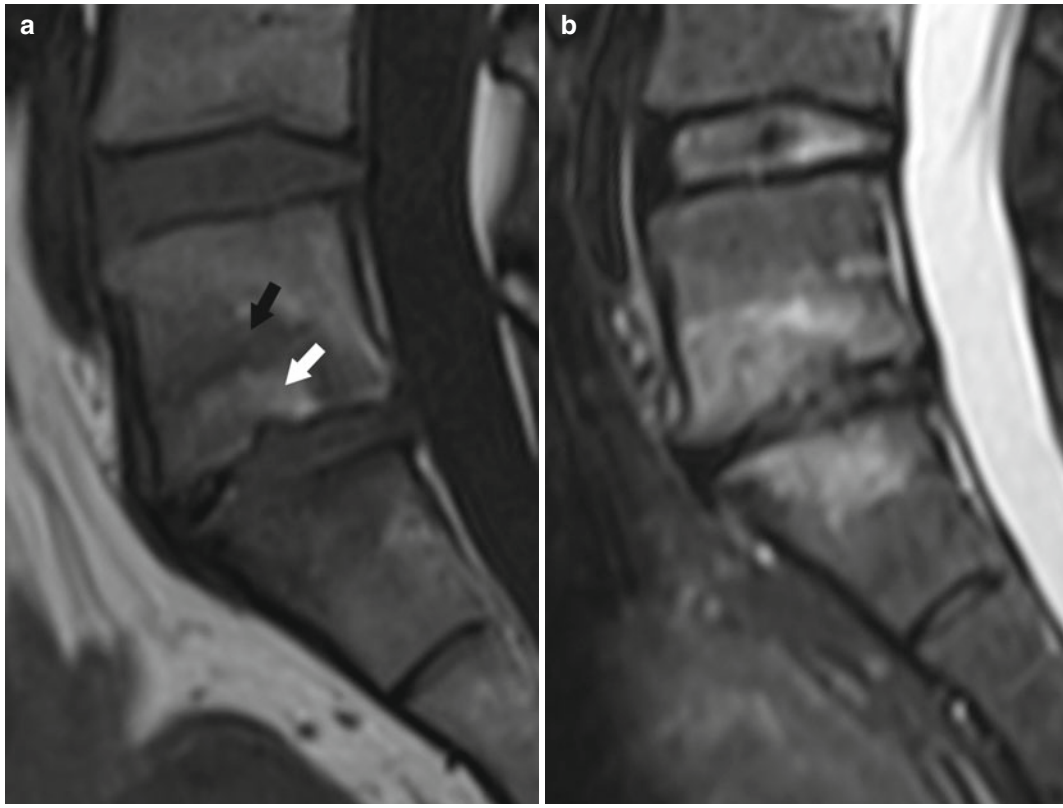

Fig. 7.17 Modic type 1 L5-S1 end plate changes with partial conversion Modic type 2. End plates appear mainly hypointense on T1 (*black arrow* on **a**) and hyperintense on T2 (**b**) sagittal MR images, but area of high signal appears next to the disk on T1w images (*white arrow* in **a**)

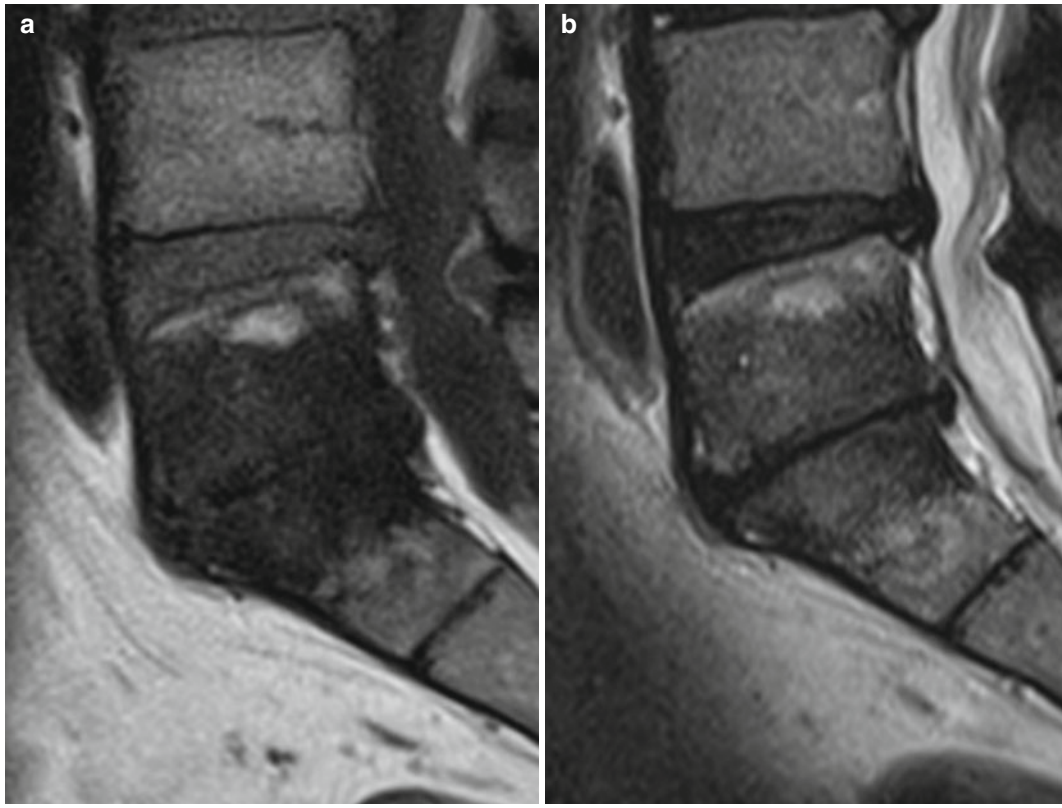

Fig. 7.18 L5-S1 type III end plate changes hypointense on T1 (**a**) and T2 (**b**) in keeping with end plate sclerosing

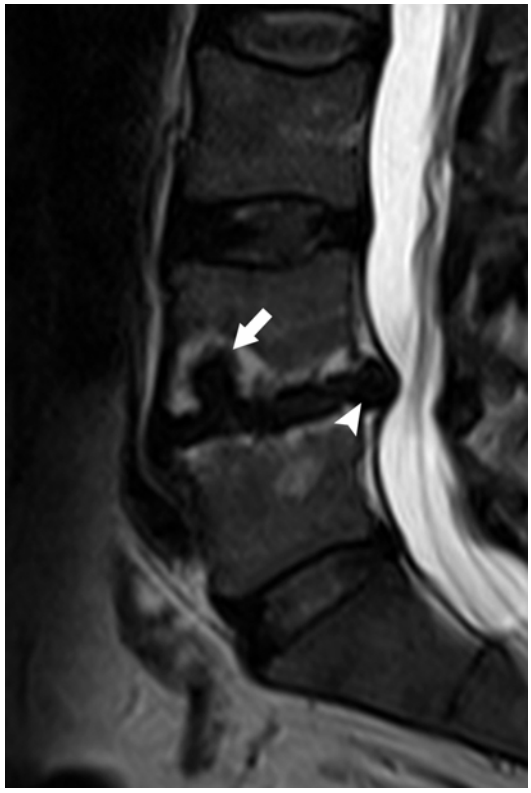

Fig. 7.19 Cartilaginous Schmorl node (*arrow*) with hyperintensity on T2 areas (*arrow*) involving the surrounding bone marrow indicating edema related to inflammatory changes. Posterior disk bulge is present (*arrowhead*)

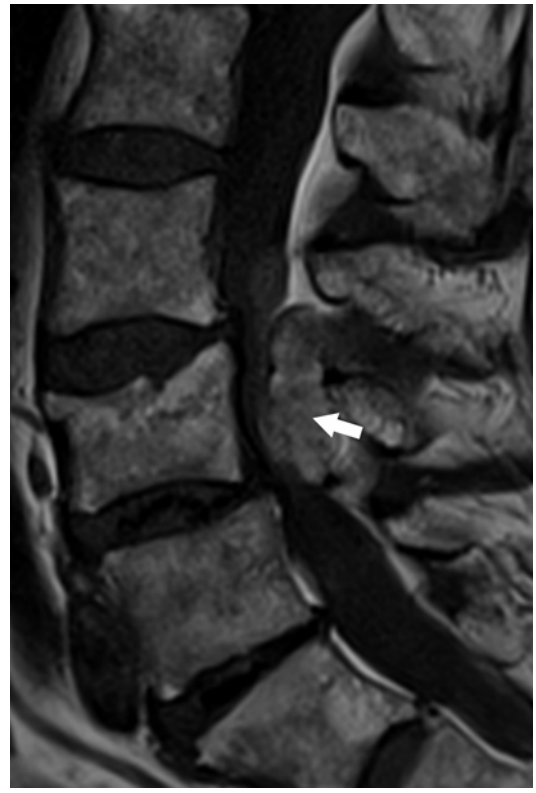

Fig. 7.21 Hemorrhagic facet joint cyst with canal mass effect. Sagittal T1w MR image shows hyperintense lobulated mass before facet joints (*arrow*)

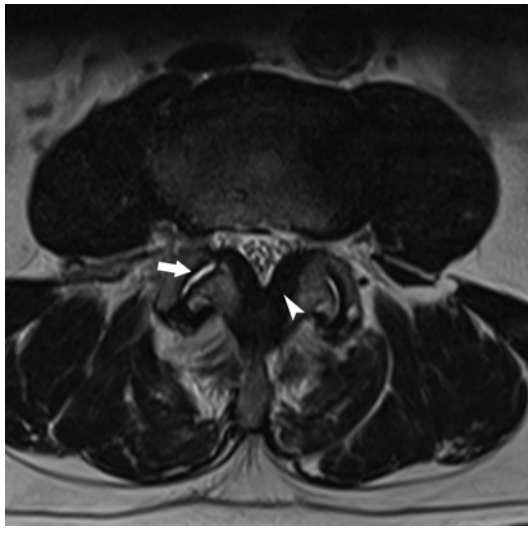

Fig. 7.20 Degenerative changes involving L4-L5 facet joints. Hyperintense signal consistent with facet joint effusion (*arrow*) and hypertrophy of ligamentum flavum (*arrowhead*) are seen on axial T2w MR image

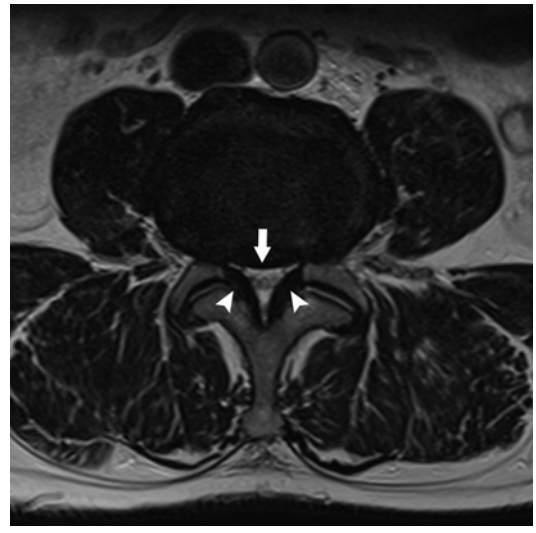

Fig. 7.22 Canal stenosis secondary to degenerative changes. Image T2w MR image shows canal narrowing due to posterior disk bulge (*arrow*) and facet joint and *ligamentum flavum* hypertrophy (*arrowhead*)

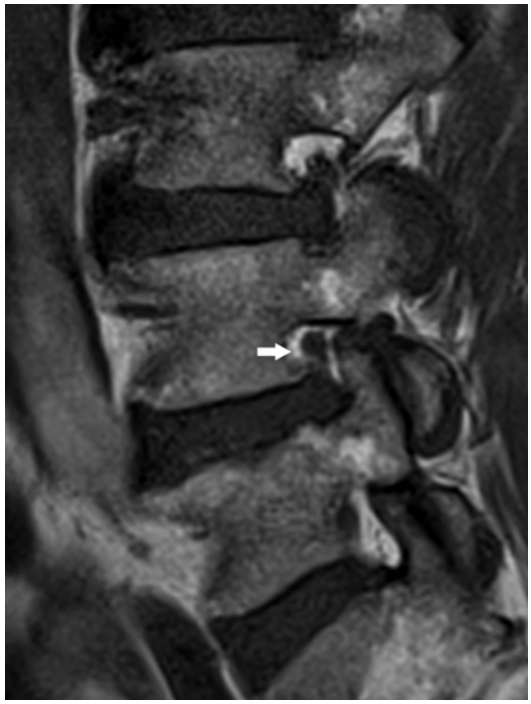

Fig. 7.23 Intervertebral foramen narrowing. Sagittal T1w MR images show mild reduction of fat around the nerve root (*arrow*) secondary to posterior disk bulge and facet hypertrophy

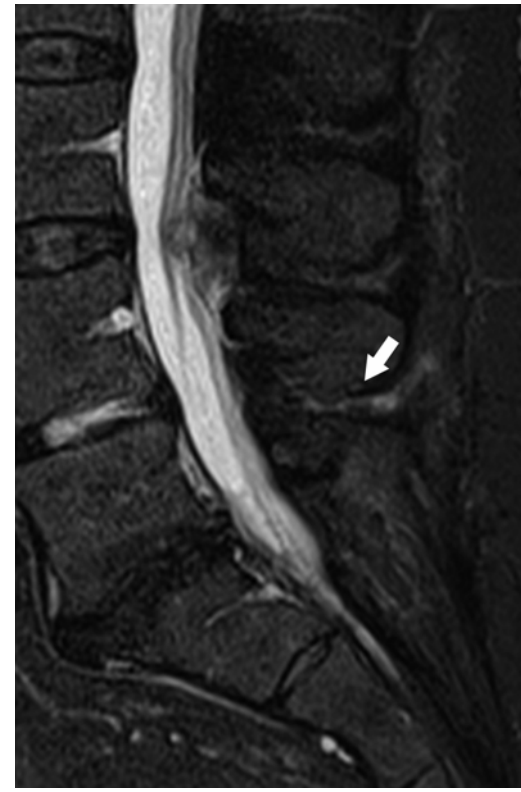

Fig. 7.24 Baastrup disease involving the L4-L5 interspinous space. Fluid within the interspinous space appears hyperintense on sagittal fat-saturated T2 MR images (*arrow*). Note severe L5-S1 disk space narrowing

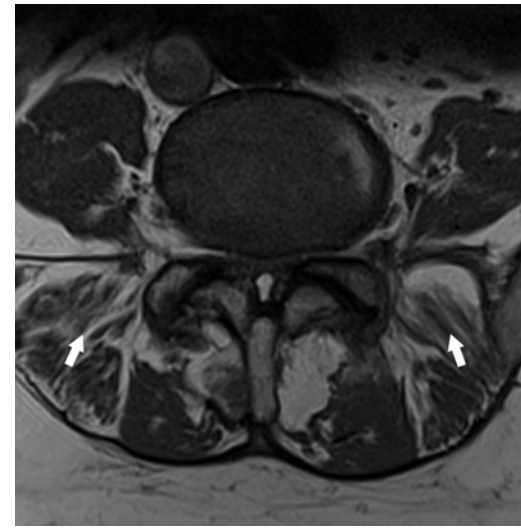

Fig. 7.25 L4-L5 facet joint osteoarthrosis associated with paraspinal muscle atrophy with fatty replacement (*arrows*) visualized on axial T1 MR image. Severe canal stenosis secondary to posterior disk bulge and facet hypertrophy is present

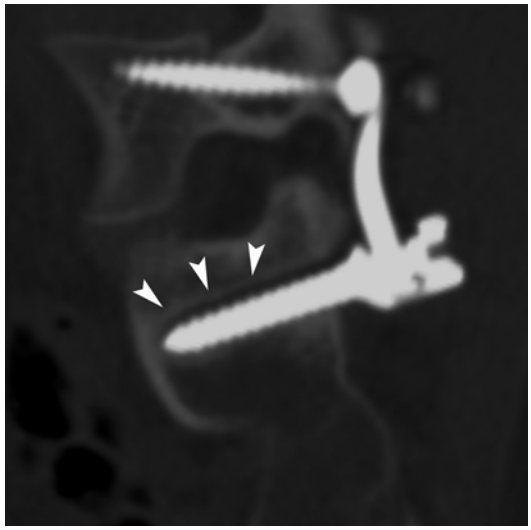

Fig. 7.26 Aseptic loosening of S1 screw after L5/S1 arthrodesis. CT sagittal reformat shows lucency around screw (*arrowheads*)

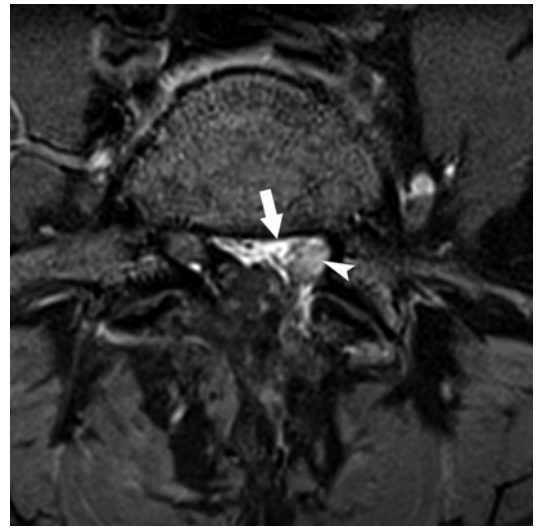

Fig. 7.28 Persistent radicular pain after diskal surgery. Axial gadolinium-enhanced T1w MR image shows enhancement of periradicular space consistent with fibrosis (*arrow*) as well as moderate nerve root enhancement (*arrowhead*)

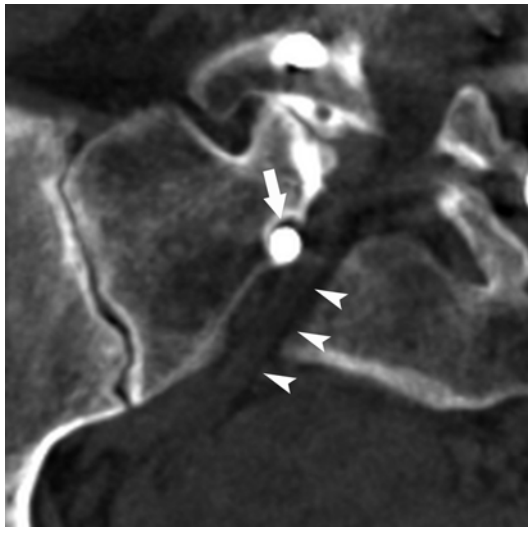

Fig. 7.27 Radicular pain after lumbar arthrodesis. CT oblique reformat demonstrates low and medial position of S1 screw (*arrow*) that displaces S1 root (*arrowheads*)

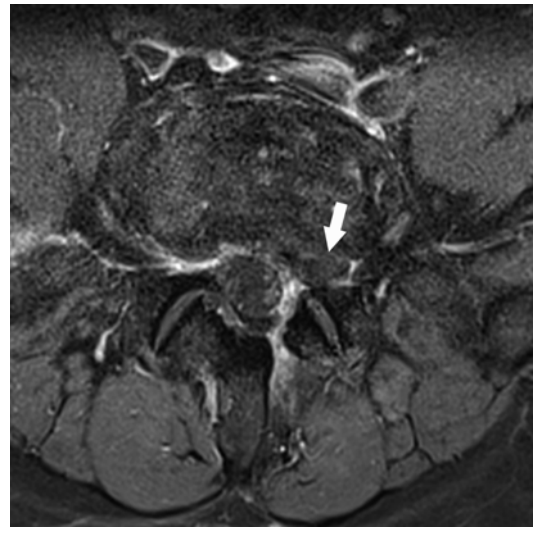

Fig. 7.29 Persistent radicular pain after diskal surgery. Axial gadolinium-enhanced T1w MR image shows a non-enhancing mass within foramina consistent with hernia recurrence (*arrow*)

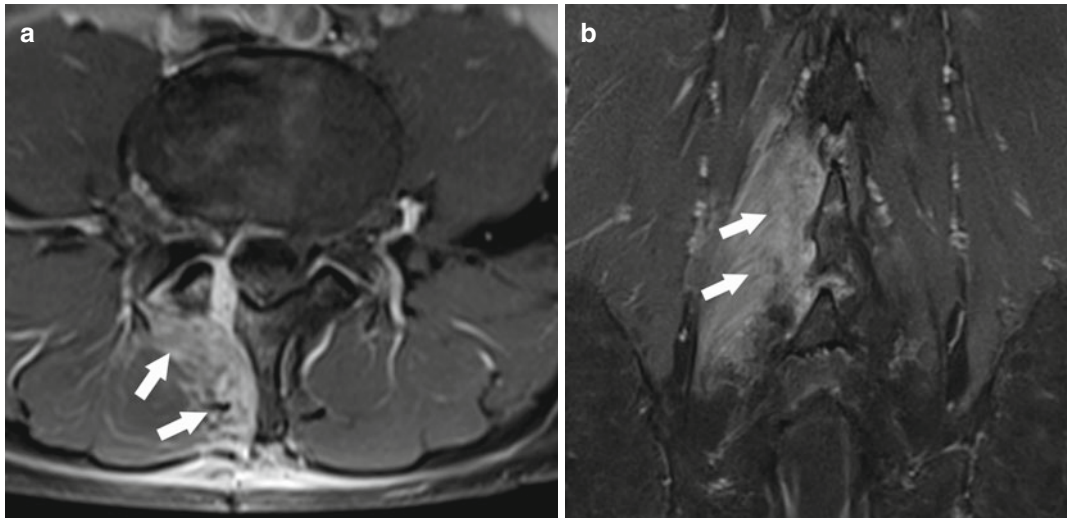

Fig. 7.30 Back pain after diskal surgery. Axial gadolinium-enhanced T1w MR image (**a**) and coronal fatsat T2w image (**b**) demonstrate multifidus edema consistent with postoperative denervation (*arrow*)

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Diskography

8

Richard Derby, Lee R. Wolfer,
and Milton H. Landers

8.1 Introduction

Until the introduction of diskography by Lindblom in the 1940s, oil-contrast myelography was utilized to diagnose disk herniations [1–4]. During the era of the "herniated disk" in the 1930s [5], both axial pain and referred pain were thought to be due to the disk compressing neural elements. Myelography was limited in that it only visualized the thecal sac and dural root sleeves. Diskography allowed visualization of the disk itself, including internal morphology and lateral protrusions which were missed on myelography. Diskography was initially utilized to diagnose disk herniations prior to surgery in patients with radicular pain [1–3]. Interestingly however, most of the disks examined by diskography exhibited annular disruption, but no frank herniation or protrusion. More importantly, upon injection of contrast media into these internally disrupted disks, some patients experienced reproduction of their familiar pain [6, 7]. These observations led surgeons to use provocation diskography not only to reveal structural abnormalities but also to identify and treat painfully internally disrupted disks. Diskography became a sophisticated extension of the physical exam, a means of "palpating" the disk to elicit pain [8]. Previously, diskography was only used as a presurgical planning test; however, with the introduction of new "regenerative medicine" techniques such as platelet-rich plasma, there is a renewed interest in understanding and treating the disk as a pain generator.

Over the most recent decades, histochemical and anatomical studies have provided evidence that the disk is an innervated structure capable of transmitting pain. There is no doubt that the disk can be a source of pain. Typically, in a normal disk, innervation is limited to the outer annulus; however, we know that pathologically painful disks (based on positive diskogram pre-fusion) show neo-innervation to the inner annulus as well as nucleus pulposus [9–11]. It is believed that injection of contrast dye into the nucleus stimulates nerve endings [12] via two mechanisms: a chemical stimulus from contact between contrast dye and sensitized tissues and a mechanical stimulus resulting from fluid-distending stress. What is controversial is not whether the disk is a source of pain, but whether disk pain can be reliably diagnosed?

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_8

The validity and accuracy of diskography have been challenged, particularly in the last 10 years, with reports of unacceptably high false-positive rates in asymptomatic subjects, particularly in patients with chronic pain or evidence of psychologic pathology. However, these negative studies have been refuted after close review and a performance of a meta-analysis of false-positive rates of lumbar diskography. Combining all the major studies on diskography in asymptomatic subjects, a false-positive rate of less than 10 % can be achieved if the diskographer adheres to strict operational standards and interpretation criteria [13]. Although MRI and CT are the most commonly used advanced imaging modalities for low back pain, diskography still occupies a critical place in the diagnostic algorithm. We know that abnormal disk morphology alone is not diagnostic of diskogenic pain, as many individuals with abnormal CT scans or MRIs are asymptomatic of low back pain [14, 15]; however, MRI cannot distinguish between a painful and painless disk.

In contemporary practice, the criterion standard for diagnosis of a painful internally disrupted disk by provocation diskography is pain ≥7/10, pressure <50 psi a.o. (above opening pressure), concordant pain, ≥grade 3 annular tear, volume ≤3.5 ml, and the presence of a negative control disk [16].

In this chapter, the indications for diskography, technical considerations, as well as complications of lumbar diskography are discussed. Procedural descriptions have also been extensively described in our prior publications [17, 18]. The technical section of the chapter is followed by a brief updated literature review in regard to the role of diskography as a diagnostic test (versus MRI and CT), the false-positive controversy, predictive value, as well as an update on analgesic diskography.

8.2 Indications and Contraindications

Diskography is not an initial screening examination. Disk stimulation follows failed conservative treatment modalities and is only used when other less invasive diagnostic tests are inconclusive. Diskography is invasive, and irreversible surgical procedures may be chosen based on the results. The principal indication for provocation diskography is to determine whether or not a disk is pathologically painful and to determine the extent of annular or end plate disruption. Results of diskography may then used to guide the surgeon or spine interventionalist. Pertinent clinical information is then used to establish a diagnosis of diskogenic pain and consideration of targeted disk therapies. Only diskography followed by CT scanning can define the internal anatomy of the disk [19]. Post-diskography CT scanning is also particularly useful in post-diskectomy patients with suspected residual or recurrent disk herniations. Diskography is useful in problematic cases unresolved by MRI or myelography and in patients for whom surgery is contemplated [20]. Diskography can offer a potential solution to the diagnostic dilemma concerning which patients to treat surgically and at what segmental level. When a single disk is found to be symptomatic in the presence of adjacent asymptomatic disks, focused intradiscal or surgical therapy can be entertained. A no less important application is to identify asymptomatic disks which do not need intervention. Patients with symptomatic or abnormal disks at multiple levels (≥3) constitute a greater surgical challenge.

If the patient is not a surgical candidate, diskography is useful to provide a diagnosis that can be used to bring the workup to closure and direct the patient to non-interventional pain management treatment options. The position statement of the North American Spine Society on diskography is as follows [19]:

> Diskography is indicated for the evaluation of patients with unremitting spinal pain, with or without extremity pain, of greater than four months' duration, when the pain has been unresponsive to all appropriate methods of conservative therapy. Before diskography, the patient should have undergone investigation with other modalities which have failed to explain the source of pain; such modalities should include, but not be limited to, either computed tomography (CT) scanning, magnetic resonance imaging (MRI) scanning and/or myelography.

Inclusion criteria:

1. Failed conservative treatment for low back pain of probable spinal origin.
2. Pain has been ongoing for greater than 3 months.

3. Symptoms are clinically consistent with disk pain. Ideally the zygapophyseal joints and sacroiliac joints have been ruled out as pain generators using appropriate dual diagnostic blocks with local anesthetic.
4. Symptoms are severe enough to consider surgery or percutaneous interventions.
5. Surgery is planned and the surgeon desires an assessment of the adjacent disk levels
6. The patient is capable of understanding the nature of the technique and can participate in the subjective interpretation.
7. Both the patient and physician have a need to know of the source of pain in order to guide further treatments.

Contraindications:

1. Unable or unwilling to consent to the procedure
2. Inability to assess patient response during the procedure
3. Inability of patient to cooperate
4. Known localized or systemic infection
5. Pregnancy
6. Anticoagulants or bleeding diathesis

Relative contraindications:

1. Allergy to contrast medium, antibiotics, or local anesthetics
2. Significant psychological overlay
3. Any other condition, medical, congenital, postsurgical, anatomical, or psychological which would increase the risk of the performance of the procedure to an acceptable level

8.3 Preprocedure Evaluation

Prior to diskography, one should obtain a complete history and perform a physical examination to reveal any procedural contraindications. Red flags such as fever, night pain, history of malignancy, or unexplained weight loss should alert the physician to an alternate diagnosis. Prior to diskography, obtain informed consent from the patient. The purpose and nature of the procedure; its risks, benefits, alternatives, and complications; and what to expect post-procedure are explained. Patients are instructed in the use of a 0–10 pain scale. Specifically, the patient should understand that diskography is commonly painful and that they will need to describe the location, intensity, and concordance of any provoked pain in respect to their ongoing complaints. A trained observer can independently monitor patient pain responses during the procedure. Some diskographers have their patients fill out a brief psychometric test such as the Distress and Risk Assessment Method (DRAM) to assess if the patient has a normal, at-risk, distressed depressive, or distressed somatic profile [21].

In patients with a history of allergy to nonionic water-soluble contrast media (iohexol or iopamidol) or other related agents, the risks versus benefits of the procedure must be weighed and discussed with the patient. For patients with iodine allergies, pretreat patients with corticosteroids and H1 and H2 blockers prior to the procedure. If the risk of allergic reaction to contrast is significant, use saline instead of contrast or add a very small volume of gadolinium to the saline and obtain an immediate post-procedure MRI [22, 23].

In all cases of lumbar diskography, an MRI or CT scan should be reviewed. The majority of diskographers select test levels according to the appearance of the MRI T2-weighted images. Most test disks with decreased T2-weighted signal intensity; an adjacent, less degenerated disk is usually selected as a control. Rarely is it necessary to inject greater than three levels.

8.4 Patient Preparation

8.4.1 Antibiotic Prophylaxis

Intravenous access is standard. Diskitis is the most common serious (albeit rare) complication. Prophylactic antibiotic (cefazolin 1 g, gentamicin 80 mg, clindamycin 900 mg, or ciprofloxacin 400 mg) is administered prior to the procedure and within 30 min of needle insertion. Sheep studies confirmed optimal antibiotic levels in the annulus 30 min post-IV administration; no antibiotics were present at 60 min [24, 25]. Post-procedure, aminoglycosides are not required for prophylaxis [26]. Along with IV antibiotics, many diskographers mix intradiscal antibiotics

with the contrast dye (between 1 and 6 mg per ml of cefazolin or an equivalent dose of another antibiotic) [27–30]. Klessig et al. [30] reported that cefazolin and gentamicin 1 mg/cc and clindamycin 7.5 mg/cc exceed the minimum inhibitory concentrations (MICs) for the three most common organisms causing diskitis: *Escherichia coli*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*. All procedures should be performed under sterile conditions with double gloves.

8.4.2 Sedation

As a provocative test, diskography is at best uncomfortable and at worst very painful. How much and which drug to use for preoperative sedation varies according to the diskographer's skill and training. Intravenous sedation should be titrated to maintain patient comfort during needle insertion while minimizing masking of the evoked pain response. The patient must be awake and conversant during disk stimulation. Doses of midazolam between 2.0 and 5.0 mg provide effective anxiolysis and sedation during diskography but cause retrograde amnesia. Many spine interventionalists, particularly those with an anesthesia background, use propofol (an ultrashort-acting hypnotic) in intermittent boluses of 10–30 mg. Propofol causes rapid sedation and amnesia during needle insertion, but because of its short half-life, the patient will be awake when during disk stimulation.

Some diskographers believe that opioids should not be utilized prior to or during diskography [31–35]. They assert that diskography is a provocational test; therefore, pain intensity needs to be compared and quantified in relation to the patient's usual pain intensity, and opioid analgesics could decrease the pain response and increase the chance of a false-negative response. Alternatively, others [36] believe that a small dose of analgesics (meperidine 50 mg, fentanyl 50 mcg, or morphine 5 mg) prior to the procedure helps decrease the rate of false positives in patients with clinically insignificant diskogenic pain. Most diskographers agree that chronically opiate-tolerant patients (who have also been NPO) should be given a reasonable dose of IV opiate to avoid false-positive responses in the setting of early opiate withdrawal and possible heightening pain responses or, at a minimum, the patients should take their usual morning pain medications with small sips of water. During diskography, patients must be monitored appropriately. Although respiratory depression is uncommon with this protocol, subjects should have a pulse oximeter and blood pressure cuff. Supplemental oxygen is supplied by nasal cannula. Personnel competent in airway management and resuscitation should be present during the procedure.

8.4.3 Sterile Technique

The skin and draping technique for diskography is similar to the sterile technique used for surgery. Standard draping to provide a sterile field may include the use of sterile towels or fenestrated drapes per the injectionist's preference. Povidone-iodine 10 % (*Betadine* solution) and/or *DuraPrep* (iodophor 0.7 % and isopropyl alcohol 74 %) are the preparations of choice. Chlorhexidine and alcohol may be substituted if the patient has allergies to the aforementioned solutions. The procedure room staff should be dressed in clean clothes (scrub suites). Surgical caps and masks are mandatory for any personnel in close contact to the sterile field. Many injectionists scrub, gown, and glove as for an open surgical procedure. The C-arm image intensifier should also be draped.

8.5 Lumbar Diskography: Technique

Diskography can be performed in a procedure room appropriate for aseptic procedures. Fluoroscopy is required for safe visualization of spinal anatomy in anterior-posterior (AP), lateral, and oblique projections. Biplanar fluoroscopy can be utilized, but most diskographers use C-arm units which allow excellent visualization without repositioning the patient. An adjustable, radiolucent procedure table is useful.

8.6 Patient Position

The patient lies in a prone position on a fluoroscopy table. Most diskographers place a pillow or bolster under the patient's abdomen to slightly flex the spine and decrease the lumbar lordosis. Elevating the target side approximately 15° allows the fluoroscopy tube to remain in a more AP projection and reduces radiation scatter. If needed, a folded towel or soft wedge can be placed under the patient's flank to prevent side bending of the lumbar spine. Monitoring and light sedation are initiated. On the side selected for puncture, a wide area of the skin of the back is prepped and draped from the costal margin to the mid-buttock and from the midline to the flanks.

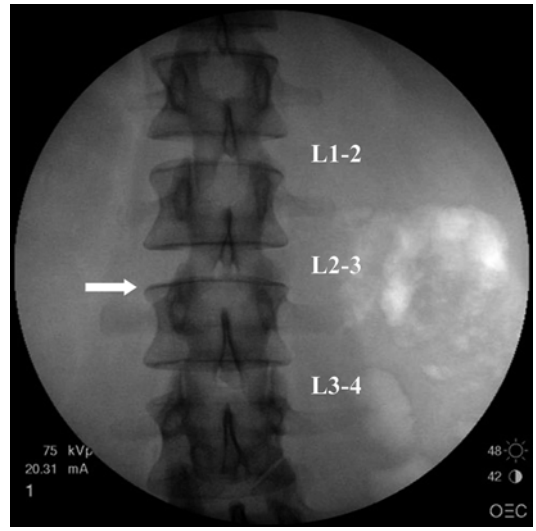

Fig. 8.1 AP view of the lumbar spine. Target disk is at L2–L3. *Closed white arrow* indicates superior end plate of L3 parallel to the X-ray beam

8.7 Disk Puncture

Until the 1960s, diskography was performed with a posterior interpedicular or transdural approach; however, this technique is seldom utilized today because it requires dual punctures of the dura. Currently, a lateral, or extra-pedicular, approach [37, 38] is used except in rare situations where anatomical variation or postsurgical changes prevent disk access by a lateral approach.

Prior to injection, a fluoroscopic examination of the spine is performed to confirm segmentation and determine the appropriate level for needle placement. The target disk is identified on AP view. The image intensifier of the C-arm is tilted in a cephalad or caudad direction until the end plate of the vertebral body, caudad to the target disk, is parallel to the X-ray beam (Fig. 8.1). The end plate is visualized as a line rather than an oval. After selecting the target disk on AP view, the fluoroscopic beam is obliquely rotated until the superior articular process of the adjacent caudal vertebrae appears to lie under the midpoint of the inferior vertebral end plate of the level above. In this view, the insertion point is 1 mm lateral to the lateral margin of the superior articular process (SAP) (Fig. 8.2). This positioning of the fluoroscope allows needles to be passed using "tunnel vision" (i.e., parallel to the beam when the skin puncture site is aligned with the target structure) just lateral to the SAP.

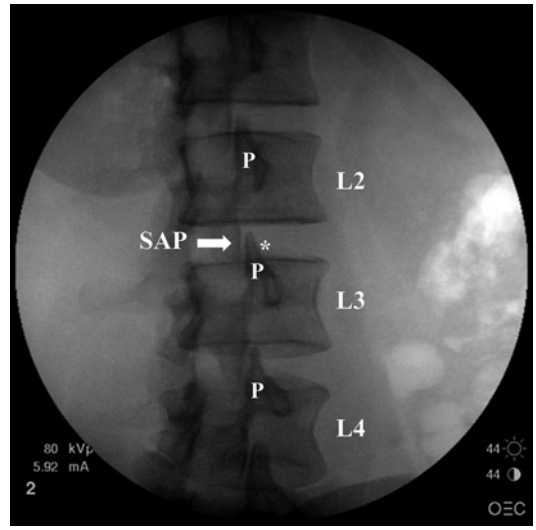

Fig. 8.2 Right oblique view. Tip of the SAP of L3 is at approximate midpoint of the inferior end plate of the L2 vertebral body (* target point, *SAP* superior articular process, *P* pedicle)

The disk is preferentially approached from the side opposite the patient's usual pain to avoid the patient mistaking discomfort secondary to needle placement with provoked pain secondary by disk

stimulation. If the patient has central pain or the pain is equal bilaterally, or if there are other impeding technical factors, needle insertion from either side is fine.

The insertion point is marked on the skin. The distance between the opposite superior articular processes increases at the lower lumbar levels. At T12–L1, the needle insertion point is about 3–4 cm lateral to the midline; at L5–S1 it is approximately 6–7 cm lateral. At L5–S1, because of the iliac crest and increased interfacetal distance, ideal access to the disk may not be possible. The fluoroscope is therefore rotated only far enough to bring the superior articular process approximately 25 % of the distance between the anterior and posterior vertebral margins.

Prior to needle placement, a skin wheal is made with lidocaine 1 % (~1 cc) using a 25 gauge 1.5 in. needle. To anesthetize the needle track, one can use a 25 gauge 3.5 in. needle advanced under "tunnel vision," i.e., parallel to the X-ray beam, to the level of the SAP. Exercise caution so as not to anesthetize the dorsal root ganglion within the foramen. Overenthusiastic anesthetization may obscure nerve root impalement and could potentially anesthetize the sinuvertebral and ramus communicans nerves, thus altering the evoked pain response during disk stimulation and creating a false-negative response.

A one- or two-needle technique may be used; however, most diskographers currently use a two-needle technique. Prior to the routine use of prophylactic antibiotics, Fraser et al. [24] reported a rate of diskitis with single non-styletted versus double needles of 2.7 % versus 0.7 %, respectively. Both the North American Spine Society and the International Spinal Injection Society recommend a two-needle approach [16, 19].

The two-needle technique utilizes a shorter, larger gauge introducer needle through which a longer, smaller gauge needle is advanced past the tip of the introducer needle into the targeted intervertebral disk, theoretically avoiding picking up any skin flora. The trend is to use a 20 gauge 3.5 in. introducer with the 25 gauge 6 in. disk puncture needle. The 25 gauge needle theoretically minimizes any trauma to the disk. Less experienced operators may start with the 18/22 gauge needle combination, particularly because the curve of the disk puncture needle is easier to maintain. The body habitus of the patient will dictate if longer needles are necessary, i.e., 5 in. introducer and an 8 in. disk puncture needle. A slight bend, opposite the bevel, is typically made at the tip of the disk puncture needle to allow the operator to "steer" the needle during extra- and intradiscal insertion [39–42]. At times a larger curve, at the distal third of the disk puncture needle, must be utilized to compensate for less than ideal anatomy or postsurgical changes.

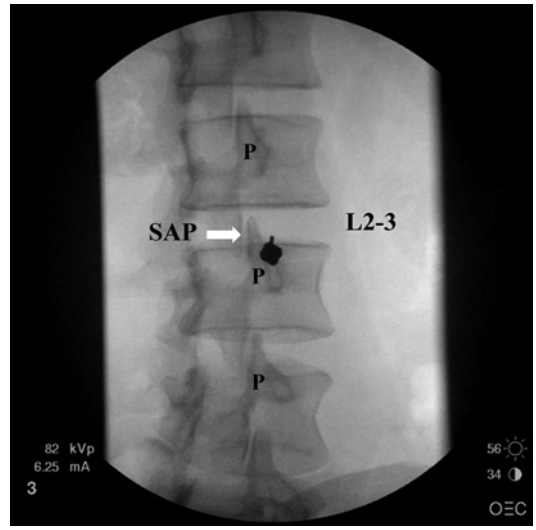

Fig. 8.3 Right oblique view. Introducer needle in lateral to SAP at L2–L3 target disk (see *closed white arrow*) (*SAP* superior articular process, *P* pedicle)

The introducer needle is passed through the skin wheal at the skin puncture point, using a "down the beam" or "tunnel vision" technique on the oblique fluoroscopic view and is often felt to enter the foramen (Fig. 8.3). To protect the diskographer's hand from radiation exposure, forceps may be used to grasp the introducing needle. To avoid potential neural injury, direct the needle into the region below the segmental nerve, just lateral to the superior articular process and above the end plate (Fig. 8.4). The disk puncture needle must travel under the segmental nerve coursing medial to lateral, and dorsal to ventral, to puncture the annulus fibrosus of the disk at the midpoint of the disk when seen in lateral and AP views. To minimize nerve trauma, one might

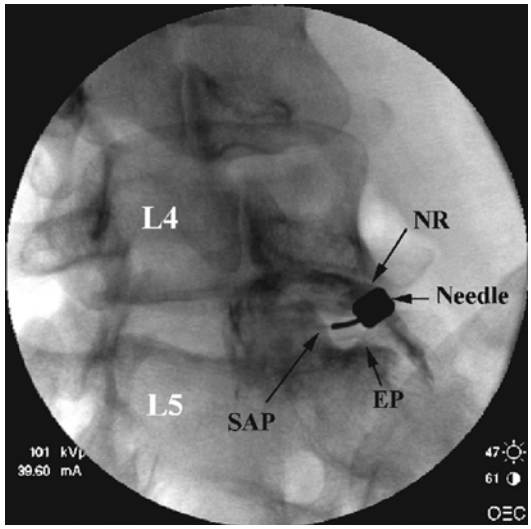

Fig. 8.4 Location for diskogram needle insertion. *NR* nerve root outlined by contrast media, *SAP* superior articular process, *EP* end plate

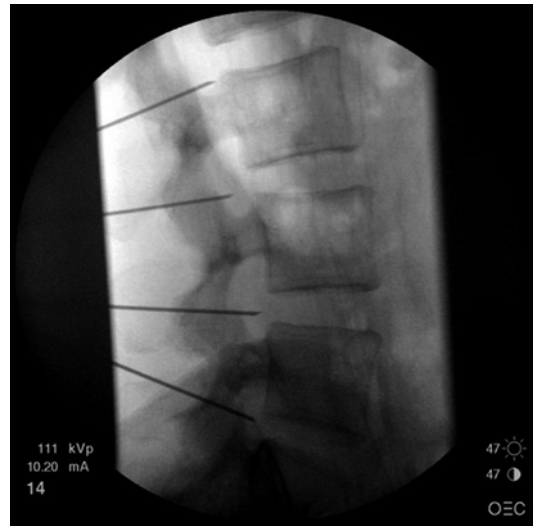

Fig. 8.5 Lateral fluoroscopic view of the lumbar spine. All introducer needles in place, at or just ventral to the posterior elements, for L1–L2 through L5–S1 disks

consider use of a needle with a short, non-cutting bevel. However, a Quinke tip spinal needle is appropriate in that contact with the ventral ramus should be a rare occurrence if a modicum of care is utilized. Forward advancement is stopped at the approximate level of the SAP, although placement within the foramen, ventral to the intervertebral disk annulus, is acceptable. Use a lateral fluoroscopic view to check needle depth (Fig. 8.5).

The stylette is then removed from the introducer, and the longer, smaller gauge disk puncture needle is advanced slowly under real-time lateral fluoroscopy. The needle will be seen to transverse the intervertebral foramen; then, a firm but distinct change in resistance will be noted as the needle touches and punctures the annulus fibrosus. On the lateral view, the needle will typically contact the posterior disk margin 1–3 mm posterior to the vertebral margin. On AP projection, the diskogram needle ideally contacts the disk margin on a line drawn between the midpoints of the pedicles above and below (Fig. 8.6). The patient may experience a brief sharp "pinch" or sudden aching sensation when the needle pierces the innervated outer annulus fibrosus. In no case should one advance the introducer or diskogram needle medial to the inner pedicle margins before contacting the intervertebral disk. Using lateral fluoroscopy, the needle is then advanced to the center of the disk as seen on both lateral and AP projections (Figs. 8.7 and 8.8). AP and lateral projections are used to assure good needle placement, and spot films saved for documentation prior to injection of contrast.

If bony obstruction is encountered, the physician should use fluoroscopy to determine whether the needle has contacted the superior articular process or the vertebral body. If the SAP is contacted, the introducer needle can be withdrawn slightly and its trajectory modified. The introducer needle can be advanced to just over the lateral edge of the superior articular process or advanced to the dorsal margin of the disk. If the vertebral body is contacted, the introducer needle is withdrawn to a point where manipulation of the slightly bent disk puncture needle can compensate for the nonoptimal placement of the introducer needle.

If the patient experiences any radicular pain or dysesthesia during needle advancement, insertion of the needle must halt. The ventral ramus may be encountered because it crosses the posterior-lateral aspect of the disk in close proximity to the disk entry site. In such a case, the needle is partially withdrawn to alter its course and redirected toward the disk. A slight

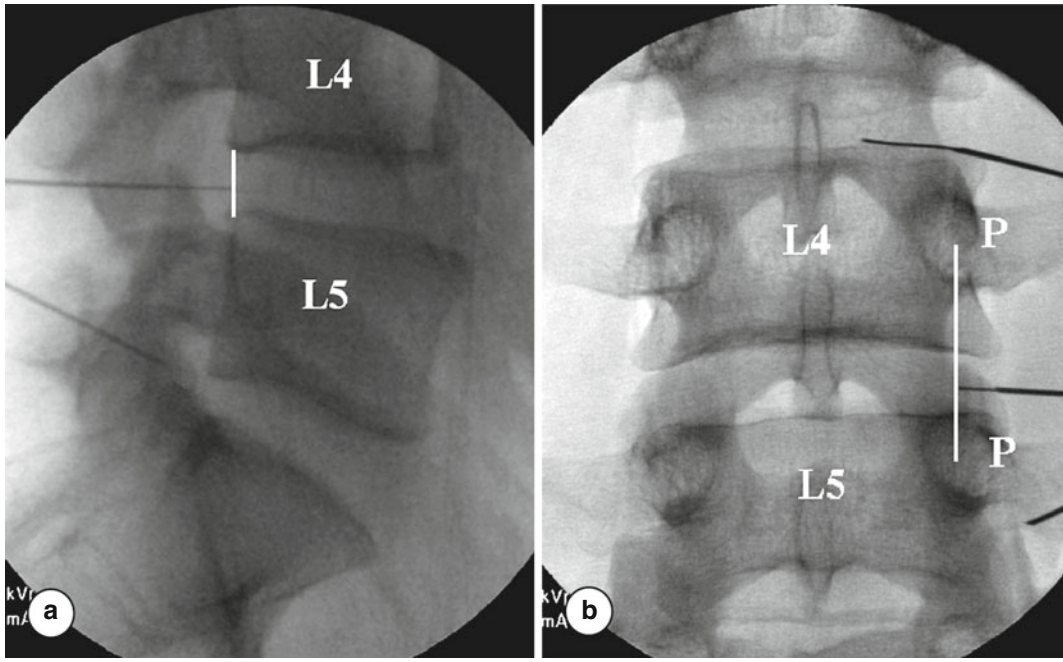

Fig. 8.6 The diskogram needle should contact the disk between the midpoint of the posterior vertebral margins on the lateral view (**a**, *white vertical line*) and at the line between the midpoint of the pedicles on the AP view (**b**, *white vertical line*) (*P* pedicle)

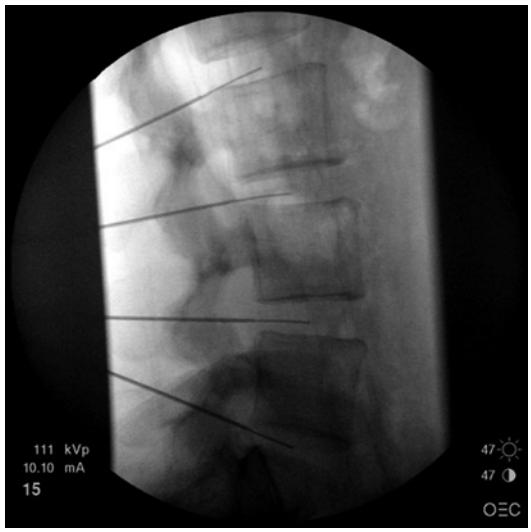

Fig. 8.7 Lateral fluoroscopic view. Diskogram needles placed into center of intervertebral disks

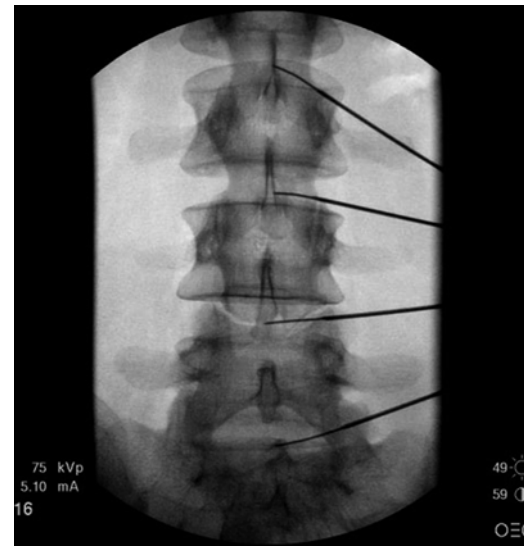

Fig. 8.8 AP view. Disk puncture needles in the center of the nucleus pulposus of each intervertebral disk

bend in the needle tip facilitates small directional adjustments. Typically, redirection of the needle more medially and caudally will avoid the segmental nerve. If greater direction changes are needed, withdraw and redirect the introducer needle as well.

The above technique can be utilized for disk puncture in greater than 95 % of lumbar disk

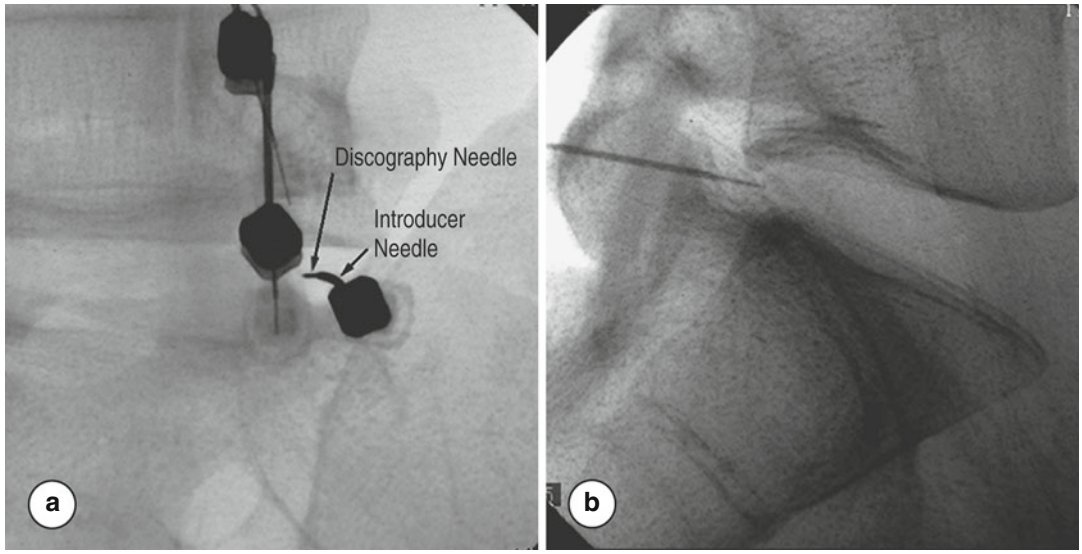

Fig. 8.9 (**a**) Oblique view of L5–S1 needle position. The tip of the diskogram needle can be seen just beyond the introducer just lateral to the S1 superior articular process and medial to the iliac crest. (**b**) Lateral view. The needle is advanced slowly under direct fluoroscopic vision, and the guide needle is simultaneously retracted. The inner needle should contact the disk 2–3 mm posterior to the vertebral margin

levels; however, occasionally, due to anatomical variations (i.e., overriding iliac crest, osteophytes) or postsurgical changes (i.e., posterior intertransverse fusion mass or fusion hardware), variations in the procedure must be utilized. A detailed description of the myriad modifications with which a diskographer might be faced is beyond the scope of this chapter; however, most involve either a more lateral or more medial needle insertion with the disk puncture needle bent or curved to varying degrees. Rarely, the posterior interpedicular, transdural, approach must be used for disk puncture. This technique increases the chance for morbidity since the dura is punctured twice. Risks and benefits of this technique must be weighed. At the L2–L3 level and above, the posterior approach should never be used due to the real risk of impaling the spinal cord.

Disk puncture at L5–S1 can be technically more challenging than the L1–L4 levels when due to the increased inter-facet distance and the proximity of the iliac crest which obscures direct access to the disk nucleus. When optimal obliquity is not possible due to bone, less rotation is required. After the L5–S1 intervertebral disk has been identified and the superior end plate of the S1 vertebral body is aligned with the X-ray beam, the image intensifier is ipsilaterally obliqued until the ilium or sacral ala obscures the disk target. Counter rotation then is used to evidence a clear path to the lateral disk access. At this point, the S1 superior articular process (SAP) may be only 25 % of the distance between lateral vertebral borders. Less than 2 cm of the L5–S1 disk is visualized between the superior articular process of S1 and the sacral ala (Fig. 8.9). Unlike the direct approach at the levels above, a slight to marked curve or "hockey-stick" bend is required for the diskogram needle insertion at this level. Under the oblique fluoroscopic view, the introducer needle is advanced toward the bony notch between the S1 superior articular process (SAP) and sacral ala. The needle tip should be immediately adjacent to the anterolateral aspect of the S1 SAP (Fig. 8.9). Next, sterile gauze is used to curve the distal 2–3 cm of the diskogram needle into a smooth arc in the direction opposite the bevel (Fig. 8.10). The degree of curve is operator dependent, based on the amount of medial deflection required to reach the center of the disk. Under a live lateral fluoroscopic view, the curved diskogram needle is advanced through the guide

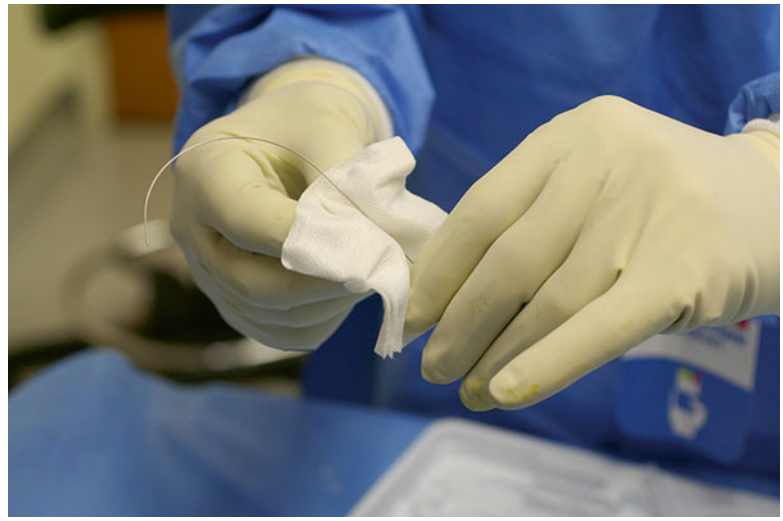

Fig. 8.10 Operator uses sterile gauze to bend the distal tip of the diskogram needle (bevel facing out). This technique is often used at the L5–S1 disk space (Photo courtesy: Richard Derby, MD)

needle until the tip emerges and is felt to gain purchase in the outer annulus. The needle is then directed in a medial and slightly posterior course around the SAP to stay within the safe region (Fig. 8.4). For some diskographers, the 18/22 gauge needle combination may be easier to direct versus the 20/25 gauge needle combination used at upper levels. Obese or muscular patients may require longer needles. Once the diskogram needle reaches the annulus fibrosus, its position is checked in both AP and lateral views. In the lateral view, the needle should contact the disk 2–3 mm posterior to the vertebral margin (Fig. 8.9b), and in the AP view, the needle should ideally be on a line bisecting the midpoint of the L5 and S1 pedicles. The needle course must be closely monitored; if the needle does not curve sufficiently in the medial direction, it will not reach the center of the disk; moreover, it may strike the ventral ramus. If the needle does not track medially and posteriorly, it must be removed and its curvature accentuated. Once the disk puncture needle is within the outer annulus and is slowly advanced, the introducer needle can be withdrawn to reinstitute and accentuate the bend on the disk puncture needle facilitating medial deviation. As mentioned previously, if the needle contacts bone, determine whether the superior articular process or the vertebral body has been encountered and make appropriate adjustments. Ideally, the final needle position is the center of the disk; however, there is leeway. In severely degenerated disks, the needle position is not as crucial because the contrast spreads throughout the disk due to loss of the intrinsic disks architectural integrity. Ideally, the needle should be within 4–5 mm of the disk center on AP and lateral fluoroscopy.

8.7.1 Disk Provocation

Diskography is a provocational test which attempts to mimic physiologic disk loads and evoke the patient's pain by increasing intradiscal pressure with an injection of contrast medium. Increased intradiscal pressure is thought to stimulate annular nerve endings, sensitized nociceptors, and/or pathologically innervated annular fissures. Historically, pressure standards have been lacking, no doubt leading to erroneous conclusions. This approach is taxonomically unsound; emerging standards require unambiguous operational criteria that establish a threshold intensity for both pain response and stimulation intensity. Both require a precise method to apply the stimulus and strict criteria for interpretation. The intensity of the provocation stimulus must be carefully controlled through the skilled operation of a manometer syringe or an automated manometer. A 3 cc syringe with manual thumb pressure is still utilized by some operators, but this does not reflect current standards. Stimulus intensity can also be quantified with a controlled inflation

syringe and digital pressure readout, permitting more precise comparisons between patient disks and between diskographers.

Most abnormal disks will be painful between 15 and 50 psi a.o. [43] and are termed "mechanically sensitive" based on a four-type classification introduced in the 1990s by Derby et al. in respect to annular sensitivity [44]. Disks which are painful at pressures <15 psi a.o. are termed low-pressure positive or "chemically sensitive" disks [44]; if painful between 15 and 50 psi a.o., they are termed "mechanically sensitive" disks. Indeterminate disks are painful between 51 and 90 psi a.o. and normal disks had no pain provocation. An important caveat is that a normal disk can hurt if pressurized too high with uncontrolled, manual "thumb" pressurization. Much of the recent research reporting a high false-positive rate for lumbar diskography in asymptomatic subjects used uncontrolled, manual thumb pressurization to 100 psi a.o. [45, 46]. If a disk is painful at >50 psi, the response must be reported as indeterminate, because it is difficult to distinguish between a pathologically painful disk and the pain evoked from simply mechanically stimulating a normal or subclinically symptomatic disk [47]. To limit false-positive responses, the most up-to-date diskography standards set a pressure criteria of <50 psi a.o. to define a positive response [16].

Injection speed is also a confounding factor and may account inter-operator variability in results and increased false-positive responses. At high injection speeds, the true intradiscal pressure (dynamic pressure) is higher than the recorded static pressure [48]. The dynamic pressure, measured only in research settings, is the actual pressure which would be recorded with an intradiscal pressure sensor. Currently, we measure pressure indirectly via a manometric syringe which records plateau static pressures postinjection. The pain during activities of daily living is more closely correlated to dynamic peak pressure [44]. Static pressure is reflective of dynamic pressure when recorded by needle sensor and manometer only at slower injection speeds (<0.08 ml/s) [48]. Currently, injection speed can be standardized with an automated manometer or manually by a skilled operator.

When all needles are positioned in the nuclei pulposi of the target disks, injection can commence. The patient should be awake and able to describe sensations produced by disk stimulation. The patient should be blinded to both the initiation of stimulation and the level of injection. Nonionic contrast medium combined with antibiotic is injected into each disk at a slow velocity using a calibrated injection syringe or automated manometer with digital pressure readout. The total volume injected should probably be limited to ≤3.5 ml. A standardized procedure form is recommended to record the stimulation parameters, patient response, and observations concerning internal disk morphology.

Opening pressure is reported first, with typical values from 5 to 25 psi, varying with the degree of disk degeneration. If the opening pressure is greater than 30 psi, this usually indicates that the needle tip is in the inner annulus and therefore must be repositioned. At each 0.5 ml aliquot, the following data is collected: total volume, static and dynamic pressures, pain response (intensity and concordance), pain behaviors (vocal or physical), and contrast pattern. Injection continues until one of the following end points is reached: pain response ≥7/10, intradiscal pressure ≥50 psi above opening in a disk with a grade 3 or greater annular tear or 80–100 psi in a disk with normal-appearing nucleogram, epidural or vascular pattern is evident, or a total of 3.5 ml of contrast medium has been injected.

Some severely degenerated disks may accept greater volume; however, the incidence of false-positive pain responses may increase. If the disk cannot be pressurized in a slow sustained manner, to greater than 50 psi above opening pressure at ≤3.5 ml volume (due to an annular or end plate leak or severe disk degeneration), one can use a rapid manual injection of a small volume to elicit a dynamic pressure of 50 psi above opening. However, the diskographer should be aware that in the setting of a leak, stimulation of structures adjacent to the disk (e.g., posterior longitudinal ligament, DRG, nerve roots, etc.) could provoke back pain or referred pain. Furthermore, with injection into the disk nucleus, the height of the intervertebral disk can increase causing motion of the contiguous vertebral bodies and possibly

stimulating an adjacent disk with pain provocation. This would be expected to a greater extent when high volumes of injectate are utilized or high pressures obtained.

8.8 Imaging

Anterior-posterior (AP) and lateral images of all injected disks are saved as part of the permanent record. A descriptive classification [49] is used for the fluoroscopic images: cotton ball, lobular, irregular, fissured, and ruptured (Fig. 8.11). A variety of patterns may occur in abnormal disks [49]. The appearance of the normal nucleus following the injection of contrast medium is classic: the contrast medium assumes either a lobular pattern or a bilobed "hamburger" pattern (Fig. 8.11). Contrast medium may extend into radial fissures of various lengths but remain contained within the disk (Figs. 8.11 and 8.12). Contrast may escape into the epidural spaces through a torn annulus (Figs. 8.11 and 8.13). In Fig. 8.13, note how epidural contrast outlines the location of the left S1 nerve root as it passes under the pedicle. This might explain how a patient could experience both axial pain and pseudo radicular pain. In some cases the contrast medium may escape through a defect in the vertebral end plate [8]. In other cases, the disk is completely fissured and disrupted (Fig. 8.14). However, none of these patterns alone is indicative of whether the disk is painful; that can be

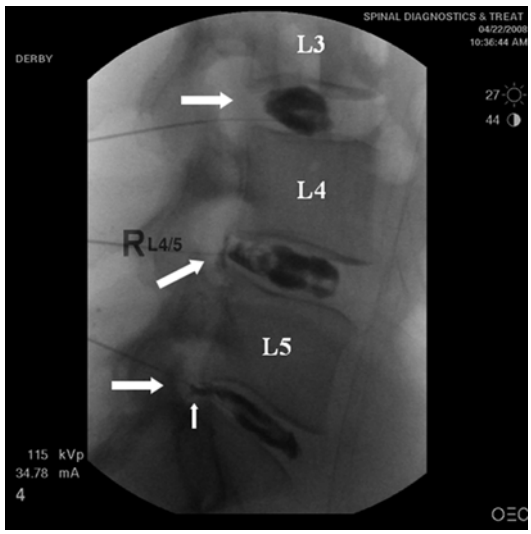

Fig. 8.11 Lateral fluoroscopic view after disk injection. Large *closed white arrows* point to disks. L3–L4 disk, classic bilobed, "hamburger" pattern; L4–L5 disk, posterior annular fissure with contrast dye outlining disk protrusion; L5–S1, posterior annular tear extends into disk protrusion with very small leak visible (*thin vertical white arrow*)

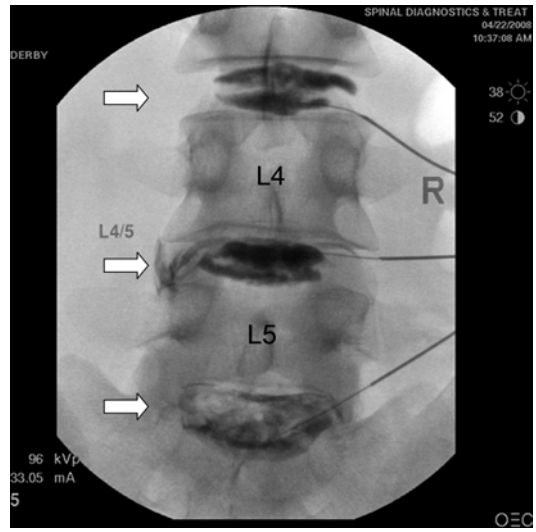

Fig. 8.12 AP fluoroscopic view of same patient in Fig. 8.11. *Closed white arrows* point to disk spaces. L3–L4 disk, bilobed dye pattern; L4–L5 disk, left-sided annular fissure extending into lateral protrusion. L5–S1 disk, marked annular disruption with small leak visible inferiorly*

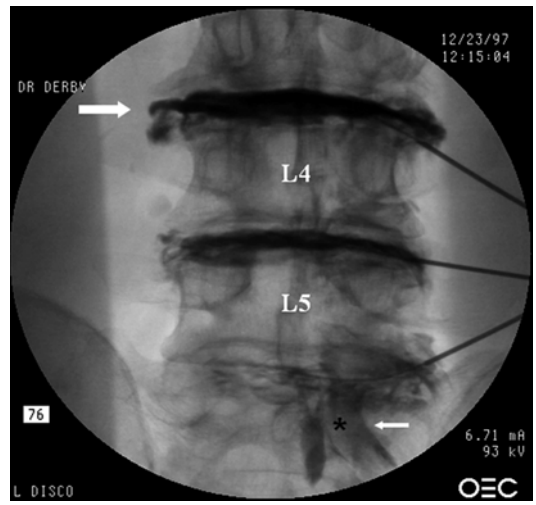

Fig 8.13 AP fluoroscopic view of lumbar spine. *, epidural leak at *left* L5–S1 level; note how contrast outlines the location of the S1 nerve root (*thin white arrow*). Large *white arrow* shows right lateral disk protrusion below L3 osteophyte

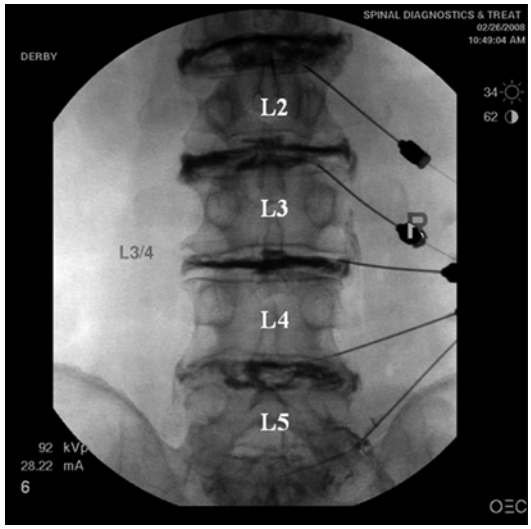

Fig. 8.14 AP fluoroscopic view of the lumbar spine. Multilevel severe degenerative disk disease from L1–L2 to L5–S1

ascertained only by the patient's subjective pain response to disk injection.

Post-diskography axial CT scanning provides the most accurate depiction of internal disk architecture. The degree of degeneration is described by dividing the disk into four quadrants [50]. If the contrast is confined to the nucleus, then no quadrant disruption is present; if the contrast is dispersed, then its location is described (e.g., single-quadrant disruption, right posterior; two-quadrant disruption, left anterolateral and right posterior, etc.). The degree of radial and annular disruption is most commonly described [50, 51] using the Modified Dallas Discogram Scale (Fig. 8.15) [16, 52, 53]: grade 0 indicates contrast is contained within the nucleus; grades 1–3 describe degree of fissuring extending to the inner, middle, and outer annulus, respectively; grade 4 describes a grade 3 annular fissure with a

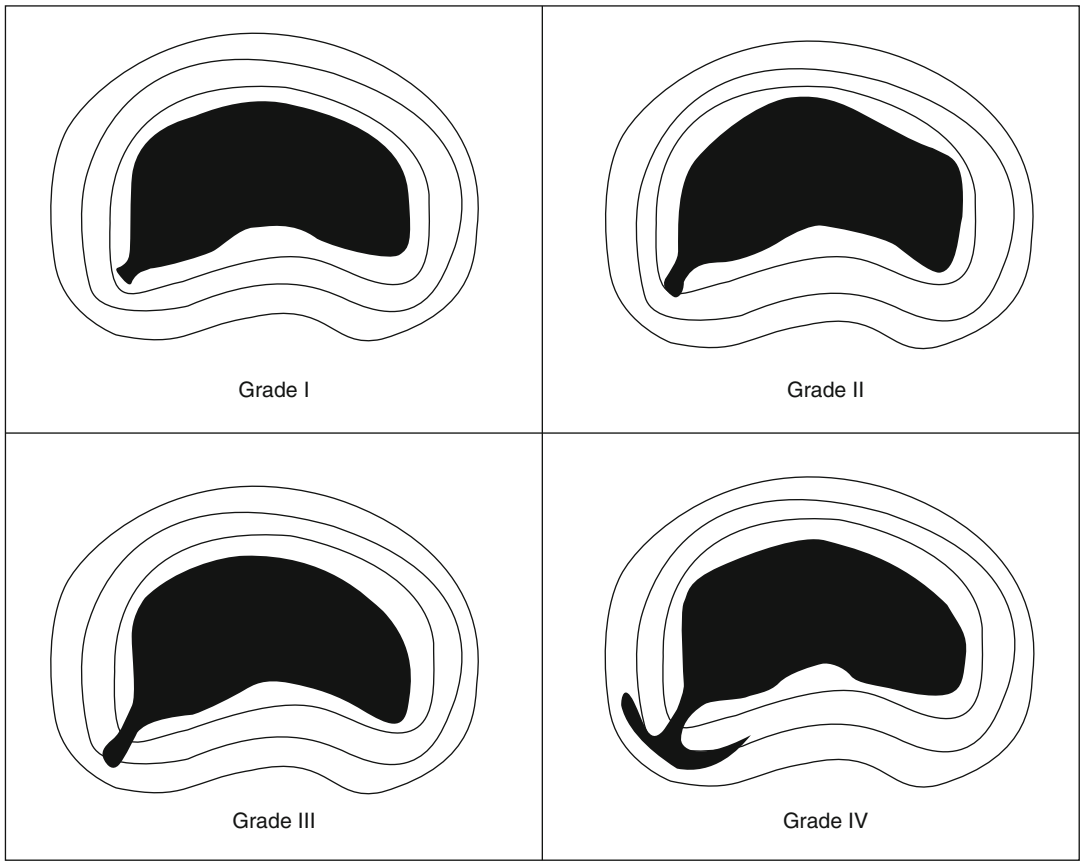

Fig. 8.15 Modified Dallas Discogram Scale. Grade 0, no annular disruption; grade 1, radial disruption into the inner third of the annulus; grade 2, contrast spread into the middle third of the annulus; grade 3, contrast into the innervated outer third of the annulus; grade 4, grade 3 with >30° circumferential tear; grade 5, spread of contrast into the epidural space (Adapted from Endres and Bogduk [29], p 23)

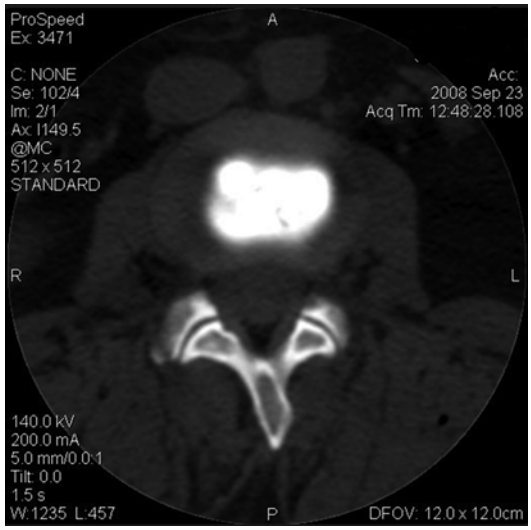

Fig. 8.16 Axial post-diskography CT scan with grade 0 annular tear. Contrast is contained in the nucleus pulposus

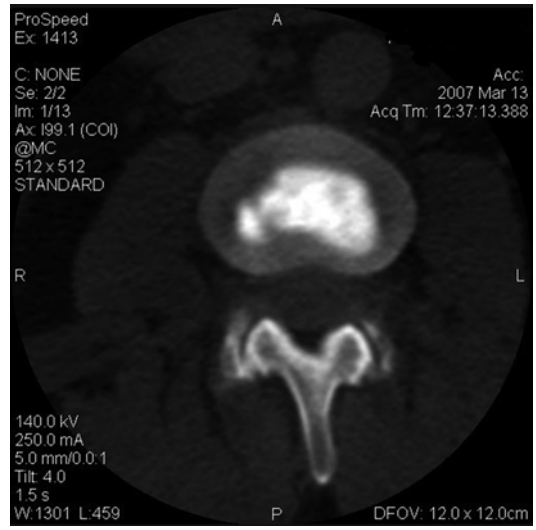

Fig. 8.18 Axial post-diskography CT scan with grade 1 and 2 annular tears. Contrast extends slightly into the inner annulus in the right posterior quadrant and into the middle annulus in the left posterior quadrant

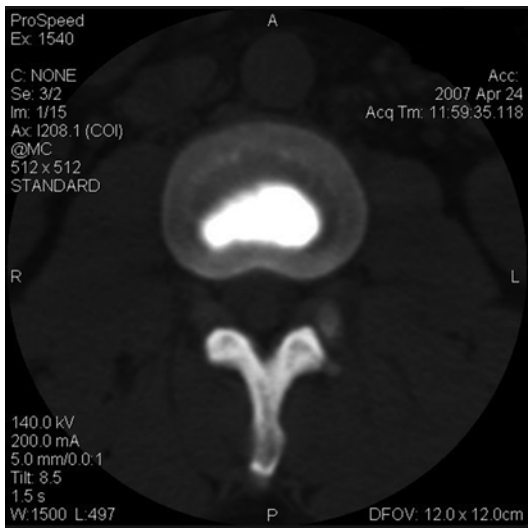

Fig. 8.17 Axial post-diskography CT scan with grade 1 annular tear. Contrast extends slightly into the inner annulus in the right posterior quadrant

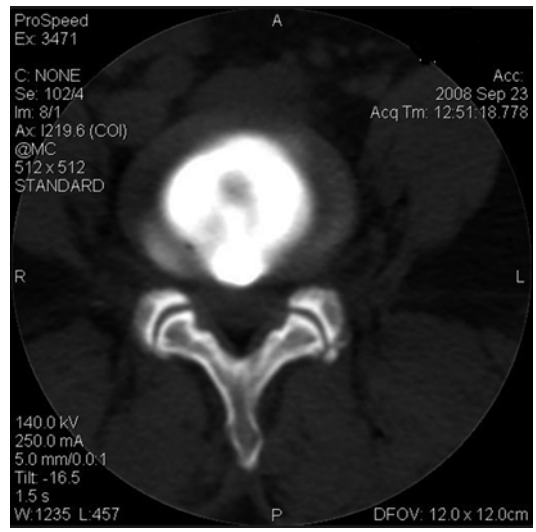

Fig. 8.19 Axial post-diskography CT scan with grade 3 annular tear. Contrast extends posteriorly to the outer annulus within a contained protrusion

greater than 30° circumferential arc of contrast (Figs. 8.16, 8.17, 8.18, 8.19, and 8.20), and a grade 5 annular tear indicates rupture or spread of contrast beyond the outer annulus into the epidural space or foramen (Fig. 8.13).

8.9 Diskography Standards

Both the techniques for performing diskography and the criteria for interpreting the findings have been in a constant state of evolution since their

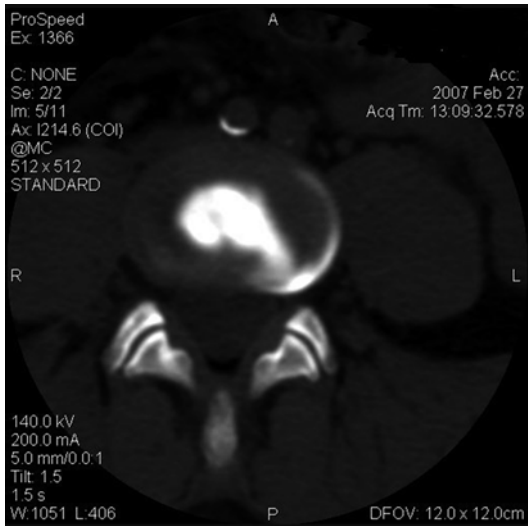

Fig. 8.20 Axial post-diskography CT scan with grade 4 annular tear. Contrast extends into the left posterior quadrant and into a circumferential tear

introduction in the 1940s. Until very recently, diskography has been performed without strict operational standards with respect to pressure limits, injection speed, volume, and validated clinical end points. The current standard for determining a positive response to diskography with the use of pressure-controlled diskography is pain ≥7/10, pressure <50 psi a.o., concordant pain, grade 3 or greater annular tear, ≤3.5 ml volume, and at least one negative control disk [16]. One can refine the criteria by adding the Walsh criteria, which stipulate that a positive response includes ≥2/5 pain behaviors (guard/brace/withdraw, rubbing, sighing, verbalizing, and grimacing) [54]. Provocation diskography is the best diagnostic test we have to diagnose diskogenic pain. However, if performed without consistent operational and interpretation standards, diskographers can obtain inaccurate results.

8.10 Caveats

The following are techniques employed by experienced diskographers to optimize performance of the test, as well as limit false-positive and false-negative responses:

1. The diskographer must be skilled in needle placement; otherwise, further pain provocation will be hard to interpret. Inexperienced diskographers often impale the adjacent segmental nerve or create significant tissue trauma from multiple needle insertion attempts.
2. Carefully evaluate pain produced ipsilaterally to the needle insertion site. Referred pain may be caused by the diskogram needle impinging upon the dorsal root ganglion. Gently "jiggle" the needle to distinguish needle pain from diskogenic pain.
3. Transient pain may be provoked if an asymptomatic fissure or previously healed annular tear with a fibrous cap is abruptly opened during pressurization. A true positive pain response is ≥7/10 and sustained for greater than 30–60 s; true diskogenic pain is less likely to decrease rapidly. Pain which resolves within 10 s should be discounted. Clinically, patients with diskogenic pain tend to have increased pain postoperatively and an exacerbation of symptoms for 3–7 days.
4. Confirm all positive responses with manual re-pressurization with a small volume. If re-pressurization does not provoke concordant ≥7/10 pain at <50 psi a.o., then the response is considered indeterminate.
5. If the patient has significant pain in a disk without a grade 3 tear (adjacent to a positive response disk), consider injecting 1 ml of 4 % Xylocaine into the painful adjacent disk and retest the normal-appearing disk in 10 min. One may find that the disk is no longer painful. There is likely segmental overlap with innervation or stimulation of the adjacent disk due to vertebral body movement.
6. Injected volume should be limited to 3.5 ml. Painless, morphologically severely degenerated disks can be made painful if excessive volume is injected.
7. When diskography is performed on disks status post prior diskectomy, the false-positive response is likely higher. The results should be reported as indeterminate unless the disk is painful at low volume and low pressure.

8.11 Post-procedure Care

After the procedure, patients are taken to the recovery room for vital sign and clinical status monitoring by nurses trained in spine injection management. The patient is checked immediately post-transfer and 30 min post-procedure for any subcutaneous bleeding. Analgesic medications (oral, IV, or IM) is provided as needed. The patient is advised to that they may experience an exacerbation of their typical symptoms for 2–7 days. The patient is instructed to contact the office if he or she develops fever, chills, or severe (or delayed) onset of pain. Patients are observed and discharged according to institutional protocol. Typically, the patient is discharged to the care of a responsible adult and instructed not to drive for the remainder of the day. All patients should be contacted by phone 2–4 days post-procedure to screen to complications or adverse side effects.

8.12 Potential Risks and Complications

Post-diskography complications are well described [25, 55]. Complications can occur secondary to the disk puncture itself and to misadventures during needle placement or can be related to medications utilized. Complications vary from minor (e.g., increased low back pain, nausea, headache) to major (diskitis, seizure, permanent neurologic injury, and death) [56].

Concern over prolonged pain after diskography has been overblown. In the 1960s, Holt reported prolonged low back pain after diskography [57]; however, serious criticisms were raised about this author's patient population (prisoners), technique, and the use of noxious Hypaque dye. More recent studies also have serious shortcomings. The claim that diskography causes prolonged pain at 1 year in subjects asymptomatic of low back pain who underwent diskography is based on six patients [58]. However, a closer look must be taken at these six patients, as they are not "psychologically" representative of patients undergoing PD. All patients had been diagnosed as distressed somatics or with somatization disorder. Two of the six patients were chronic pain patients status post failed cervical fusion, on daily opiate medications with active worker's compensation claims. Psychometric testing of these two patients also revealed that they were distressed somatics. The other four patients had a primary diagnosis of somatization disorder; two of these four patients were unable to tolerate the initial needle placement at more than one or two levels and were excluded from further study on diskography, yet they were included in the 1-year follow-up publication reporting that diskography caused prolonged pain. Such a small sample size limits generalizability of the conclusions; moreover, it is well recognized that persons with somatization disorder commonly complain of recurrent pain and conversion phenomena (pseudoneurologic symptoms) and are at risk for iatrogenic illness [59]. Furthermore, somatization disorder patients are hospitalized or undergo surgery three times as often as depressed patients [60].

Diskitis is the most common serious complication of diskography, reported to be less than 0.15 % per patient and 0.08 % per disk [19]. The incidence of diskitis has been clearly diminished with the double- vs. single-needle technique [24]. Also, with careful preprocedure screening for infection (e.g., UTI or skin), aseptic skin preparation, styletted needles, and intravenous and intradiscal antibiotics, diskitis is now very rare. Over a 10-year period, in our clinic (RD), only one case of diskitis per over 2,000 patients has been recorded, while in the practice of the other author (ML), in over 5,000 disks injected, no cases of diskitis are known. In these practices using standard prophylactic measures, the combined rate of diskitis is less than 1/11,000 or <0.009 %. To prevent diskitis, the authors recommend a surgical skin preparation and draping, a double-needle technique, and intravenous prophylaxis with antibiotics before the procedure as well as intradiscal antibiotics. However, even with prophylactic antibiotics, an epidural abscess after diskography has been reported [61, 62].

The most common causative organisms for diskitis after lumbar diskography are *S. aureus*, *S.*

epidermis, and *E. coli* [25, 63, 64] suggesting inoculation with surface flora or inadvertent bowel perforation. Clinically, the patient with diskitis presents with severe, unremitting, disabling pain in the days to weeks after the procedure. The patient may report a change in the quality of their pain as well as typical relieving factors. Some patients have a fever, although this is not a universal symptom. The workup should include a physical examination, laboratory, and imaging studies. Laboratory tests include complete blood count (CBC) with differential, C-reactive protein (CRP), sedimentation rate erythrocyte sedimentation rate (ESR), and blood cultures. The CRP usually increases within days of onset of infection; the ESR is not as sensitive and may not be elevated for a month. If the end plates have not been breached, the blood cultures and CBC will be normal. MRI is the preferred imaging modality [65–67]. Technectium-99 bone scan is less sensitive and specific than MRI [68]. MRI within 3–4 days of symptoms shows increased T2 signal in the disk and end plate hyperemia. Biopsy in the acute phase, before end plate breach, is more likely to be positive. After end plate breach, sanguineous spread creates a sterile environment and activation of the immune system [69]. Treatment of diskitis typically requires prolonged antibiotic therapy, although some mild self-limiting cases have been reported [69]. Empyema or abscess formation requires CT-guided drainage or surgical intervention [70–72].

Striking a ventral ramus is a potential hazard but may be avoided by careful attention to correct technique. The needle should be prevented from straying beyond its required and intended course. In a conscious patient, contact with the ventral ramus will be obviously indicated by a severe, sharp lancinating pain. Other complications include spinal cord or nerve root injury, cord compression or myelopathy, urticaria, retroperitoneal hemorrhage, nausea, convulsions, headache, and, most commonly, increased pain [19]. Disk herniation following diskography is very rare [73], and there is little evidence that diskography damages the disk [74]. Freeman et al. recently reported no histological damage following needle insertion into sheep disks [75]. Death after diskography was reported in a patient who inadvertently received contrast dye mixed with cefazolin (12.5 mg/ml) intrathecally. She developed intractable seizures and coma and ultimately died [76].

8.13 Diskography Controversies: Brief Literature Review

8.13.1 Utility of Provocation Diskography

While numerous papers have examined the usefulness of diskography, some physicians still question its reliability [58, 77]. Critics point toward mismatches between morphological features, clinical complaints, and false-positive rates. Lumbar provocation diskography for the diagnosis of abnormalities involving intervertebral disks has been used extensively as a diagnostic tool for evaluating low back pain (LBP) since the 1950s. Diskography has always been controversial, with both staunch proponents and opponents. Diskography is not meant to be a stand-alone test. Its proper use is in the diagnostic algorithm for chronic, intractable low back pain unresponsive to conservative care and when the patient is considering intradiscal or surgical treatments. Perhaps unappreciated is the value of diskography in ruling out adjacent segment diskogenic pain and limiting the number of levels treated surgically. Diskography remains the criterion standard for visualizing internal disk architecture. As a provocation test, despite its liabilities and limitations, diskography is also our best means of diagnosing diskogenic pain. Provocation diskography has an 81 % sensitivity and 64 % specificity for pain [78].

Provocation diskography (PD) is commonly compared to CT or MRI of the spine, yet PD is distinctive in that it is both an imaging and provocation test. MRI is unable to discern a painless from a painful disk. We are well aware that morphologic abnormalities of the disk are common in both patients with and without chronic low back pain. In one series, 78 % of patients with chronic low back pain had abnormal imaging findings on

diskography combined with post-CT scanning [73, 79]. Morphologic abnormalities also increase with age [55, 80]. Admittedly, abnormal morphological structures revealed by diskography without provocation are too nonspecific to be clinically useful; therefore, positive results should be limited to those eliciting concordant pain [54, 77]. In 1982, Millete and Melanson [81] reported retrospectively that concordant pain was evoked by injection in 37 % of patients with a diskographic morphologic abnormality. Studies in the 1990s and 2000s on the prevalence of painful internal disk disruption in patients presenting to tertiary referral centers with chronic low back pain range from 26 % to 39 % [82, 83].

For most cases, MRI is sufficient for advanced imaging; however, provocation diskography adds additional useful diagnostic information to confirm or refute the hypothesis that a particular disk is the source of the patient's pain. Neither high-resolution CT nor MRI demonstrates annular morphology with the same detail as diskography [84, 85]. CT-diskography was found more sensitive than MRI in detecting early annular disruption. In 18/177 disks with a normal T2-weighted MRIs, annular and radial fissures were revealed on CT-diskography [86]. When compared to surgical findings, in 94 % of patients, CT-diskography correctly diagnosed the type of disk herniation, including in the previously operated spine [86]. Diskography has also been correlated to pain drawings [87].

The high-intensity zone (HIZ) has been proposed as a marker for painful disks [52, 88], yet while highly specific, the sensitivity of this finding is only 26 %, limiting the usefulness of the HIZ in selecting patients for surgery [89]. However, if an HIZ is contained within a protrusion, there is a correlation with a positive diskogram response [90]. Modic changes are a highly specific marker pain at diskography [91]. These authors have suggested that diskography is not needed if the index disk level has Modic type I changes. Surgical decision-making requires a high level of diagnostic confidence, and research has shown that MRI cannot always reliably predict which disks will be symptomatic with diskography [92, 93]. Diskography has fallen out of favor in many countries due to the studies reporting a high false-positive rate and potential disk injury after PD, in spite of subsequent studies disputing these findings.

8.13.2 False-Positive Rates

Diskography's greatest liability at this time is the series of studies reporting high false-positive rates in asymptomatic subjects [46, 57]. These recent negative studies also reported a correlation between the presence of chronic pain and abnormal psychometric scores with positive diskogram responses. Early work by Holt in 1968 reported a 36 % rate of positive diskography in asymptomatic subjects, although this study contained serious methodological flaws [57]. Reanalysis of the Holt data actually reveals a false-positive rate of 3.7 % [13]. Holt's findings were also refuted by Walsh et al. [54], who demonstrated a 0 % rate of positive diskography in ten asymptomatic volunteers and established reproducible criteria for positive diskography (criteria: ≥3/5 pain (pain thermometer), concordant pain, ≥2/5 pain behaviors, pressure limited to approximately 60–70 psi a.o. (manual pressurization by a highly skilled diskographer), and abnormal disk morphology). Walsh's study was critiqued due to his asymptomatic subject choice of primarily young men in their 20s. Using strict pressure criteria and pressure manometry, Derby et al. [94] studied 13 asymptomatic volunteers and also reported a 0 % false-positive rate.

Carragee [46] performed diskography on several subject populations asymptomatic of low back pain and reported the following false-positive rates: residual pain after iliac crest bone harvest, 50 %; no low back pain and no chronic pain, 10 %; chronic cervical pain, 40 %; post-diskectomy, 35 %; and somatization disorder, 75 %. He also studied symptomatic subjects with "benign" or "mild persistent low back pain" and reported a false-positive rate of 36 %.

More recent literature has reached different conclusions. A critical examination of all the

studies since the 1960s including a systematic review and a meta-analyses of false-positive rates [13] shows that an acceptably low false-positive rate can be achieved using PD utilizing the ISIS/IASP standards for a positive diskogram: pain ≥7/10, concordant pain, pressure <50 psi a.o., ≥ grade 3 annular tear, volume limit ≤3.5 ml, and presence of a negative control disk. A recent meta-analysis of all studies of asymptomatic subjects undergoing diskography obtained a specificity of 0.94 (95 % CI 0.89–0.98) or a false-positive rate of 6 % per disk and 9.3 % per patient [13]. Among subjects asymptomatic of any confounding factors, one can obtain a false-positive rate of 3 % per patient and 2.1 % per disk; for subjects with chronic pain, the rate is 5.6 % per patient and 3.85 % per disk. Taken alone as a group, post-diskectomy subjects appear to have a slightly higher false-positive rate of 15 % per patient and 9.1 % per disk. Given our limited knowledge of diskography in post-diskectomy patients and the possibility that provocation may open previously healed granulation tissue along surgical planes, diskographers may consider pressure- and speed-controlled manometry and low pressure and volume limits for defining a positive value. Among subjects with somatization disorder, the false-positive rate is 50 % per patient (95 % CI 0–100 %) and 22 % per disk. Concern has also been raised regarding chronic pain and psychologic comorbidity as significant confounding factors in patients undergoing diskography. Is chronic pain a significant confounding factor? Evidence indicates that patients with chronic or chronic intermittent low back pain respond similarly to disk stimulation as do asymptomatic volunteers undergoing diskography. Derby studied the effect of chronic low back pain on negative and positive disks versus asymptomatic controls [94]. For example, comparing disk stimulation in disks with grade three annular tears, there was no difference in pain scores (1.6/10 versus 1.1/10) reported by asymptomatic volunteer disks compared to negative patient disks. Patients undergoing diskography can readily distinguish between a negative and positive disk level [94, 95]. Shin et al. also recently reported that a majority of patients with grade 4 patients could distinguish between positive and negative disks by magnitude of pain response [95]. The argument that a majority of patients with chronic pain who undergo diskography will overreport pain is not supportable.

Are psychologic comorbidities confounding factors? Perhaps, but the data is conflicting. Carragee [46] studied six subjects with somatization disorder. Only 4/6 subjects were able to complete their diskogram because of pain (the cause of the pain is not reported, i.e., secondary to placement of diskogram needles versus disk stimulation). From this small sample size, a 75 % false-positive rate with a 95 % confidence interval from 0 % to 100 % was reported. Given the type of patients studied and the statistical shortcomings of the analysis, the generalizability of these findings is limited. Furthermore, contrary to these previous findings, a larger, randomized-controlled trial comparing diskography results of 25 patients with and without somatization disorder found no significant difference in positive responses between groups [96]. There was also no difference in positive responses in patients with depression and/or general anxiety disorder. Derby et al. [21] reported Distress and Risk Assessment Method (DRAM) scores of 81 patients undergoing diskography: 15 % (12/81) were normal, 52 % (42/81) were at risk, and 33 % (27/81) were abnormal (distressed depressive or somatic). The positive rates of diskography were not statistically significant by subgroup ($p > 0.05$). In patients with chronic low back pain, no correlation was found between presenting DRAM score and diskography result.

Concern has also been raised that diskography is falsely positive in patients with "benign" or chronic persistent mild low back pain [97]. To be considered a subject with "benign" low back pain, subjects reported that they did not restrict their activity or seek medical care for their back pain. They reported their pain as mild to moderate or 2–4/10. Provocation diskography was reported as positive in 9/25 patients; thus, the author reported obtaining a 36 % "false-positive" rate. Of note, 72 % (18/25)

of the patients had chronic pain due to failed cervical surgeries and were on medications, including opiates for their pain, which may have masked their pain. In addition, patients taking narcotic medications for as little as 1 month might be expected to evidence hyperalgesia and allodynia resulting in an inaccurate rate of false-positive results. Moreover, such subjects may have been understandably reluctant to seek medical care for their low back pain after a failed cervical surgery. The 36 % reported false positives are arguably true positives. One could argue that these chronic low back pain volunteers are no different from patients undergoing diskography who often have varying degrees of and duration of pain flare-ups. Given the history of neck pain in these patients, the fact that some have painfully internally disrupted disks in their lumbar spine is not surprising. In fact, the reported prevalence of positive diskograms in patients referred for chronic low back pain ranges from 26 % to 39 % [83, 98]. The argument that these positive responses represent "false-positive responses" is not supportable. Diskography was not developed and should not be used to determine the clinical significance of a patient's perceived suffering and disability related to chronic low back pain.

In fact, one of the reasons researchers [45, 46] obtained so many false-positive responses may have been because of the high pretest probability of diskogenic disease in the majority of the research subjects. All subjects, except for the somatization disorder and iliac crest pain patients, had a history of known diskogenic pain severe enough to require surgery. The subjects may have had asymptomatic or minimally symptomatic disease provoked with the use of high pressurization (up to 100 psi a.o.) or high dynamic pressures in the setting of manual diskography. Also, we know that the co-occurrence of cervical and lumbar diskogenic disease is commonplace. MRI studies of twins showed 79 % and 64 % heritability for "severe" disease in the cervical and lumbar spine, respectively [99]. In one follow-up study of 200 patients who underwent cervical surgery, 100 % had significant low back pain episodes (suggestive of disk herniation) and/or underwent back surgery [100]. Another reason for reported high false-positive rates may have been the use of uncontrolled manual pressurization (to 100 psi a.o.) with measurement of only static pressures [48]. Lastly, in some prior studies, false-positive rates are reported per patient instead of per disk (subjects status post iliac crest harvesting, status post-diskectomy, or with somatization disorder), leading to a significantly higher absolute number. Provocation diskography is a test designed to confirm or refute the hypothesis that a particular disk is a source of a patient's pain; however, a positive diskogram does not rule out other significant sources of pain.

Diskography continues to be controversial. In 2009, researchers reported [101] that modern diskography techniques utilizing a small-gauge needle and limited pressurization resulted in accelerated disk degeneration, disk herniation, loss of disk height and signal, and the development of reactive end plate changes compared to match controls [101]. In 2013, Ohtori et al. [102] obtained follow-up MRIs 5 years after diskography, utilizing contrast and bupivacaine ("diskoblock" or analgesic diskography). One concern raised by opponents of diskography in addition to the effects of disk puncture is a possible toxic effect to disk cells due to anesthetic. Ohtori found neither evidence of accelerated disk degeneration in patients who underwent modern diskography with contrast nor accelerated degeneration with the use of bupivacaine versus controls.

An additional concern raised by the recent study [101] was the effects of disk puncture as a cause of disk injury. Martin et al. [103] compared the effects of 29 gauge versus 26 gauge needles placed into mouse disks. The larger needle led to increased disk degeneration at 8 weeks; the smaller needle did not initiate degenerative changes. If this model is extrapolated to human disks, a 29, 26, or 25 gauge needle placed into the disk of a 70 kg male versus that of a mouse weighing an average of 1 oz. would not be likely to cause any radiologically or clinically significant disk degeneration. Continued long-term follow-up MRI of subjects undergoing diskography is needed to clarify long-term effects.

8.14 Analgesic Diskography

Due to the controversies over provocation diskography and conflicting studies regarding high false-positive rates, new diagnostic methods have arisen. Just as facet pain is diagnosed by blocking a medial branch nerve with local anesthetic, the concept of blocking intradiscal nociceptors arose. Previously, anatomists reported that only the outer annulus of the disk was innervated; however, in painful disks, sensory nerves extend to the inner annulus and nucleus pulposus [10, 104, 105]. Painful internally disrupted lumbar disks also have greater concentrations of sensory fibers in their nucleus and end plates than normal disks and along annular fissures [9, 11, 106]. In disks sampled from surgery, researchers find higher levels of pro-inflammatory cytokines, including IL-8 and PGE2, thought to create hyperalgesia, thus "sensitizing" the disk mechanoreceptors [107, 108].

The first reported use of analgesic diskography (AD) was in 1948 by Hirsch [109]. He injected 0.5 cc of 1 % Novocain into the disks of patients who reported pain during disk puncture or needle movement. For the ensuing 2–4 h, after local anesthetic injection, these subjects were essentially free of back pain with normal mobility and negative straight-leg-raise testing. Subsequently, various surgeons have used the injection of local anesthetic to confirm the results of PD [11, 109, 110]. In the 1970s, Roth [110] studied AD in the cervical spine and reported that analgesic diskography was diagnostically superior to PD. He reported 93 % good to excellent surgical outcomes in 71 patients undergoing cervical fusion. Other descriptions of AD have largely been "embedded" in the methods sections of various diskography studies. Coppes et al. [11] used 0.5–1.0 ml of bupivacaine as a confirmatory test after provocative diskography and reported 1–4 h pain relief.

Alamin [111–113] was the first to formally study analgesic diskography using a balloon-tipped catheter (Functional Analgesic Diskography, FAD, Discyphor™ Kyphon, Sunnyvale, CA, USA) which he codeveloped. The catheter can be anchored in the disk for pre- and post-functional positional testing after instilling the disk with local anesthetic. Alamin et al. [113] compared the results of standard pressure-controlled PD to functional anesthetic diskography (FAD) in a study with 52 chronic low back pain. PD was performed first; FAD was performed in positive cases or in patients with clinical features and imaging studies highly suggestive of symptomatic disk degeneration. A positive FAD response was defined as a 2 or greater decrease in VAS. Discordant results were found in 46 % of the patients; 26 % of patients with positive PD had negative findings on the FAD test; 16 % had positive findings at a single level where the PD had found 2 or more positive levels; 4 % of patients had new positive findings on FAD. He reported that using FAD immediately following PD, the false-positive rate of PD could be significantly reduced.

DePalma [114] investigated whether outer annulus fissures stimulated during PD are a source of diskogenic pain. He found that 80 % of painful disks diagnosed by PD were also diagnosed with FAD, demonstrating >50 % pain reduction. Approximately 10 % demonstrated partial pain reduction. Unlike Alamin's results [113], DePalma found no correlation between psychiatric history and positive PD/FAD. The study did not report the percentage of discordant findings between PD and AD. DePalma found a similar percentage of patients with a positive PD and negative FAD as did Alamin et al. equal to 20 % in the second published study using the FAD system.

Subsequently, Derby et al. [115] correlated data from different analgesic protocols (including the DePalma study with FAD) where compared to obtain the incidence of pain relief following injection of local anesthetic (LA) into lumbar disks that caused concordant pain during provocation testing. Subjective pain relief was compared at three separate facilities: 23 patients undergoing routine provocation diskography (PD), 47 patients undergoing combined provocative diskography (CPD) with equal volumes of LA and contrast, 120 patients injected with LA following routine PD (AD/PD, same session), 33 patients undergoing stand-alone analgesic diskography (SAAD, separate sessions), and 28

patients injected with LA through a catheter (FAD) placed during provocative diskography testing. If the criterion standard to confirm annular tears is concordant pain provocation and 80 % or greater pain relief following LA injected into lumbar disks, the SAAD, AD/PD, and FAD protocols show statistically similar 20–30 % prevalences of diskogenic pain. As yet, there is no single validated technique for analgesic diskography.

At this time the evidence is insufficient to recommend that AD or FAD replace PD. However, these tests may be useful confirmatory tests. Further research is needed to compare PD to AD, to refine technical performance of the test, to determine if AD has a lower false-positive rate than PD, and to determine if surgical outcomes are superior with AD.

8.15 Predictive Value

One of the obvious challenges with diskography, whether using provocative or analgesic diskography, is the lack of a clear "gold standard" to which the outcomes of testing for diskogenic pain can be compared. The best proxy we have for a gold standard is the outcome from the surgical intervention. Various intradiscal procedures remain poorly tested; therefore, surgical fusion is the current standard treatment for diskogenic LBP unresponsive to conservative therapy. However, this proxy also has limitations, as there are many different surgical fusion techniques used to treat diskogenic pain. Carragee et al. [116] compared circumferential fusion for single-level diskogenic pain determined by PD with the results of the same surgery for single-level isthmic spondylolisthesis. High-grade clinical success was achieved in 72 % (23 of 32 patients in this control group) of the patients with isthmic spondylolisthesis versus 27 % (8 of 30 patients) with presumed diskogenic pain. The authors of this study attributed the poor response of the "diskogenic pain" patients to the high false-positive rate of PD; however, other authors also point out that isthmic spondylolisthesis and painful internal disk disruption are fundamentally different clinical entities in terms of their predictable response to fusion.

Several other studies have reported on surgical outcomes in patients undergoing diskography.

Colhoun et al. [117] studied 195 patients with axial pain and reported that of 137 patients with diskogram positive for disk disease and provoked concordant pain, 89 % derived significant, sustained clinical benefit from operation. Twenty-five patients showed morphologic disk abnormalities, but no provocation of concordant pain on diskography. Among this group, only 52 % had clinical success. Blumenthal et al. (1988) [118] reported that 74 % of patients with internal disk disruption returned to work following anterior lumbar fusion performed based upon diskography. In a multicenter surgical and nonsurgical outcome study after pressure-controlled diskography, Derby et al. [44] stated that precise prospective categorization of positive diskographic diagnoses may predict treatment outcomes, surgical or otherwise, thereby greatly facilitating therapeutic decision-making. In addition, patients with highly sensitive disks at low pressure appear to achieve significantly better long-term outcomes with interbody/combined fusion than with intertransverse fusion. Lettice et al. [119] used pressure-controlled manometric PD with strict criteria (pressure <50 psi a.o. with grade III annular tear) to compare results of short-segment (1–2) vs. long-segment (3–5) fusions. Typically long-segment fusions show progressively poorer clinical outcomes. In an SF-36-based outcome study of total joint arthroplasty, PCS score increments of 10 and 12 have been reported. Similar PCS score improvements (11.35 and 10.06 for the short- and long-segment groups during the 2-year follow-up, respectively) [120] were obtained in this study. The authors attributed this success to the use of criterion-based pressure-controlled, manometric PD.

Recently, Cooper et al. [121] studied the prognostic value to lumbar disk stimulation and to

validate the ability of disk stimulation to predict treatment response, using the ISIS guidelines for positive (>70 points), negative (40–60 points), and indeterminate (<40 points) responses [16] and physician determination of diskography: positive, indeterminate, and negative. He performed an opportunistic audit of patients who underwent diskography and their surgical outcomes; the data was collected retrospectively; thus, no interference occurred with respect to diskographer or surgeon. Patients agreed to be followed up regarding response to treatment, pain scores, the use of health care, and functional status. Eighty-nine patients were included in the study. The results demonstrated that diskography was predictive of treatment response. A cutoff score of >50 and physician interpretation both showed statistical significance. A patient undergoing fusion with a score of >50 had the following results: 5× more likely to return to >25 % ADLs, 3.4 times more likely to return to >50 % ADLs, and 3.3 times more likely to have less pain than patients who did not choose fusion. With an ISIS score of >50, fusion outcome was superior to IDET. With a score of <50, conservative treatment was superior to fusion. Cooper et al.'s [121] final recommendation was to utilize an ISIS score of 50 as a cutoff with clinical judgment to obtain the best patient outcome.

Two authors have reported on surgical fusion outcomes using FAD or AD. Alamin [111, 112] has followed 16 patients out to 6 months: the mean Oswestry score decreased from 55 to 25; mean back pain VAS decreased from 6.9 to 2.6. Ohtori et al. [122] performed an RCT comparing surgical outcomes of 15 patients undergoing PD versus AD. At 3 years, the VAS score, Japanese Orthopedic Association Score, Oswestry Disability Index, and patient satisfaction score were superior ($p < 0.05$) in the AD group.

Finally, although imperfect, diskography is safe in experienced hands, shows substantial sensitivity for identifying painful disks, and may predict surgery-related outcomes. Analgesic diskography may give additional value to confirm a positive finding on PD.

8.16 Summary

For over 50 years, lumbar diskography has been widely used for evaluating diskogenic low back pain. Since these earlier negative studies, diskography techniques and diagnostic criteria have also advanced. Complications are minimal in skilled hands. Most importantly, pressure- and speed-controlled manometric diskography has been adopted. Previous diskogram studies assessing false-positive rates had limitations including the use of excessive pressurization, manual injections, uncontrolled injection rates, unrecorded and/or unreported opening, and dynamic pressures, volumes, and maximal volumes. Walsh et al.'s [54] study performed by a skilled operator with strict criteria reported a 0 % false-positive rate. Derby et al. [123] used pressure-controlled manometry and precise criteria for positive diskography and also obtained a 0 % false-positive rate. We recommend positive criteria for lumbar pressure-controlled manometric diskography as follows per ISIS/IASP standards: pain ≥7/10, concordant pain, <50 psi a.o., at least grade 3 annular tear, ≤3.5 ml total volume, and at least one negative control disk [16]. Based on the use of these standards, our best estimate of the false-positive rate for lumbar diskography is acceptable. A recent meta-analysis combining all the recent diskography studies in asymptomatic subjects (including data from Carragee) obtained a 6 % false-positive rate per disk [13]. Analgesic diskography is an emerging test in which local anesthetic is used to attempt to block intradiscal nociceptors. Proponents of AD report that it has a lower false-positive rate than PD; other researchers have found various AD protocols reporting 20–30 % prevalence. AD is currently being used as a confirmatory test to PD. Recently, researchers reported an increased incidence of disk degeneration on follow-up MRI in patients undergoing diskography [101]. However, more recent study [102] has not replicated these findings. Clearly, continued research is needed. Diskography remains an important diagnostic test for diskogenic pain.

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9 Modic Changes and Symptomatic Lumbar Degenerative Disk Disease: Is There Any Correlation?

João Luiz Pinheiro-Franco and Philippe Esposito

9.1 Introduction

Low back pain (LBP) is the most common health problem for individuals between the ages of 20 and 50 years [1]. The lifetime prevalence of LBP is approximately 80 % [2]. According to the United Nations, the population is estimated to increase from 13 % of those older than 60 years now to 20 % by 2050. One out of every ten persons is now 60 years or older; by 2050, one out of five will be 60 years or older [3]. This exponential increase in age carries direct correlation with the increase of LBP. Consequently, chronic physical disability originating from LBP will become a public health priority [4]. Chronic LBP carries tremendous socioeconomic and psychological impact in modern societies.

Diagnosis of LBP is challenging. Diverse structures in the lumbar and adjacent regions have nociceptors and are, therefore, potential pain generators. Only about 20 % of LBP diagnoses can directly be linked to a specific pathoanatomical entity [5]. A primary source of LBP, lumbar degenerative disk disease (DDD), is intimately related to aging and oftentimes may not be symptomatic. LBP due to DDD is often referred in the nomenclature as "nonspecific LBP" differentiating it from specific, e.g., tumoral, infectious, inflammatory, and traumatic, causes of LBP. The term "nonspecific LBP," which accounts for 80 % of diagnoses, however, is not a satisfying diagnosis for both the patient and physician [6].

Lumbar pain in the setting of DDD may be a symptom of many complex and intricate underlying processes with multiple variables involved. The identification and diagnosis of relevant subgroups of patients with persistent, chronic LBP, preferably with a sound patho-anatomical basis, is strongly needed. Attempts to subclassify patients with LBP may result in a better targeting of treatment [7].

The aging of the functional spinal unit (intervertebral disk + facet joints) is related to LBP. The disk has its nourishment supplied by the cartilaginous end plates. Working as a double way crossroad and permitting disk nutrition and elimination of metabolites, the vertebral end plates have a crucial place in maintaining disk health. So far, the exact place of vertebral end plate degeneration in the degenerative cascade is not fully understood. Recently awarded research demonstrated that the histological degenerative changes found in the vertebral end plates preceded the degenerative changes of the nucleus pulposus [8].

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_9

This chapter attempts to (1) understand how the vertebral end plate signal changes (VESC) on magnetic resonance imaging (MRI) – named Modic changes (MC) – especially the inflammatory type 1 MC (M1) may reflect disturbances in the dynamics of the unit intervertebral disk-cartilaginous end plate-vertebral bone marrow and (2) to analyze correlations between LBP and MC.

Whether vertebral end plate degeneration, in association with mechanical and genetic factors, precedes nuclear degeneration, it remains to be definitively proved. We indeed emphasize the necessity of understanding vertebral end plate function and dysfunction and the need to comprehend eventual associations between their assumed mirror MRI images (Modic changes) and clinical manifestations. Despite conflicting evidence in the literature that MC may or may not be associated with clinical findings, a wide review of the facts is necessary.

As clinicians, we have a duty to apply basic scientific principles in our practice. In physical science, just one validated exception is sufficient to invalidate any theory. In biological science, however (where individual "natural" variation prevails), less rigor must frequently be tolerated [9]. This may be the case of MC and LBP.

9.2 Lumbar DDD: A Physiopathological Review

A detailed analysis of the physiopathological processes of DDD is beyond the scope of this chapter and is discussed elsewhere in this book. A brief overview, however, is necessary.

Disk degeneration is a natural phenomenon of the aging spine, and the distinction between physiological and pathological DDD is not obvious. DDD is deemed to be induced mechanically and mediated by biochemical responses, often concurrent with aging and probably influenced by genetic particularities [4]. Identification of apoptotic cells in intervertebral disks indicates that programmed cell death may also play a non-negligible role in the pathophysiology of disk degeneration [10–13].

The intervertebral disk is a highly specialized structure working as a fixed cushion that resists loads and allows controlled movement between vertebrae. The end plates are considered to be a dynamic barrier. The movement of molecules through osmosis allows the passage of nutrients and the elimination of metabolites [14], in such a manner that local metabolism acts in equilibrium. Disk degeneration may result from an imbalance between the anabolic and catabolic processes or the loss of steady-state metabolism. The dynamics of such end plate barrier is thought to play a key role in the onset and progression of degeneration, but the biochemical progression that regulates these changes remains poorly understood.

Disk nutrition disturbance has therefore a definitive importance in DDD process. The normal disk is the largest non-vascularized structure in the adult human body [15], and its nutrition is supplied through the vertebral end plates and thin cartilaginous plates between the vertebrae surface and the disk. The mineralized portion of the end plate is penetrated by marrow contact channels (MCC), through which capillary buds emerge. These capillary buds connect the trabecular spaces to the cartilaginous end plate, but do not penetrate into it [16]. For small solutes, diffusion may predominate, but transport of larger solutes such as proteins are believed to be significantly facilitated by the bulk flow of fluid [17] through MCC. End plate blood vessels have been observed to diminish after the first decade of life when the first signs of disk degeneration are evident [18]. Also, reduced permeability of end plates is generally seen in association with DDD and age-related changes [16]. Both of these changes may be due to calcification of the end plates and occlusion of the MCCs observed with disease and age [19–21].

The biochemical composition of the end plates, from normality through the spectrum of degenerative conditions, has been documented extensively [22]. Benneker et al. [15] demonstrated an indirect correlation between the density of openings in the osseous end plate and the morphologic degeneration grade of the disk. These results support the hypothesis that occlu-

sion of these openings may deprive the cells of nutrients, leading to insufficient maintenance of the extracellular matrix and disk degeneration.

All disk degeneration processes start early in life [8, 23]. A recent extensive study on histologic degeneration noted unequivocal signs of degeneration of disk tissue as early as the first half of the second decade (11–16 years of age) [8, 24]. In small children's disks there is a net of fine capillaries that promotes disk nutrition. During early childhood this blood supply to the vertebral end plate begins to decrease and remains as a small nutrition supporting network in the outer boundaries of the posterior anulus fibrosus. With aging, loss of proteoglycans in the nucleus pulposus occurs which is believed to be a critical factor in DDD [23, 24]. The nucleus becomes dehydrated, and the anulus fibrosus loses its organization. The load bearing in the disk structures changes and, per se, contributes to a continuum of disk degeneration. Progressive DDD may impair the disk's ability to defend against mechanical loads. A recent study demonstrated the sequential histological degenerative changes across nine decades [8]. Generally, these changes affect the end plate first, then the nucleus, and, finally, the anulus. Different spine levels behave likewise, the same sequence [8].

Tremendous changes in cellular phenotype and extracellular matrix composition are associated to DDD [23, 25] and are intimately related. Collagenous disk matrix modifies itself during aging and disk degeneration. The huge phenotype modifications may ultimately lead to disk's biomechanical failure.

Chemical events have a remarkable role in symptomatic DDD. Proinflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF) are known mediators of the peripheral inflammatory response [26, 27]. It has been demonstrated that painful disks secrete higher levels of proinflammatory mediators, such as TNF, IL-6, and nerve growth factor (NGF) compared with asymptomatic disks [28, 29]. The nucleus pulposus can produce a formidable range of proinflammatory cytokines [30–35]. The impact of these mediators in the nucleus pulposus has been confirmed in both animal and human studies of lumbar disk herniation [36]. Although inflammatory mediators seem to be native to the disk, their presence, such as cytokines and proteinases, is also conspicuous in granulation tissues [31, 37]. The influx of cytokines (TNF, IL-6, IL-1) and proteinases (stromelysin) is a common phenomenon in degenerated disks [33, 38, 39]. Degenerative disks also contain significantly upregulated activity of major matrix-degrading enzymes, the matrix metalloproteinases [40, 41]. Despite all scientific advances, the exact pathomechanism leading to increased production of inflammatory mediators by the nucleus pulposus in patients with diskogenic LBP is not fully known [28]. It has been proposed that as some disks degenerate the cells of the nucleus may be exposed to a proinflammatory stimulus leading to the formation of inflammatory degeneration which gives rise to LBP [28].

Intranuclear innervation has been suggested to be involved in pain generation. Painful disks have higher concentrations of sensory nerves than those which are asymptomatic [42]. The sensory nerves in painful disks were found in the nucleus and in the end plates. Nerve ingrowth into degenerated symptomatic disks may be mediated by chemotactic substances released by the degenerating disks [43]. Therefore, a combination of increased production of proinflammatory mediators and innervation of the nucleus pulposus may constitute the basis for diskogenic LBP. Hyperalgesia, which is known to be induced by IL-8 and PGE2 [40], may be responsible in part for diskogenic LBP.

Pain provocation studies have correlated severe LBP with relatively innocuous mechanical stimulation of the outer posterior anulus and end plate [44]. In normal disks, the posterior anulus and its adhering longitudinal ligament are innervated by the sinuvertebral nerve, a mixed autonomic and somatic nerve believed capable of nociception. Nociceptive nerve fibers normally penetrate only the outermost 1–3 mm of the annulus [45, 46]. In painful and disrupted disks, the ingrowth progresses anteriorly into

the nucleus [45]. The vertebral end plate has a similar density of innervation [47]. It has been shown that in patients with severe LBP and disk height collapse, there is an increase in the density of sensory nerve fibers into the end plates with associated defects in the end plate cartilage, strongly suggesting that the end plates and vertebral bodies are sources of pain [48]. Hence, the ingrowth of nerves and blood vessels is a significant feature of structurally disrupted disks and appears to be directly, though variably, associated with pain [45].

Other events that may contribute to nerve ingrowth are (1) the loss of hydrostatic pressure of an intact disk followed by collapse of hollow capillaries [49] and (2) the reduction in proteoglycan content [50] as aggrecan can inhibit nerve ingrowth in vitro [51].

Despite the increasing data on the pathogenesis of disk degeneration, very little is as yet known on any putative markers that identify the early and "active" stages of disk matrix alterations. Advances in imaging techniques may intend to associate histological markers with imaging findings and provide a foundation for an earlier treatment of lumbar DDD.

9.3 History

In 1984, 4 years before the classic manuscript, Modic et al. [52] noted a high MR signal intensity (suggesting inflammation or scarring) in the vertebral end plates adjacent to a marked degenerated disk in a patient who underwent chymopapain (CP) injection.

Three years later Hajek et al. [53] studied retrospectively spine MRIs from 120 patients and observed that 60 % of cases depicted localized or spotty bone marrow alterations (usually affecting vertebral bodies adjacent to the end plates) with a characteristic fat signal intensity. The study group was quite heterogeneous including proved metastasis and operated patients. The authors concluded that focal fatty replacement of hematopoietic bone marrow is a common phenomenon at all ages in both sexes, hence a physiologic process.

De Roos et al. [54] published in 1987 a review of lumbar MRIs and observed band-like sheets adjacent to lumbar vertebral end plates in 50 % of 203 degenerated disks. These signs didn't relate to infection or tumor, but were deemed to represent inflammation or ischemic necrosis, as well as fat replacement and fibrosis/sclerosis. The authors noted that 100 % of these findings were associated with DDD [54–57]. Furthermore, patients with lumbar DDD and these signal changes were usually older than patients with lumbar DDD without such changes. Signal changes compatible with fatty replacement were found in 83 % of degenerated disks. These findings support the premise that MC represent natural evolutions inside DDD, often associated with the aging process.

In 1988, Modic et al. [55] developed a classification system of vertebral bone marrow changes based on representative MR T1- and T2-weighted images. Modic type 1 changes (M1) demonstrated hypointense signal findings on T1-weighted images and hyperintense signal changes on T2-weighted images. Modic type 2 changes were characterized by hyperintense signal on T1-weighted images and isointense or slightly hyperintense signal changes on T2-weighted images. Rare type 3 (M3) changes (hypointense signal on both T1- and T2-weighted images) were added to the classification at a later time.

Modic et al. hypothesized that these signal changes reflect a spectrum of marrow changes related to DDD that could be distinguished from vertebral osteomyelitis and other vertebral body abnormalities [55].

9.4 Physiopathology of Modic Changes

The pathophysiology of MC remains obscure. The factors that lead to the onset of signal changes in the vertebral bone marrow adjacent to degenerative disks in MRIs are not well understood. It is of general agreement, however, that the physiologic association between the end plates, subchondral bone, and intervertebral disk is of

paramount importance to the understanding of DDD [58].

MC and the dual complex of aging/DDD are intimately, but not specifically, related. Mechanical loads, inflammation, genetics, and apoptosis have all been implicated in the genesis of MC and will be briefly discussed.

The cartilaginous end plate degenerates with aging. It is known to decrease in thickness and tear and eventually disappear with aging. Matrix production and accumulation within the cartilaginous end plate (CEP) decrease with aging [19, 22, 59], possibly because of decreased cell viability and reactivity of viable cells within the CEP [60]. The cause of these age-related changes remains unclear.

Programmed cell death has been implicated in this age-related end plate regression. Using a mouse spondylosis model, Ariga et al. [60] investigated the role of apoptosis in DDD. They analyzed operated and non-operated disks and controlled for age. The operated group was considered as having been exposed to marked mechanical stress. Apoptosis, particularly noticeable in the cartilaginous end plates, increased with age and resulted in a marked decrease in cell density. Interestingly, the extensive occurrence of apoptosis seen in the CEP was not observed in the nucleus pulposus. The authors speculated that CEP changes may possibly occur first and may cause the changes in the nucleus pulposus [60].

Ariga et al. [60] concluded that apoptosis was more evident in the surgically treated group than in the naturally aging group. The structure of the end plate began to disappear more rapidly in the surgically treated group supporting the role of mechanical stress in the degenerative process. Their conclusion was in parallel to reports demonstrating that cells within the CEP may be induced into apoptosis by the application of mechanical stress [13]. These observations suggest that acceleration of apoptosis in the CEP is involved in the cascade of events constituting disk degeneration and that mechanical stress may be one of the factors that induce apoptosis within the CEP [60].

Mechanical factors are supposed to induce end plate degeneration. The vertebral end plates were considered the spine's "weak link" in compression. Nachemson [61] affirmed that the degenerative process within disks results in greater axial loading and increased stress on the vertebral end plates. In patients with nonspecific LBP, it was hypothesized that disk degeneration leads to increased loading and shear forces on the end plates, which might lead to fissures of the end plate [62]. Animal models have demonstrated that injury to the disk induces changes in the adjacent vertebrae with subsequent bone marrow depletion and degeneration followed by bone regeneration [58, 63, 64].

It is speculated that MC may represent vertebral bone marrow reactions occurring after end plate damage or a bone marrow response to an acute or chronic inflammatory reaction in the disk.

Whatever might be the origin of MC, the importance of the end plate and subchondral bone [65] on the integrity of the intervertebral disk has been firmly established. The normal nucleus pulposus is designed to distribute weightbearing forces evenly onto the adjacent vertebral bodies. When the normal weightbearing properties of the nucleus pulposus are altered, weightbearing forces on the spine become distributed unevenly on the adjacent vertebrae, resulting in microfractures and bone necrosis [58]. These events result in inflammation of the adjacent bone marrow. Microtrauma to the end plate would permit contact between chemical agents in the degenerative disk and cells in the bone marrow [62, 66] and therefore may be considered the initiating inflammatory or autoimmune event in a progressive deteriorating process.

End plate damage decompresses the adjacent nucleus and transfers load onto the anulus, causing it to bulge into the nucleus cavity [67, 68]. Accumulating trabecular microdamage [69] probably explains why the nucleus increasingly bulges into the vertebral bodies in later life [70]. If the nucleus pulposus herniates through a damaged end plate, then subsequent calcification may create a "Schmorl's node."

MC are more frequent in lower lumbar levels [71]. This provides indirect evidence that there is a mechanical component to MC [71, 72]. A

mechanical cause is also supported by the higher prevalence of DDD in the lumbar rather than the cervical or thoracic spine [73]. This is also supported by a report associating MC changes with physical loading [74].

9.4.1 Surgical Rupture of the End Plate

Animal models demonstrate that surgical disruptions of the end plate or anulus will inexorably provoke degenerative changes in all disk structures [58, 68, 75]. Perforation of the end plate from the side of the vertebral body causes nucleus decompression, proteoglycan loss, and internal disruption of the annulus [68]. The anulus disruption model, which simulates a peripheral rim tear, causes subsequent changes in the nucleus and end plate [63, 75]. An injury to the end plate has been found to provide a potent mechanical stimulus for disk degeneration [66] and end plate trauma following fracture. It has been suggested to cause accelerated intervertebral disk degeneration [76].

9.4.2 End Plate Fracture

A noteworthy hypothesis regarding MC origin concerns end plate fractures. Histopathologic studies have confirmed the existence of end plate cartilage in herniated disks. This kind of herniation, described as "avulsion of end plate cartilage," represents the predominant histopathologic type of disk herniation in the elderly population [77]. These avulsion fractures of the cartilaginous end plate take place in the middle third of the sagittal diameter of the end plate [77].

Clinical relevance of cartilage material in disk herniation remains unclear. Schmid et al. [78] demonstrated that MC are associated with cartilage material in the extruded disk herniation. They compared preoperative MC and corresponding herniated disk tissue ($n=51$, mean age = 40, range 17–62) and found 59 % of preoperative MC adjacent to surgically treated disks (M1 in 11 % and M2 in 47 % of patients). There was a significant statistical correlation between MC extending over 33 % of the vertebral end plate and the presence of cartilaginous end plate material in the extruded disk. End plate cartilage avulsion would theoretically provoke a reaction in the adjacent bone marrow, resulting in MC.

It has been hypothesized that if hyaline cartilage from the vertebral end plate was found in herniated disk material, the end plate avulsion may have preceded the process of disk herniation [78]. Therefore, vertebral end plate signal intensity changes may be regarded as osteocartilaginous fracture signs similar to other skeletal manifestations. This data supplemented the knowledge that signal intensity changes along the end plates may be caused not only by edema, fissuring of the end plates, and formation of granulation tissue but also in part by end plate avulsion. The end plate cracks/fractures/avulsions may cause inflammation in the adjacent bone marrow with corresponding M1 signs on MRI.

Histopathologic studies [79–81] demonstrated that hyaline cartilage from the end plate present in an extruded disk material may suppress the process of neovascularization. Neovascularization is important for extruded disk material absorption. Therefore, the presence of hyaline cartilage from the end plate present in an extruded disk material would suppress disk absorption. M1 changes have been associated with the presence of hyaline cartilage in an extruded disk; therefore, an extruded disk is less likely to disappear when associated with adjacent M1 changes. It may be hypothesized that patients with M1 changes and an extruded disk would have less benefit from conservative treatment since the disk would probably not be reabsorbed. Patients without M1 changes and an extruded disk may respond better to conservative treatment [78].

9.4.3 Chymopapain and the Brutal Acceleration of Disk Degeneration

The theory exposed above may explain some consequences of chymopapain (CP) injection into intervertebral disks. CP injection for the

treatment of disk herniations can result in M1 inflammatory signs [55]. An accepted model of accelerated disk degeneration, intradiscal CP, provokes acute disk desiccation. This "shrinking" process may result in the acute detachment of the vertebral end plate. This causes an abrupt interruption of disk nutrition through the acute loss of end plate vascularization. Disk metabolism has adapted itself to chronic slow degenerative changes but does not seem adapted for sudden changes in its local environment. Sudden changes to the disk architecture may provoke acute inflammation.

Meanwhile, a normal nucleus is supposed to distribute weightbearing forces evenly onto the adjacent vertebral bodies. When the normal weightbearing properties of the nucleus pulposus are altered, weightbearing forces on the end plates become distributed unevenly, resulting in microfractures and bone necrosis [58]. These events would result in inflammation of the adjacent bone marrow.

When the process is chronic, a process of end plate healing ensues followed by stabilization of disk function [82]. This theory would in part explain why M2 anomalies (chronic, fatty replacement) are less seldom associated with pain production. Bone remodeling is thought to be induced by changes in the mechanical stress on vertebral bodies caused by DDD. Such stresses may result in pathological changes in the vertebral bone marrow. An insufficient healing process, with impaired bone remodeling, beginning with bone marrow edema and necrosis [65, 71] may result in an end plate defect. Inflammation within the end plates with M1 subchondral signal changes has been suggested to be induced by TNF [83].

9.4.4 Genetics and MC

Genetic evidence of MC prevalence was observed by Karppinen et al. [84]. These authors studied whether genetic factors were associated with MC in vertebral lumbar end plates and noted an association between a combination of IL1 and MMP3 gene variations and M2.

9.4.5 Inflammation

Inflammation is suggested to play a formidable role in MC as it does in DDD. The inflammatory nature of M1 was recently confirmed. Ohtori et al. [28, 83] presented immunohistological evidence that M1 is associated with inflammation of the vertebral end plates. The study suggested that TNF expression in chondrocytes gives rise to inflammation in the end plate of patients with M1. Furthermore, they noted that an increase in nerve fibers within the vertebral end plates in patients with M1 and M2 changes may be a cause of LBP, suggesting that the pain may originate from abnormal end plates [83].

Burke et al. [85] demonstrated that MC in patients with symptomatic (painful) disks are associated with high levels of production of proinflammatory mediators. These observations support their part as an objective marker of diskogenic LBP [85]. These authors studied the levels of IL-6, IL-8, and prostaglandin E2 (PGE2) in the disks of a surgically treated cohort of patients with sciatica ($n=40$, with 12 % of M1) and a surgically treated cohort of patients with (positive discography) diskogenic LBP ($n=12$, with 40 % of M1). There was a statistically significant difference between levels of IL-6, IL-8, and PGE2 production by M1 and M2 groups compared with the group without MC. The authors speculated that these findings were firm arguments favoring the link between MC and pain. M1 was more common in patients with diskogenic LBP, whereas M2 changes occurred in 50 % of patients who underwent surgery for sciatica. The cause of this high prevalence of M2 in the sciatic group is unknown.

MC may be considered in at least some cases (probably M1) a secondary sign of "internal disk disruption" [72].

9.4.6 Are Modic Changes a Result of Infection?

Albert et al. performed a double-blind RCT with 162 patients whose only known illness was chronic LBP of greater than a 6-month duration

occurring after a previous disk herniation and who also had M1 changes in the vertebrae adjacent to the previous herniation [86].

Patients were randomized to either 100 days of antibiotic treatment (Bioclavid) or placebo and were blindly evaluated at baseline, at end of treatment, and at 1-year follow-up. The antibiotic protocol in their study was significantly more effective for the LBP group (chronic LBP associated with M1) than the placebo in all the primary and secondary outcomes.

This subject remains a matter of debate. Recently, several issues concerning the previous study were pointed out [87]: very high treatment effect vs no benefit at all in the placebo arm; arguments about placebo masking (patient can detect whether or not they are receiving antibiotics); probably underpowered as two different antibiotic doses tested; no evidence of culture-positive infection at baseline, so a Koch postulate (the microorganism must be isolated from a diseased organism and grown in pure culture) fails if no known means of culture organisms (e.g., prions) are not fulfilled; is this optimum antibiotic regime, should we focus on *P. acnes* or other microflora as well?; precisely equal numbers in each group weakens the case for complete blinding, no description of skin preparation regime of culture from wound edges. Finally there is a concern relative to use of 100 days of antibiotics, that it would be maybe acceptable to treat diskitis but not if treating unconfirmed infection: with many public health/safety issues attending extended courses of antibiotics.

9.5 Epidemiology of Modic Changes

The prevalence of MC varies greatly between studies, from 19 to 60 % [54–56, 72, 74, 82, 85, 88]. This wide range in reported prevalence rates may be due to the high variation in study design including patient selection, age and sex distribution, clinical (surgical vs nonsurgical) or nonclinical (asymptomatic) series, clinical series of patients with LBP and/or sciatica, or occupational particularities. The real MC prevalence in asymptomatic and symptomatic populations is yet to be determined.

Jensen et al. [73] performed a systematic literature review to investigate the relation of the prevalence of vertebral end plate sign changes (VESC) (including MC) and the association with nonspecific LBP. The median prevalence of the reported prevalence rates for any type of VESC (M1 + M2) was 43 % in patients with nonspecific LBP and/or sciatica and 6 % in nonsymptomatic populations. The prevalence was positively associated with age and was negatively associated with the overall quality of the studies. A positive association between VESC and nonspecific LBP was found in seven of ten studies describing general, working clinical populations. VESC was a common MRI finding in patients with nonspecific LBP and was associated with pain. However, it may be present in individuals without LBP.

Weishaupt et al. [88] confirmed this finding demonstrating that MC were uncommon in 60 asymptomatic volunteers aged 20–50 years (mean age 35). According to the authors, the low prevalence of MC supported the hypothesis that MC may be predictive of LBP. Kjaer et al. [57] did a well-conducted study of 412 Danes older than 40 years old divided into three groups: MC and DDD, DDD but no MC, and the absence of DDD and MC. They observed a 15 % incidence of M1 and 7 % incidence of M2 for a total MC prevalence of 22 %. They concluded that there is an association between MC and LBP.

Most studies have demonstrated an association between the presence of MC and DDD [53–55, 72]. However, MC may also be found in the absence of DDD. Kjaer et al. [57] observed MC in 9 % of 198 non degenerated disks. Modic et al. [55] retrospectively reviewed lumbar MRIs of 474 consecutive patients referred for LBP or sciatica. They observed 4 % of M1 and 16 % of M2. Every MC was adjacent to a degenerated disk. The reverse, however, is not true, as only a minority of degenerated disks present with MC [57]. These relations are therefore not understood. The fact that MC have great specificity but a relative small sensitivity for the presence of DDD remains unclear. MC have great specificity but a relative small

sensitivity for the presence of DDD is unclear. It is not known why some degenerative disks are associated with MC, while others are not [72]. MC (especially M2) may correspond or represent at least part of the natural evolution of DDD. The association between MC and LBP seems to be stronger than that between DDD and LBP [57].

In the same line of previous studies, there is general agreement that vertebral marrow signal changes occur with increasing frequency with age [55, 89, 90]. This seems plausible as VESC has been correlated with disk degeneration [55, 57], which in turn is correlated with age [91].

Other variables were also analyzed. There was no apparent difference regarding gender. Kjaer et al. [74], in turn, found no significant gender difference among those with MC. They noted a 23 % prevalence of MC among 40-year-old men and women. A recent study, however, observed that MC were significantly associated with the male gender [90].

Most studies have demonstrated a predominance of M2 changes [54–56, 72, 85, 89, 92]. Hajek et al. [53] noted an age-related prevalence of "focal fat deposition" (M2). They observed these changes in 52 % of patients aged 31–40 years, 93 % in those aged 51–60 years and 100 % of those older than 60 years of age. It is known that there is a physiologic conversion of red marrow to fat marrow throughout life. A few studies have noted a predominance of M1 [57, 72, 93, 94]. Mixed forms and M3 were more rarely reported in the literature. The prevalence of mixed M1/M2 anomalies is estimated at approximately 8 % [93].

9.6 Reproducibility

Weighted kappa statistics are generally performed to analyze both intraobserver reliability and interobserver reproducibility. The kappa coefficient represents the percentage of instances of agreement, while the likelihood of agreement based on chance alone is taken into account. A kappa coefficient of 1.00 indicates perfect agreement, whereas a kappa coefficient of 0.00 implies no more agreement than would be expected by chance alone.

Recent studies have demonstrated that the Modic classification is both reliable and reproducible. High kappa values were demonstrated in the identification of MC [95]. These MRI signal changes were also comparable between specialties [95].

Jensen et al. [93] evaluated MRI scans of 50 individuals representative of the general Danish population aged approximately 40 years of age. Intra- and interobserver agreement of the detailed evaluation of variables describing vertebral signal changes (Modic type, location, volume, maximum height, and end plate area) were all found to have substantial to almost perfect agreement.

VESC is an MRI finding easy to evaluate [93] and is supported by studies that have reported the interobserver reproducibility of a detailed evaluation of VESC with kappa values ranging from 0.64 to 0.91 [89, 90, 93, 96, 97].

9.7 Bone Marrow Anatomy, Histology, and Physiology

Being MC a reflection of vertebral bone narrow structure, a brief review of its anatomy, histology, and physiology is needed.

9.7.1 Bone Marrow Structure and Its Aging Natural History

Vertebral bone marrow consists of red and yellow marrow. "Red marrow" is considered hematopoietically active, being responsible for the production of red cells, white cells, and platelets. "Yellow marrow" is hematopoietically inactive. Red marrow contains approximately 40 % water, 40 % fat, and 20 % protein, while yellow marrow presents 15 % water, 80 % fat, and 5 % protein. There are also structural differences. Conversion of red to yellow marrow occurs during growth and development and has a predictable and orderly pattern [98].

Modic MR changes are MR imaging mirrors of vertebral bone marrow histological structure. While portions of the end plate can be harvested at the time of surgery, the in vivo removal of unadulterated vertebral bone marrow for

histopathological study in the setting of lumbar DDD cannot be easily obtained. Thus histological data concerning vertebral bone marrow changes are scarce. To our knowledge there is one cadaver study that correlated MC and vertebral bone marrow histological changes. Hajek et al. [53] performed a macroscopic evaluation of sectioned cadaveric spine specimens and observed well-defined, yellow areas within the bone marrow that corresponded precisely with the localized zones of characteristic fat signal intensity on MR images (M2). Histologic evaluation of these regions demonstrated typical focal fatty replacement of normal hematopoietic marrow. The authors argued that fat in the bone marrow would exclude the presence of inflammation. Later on it would be proved that both fat and inflammation can coexist.

9.8 Vertebral End Plate MR Signal Changes (Modic Types)

Modic 1 Changes: Inflammation

M1 consists basically of inflammatory changes within the cartilaginous end plate and vertebral bone marrow. Modic et al. [55] examined histologically end plate material in specimens demonstrating M1 and M2 changes. End plate specimens were obtained during lumbar surgery for DDD in three patients with M1 and three patients with M2. M1 histology revealed disruption and fissuring of the end plates with regions of degeneration and regeneration and vascular granulation tissues adjacent to the end plates. There was an increased amount of reactive woven bone with thickened trabeculae and prominent osteoclasts and osteoblasts [55].

In M1 histologic tissue, the adjacent marrow of the vertebral body is replaced by loosely textured fibrous tissue with multiple small blood vessels. A fairly abrupt transition of these changes to normal cellular marrow at a variable distance from the end plate occurred [55]. Vande Berg et al. [99] observed granulation tissue with marked immature fibrosis, vessels, and few areas of subchondral necrosis along with thickened trabeculae. All these changes are compatible with M1 findings on MRI.

Among Modic types, M1 has been suggested mostly to correlate with pain. Kuisma et al. [56] affirmed that the suggestion of pain related to M1 findings is not surprising as this type is thought to have an inflammatory component. Crock [100] suggested that repeated trauma to the intervertebral disk results in the production of inflammatory mediators in the nucleus pulposus and that the diffusion of such toxic chemicals through vertebral end plates could result in a local inflammatory reaction resulting in LBP.

The inflammatory nature of M1 was confirmed in a recent observational immunohistological study on patients with diskogenic LBP [83]. Ohtori et al. [83] evaluated TNF expression and the existence of nerve fibers in the end plate of patients with diskogenic LBP. The results of immunohistochemistry were compared with end plate changes observed by MRI. There were two cohorts: a cohort of 14 patients who had LBP and disk degeneration on MRI and a control group of 4 patients. Vertebral end plates from patients suffering LBP with M1 and M2 changes had significantly more PGP 9.5-immunoreactive nerve fibers and TNF-immunoreactive cells in comparison with patients with normal end plates on MRI ($P<0.01$). The number of TNF-immunoreactive cells in end plates exhibiting M1 was significantly higher than in end plates exhibiting M2 ($P<0.05$) [83].

The results of their study suggested that TNF expression in chondrocytes results in end plate inflammation in patients with M1. TNF and the resulting inflammation affect sensory nerve fibers causing pain. The authors didn't specifically examine TNF expression and PGP 9.5-immunoreactive nerve fibers in patients with degenerated disks, but they speculated that the presence of nerve ingrowth in the inner disk layers caused diskogenic LBP in patients without MC. In the same line, an additional significant positive correlation was identified for nuclear TNF expression, disk degeneration, and age. TNF expression in the setting of M1 and M2 changes may also induce nerve ingrowth into the end plates [83]. Sensory nerve fibers innervating the vertebral end plate have previously been described [48].

Rannou et al. [101] performed a pilot prospective study of patients with chronic LBP and "no Modic" M1 and M2 changes and their relationship to high-sensitivity C-reactive protein (hsCRP) levels. hsCRP is a sensitive systemic marker of low-grade inflammation (IL-6 is the major upregulator of CRP gene expression). Their conclusion was that hsCRP is increased in patients with chronic LBP and M1, which supports a local inflammation phenomenon occurring at the vertebral end plate level.

Differential Diagnosis of Inflammatory M1 Changes

Vertebral end plate signal changes consistent with marrow edema may be seen in infectious diskitis [102], accompanying Schmorl's nodes [103] and within 3 months of chemonucleolysis [104]. However, in the absence of such predisposing causes, VESC have only been identified adjacent to degenerated disks [72]. In spondylodiskitis the T2 signal intensity of the disk and end plate is typically increased [105–107], and the end plates are eroded infection [105, 107]. The presence of paraspinal or epidural inflammation and/or a collection [105] as well as the clinical presentation and erythrocyte sedimentation rate and C-reactive protein (CRP) may help guide the diagnosis of an infectious process [105]. CRP is a very reliable indicator of disk infection, being elevated in up to 100 % of patients at the time of diagnosis. Diffusion-weighted imaging (DWI) is a sensitive and fast sequence that offers the possibility of quantifying diffusion coefficients of the lesions, which could help to discriminate between spondyloarthritis axial active inflammation and type 1 Modic changes [108].

Modic 2: Fatty Replacement

Histological specimens [55] demonstrated disruption of the end plates with evidence of chronic repetitive trauma (increased reactive bone and granulation tissue) similar to that seen with M1. However, the adjacent marrow was devoid of hematopoietic elements and was replaced by abundant fat (yellow marrow). These regions also showed a return to normal hematopoietic marrow at a variable distance from the end plate. Toyone et al. [82] stated that these changes are common in patients with late-stage DDD, which may represent the "restabilization phase" described by Kirkaldy-Willis and Farfan [109]. Thus, M2 may simply accompany aging or may coexist with the natural healing/restabilization phase of the chronic degenerative process.

Modic 3 Changes

M3 means a sclerotic state, corresponding to sclerosis on radiographs [110]. The presence of sclerosis is better appreciated with plain radiographs than with MRI, as it is a reflection of dense woven bone within the vertebral body. MR imaging reflects or displays the presence of marrow elements such as normal hematopoietic tissue, fibrovascular tissue, and lipid content between the bony trabeculae.

Mixed Forms

Mixed forms of MC consist of different histological substrates (e.g., M1 inflammatory changes + M2 fat replacement, often referred to as M1/M2) concurrently in the same vertebral body marrow adjacent to a degenerated disk [72]. Marrow content over time may and will often progress from one to another type. Many studies have confirmed these transformations [55, 72, 111, 112]. The most common type of mixed MC is M1/M2. Longitudinal studies confirmed that often there is a progression from M1 to M2 or from M1/M2 to M2 [112]. This may correspond to a transition from an (less stable) inflammatory state to a more stable (chronic, not meaning pathology) state (M2) [55].

The distinction between M1 and M2 is very specific as inflammation and fat replacement are distinct histopathological configurations. It is therefore obvious to refer to M1 or M2 and not the "generic" "Modic changes" expression, as M1 and M2 represent different histologies. These more specific M1 and M2 definitions are requested when studying the presence of LBP or MC natural history [113].

Inflammatory changes (M1) may be masked if they are superimposed by fatty replacement tissue (M2) [88]. Traditional T1 and T2 sequences may not be precise enough to distinguish between

various Modic types [72]. MR accuracy can be improved through supplementary fat suppression techniques followed by contrast injection or STIR (short TI inversion recovery) sequence. Using the first protocol, the sensitivity of detecting M1 changes improves as gadolinium enhances bone marrow inflammation in sites where fat is suppressed. STIR is a sequence with specific timing so as to suppress the signal from fat. These techniques improve the detection of inflammation.

9.9 Natural History: Modic Changes

Little is known about the natural history of MC. There are no studies analyzing the natural course of MC in asymptomatic populations. Existing data basically concerns clinical and surgical series [6, 55, 89, 112, 114]. Kuisma et al. [89] performed a longitudinal study in patients with symptomatic sciatica and noted a 6 % incidence over 3 years of new MC. All new cases of MC were primarily M1 and adjacent to herniated disks.

As previously stated, MC may convert from one type to another [55, 72]. The identification of several mixed forms is consistent with this idea and may represent different stages of the same pathological process [72]. It has been suggested that M1 represents an acute stage and may later transform to M2 [55, 112], as the subchondral bone heals. While several clinical and surgical series demonstrated this type of evolution [55, 111, 112, 114], it is not known whether all M2 are preceded by at least a discrete M1.

The mixed forms M1/M2 are thought to be transitory states during this transformation [89, 111]. Modic et al. [55] followed longitudinally 16 patients (6 M1 and 10 M2) in a series of 412 patients referred for MRI due to LBP/and sciatica. Five out of six M1 had at least partial conversion to M2 over a time period of 14 months to 3 years. All six patients with M2 changes remained unchanged.

Mitra et al. [112] observed M1 in 18 % of 670 patients referred for MRI due to LBP or sciatica. These patients were rescanned 12–72 months later. M1 transformed accordingly: 37 % M1 converted fully to M2, 15 % converted partially to M2, and just 8 % underwent no change. Forty percent of M1 changes increased in size. The authors correlated the evolution of M1 with the patients' symptoms and noted that in patients whose symptoms had improved, M1 transformed into M2. In patients reporting a worsening of their symptoms, M1 changes had progressively worsened. The conditions that govern the transit of a theoretically less stable M1 to a more stable M2 are unknown.

Albert and Manniche [6] observed that M1 changes were closely related to a previous disk herniation. The authors performed a longitudinal study where 181 patients were recruited from a randomized controlled study (RCT) comparing two active conservative treatments. The patients, who at baseline had radicular pain ending or radiating below the knee, had follow-up MRIs 14 months later. The prevalence of M1 increased from 9 to 29 %. M2 and M3 remained unchanged.

Modic et al. [55] believed that M1 didn't seem to invariably transform into M2. M1 could eventually regress to M0 or convert to M3 [71]. In a longitudinal series of sciatic patients, it was observed that no patients evolved from M1 to M2 over a 3-year period, and only two patients with M1/M2 changes converted to M2 [89]. The same study observed that several patients with M1 inflammatory changes regress to M0.

Considering that M2 represents a chronic state and M1 an acute inflammatory state, it is reasonable to think that the change from M2 to M1 would represent a sudden decompensation of the chronic degenerative state that M2 characterizes [115]. A new ongoing acute process may aggravate the degenerative process and provoke M1 inflammatory changes [89]. Marshman et al. [9] described two cases of M2 conversion to M1. Follow-up MRI of one of these patients demonstrated a vertebral slippage appearing concurrently with the transformation of M2 to M1. Luoma et al. [71] observed three cases in which M2 regressed (disappeared or decreased), concomitant with enlargement of M1 changes (conversion of M2 to M1). Kuisma et al. [89] noted eight individuals who had M2 changes which transformed into the intermediate form M1/M2

(six cases) and to M1 (two cases). Some patients evolved from the theoretically more stable M2 state to the less stable M1 state [89]. In contrast to previous findings, these authors suggested that M2 may be less stable than previously assumed. Most transformations occurred at L5–S1 and were associated with a symptomatic disk herniation.

M1, M2, and M3 size may remain stable or increase in size [6, 71, 112]. One series demonstrated that 41 % of M2 changes enlarged over time [71]. The increase in M2 size was more prevalent in those that did not convert to another type [89].

The factors that determine the fate of M1 inflammatory changes are not fully understood.

Luoma et al. [71] studied the natural course of M1 changes. They grouped together M1/M2 and pure M1 findings but labeled them all as M1. Moreover no clinical correlation was made with MC evolution. The study included 1015 consecutive nonspecific chronic LBP patients, and 24 (2,4 %) of the patients had 54 M1 (28 M1 and 26 M1/M2). These 24 patients underwent a follow-up MRI study within 18–72 months. Almost 100 % of new M2 (22 from 23) evolved from M1, supporting the M1 to M2 evolution hypothesis. However, most (67 %) of the 54 M1 (28 M1 and 26 M1/M2 grouped together) regressed over time, disappearing or undergoing size reduction possibly suggesting a total or partial resolution of the inflammatory process. The longer the interval, the more likely M1 tended to decrease or disappear. It is possible to conclude from this study that most M1 regress with healing and that most M2 evolve from M1. However when considering a general population, M2 would not be expected to always originate from M1 as fatty conversion of the marrow is part of a physiologic process. Another study showed that 34 % of M1 persisted or enlarged over time, and therefore subchondral edema may last for years [111].

Chymopapain injection, due to its mechanism of action of provoking sudden nucleolysis, is considered a model of accelerated disk degeneration. In this scenario M1 inflammatory changes may appear over a time period of 6–12 weeks [55]. M1 changes may therefore be viewed, at least in this clinical situation, as the result of an aggressive acceleration of the physiological degenerative cascade or an abrupt decompensation of the very slow degenerative disk process.

A disk herniation, when aggressively surgically removed (aggressive diskectomy), would theoretically provoke a similar "sudden loss of disk height" effect, resulting in a loss of vertebral body support. In a series [6] of 181 patients with sciatica in which the majority were treated conservatively, 12 patients underwent surgery for a lumbar disk herniation (LDH) during the 1-year follow-up period. Follow-up MRI at 1 year demonstrated a trend (though not statistically significant) for the operated patients to develop MC (especially M1).

Kerttula et al. [116] stated that M1 is a sign of a fast progressing and deforming "pathologic" disk degeneration. These authors affirmed that the accelerated process of degeneration in disks with an adjacent M1 may lead to deforming changes in the diskovertebral unit in a much shorter time than would be expected with age-dependent degeneration. They performed a prospective MRI study in chronic LBP patients evaluating the natural course of degenerative lumbar spine changes in relation to M1 (or a mixed Modic change M1/M2 or M1/M3) within 1 year. From 3,811 consecutive chronic LBP patients referred to lumbar spine, MRI 54 patients had M1. Follow-up MRI was obtained within 11–18 months. In follow-up, an unstable M1 was associated both with an increase of end plate lesions, decrease of disk height, and change in disk signal intensity, most found at L4/L5 or L5/S1. In disk spaces without M1, progression of degenerative changes was rare [116].

9.10 Clinical Correlation

There are no precise clinical, diagnostic, or imaging pathognomonic patterns that define the exact source of LBP. Radiological lumbar degenerative findings do not imply clinical symptoms. Several studies have demonstrated a high prevalence of morphologic abnormalities in both symptomatic and asymptomatic individuals [117, 118].

Most of the studies concerning MC and LBP have been performed in selected series of patients

[56]. Only one population-based study has focused on the association of MC and LBP [57]. In a population-based sample of 412 forty-year-old Danes, information including MRI findings, patient questionnaires, and clinical examination was collected. Three subgroups of patients were created: those with both DDD and MC, those with only DDD, and those with neither DDD nor MC. Clinical characteristics of each group were investigated to see if there was a distinct difference between subgroups [57]. The authors observed an association between MC and LBP.

MC are uncommon in an asymptomatic adult (aged 20–50 years) population. The low prevalence of end plate abnormalities in the asymptomatic population supports the hypothesis that end plate changes may be predictive of LBP [88]. However, MC are not specific of LBP. Many authors have suggested that M1 is associated with a higher prevalence of LBP [6, 56, 73, 82, 85, 111, 114, 119–121] thought secondary to DDD [6, 55, 57, 72, 82, 120]. Other authors have noted an association of M2 with LBP [6, 9, 56, 72, 94]. M1 may be more strongly associated with pain compared to M2 [6]. Albert and Manniche [122] observed from their outpatients' clinic that a large proportion of patients with persistent LBP had MC and patients with sciatica who were treated conservatively were three times as likely to report LBP if they had developed MC at 14 months of follow-up as compared to those who had not. These authors [6] conducted an RCT of 181 patients with severe sciatica treated with two active conservative treatments. Nonspecific LBP was more frequent in people with M1 compared to those with M2, but the difference between types was not statistically significant. The prevalence of MC was higher in patients who had undergone surgery for a herniated disk. A lumbar disk herniation was a strong risk factor for developing MC (especially type 1) during the following year, and the development of new MC was closely related to the level of a previous disk herniation [6].

Kuisma et al. [56] studied a population of 228 middle-aged male workers (159 train engineers and 69 sedentary controls) with a mean age of 47 years (range 36–56). MC was present in 56 % of patients, divided into M1 = 15 % and M2 = 32 %. Train engineers had on the average higher sciatic pain scores than the sedentary controls, but the prevalence of MC was similar in both occupational groups. The presence of MC was associated with an increased number of LBP episodes, with higher LBP scores during the past week and past 3 months. At specific disk levels, an association of LBP with MC was seen only at L5–S1, with MC being associated with a higher number of previous LBP and sciatica episodes and with a higher LBP score during the past week. MC at the upper lumbar levels or at L4–L5 were not associated with any pain variables [56]. M1 at any level (all levels combined) was related to a higher number of previous LBP episodes, higher LBP scores during the past week and past 3 months, and higher sciatic pain score during the past 3 months. At L5–S1, the associations were similar. At the upper levels, analyzed separately, the authors found no association between pain symptoms and M1 and M2 changes at any level (all levels combined). At L5–S1, M2 changes were associated with a higher number of previous LBP episodes.

The authors concluded that MC at L5–S1 and M1 are more likely associated with pain than other types of MC or changes located at other lumbar levels. The importance of this study was that it was the first to correlate occupation and MC [56]. The authors speculated that the association of LBP with the L5–S1 level might be due to mechanical factors, but the pathophysiology of this phenomenon needs further investigation.

A systematic review of the literature concerning VESC and nonspecific LBP [73] was performed. The authors defined manuscript quality criteria and reviewed 137 full text articles. They verified a positive association between VESC and nonspecific LBP in the majority of studies regardless of country of origin or whether it included a working or nonworking population [56, 74, 123]. The median prevalence of VESC changes in the nonspecific LBP population was 43 % and only 6 % in the nonclinical population. The authors hypothesized that if VESC is a condition that results in LBP, then the prevalence would be highest in study samples of patients

with LBP, lower in study samples of the general and working population, and lowest in individuals without LBP. When all populations of patients were combined into one group, the prevalence of VESC was found to be more than seven times higher among patients with nonspecific LBP than in asymptomatic (nonclinical) patients [73].

A recent 14-month longitudinal cohort study with MRI demonstrated that the presence of M1 at both baseline and follow-up is associated with a poor outcome in patients with persistent LBP [124]. Bailly et al. [125] compared, in a case-control study, clinical characteristics of patients with LBP with and without M1. On multivariate analysis, M1 patients were associated with sedentary work, pain with lumbar extension, and inflammatory pain pattern.

Kerttula et al. [116] studied the relation of the sizes of M1 and M2 and the Modic type (mixed M1-M2 or pure M1) with the intensity of LBP and level of perceived disability in 62 patients with large M1 and chronic LBP. They observed that the size of M1 did not directly correlate with clinical symptoms, but the Modic type (M1) was more important. They suggested that pure M1 may exist for a relatively short time after the onset of the process and then turn into M2 gradually. The authors remarked that when the inflammatory process turned to the mixed M1-M2 lesions, clinical symptoms improved [116].

9.11 Discography or MC or None to Define Painful Disk?

Provocative discography is not universally accepted as a pathognomonic test for diskogenic pain but remains the only useful functional study used to localize the pain generator in the setting of a degenerated disk. Diverse patient and operator variables may alter and influence patient responses and may lead to false-positive and false-negative findings. A correlation between provocative discography and MC has been evaluated by many authors [72, 94, 120, 126]. A verifiable positive association between MC and a painful disk would obviate the need for provocative discography. The presence of MC in a grouping of degenerative disks would allow a surgeon to target more appropriately treatment after excluding other causes of LBP. Such an association to date has not been verified [126].

Braithwait et al. [72] reviewed MRI studies and diskograms of 58 patients with supposed diskogenic LBP. The presence of MC was correlated with pain reproduction at 152 disks. MC occurred in 48.3 % of patients and 24.2 % of degenerative disks. There were 23 disks with associated MC that underwent discography, and the vast majority (21 out of 23) was associated with pain reproduction. However, pain was also reproduced at 69 levels where no MC was present. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for an MC as a marker of a painful disk was 23.3 %, 96.8 %, 91.3 %, and 46.5 %, respectively. These authors concluded that the presence of MC was a relatively specific but an insensitive sign of a painful lumbar disk in patients with diskogenic LBP.

Weishaupt et al. [94] affirmed that moderate and severe end plate abnormalities appear to be useful in the prediction of a painful disk in patients with symptomatic LBP. The authors performed a retrospective MRI review of 30 consecutive patients aged 20–50 years with long-standing LBP who underwent both MR imaging and discography. MC existed in 53 %. When only moderate and severe M1 and M2 were considered, all injected disks caused eed pain with provocation (sensitivity, 38 %; specificity, 100 %; PPV, 100 %).

Jensen et al. [73], in their literature review, similarly stated that the presence of VESC increases the likelihood of a concordant response during provocative discography. Buttermann et al. [121] noted a positive association between discography and M1 and M2, but the series was quite small. Sandhu et al. [126] retrospectively reviewed 53 consecutive patients who underwent discography and MRI for MC analysis. Their data showed no significant relationship between these distinct diagnostic tools. They concluded that both diagnostic entities had poor specificity for the diskogenic LBP and that each method may identify distinct pathologic entities.

9.12 Modic Changes and Surgical Series

9.12.1 Fusion

The first correlation of bone marrow changes on MRI and surgical intervention was published by Lang et al. [119]. These authors clearly described M1 changes in 10 out of 14 patients in which a diagnosis of pseudoarthrosis was suspected after segmental fusion. They also found M2 changes in 16 out of 19 patients who had solid fusions. These findings are in agreement with the presumed role of segmental hypermobility [82] in the genesis and/or persistence of degenerative vertebral end plate inflammatory changes.

Chataigner et al. [127] retrospectively reviewed 56 patients with symptomatic DDD surgically treated with an anterior lumbar interbody fusion (ALIF) technique. Improved clinical results were present in patients presenting with M1 changes compared to those with M0 or M2 changes. They concluded that an interbody fusion was an effective treatment method in lumbar DDD associated with M1 changes. Clarke et al. [128] prospectively compared 13 patients without MC with 13 patients with 2 M1 and 11 M2 changes and observed that MC did not predict improved outcome after instrumented posterolateral fusion. However, no statistical comparison between Modic groups was possible due to the very small number of M1 patients. Vital et al. [114] published a consecutive series of 17 surgically managed patients with DDD and M1 changes. All patients experienced improved pain and disability at a follow-up ranging from 12 to 72 months. The authors also reported conversion to M2 ($n=13$) or M0 ($n=4$) in all cases within 6 months after arthrodesis. This supports the contention that segmental arthrodesis may accelerate healing in patients with M1 changes by modifying loads exerted on the degenerated disk.

Esposito et al. [111] reported the findings of a prospective study of a cohort of 60 consecutive patients with chronic diskogenic LBP (duration >6 months) refractory to conservative treatment. The population of 30 men and 30 women constituted a clinically homogeneous cohort. All were severely disabled (visual analog scale [VAS] scores >= 6; Japanese Orthopedic Association [JOA] scores <=10), with advanced disk degeneration (Grades 3–5 according to Pfirrmann classification). When there were more than one degenerated disk on MRI, discography was performed to determine the painful level. Patients underwent either a posterior 1-level instrumented arthrodesis and posterolateral fusion with autograft (38 patients) or an interbody fusion with a carbon fiber composite (polyetheretherketone) cage filled with bone graft (22 patients). Changes were classified as Modic 0 in 15 patients, M1 in 22, M2 in 14, and M1/M2 (defined by them as a transitory state) in 9. The Wilcoxon paired sample test was used to assess significance ($p<0.05$ considered significant) in comparing the results of pre- and postoperative evaluations of pain and functional status. Patients with M1 improved much more than others ($p<0.01$), with good to excellent results noted in 72.7 % of patients. In the M2 group, the results were generally poor, with good to excellent results observed in only 14.3 % of patients. For the M1/M2 group, clinical outcomes were comparable to patients who had presented with pure M1 ($p<0.01$). In the group without MC, there were also significant improvements in both VAS and JOA scores, but in a smaller proportion of patients than in the M1 and M1/M2 groups ($p=0.0395$). The authors concluded that patients with LBP of presumed discal origin and severe DDD with an M1 may expect an optimal outcome following fusion. They also concluded that an arthrodesis in patients with an M2 lesion may experience less benefit of doubtful clinical significance. Despite the absence of a clinical control cohort, the results of this study provide important contributions to the understanding of the pathomechanism of MC and their relationship to LBP and its response to surgery. Surgery may be considered an artificial means of acceleration, the healing process/ bone remodeling of this inflammatory state leading to symptom improvement especially in patients with M1 changes.

Ohtori et al. [129] examined the change of M1 to M2 after instrumented posterolateral fusion plus decompression surgery for lumbar canal stenosis and observed that M1 changed to M2, but M2 didn't convert to M1. M1 and M2 changed to normal bone marrow signals in four cases. This suggested that M2 is the final stabilized stage;

however, the bone marrow may be able to "regenerate" after surgical stabilization [129].

9.12.2 Dynamic Fusion

Dynamic systems for treating MC were described. A dynamic stabilization in theory would avoid drawbacks of fusion, leaving the segment mobile and controlling load-bearing pattern of the motion segment and abnormal motion at the segment [130]. Eser et al. [131] operated 88 patients with chronic LBP and M1 and M2 using dynamic systems Cosmic (Ulrich GmbH & Co. KG, Ulm, Germany) and Safinaz (Medikon AS, Turkey) consisting of dynamic pedicle screws and a rigid rod system. The authors performed microdiskectomy in all patients. All cases of M1 turned into M2 or M3 in the 2-year follow-up.

9.12.3 Disk Arthroplasty

Blondel et al. [132] studied the clinical results of lumbar total disk arthroplasty in accordance with Modic signs, with a 2-year minimum follow-up, and observed superior clinical results in M1 patients compared to M2 and no Modic sign.

Siepe et al. [133] analyzed the effect of MRI end plate changes on outcome after lumbar arthroplasty. They followed 92 patients for a minimum of 24 months. Patients were divided into four groups: isolated DDD, DDD associated with disk herniation, DDD associated with MC, and postdiskectomy syndrome. At final follow-up, a significant clinical improvement was reported for the entire cohort, and the best results were achieved in the group with an associated disk herniation. MC were not associated with significantly better clinical outcomes.

9.12.4 Diskectomy

Chin et al. [134] performed a prospective case-control study to assess the outcomes following microdiskectomy in 15 consecutive patients with symptomatic disk herniation and sciatica associated with LBP and M1 and or M2 changes compared with similar patients without MC. Relief of LBP was less predictable than sciatica. The authors suggested that the substantial improvement seen in both groups supports the premise that a diskectomy alone is adequate in patients with MC and sciatica correlating with a disk herniation. There was a trend toward greater improvement of LBP in patients without any MC.

Sørlie et al. [135] found that patients with M1 who were operated for lumbar disk herniation had less improvement of LBP 1 year after surgery, compared to those who had no or other types of MC. However, in the multivariate analyses, this negative association no longer showed statistical significance when adjusted for smoking, which remained the only independent risk factor. Patients with preoperative M1 can expect less but still significant improvement of LBP 1 year after microdiskectomy, but not if they smoke cigarettes. Lurie et al. [136] stated that patients with M1 had worse outcomes after diskectomy for lumbar disk herniation. They affirmed that patients with small disk herniations and M1 may not benefit substantially from diskectomy.

Braithwait et al. [72] affirmed that patients with M1 and severe LBP did well after anterior diskectomy and fusion, but that the outcome was less predictable in M1 absence. Buttermann et al. [121] observed that when diskectomy was followed by the development of M1, patients often experienced continued LBP. Of the 24 patients with M1, 18 had undergone a prior procedure: 17 a diskectomy and 1 a nucleolysis. Another group of 24 patients, most of whom had also undergone a prior diskectomy, had M2. Most of the patients with LBP and M2 also had an inflammatory component manifested as mixed M1/M2. In their series, 19 out of 24 patients with M1 who underwent fusion continued to experience LBP ($p<0{,}03$). Precise data regarding pseudoarthrosis rates were not reported. The authors noted a correlation between clinical failure of a posterior fusion and the presence of M1 at the symptomatic level.

9.12.5 Intradiscal Steroid Injection

Fayad et al. [137] analyzed a series of 74 patients with LBP and found that patients with chronic

LBP and predominantly M1 had better short-term relief of symptoms following lumbar intradiscal steroid injection (IDIC) than M2. They noted that at 3 and 6 months, IDIC tended to be more effective in patients with M1 and M1/M2 changes, although this was not statistically significant. Similar findings were reported by Beaudreuil et al. [138] who reported that patients with disabling chronic LBP and M1 have specific acute response to intradiscal injection of methylprednisolone.

Conclusion

Much has been written recently concerning Modic changes and their relationship to symptomatic low back pain. Despite anedoctal evidence that Modic changes, especially M1 subchondral inflammatory changes, may be causally related to symptoms of low back pain, well-designed studies are needed to develop a better understanding of their true significance and prognostic value.

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10 Degenerative Marrow Changes: Natural History Biomechanics in Relation to Symptoms

Michael T. Modic

Signal intensity changes of the vertebral body marrow adjacent to the end plates of degenerated disks are a long recognized and common observation on MR images of the lumbar spine [1, 2]. However, despite a growing body of literature on this subject, their clinical importance, etiology, and relationship to symptoms remain unclear [3].

These marrow changes appear to take three main forms on MR imaging. Type I changes demonstrate decreased signal intensity on TI-weighted images and increased signal intensity on T2-weighted images (Fig. 10.1). They have been identified in approximately 4 % of patients scanned for lumbar disease [2], approximately 8 % of patients after diskectomy [4], and in 40–50 % of chymopapain-treated disks, which may be viewed as a model of acute disk degeneration [5]. Histopathologic sections of disks with type I changes show disruption and fissuring of the end plate and vascularized fibrous tissues within the adjacent marrow, prolonging T1 and T2. Enhancement of type I vertebral body marrow changes is seen with administration of gadolinium that at times extends to involve the disk itself and is presumably related to the vascularized fibrous tissue within the adjacent marrow. Type II changes are represented by increased signal intensity on T1-weighted images and isointense or slightly hyperintense signal on T2-weighted images (Fig. 10.2). They have been identified in approximately 16 % of patients at MR imaging. Disks with type II changes also show evidence of end plate disruption, with yellow (lipid) marrow replacement in the adjacent vertebral body resulting in a shorter T1. Type III changes are represented by decreased signal intensity on both T1- and T2-weighted images and correlate with extensive bony sclerosis on plain radiographs (Fig. 10.3). The lack of signal in the type III change no doubt reflects the relative absence of marrow in areas of advanced sclerosis. Unlike type III, types I and II changes show no definite correlation with sclerosis at radiography [6]. This is not surprising when one considers the histology; the sclerosis seen on plain radiographs is a reflection of dense woven bone within the vertebral body, whereas the MR changes are more a reflection of the intervening marrow elements. While the aforementioned histologic changes appear to describe the underlying anatomic substrate for the MR signal changes, they by no means describe the etiology of the underlying causative process.

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Editor's Note Dr. Modic gave us the great honor of a chapter written by himself about the radiological findings that were marked in medicine as Modic changes. We are very grateful to him for his current appraisal of the matter.

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_10

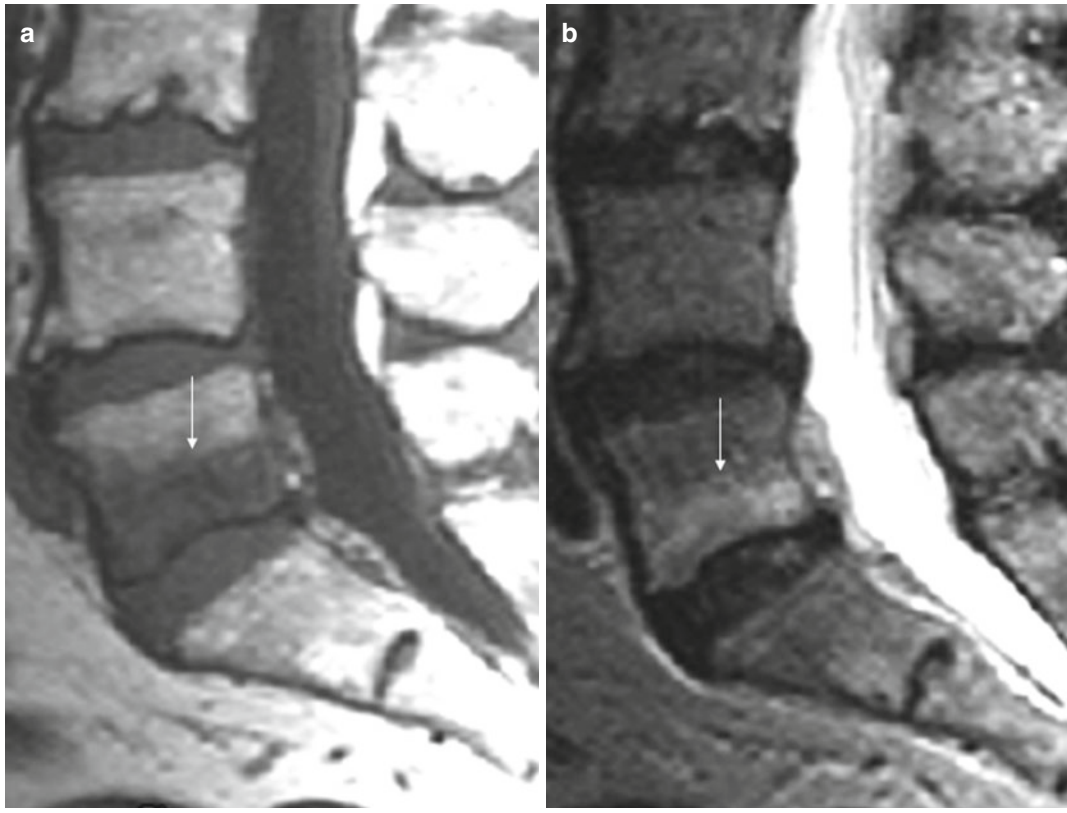

Fig. 10.1 Degenerative type I marrow changes: sagittal midline T1 (**a**) and T2 (**b**) spin-echo images of the lumbar spine. There is decreased signal intensity of the inferior aspect of the L5 vertebral body on T1 (→) and increased signal intensity on T2 (→). The L5/S1 disk is degenerated

Similar marrow changes have also been noted in the pedicles. While originally described as being associated with spondylolysis, they have also been noted in patients with degenerative facet disease and pedicle fractures [7, 8] (Fig. 10.4). We do not know the exact mechanism by which these marrow changes occur. Their association with degenerative disk disease, facet changes, and pars and pedicle fractures suggest they are a response to biomechanical stress. This then suggests the first and likely most common etiology – mechanical.

The bone is a dynamic architectural substance that responds to changes imposed upon it. When stressed, the bone behaves according to Wolff's law [9]. Wolff's law of bone states that the architecture of a bone is determined by the mechanical stresses placed upon it and the bone's adaptation to withstand these stresses. Wolff's law is an example of the complementarity of form and function, showing that the form of a bone is shaped by its functional experience. The trabeculae of spongy bone often develop along lines of stress. The major trabecular orientation in the vertebral bodies and pedicles is in-line with the principal direction of loading, whereas perpendicular laid-down support elements or "struts" increase the overall strength. As the bone comes under consistently applied stresses, it may react through the development of microfractures as well as osteoblast depositing new osseous tissues. The orderly remodeling of bone depends on a precise balance between deposition and resorption, between osteoblasts and osteoclasts, a process which repairs microfractures. The remodeled bone is known to contain microfractures that can demonstrate abnormal uptake at scintigraphy. It has been suggested that the type I MR signal intensity changes may be a reflection of remodeling trabecular bone with microfractures and associated marrow changes [10–12].

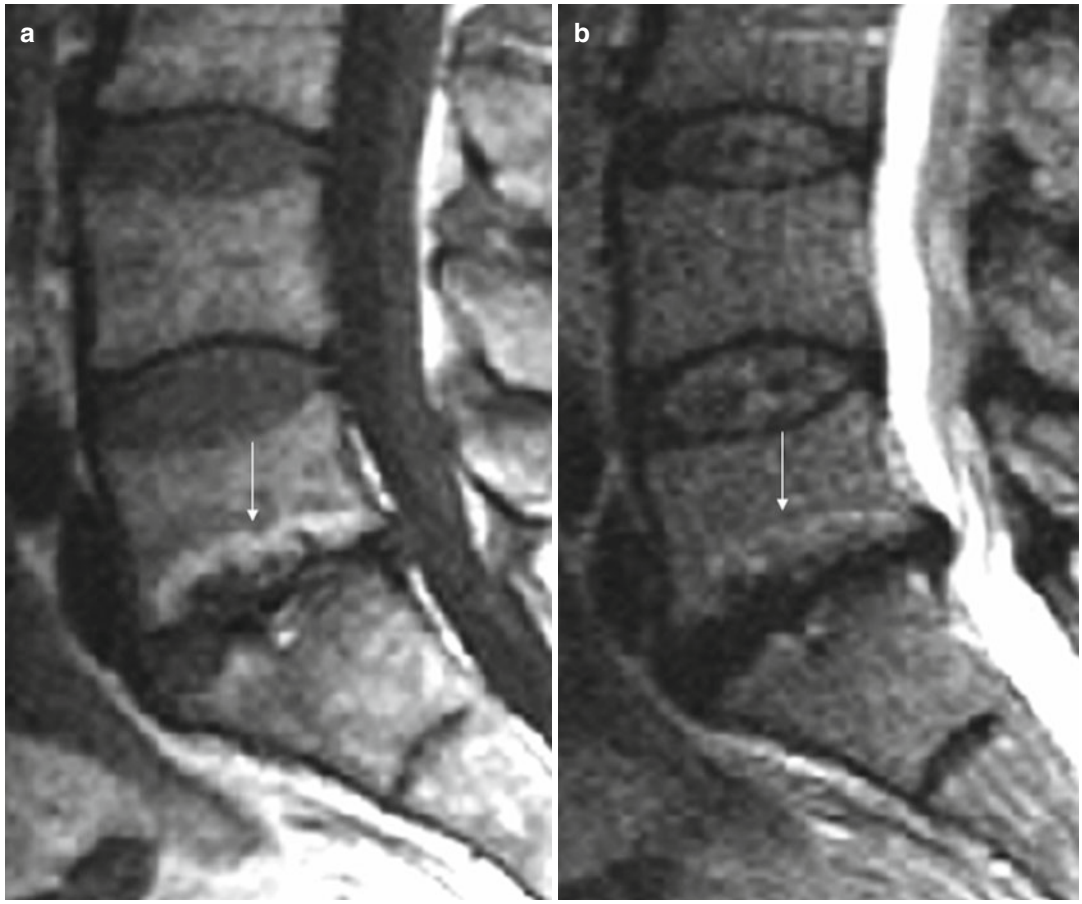

Fig. 10.2 Degenerative type II marrow changes: sagittal T1 (**a**) and T2 (**b**) spin-echo images of the lumbar spine. On the sagittal T1-weighted images, there is increased signal intensity of the inferior aspect of L5 (→) and superior aspect of S1. The signal intensity on the T2-weighted images is slightly increased in this same region. The disk space is degenerated and there is evidence of a disk protrusion

Of these three types, type I changes appear to be more fluid and variable, a reflection of some ongoing underlying pathological process such as continuing degeneration with resulting changing biomechanical stresses. Of the three types, type I is most often associated with ongoing low back symptomatology [13–17]. In a longitudinal study, the incidence of new degenerative marrow changes was 6 % over a 3-year period, most of these being of type I [15]. In a study of nonoperated patients with low back pain, Mitra [14] found that 92 % of type I changes converted either wholly or partially into type II (52 %), became more extensive (40 %), or remained unchanged (8 %). There was an improvement in symptoms in patients where type I changes converted to type II.

Some studies of diskography in patients with degenerative marrow changes have suggested that type I marrow changes are invariably associated with painful disks [18, 19]. Others [20, 21] have failed to be able to reproduce this association, and thus the relationship of degenerative marrow changes and diskogenic pain remains unproven.

In most cases, type II degenerative changes appear to be associated with a more stable state. Type II changes, however, are not always permanent and conversion between type II and I has been demonstrated. In general, when type II marrow changes convert to type I, there is usually a superimposed process such as continued or accelerated degeneration or vertebral

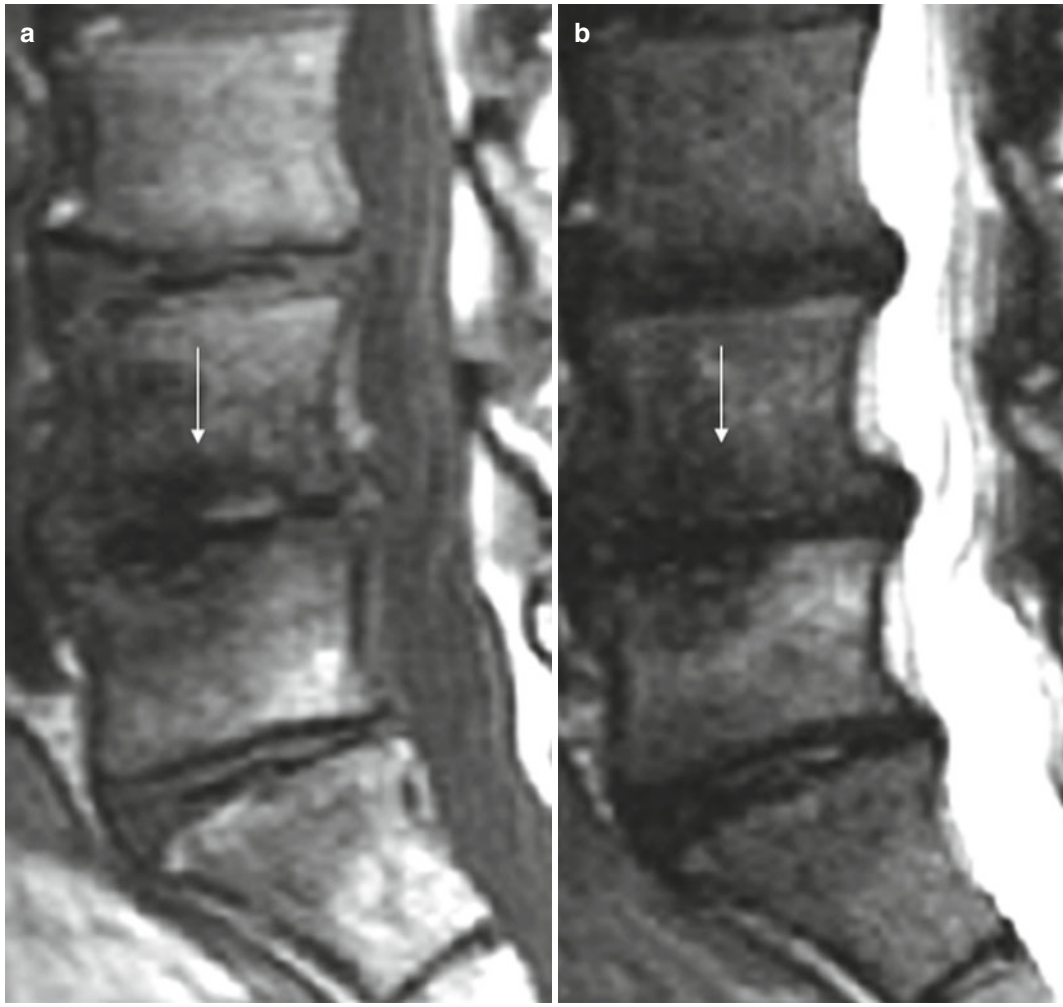

Fig. 10.3 Degenerative type III marrow changes: sagittal midline T1 (**a**) and T2 (**b**) spin-echo images of the lumbar spine. There is decreased signal intensity of the adjacent portions of L4 and L5 (→) with an intervening degenerated disk on both T1- and T2-weighted sequences

osteomyelitis. Some authors have suggested that mixed lesions are more common than originally thought and indicative of overlap and progression of one type to another [15] (Fig. 10.5).

In most studies of marrow changes, type II are the most prevalent and the prevalence increases with age [15, 22, 23]. Others have suggested that type II changes are less stable and may be as active as type I and equipotent relative to symptomatology [15, 24, 25]. In a study by Määttä et al. [26], there was a 46 % prevalence of marrow changes in patients referred to spinal surgery. In a study by Jensen [25], this prevalence was 43 % in patients with low back pain seeking care. In fact, Marshman et al. [24] reject the contention that type I lesions are more active. They speculate that the bone marrow appearances are merely epiphenomena. As such, they detract one from the more important consideration that the de novo pain afferents have traversed the disk space providing a substrate for diskogenic pain which is a more important consideration than the gross histological appearance and MR signal intensity change of the vertebral body marrow. This last point is valid in that MR changes are likely a con-

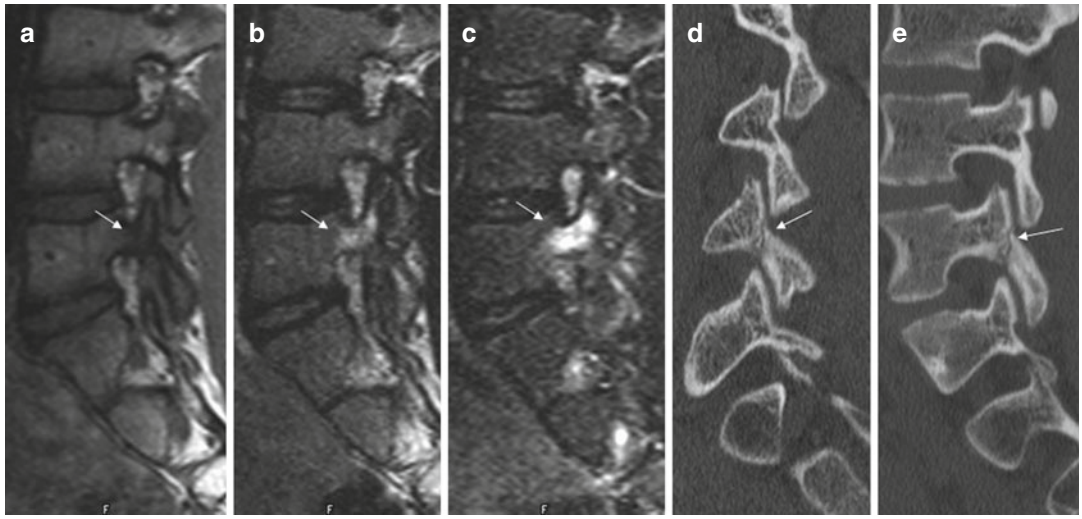

Fig. 10.4 Pars fracture and pedicle hyperintensity: (**a**) parasagittal T1-, (**b**) T2-, and (**c**) STIR-weighted images of the lumbar spine (**d**, **e**) are oblique and sagittal multiplanar reformatted (MPR) CT images (respectively) of the lumbar spine. Note the decreased signal intensity on T1 (→ Fig. 10.4a) and increased signal intensity on T2- and STIR-weighted images (→ Fig. 10.4b, c) within the pedicle of the L4 vertebral body on the *right*. A subtle pars fracture is demonstrated on the oblique (**d**) and sagittal (**e**) MPR CT images (→)

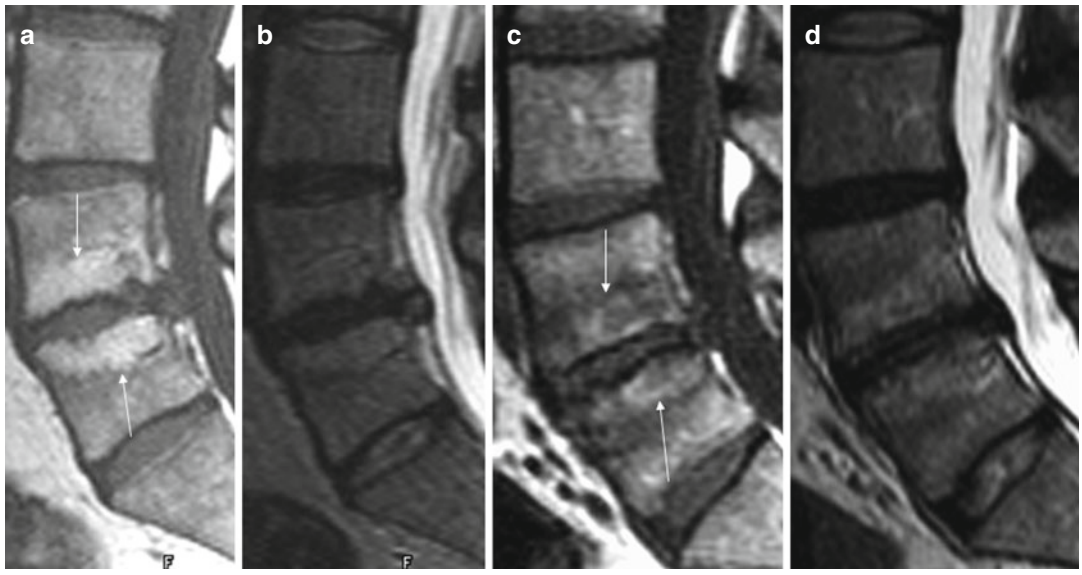

Fig. 10.5 Type II marrow conversion: sagittal midline T1 (**a**) and T2 (**b**) spin-echo images of the lumbar spine in a patient with low back pain and radiculopathy. This patient underwent a diskectomy at L4/L5 and initially did well but 1 year postoperatively developed recurrent low back pain and was reimaged. Figure 10.5c, d is sagittal midline T1 and T2 spin-echo images which demonstrate a loss of the lipid marrow signal intensity (Fig. 10.5a) typically seen in type II degenerative marrow changes at L4/5. There is now a more mixed signal intensity of the marrow space (**c**). There is subtle increase signal intensity on the T2-weighted images (**d**)

sequence of the biomechanical, cellular, and immunological factors that are primarily responsible for symptomatology. The signal intensity changes on MR are a secondary reflection. However, I believe the available data would support that type I marrow changes are more

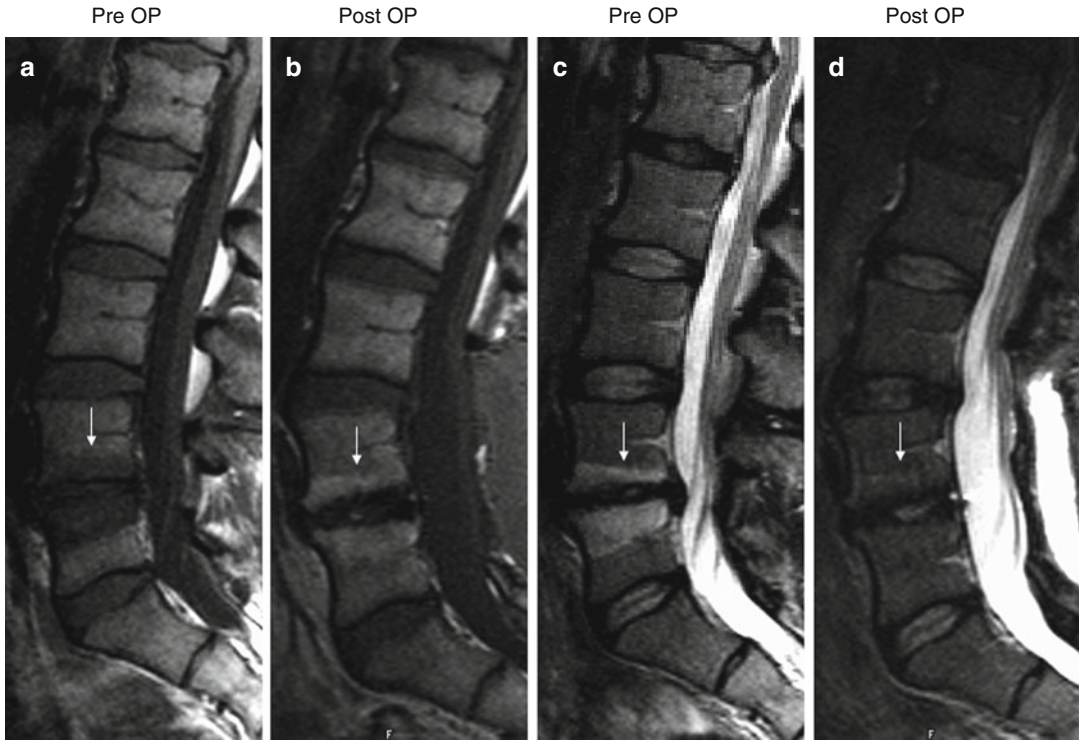

Fig. 10.6 Type I marrow conversion following lumbar fusion: sagittal midline T1 spin-echo images of the lumbar spine preoperatively (**a**) and postoperatively (**b**). Figure 10.6c, d is sagittal midline T2-weighted images of the lumbar spine preoperative and postoperative, respectively. Note the typical type I degenerative marrow changes at L4/5 preoperatively (**a**, **c**) which covert to type II degenerative marrow changes (**b**, **d**), respectively, following lumbar fusion. Note the laminectomy defect and posterior fluid on the postoperative images (**b**, **d**)

strongly associated with symptomatology than type II and more fluid, and their resolution or change is more common and associated with clinical improvement.

Type III degenerative marrow changes are the least common and probably are a reflection of end-stage degenerative disk disease. There is no enough data to make meaningful comments about its relationship to symptomatology or even the preceding two types.

In a study by Toyone [13], 70 % of patients with type I marrow changes had segmental hypermobility versus 16 % with type II. Probably the greatest support for suggesting these marrow changes, particularly type I, is related to biomechanical instability and is based on observations following fusion. Chataigner [27] has suggested that type I marrow changes have much better outcomes with surgery than those with isolated degenerative disk disease and normal or type II marrow changes. In addition, resolution of type I marrow changes to either normal or type II was associated with higher fusion rates and better outcomes. Other studies support the contention that persistence of type I changes after fusion suggests pseudoarthrosis and is associated with a greater percentage of patients with persistent symptoms. Conversely, resolution of type I marrow changes to either normal or type II was associated with higher fusion rates and better outcomes [28–30]. The conclusion then would be that fusion produces greater stability, reduces biomechanical stresses, and accelerates the improvement in the course of type I marrow changes (Fig. 10.6).

As further support for these fluid marrow changes reflecting biomechanical stress, we have seen similar marrow conversion in the pedicles of vertebral bodies associated with symptomatic pars and pedicle fractures as well as

severe degenerative facet joint disease. Twenty-two patients with type I marrow changes of the pedicles and back pain were followed longitudinally. The type I pedicle marrow changes resolved in 17 patients but persisted in 5. Self-reported pain scores tended to improve over time with concordant resolution of marrow signal intensity, but this was not statistically significant – functional improvement was. Of the 17 patients with resolution of the type I marrow change, 6 converted to type II and 11 turned to normal marrow signal. This result suggests that the pedicle marrow type I conversion to a normal or type II appearance is associated with improved symptoms [31].

While the data is strong that there is a mechanical etiology to many of these marrow changes, there is a growing body of literature that suggests that in some there is a true infectious or inflammatory cause [32]. Multiple authors have observed a variety of inflammatory mediators in association with degenerative marrow changes. Burke et al. [21] observed an increase in proinflammatory mediators such as interleukin-6, interleukin-8, and prostaglandin E-2 in the disks of patients with type I marrow changes and in patients undergoing fusion for LBP. Ohtori et al. [33] found that the cartilaginous end plates of patients with type I marrow changes had more protein gene product (PGP) 9.5 immunoreactive nerve fibers and tumor necrosis factor (TNF) immunoreactive cells than those with normal end plates. PGP 9.5 immunoreactivity was seen exclusively in patients with diskogenic LBP. TNF immunoreactive cells in end plates with type I marrow changes were higher than those with type II marrow changes. These authors concluded that type I marrow changes represented a more active inflammation by mediated proinflammatory cytokines, whereas type II and type III changes appeared to be more quiescent [3]. Korhonen [34] in a study of infliximab, a monoclonal antibody against TNF-alpha, suggests it was most effective when there were degenerative type I marrow changes at the symptomatic level. Nevertheless, the relationship to immunobiologic and cellular response mechanisms, while probably important, remains unclear.

In patients with the low back pain and type I marrow changes, an important differential consideration is vertebral osteomyelitis. Disk space infection typically gives rise to similar vertebral body marrow signal changes which are manifested by low signal intensity on T1, high signal intensity on T2, and nonanatomic high signal intensity within the intervertebral disk. Contrast enhancement of the disk and end plates may occur in both disk space infection and degenerative type I marrow changes (Fig. 10.7). The vertebral end plates are usually preserved in degenerative type I marrow changes rather than eroded, destroyed, and indistinct as in disk space infection. There is more often an associated paraspinal or epidural soft tissue mass with disk space infection than degenerative disk and type I marrow changes. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are almost invariably elevated in vertebral osteomyelitis and usually normal in uncomplicated degenerative type I marrow changes [35]. While classic pyogenic and fungal osteomyelitis may, in their earliest stages, overlap in appearance on MR with type I marrow degenerative changes, classic osteomyelitis has a distinctly different clinical and more rapidly changing imaging picture. More recently, it has been proposed that some type I marrow changes which here to fore have been presumed to be degenerative may in fact been secondary to a low virulent anaerobic bacterial process [36].

This hypothesis rests on several observations and studies. Stirling [37] used a newly developed serological test to diagnose deep-seated infections caused by low virulent gram-positive organisms. They studied disk material from 36 patients obtained during microdiskectomy. Nineteen (53 %) had positive cultures after long-term incubation. *Propionibacterium acnes* was the organism isolated in 16 of 19 (84 %). They proposed that these microorganisms colonized degenerated and herniated disks because of access provided by minor trauma and tissue disruption.

Albert reproduced some of these same observations [38]. They acquired disk samples from 61 patients who underwent disk surgery and subjected them to microbiologic analysis. All

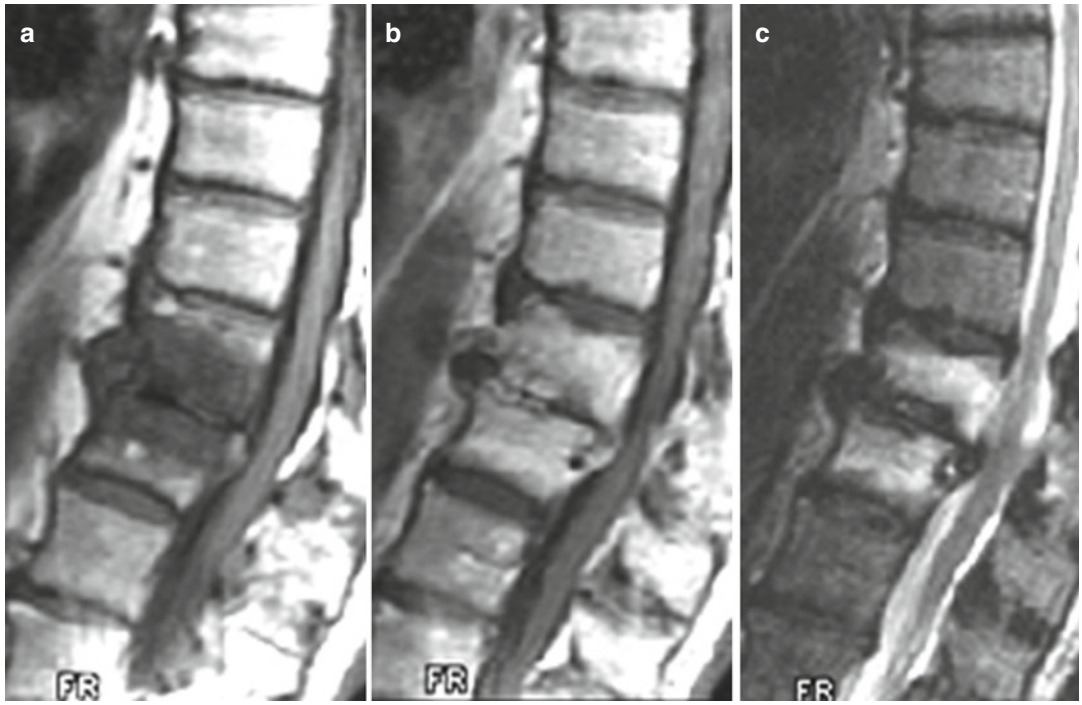

Fig. 10.7 Type I marrow conversion following lumbar fusion: sagittal midline T1 spin-echo images of the lumbar spine preoperatively (**a**) and postoperatively (**b**). Figure 10.7c, d is sagittal midline T2-weighted images of the lumbar spine preoperative and postoperative, respectively. Note the typical type I degenerative marrow changes at L4/5 preoperatively (**a**, **c**) which covert to type II degenerative marrow changes (**b**, **d**), respectively, following lumbar fusion. Note the laminectomy defect and posterior fluid on the postoperative images (**b**, **d**)

patients then had an MR at baseline prior to surgery and 1–2 years postsurgery and disk sampling. Microbiologic cultures were positive in 28 of 61 (46 %) of which 26 (43 %) grew anaerobic organisms and 4 (7 %) dual microbial organisms. In the disk with anaerobic bacteria, 80 % subsequently developed new type I marrow changes on MR. This study confirmed the original findings of Stirling et al. [37] demonstrating the extruded nuclear material frequently has microorganisms present. As a counterargument of contamination being the cause of infection, a control group of 27 patients who had undergone spinal procedures for scoliosis, trauma, or a malignancy were sampled and studied in a similar fashion. In this control group, no organisms were isolated [39]. None of the aerobic positive cultures (presumably contaminates) developed marrow changes. Additionally, in patients where all cultures were negative, only 44 % developed new marrow changes by MR.

The theory of infection as an etiology for marrow changes has been tested further. In a subsequent study, Albert and his group proposed the hypothesis that disk herniations provide an environment conducive to low-grade anaerobic infections. If these infections were responsible for symptoms and marrow changes, they should be responsive to antibiotic therapy. The aim then of their study was to test the efficacy of antibiotic treatment in patients with chronic low back pain and MC type I. In order to test this hypothesis, the authors performed a double-blind randomized controlled trial in a patient cohort with chronic low back pain. The initial group was composed of patients with low back or low back and leg pain with a demonstrable disk herniation on MR for back or back and leg pain which demonstrated a disk herniation on MR. To be eligible for randomization, the patients would then subsequently have to have had continued chronic low back pain for 6 months or longer and

on follow-up MR examination have developed type I marrow changes. One hundred sixty-two patients meeting the entry criteria were randomized to either 100 days of antibiotic treatment or placebo. Patients treated with antibiotics showed statistically significant improvements compared to the placebo group in all measured parameters including MR appearance. In addition, the authors observed that the improvement achieved in the antibiotic-treated group was greater than those described with other established conservative treatments.

The authors hypothesize that the marrow changes are a side effect of the cytokine propionic acid production from the bacteria entering the adjacent marrow space, presumably through degenerative changes related to disk herniation and underlying degenerative disk disease. Their hypothesis then is following a tear in the outer fibers of the annulus with disk herniation, there is neovascularization and new capillary formation associated with reparative/inflammatory changes surrounding the herniated disk material. Through these new vascular channels, anaerobic bacteria could enter the anaerobic disk environment and produce a slowly developing low virulent infection. The associated marrow changes could be the visible signs of the inflammatory and low-grade bony destructive changes.

Conclusion

Degenerative marrow changes appear to be an age-related process associated with degenerative disease. Type I changes are strongly associated with active low back symptoms and probably some degree of biomechanical instability. Type I changes have been suggested to predict an excellent outcome following stabilization with fusion. Resolution of type I marrow changes has been associated with the reduction of symptoms. There can be conversion between types, most commonly type I to type II or normal. Type II changes appear to be more stable over time and less strongly associated with low back pain. They are most common at L4/5 and L5/S1. They may convert to type I with superimposed changes such as infection or accelerated degeneration. A biomechanical cause is felt likely because of the strong association with degenerative disk disease, improvement with fusion, and relationship to and resolution with changing symptoms. While the data is strong that there is a mechanical etiology to many of these marrow changes, there is a growing body of literature that suggests that in some, they are a reflection of an inflammatory or infectious process facilitated by the degenerative change. The altered signal intensity detected by MR imaging is not, in and of itself, the causal pathological process, but rather a reflection of the causal process that is probably some type of mechanical stress or instability and superimposed or concomitant immunobiologic, cellular, or possibly even infectious response.

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Part III

General Important Aspects When Treating Symptomatic Lumbar Degenerative Disk Disease

Psychosocial Aspects and Work-Related Issues Regarding Lumbar Degenerative Disk Disease

11

Clayton L. Haldeman, Andrew Bauer, Daniel K. Resnick, and Nathaniel Brooks

11.1 Introduction

The latest Global Burden of Disease Study ranks low back pain as the leading cause of disability worldwide [1]. The one-year incidence has been estimated to be as high as 36 %, while the lifetime prevalence is thought to be close to 80 % [2]. Regardless of treatment most patients enjoy full recovery from their symptoms [3]. However recurrence is common. And while the prevalence is difficult to estimate, some patients go on to develop chronic back pain, typically defined as pain lasting longer than 3 months.

Back pain is not a new ailment. The oldest known surgical text, the Edwin Smith papyrus from 1550 B.C., contains a description of sciatica. However the idea of disability as a result of chronic back pain does seem to be a relatively new concept [4]. There is no reason to think that back pain today is any more severe, frequent, or otherwise different from the pain our ancestors experienced. A more recent book, "The Back Pain Revolution," authored by Gordon Waddell highlights this point [5]. Dr. Waddell discusses his time spent in Oman as it transitioned from an underdeveloped country to become more "westernized." New oil money brought modern medical treatments to this country in the mid-1980s. At the time, patients with back pain flooded into the newly established clinics seeking treatment for their pain. These patients had very similar problems with similar etiology to patients in developed western countries. The interesting part is that nearly none of them were off work or "disabled" from their pain. Waddell's observation was that the patients who were able to escape the confines of their country to have "modern" medical procedures in other countries became disabled after surgery at a much higher rate than those who did not have access to modern medical care. This is an illustration that suggests that low back pain is nothing new, but low back disability is largely a product of modern western medicine. What has changed then? One theory is that as physicians have embraced the scientific method, they have lost touch with the more ancient aspects of medicine, which were equipped to treat the psychological and social aspects of illness.

Over previous centuries, back pain was poorly understood. More recently it was proposed that pain was a direct indication of tissue injury and that repair of the injuring mechanism would

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_11

relieve the pain. The first notion that back pain came from spine and nervous system dysfunction came from Brown in 1828 [6]. This was followed by the discovery of the ruptured disk by Mixter and Barr [7] in 1934. King [8] declared that "pain in the back, as a result of injury, is the most frequent affection for which compensation is demanded from the casualty company." As the twentieth century progressed, physicians imagined that an incomplete understanding of the pathology was the only thing standing in the way of a cure to back pain.

This approach, also known as the disease model of illness, depends upon physical pathology causing symptoms proportional to severity. However, despite the remarkable advances in imaging, surgical technique, antibiotics, and pain medicines that have occurred since the early 1900s, low back pain continues to be one of the most common reasons for loss of work today. It is now understood that some components of low back disability may be a manifestation of actual physical pain, but the vast majority of such may be due to the psychological reaction to pain.

Many clinicians have found the disease model of illness to provide an inadequate understanding of low back pain and have turned to the biopsychosocial model. Psychiatrists pioneered this model in an effort to better understand and treat mental illness; however, many have found it advantageous to think about chronic pain using this model as well [9]. In a review of the model, Borrell-Carrio summarizes it as "… a way of understanding how suffering, disease, and illness are affected by multiple levels of organization, from the societal to the molecular" [10]. Where the disease model assumes disease to be fully accounted for by deviations from the norm of measurable biological variables, the biopsychosocial model "is a way of understanding the patient's subjective experience as an essential contributor to accurate diagnosis, health outcomes, and humane care." In a decade where prescriptions for opioid pain medications have doubled, and low back pain remains the most common cause of disability, the biopsychosocial model provides paradigm shift for understanding chronic pain [11].

11.2 Epidemiology and Risk Factors

Studies regarding the epidemiology of low back pain are highly variable. The incidence of developing a new episode of back pain has been estimated to be as low as 4 % and as high as 93 % [12–15]. Larger longitudinal studies indicate that this incidence is much lower, i.e., between 3 and 5 %. The incidence of back pain that did not require professional medical care was much higher at 30 % [13]. Prevalence is difficult to study due to variance among study populations and the varying factors that may affect the development of low back pain. Studies estimate that 15–20 % of adults experience memorable low back pain within 1 year. Up to 80 % experience such pain over a lifetime [16–19].

Back pain varies with age as well. Back problems are more often related to claimed disability during the third to fifth decades. These are the prime working years where low back pain leads to the greatest disability and days off work. Interestingly, the symptoms of low back pain do not worsen with age-related degeneration of intervertebral disks [20–24]. Back pain in the elderly is thought to be one of the most important factors to affecting the state of health [25]. Similar to younger adults, the prevalence of back pain in patients older than 65 has been to be 13–49 % [26], but such pain seems to be more episodic and intermittent with a lesser occurrence of chronic pain [27]. Despite the relatively high prevalence of abnormal curvature of the spine in adolescents, the incidence of low back pain is quite low. Some studies suggest that the peak age for development of back pain in children is 13–14 years. Beyond this age, the risk for developing back pain is similar to that of adults [28–30].

Risk factors for the development of low back pain include demographic, physical, socioeconomic, psychological, and occupational factors. It is typically comorbid with other chronic pain and medical conditions. In one study of chronic spinal pain, 68 % reported some type of other chronic pain, 55 % had chronic illness, and 35 % had a mental disorder [31]. Many

studies of these risk factors are small and include only self-reports of the variables. A review by Hildebrandt discusses 55 factors related to the individual and 24 occupational factors that have been linked to low back pain [32]. Many studies have looked at the relationship between socioeconomic status and level of education with the development of back pain. The association seems to be not so much with the incidence of pain, but with the ability to adjust to pain. The incidence of disability from back pain was 22–25 times higher in patients with less than 7 years of education compared with those with college degrees [4].

11.3 Observations Regarding Low Back Pain and Disability

Many people live with low back pain without disability. What is the difference between these patients and disabled patients? In order to understand this, it is important to differentiate between pain and disability. Both are related in that they are generally subjectively relayed by the patient and are not viewed the same in any two patients. There is no objective measure for either of these disorders. Pain is an unpleasant feeling often caused by intense or damaging stimuli. Disability is related to the patient's perceptions and attitudes *about* pain [33, 34] and is therefore made up of a host of psychological, social, and cultural issues. It is often based on avoidance, previous painful experiences, and maladaptive coping skills [24, 35, 36].

It is also useful to discuss the difference between acute and chronic pain. Acute pain often bears a close relationship to an inciting event and may be thought to stem directly from tissue injury. Chronic pain, on the other hand, is often due to behavioral adaptations which may have little relationship to the initial physical injury. Therefore it is difficult to treat by medical or surgical means. An example of this is the "failed back syndrome." Chronic pain becomes a syndrome of emotional distress, depression, and disease conviction [24].

Despite low back pain and sciatica taking center stage in many medical circles today, there is no evidence that the biology of the problem has changed at all over the years. Back pain is the same as it always has been. It is low back disability that is a new concept. Ninety percent of patients with low back pain get better within 6 weeks, in spite of technologically advanced medical and surgical care or interestingly no care at all [3, 21, 24, 37]. This is likely a product of the explosion in the size and complexity of the healthcare systems of western countries and people's perceptions that the abilities of modern health care should be able to "eliminate" pain. Physicians bear some responsibility in this regard. It is they who "certify" patients with pain to be excused from work, thereby amplifying the global problem of low back disability.

11.4 Breakdown of the Disease Model of Illness

Recent functional imaging studies have borne out what humans have always intrinsically known – pain perception is a multifaceted sensory and emotional experience and thus can be modified by mental, emotional, or sensory mechanisms [38, 39]. It makes most sense, therefore, to attempt to understand primary pain disorders by addressing the entire context of the patient's illness; this is best approached with the biopsychosocial model. This model stresses the integration of the subjective experience of the patient with the objective physical findings of illness, and that both contribute to the patient's perception of disease. Engel, the father of this model, emphasizes the responsibility of the physician to treat the body, but also to assist the patient in understanding and adjusting to their illness, along coping with it mentally.

Just as physicians are often frustrated with the inadequacy of treatments available for back pain, many patients are not satisfied with the office visit either. Without the establishment of a diagnosis based on real pathology, the patient often has difficulties putting their pain in context, which can exacerbate anxiety and illness. Disk disease has become so ubiquitous, and patients may be given the nominal diagnosis of disk

prolapse, without any signs of nerve root compression or radiographic evidence. It is not long until this nominal diagnosis is confused with real disease pathology, and the patient receives the label of discogenic low back pain. These patients may eventually be treated with surgery that was not indicated and then "bounce" from clinic to clinic when their "curative operation" failed. Clinics are clogged with these patients, thus making it difficult to care for patients with true pathology. Making matters worse, patients will often go from clinic to clinic until a diagnosis is made, resulting in an incentive for physicians to make nominal diagnoses or risk losing patients. Indeed, a large study of the indications for spinal surgery in the mid-1980s showed that surgical decision-making was often driven by the duration and severity of pain and disability, the patient's illness behavior, and the failure of conservative treatment [40]. As might be expected, the success rate for surgical treatment based on a nominal diagnosis is at best 30–40 %. Interestingly, nearly every study in the last 50 years has shown presence of a psychiatric disease as an extremely poor predictor for good surgical outcome [24, 41–49]. Thus, the responsible surgeon must use the history and physical examination to tease out signs of psychiatric imbalance and consider this carefully prior to proceeding with surgery.

11.5 Work-Related Issues

Since complaints of low back pain peak during productive working years, one must discuss this process as it relates to time off work. First, this problem is most prominent in the group of chronic low back pain patients. In a study by Volinn et al., 2 % of workers eligible for industrial insurance filed a claim for back pain in 1 year. Of those, 12 % were off work for 90 days or more, thus consuming more than 88 % of the wage and medical compensation paid by insurance carriers [50]. This same study found that the complaints of back sprain and pain were closely related to workplace dissatisfaction and monotonous job tasks. The medical costs were largely comprised of surgery and hospital stays for "medical back problems." A study of Medicare patients found that 71 % of these "medical back" hospitalizations were inappropriate [51]. In their review of low back pain and healthcare utilization, Volinn et al. suggest that the level of both cognitive and economic investment in low back pain drives the therapy [52]. Only when further knowledge and education of outcomes regarding the treatment of low back pain become available and third party payers invoke more stringent guidelines for what will and will not be reimbursed will the trends in surgical and medical management change.

The historical and still common practice of "therapeutic rest" appears to be based on multiple fallacies. First, that pain is related to tissue injury and inflammation in the spine, and that rest will help to reverse or alleviate this process. Second, if the pain does not come from inflammation of the spine, it must come from degenerative disk disease, and the only way to allow the disk to heal is with rest. By the disease model of illness, this seems to be a logical progression, but as previously discussed, the disease model of illness does not translate well into the world of low back pain. Considering the biopsychosocial model and assuming that chronic pain is not due to significant injury or to instability of the spine, this treatment does not make sense at all. It aims to treat a process that likely is not active and fails to treat, and may actually *worsen*, the psychological aspects of the disease. Therefore, it may encourage the assumption of the "sick role." Indeed, there is only marginal evidence in the literature that suggests that rest improves low back pain or even sciatica. This is a somewhat difficult area to study without a high degree of bias, and as one might expect, the major studies are methodologically flawed. In the majority of these studies, it was found that shorter periods of rest were more beneficial (or less harmful) than longer periods [24]. There have been no studies that suggest that activity worsens pain or tissue injury in the absence of a known pathological correlative lesion. Many of these patients will continue to complain of the same degree of pain, whether they are performing their daily activities or not. It is clear that prolonged rest is harmful to both the

body (bone demineralization [53], cardiac deconditioning [54, 55], loss of muscle strength) and mind with depression and anhedonia [56, 57]. The physician who has prescribed rest to the patient with low back pain has clearly done them no favors in the majority of cases.

Similarly, regarding the notion that a person's back pain can affect their job, the characteristics of their job can affect their back pain. A study by Boos et al. showed that the characteristics of one's job (listlessness, job satisfaction, working in shifts) were more likely than MRI identified disk abnormalities to predict which patients would seek medical treatment [58]. Similarly, these factors also are useful in predicting which patients are likely to be off work at follow-up.

All of these issues have opened up much controversy regarding litigation and workers' compensation in our current healthcare system. In the present system, compensation is largely tied to the presence of physical examination findings and imaging confirmation of disk herniation. Some studies suggest that psychological factors may also be tied in to the selection of patients for workers' compensation benefits and that patients with emotional instability may be less likely to receive compensation [59]. There is decent evidence to suggest that patients who receive time-limited workers' compensation, as opposed to long-term disability, are more likely to return to work and have a good outcome [60]. Another study by Atlas et al. also revealed that patients who were receiving workers' compensation at baseline prior to their low back disability were more likely to be receiving long-term disability benefits than those who were not (27 % vs 7 %) and were also slightly less likely to be working at a 4-year follow-up [61]. This correlates with our earlier assertion that time off work and prolonged compensation benefits allow patients to more easily adopt the sick role.

Conclusions

It is clear that low back pain and disability are epidemic in virtually all parts of the industrialized world today [1]. The main differences among countries are manifested by the way back pain is viewed and treated. In the western society, the expectation from patients is generally that they will benefit from surgery, and if not, rest and time off work will be their best treatment options. It is also clear that low back pain does not fit into the classic treatment paradigm of the disease model of illness. In this case, the biopsychosocial factors may be more at play than actual physical tissue injury. These patients place a large burden on the medical system and often bounce from clinic to clinic until they find a physician who will treat them. They then are often the victim of unindicated surgery and fall into the category of failed back syndrome. It is clear that when surgical candidates are chosen carefully and selectively, surgical therapy can lead to the best and most efficient outcomes with early return to work and relief of symptoms. It is also apparent that the traditional method of therapeutic rest is inadequate and may actually lead to a decline in the patient's functional status. The exact role of workers' compensation and disability is still somewhat unclear, but it is likely that these will only reinforce sick behavior. We advocate for a multidisciplinary approach that involves spine surgeons, occupational therapists, physical therapists, mental health professionals, sports medicine specialists, and social workers. Via this method, appropriate surgical candidates can be selected, and the remainder of patients can be funneled into a low back training program that encourages them to become empowered and take control of their "disease" and avoid their "shopping around" for further treatment. Only by addressing all of these issues can patients with low back pain be adequately and efficiently managed.

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Legal Aspects in the Surgical Treatment of Lumbar Degenerative Disk Disease

12

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Legal issues and the practice of medicine are intrinsically intertwined. This is especially true in terms of the management of symptomatic lumbar degenerative disk disease (DDD). This chapter will focus on some of the legal aspects as they relate to lumbar DDD with particular emphasis on the surgically treated patient. Medicolegal issues, as they relate to the preoperative, intraoperative, and postoperative periods, will be individually addressed. Additionally perspectives on the management of worker's compensation cases and injuries which are being litigated will be included.

Lumbar surgery is indicated for those patients who experience symptoms due to a surgically treatable lesion despite appropriate nonoperative therapy. Once these conditions are met, a candid discussion should be held with the patient. The purpose of this discussion is to inform the patient of the numerous facts and, in essence, begin the process of obtaining informed consent. Within the USA, the legal concept of informed consent relative to health law began about 50 years ago. The first court records addressing a physician's duty to discuss the details and information concerning a proposed procedure appeared in 1957 [1, 2]. Since then, there have been numerous rulings and judgments related to informed consent, and this concept has been embraced almost universally by patients. Over 90 % of patients want the proper information to allow them to actively participate in their medical decision-making process. This is not always fully appreciated by physicians, and, in fact, many surgeons not only underestimate patients' desire for information but also overestimate how much time they spend obtaining consent [3].

In the USA, informed consent is formed from both civil law (tort law) and constitutional law (codified law). The foundations of US civil law are rooted in decisions regarding injuries inflicted upon one individual by another formulated by the medieval English courts of law. Civil law may be codified into state or federal laws and/or statutes if legislative bodies perceive that such an action is in the best interest of the society. Overall, the law of informed consent is based predominantly on civil law with constitutional laws codifying some essential elements. Informed consent is not a document and does not have to be written but rather a process which begins with a dialogue between the surgeon and the patient. The discussion should establish the expectations of both the patient and surgeon with regard to the procedure. The written documentation serves as a record that the discussion took place, but such notations usually do not completely describe the entire

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_12

exchange of information between the patient and physician. It is important to record the key features of the discussion, and certainly the more detailed the written documentation, the greater its benefit should there be some question at a later date as to what transpired during the informed consent process.

The surgeon has many obligations in the informed consent process. The primary duty is to inform the patient and obtain the patient's consent to proceed with a treatment plan in a respectful manner. The information exchange should include the results of pertinent diagnostic studies, explanation of the surgical procedure, and probable outcome of surgery. Alternative management strategies need to be listed, and the risks, benefits, outcomes, and potential complications of these options are reviewed. This portion of the discussion is critical; intentional suppression of such information has been judged by the courts to invalidate consent. Many surgeons do not discuss their specific surgical outcomes but, rather, rely on what is published in selected articles; this practice places the surgeon at great legal risk [4].

Providing reliable information on the outcome and benefits of surgery for degenerative lumbar disk disease is not easy. There are many conflicting opinions regarding the management of symptomatic lumbar spondylosis, and often even experts do not agree on the best treatment. For these reasons, a great effort to present an honest appraisal of the proposed procedure is necessary. It may be reasonable in many instances to explain that surgical treatment of degenerative disk disease is not an exact science, and there are many differing opinions. On the other hand, it is important that the surgeon adheres to the procedure for which the consent was obtained. Failure to do constitutes breach of contract, and battery may also be charged [5].

Spinal surgery dominates neurosurgical malpractice claims in the USA accounting for over 40 % of all claims. A widely publicized study from the New England Journal of Medicine revealed that neurosurgeons are the physicians most prone to face a malpractice claim – the yearly risk may be as high as 19.1 % [6]. Orthopedic surgeons followed closely in fourth place [6]. Most claims faced by neurosurgeons are related to elective lumbar surgery [7, 8]. While the reasons for these claims are many, a few of these complications require mention, particularly the infrequent and catastrophic ones. Introduction of sharp instruments such as rongeurs and curettes into the abdominal cavity may occur if the anterior annulus is violated. These instruments may harm the major blood vessels, ureters, or bowel. Such injuries are potentially life-threatening, and the lumbar surgeon should be aware of their various signs and symptoms and act promptly to diagnosis and treat the problem. Though frequently overlooked when obtaining consent due to its presumed rarity, symptomatic injury of intra-abdominal contents is estimated to occur in around 100 cases per year in the USA [9]. A 1998 study focusing on the medicolegal aspects of this potentially catastrophic injury demonstrates that it can be successfully defended, especially if immediately recognized and treated, but it still resulted in a verdict for the plaintiff or a settlement in 48 % of the time [9].

Postoperative vision loss (POVL) is another infrequent but potentially catastrophic complication of surgery for lumbar degenerative disk disease. POVL can happen due to ischemic optic neuropathy, central retinal artery occlusion, cortical blindness, or another unexplained mechanism [10]. Long associated with prone positioning, other risk factors include elevated blood loss, duration of surgery longer than 6 h, patient comorbidities (particularly diabetes), and systemic hypotension during surgery [11]. Its estimated incidence is 0.2 % of all prone lumbar surgeries, thus making it a very infrequent complication, though with life-altering consequences. Unfortunately, POVL is often not discussed by surgeons during informed consent. The American Society of Anesthesiologists issued an advisory suggesting that a physician "consider" disclosing the risk of POVL to high-risk patients; it does not address who (anesthesiologist versus surgeon), how, or when to do it. A possible reason for surgeons refraining from discussing this complication is a belief that patients would not accept surgery if told of the risk for POVL; however, Corda et al. have recently shown that a vast

majority of patients would prefer to be informed of POVL in a face-to-face discussion with the surgeon, and it would still not affect their decision to undergo surgery [12].

Cauda equina syndrome (CES) is also one of the main diagnoses quoted in legal claims related to spine surgery. Despite a low incidence (1–6 % of all disk herniations), it possesses a disproportionately high medicolegal profile [13]. It is a classical neurosurgical teaching that decompression should be achieved on an emergent basis, particularly if the syndrome is incomplete and either residual motor or urinary function is present [14]. Despite a number of meta-analyses published in recent years claiming benefit for decompression within 24 or 48 h, in reality the available evidence is of very low quality. Between 50 % and 70 % of cases have a very quick onset and progress to a complete syndrome rapidly; it may be argued that these patients already have their outcome set by the time they present to the hospital [14]. Ultimately, 75 % of CES patients will recover acceptable urinary function; this number may be higher in patients presenting with an incomplete injury. Most legal claims made over CES cases involve a delay in diagnosis and/or treatment; therefore, not only physicians of other specialties may be involved as well but actually be the main target of the claim. Gardner et al. reported on 63 claims made in the UK that 48 were directed to a general practitioner or an emergency physician, 2 against radiologists, and 13 to the spine surgeon [14]. Daniels et al. also found a significant correlation between verdict for the plaintiff and time to surgery >48 h [13]. Significant, persistent disability, on the other hand, has not been always associated with increased claims or verdicts for the plaintiff [13–15].

Considerable controversy is found in the recent medical literature over wrong-site and wrong-level surgeries. Wrong-site surgery not only fails to improve the patient's symptoms, but has major medical, legal, social, and emotional implications. An American Academy of Orthopedic Surgeons (AAOS) bulletin report stated, "A successful legal defense to surgery performed on the incorrect limb is almost impossible" [16]. In 2012, wrong-patient, wrong-site, wrong-procedure-type events were reported to be the second most common sentinel event (12 %) by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [17]. Preoperative marking of the surgical site, "time-out" verification routines, and intraoperative radiographic verification are some interventions designed to minimize the occurrence of this serious problem [18]. Utilization of intraoperative imaging is believed to be one of the most effective measures to reduce wrong-level surgery – Ammerman et al. demonstrated that incorrect identification of a lumbar disk level by an experienced surgeon without intraoperative imaging may happen in up to 15 % of cases. Despite having been designated a "never event" by the National Quality Forum, there is controversy in grouping wrong-level surgery in the same category as wrong-site, wrong-patient, or wrong-procedure errors [19]. While laterality or identification can be easily determined by anybody without medical training, identification of a specific thoracic or lumbar vertebral level is dependent on variable anatomy and interpretation of radiological studies, and therefore wrong-level errors should not be grouped in the "never event" category [20]. This may explain why over 90 % of spine surgeons report a "close call" of wrong-level error during surgery, and over 50 % admit to having performed a wrong-level procedure at least once; in two thirds of these cases, the error was identified and corrected still during the index procedure [21]. It may also contribute to a perception that while self-verification (i.e., by the patient) and "time-out" procedures have effectively contributed to decrease the number of wrong-site procedures, they may be ineffective to prevent wrong-level errors [20, 21]. In contrast to the fact that wrong-site surgery is virtually indefensible, Goodkin and Laska reviewed 68 cases of wrong-level surgery taken to court up until 2004 and found that in 13 of them a verdict in favor of the surgeon was achieved [9]. Perhaps their most important finding was that there was only one case in which the surgeon identified the wrong-level error during the index procedure and corrected it and was ever taken to court; in that

specific instance, settlement was based on the occurrence of an aortic laceration and death and not the wrong-level surgery [9]. In contrast, failure to identify the error, delays in addressing it, and alteration of medical records have all been associated with higher payments [9, 22].

Degenerative disk disease also has a profound societal impact based on the direct and indirect costs associated with it. Several studies have attempted to estimate the costs associated with LBP utilizing diverse methodology, but a common finding is that the indirect costs resulting from loss of productivity far exceed the direct costs of the treatment itself. In Sweden, Hansson and Hansson calculated that the total costs associated with treatment of degenerative disk disease were equivalent to 1 % of the Swedish gross national product. Direct costs accounted for only 7 % of the total costs; despite these monetary costs, only 28 % of patients placed on disability for DDD ever returned to work. Return-to-work rates after 2 years of disability were virtually nil [23]. Wieser et al. performed a similar study in Switzerland and calculated that the direct costs of treating low back pain in 2005 amounted to 2.6 billion euros or 6.1 % of the national spending in health care. Indirect costs, including social security payments, reached 4.1 billion euros; both figures combined represented 2.3 % of the Swiss GNP during that year [24].

The lumbar surgeon is also confronted with a spectrum of special issues when dealing with the patient who became symptomatic while working. Compensation status has been reported to be associated with poor outcome after surgery since the late nineteenth and early twentieth centuries in conditions compensated through litigation, such as the "railway spine" [25]. This issue has become much more important with the establishment of worker's compensation laws in industrialized countries [26, 27]. Harris et al. performed a meta-analysis on the literature examining the association between compensation status and outcome after surgery [28]. They reviewed 211 publications addressing this topic and found that 175 stated that the presence of compensation (worker's compensation with or without litigation) was associated with a worse outcome, and 35 found no difference or did not describe a difference, and 1 described a benefit associated with compensation [28]. A meta-analysis of 129 studies with available data ($n = 20{,}498$ patients) revealed the summary odds ratio for an unsatisfactory outcome in compensated patients to be 3.79 (95 % confidence interval, 3.28–4.37 by random effects model). Secondary analyses examining the data by country, procedure, length of follow-up, total follow-up, study type, and type of compensation showed the association to be consistent for all subgroups. This review demonstrated that the higher the compensation incentive, the greater the possibility of a negative outcome [29]. Other potential types of secondary gain such as pending litigation from an alleged accidental nonwork-related injury probably also adversely impact the surgical outcome of patients with lumbar degenerative disk disease.

The current legal system in the USA for adjudication of alleged medical malpractice and determination of damages has shortcomings. Surgeons may be assessed damages for medical malpractice when appropriate care was rendered or forced into a situation where a settlement within the limits of an insurance policy is the most advantageous way out of a lawsuit. Legislative restrictions on medical liability have been helpful in limiting such activity, but a few of these recent legal reforms have been overturned [9, 30]. A myriad of interests are at stake when these discussions are undertaken at the legislative level, and it is uncertain, at this point, if these recent changes will continue or be reverted. Other legal systems allow for a different malpractice environment. In Brazil, a Roman law-based system dictates that civil cases are not decided by a lay jury but by the judge him or herself. While by no means infrequent, the necessity of a strong demonstration of departure from accepted medical standards and harm done to the patient keeps malpractice lawsuits at a minimum, resulting that very few spine surgeons even maintain insurance coverage for legal actions. It has been repeatedly affirmed in Brazilian courts that the contract between the patient and surgeon is one of the means and not the results: as long as documentation demonstrates that the surgeon was available,

had the necessary expertise, and applied every reasonable effort on the patients' behalf, a final, unfavorable verdict is extremely rare [31]. Despite specific regional differences, two very simple measures, however, are universally known to reduce the number of lawsuits. Patients and their families are extremely unlikely to sue a surgeon they respect and perceive to work on their behalf; similarly, maintenance of poor records has been identified as a major complicating factor in a successful legal defense. Addressing these two simple problems through efficient communication and documentation is a prerequisite for a successful spine practice; before being surgeons, we should be staunch patient advocates.

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Cost-Effective Spinal Surgery: Reality or Oxymoron?

13

Casey Madura, Daniel K. Resnick, and Nathaniel Brooks

13.1 Introduction

Economic inquiry regarding the cost-effectiveness of medical treatments is necessary but not sufficient for medical decision-making. Nowhere is this more obvious than in spine surgery. Fusion surgery in particular has been singled out as expensive, dangerous, and ineffective [1,2]. Recent congressional inquiries into the relationship between surgeons and industry [3] reflect the depth of concern political leaders, and by proxy the public, have regarding these issues.

This chapter is an overview of cost-effectiveness research. A description of the process of cost-effectiveness analysis (CEA) is presented along with several examples of these types of analyses that have been applied to different types of spinal surgery. The goal of this chapter is to provide a working knowledge of the elements of a cost-effectiveness analysis and to help you understand the benefits and pitfalls of this type of research. This should aid in determining the quality of cost-effectiveness studies.

13.2 Cost-Effectiveness Analysis (CEA)

CEA is a method of comparison of the costs and effects of two competing medical technologies (in this sense, a medical technology is any new therapy, whether medical or surgical). It is a method of study that helps determine the most efficient way to spend resources that have already been committed. CEAs are used to answer the question "What is the best way to spend resources that have already been committed to health care?"

At the most basic level, CEAs are conducted in order to determine the cost of one technology versus another (the comparison technology is often referred to as the *comparator*) relative to the health benefits of each. Cost-utility analysis (CUA) represents a special case of CEA in which the outcome is in terms of cost per QALY.

Health effects (either negative or positive) are often referred to as *health utilities*. By convention, a state of perfect health is given a health utility of 1, while death is given a value of 0. Various levels of health are then assigned values declining from a maximum of 1 with each decrement in health (note that negative utilities are possible,

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_13

representing health states worse than death). These utility values are then translated to *quality-adjusted life years* (QALYs).

The difference in cost between the two procedures is then calculated and compared to the difference in benefits. This outcome, the incremental cost-effectiveness ratio (ICER), represents the expenditure necessary to gain one additional unit of the measure of choice (e.g., 1 year of life in perfect health (1 QALY) in a CUA).

The results of these studies can be represented graphically. Figure 13.1 demonstrates the four possible cost-effectiveness scenarios. As you can see the "dominant" situation in the "southeast" corner of the graph is obviously good, i.e., increased benefit with decreased costs. The next situation, the "northeast" corner, represents increased benefit at increased cost. This can be good or bad depending on how costly and how significant the benefit and is by far the most common modern-day scenario. For example, an expensive instrumented fusion following decompression in a patient with a cauda equina syndrome may only slightly improve the QALYs and may not be considered worthwhile the cost. But a simple laminectomy in an incompletely paralyzed patient that allows full recovery would be considered good by almost everyone.

The "northwest" corner of the graph is considered to be bad. This will also give a negative ICER and corresponds to a more expensive worse outcome. This situation does occur from time to time and illustrates the need for high-quality research to investigate "standard" practices. For example, the use of steroids in patients with severe head injury was studied and was found to both worsen outcome and accrue increased costs. The "southwest" corner reflects a less expensive but worse outcome. Again, whether this is a good or bad result can be subjected to interpretation.

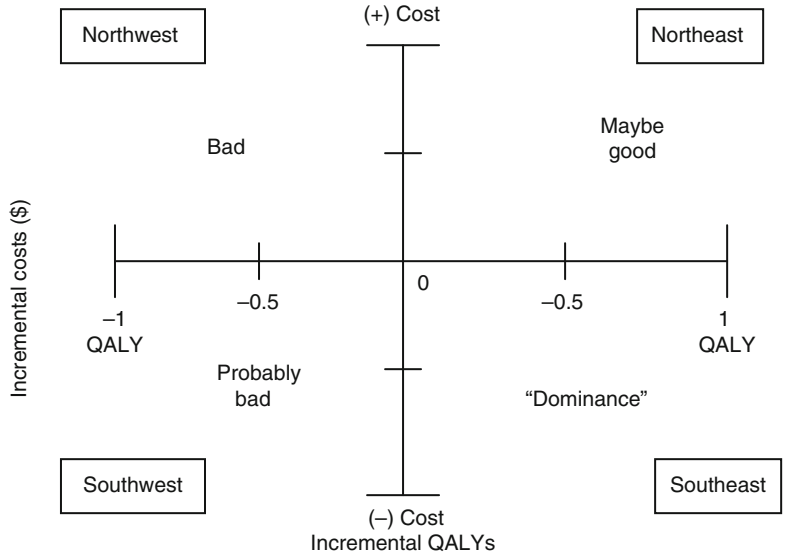

Fig. 13.1 This is a typical graph seen in cost-effectiveness analysis literature comparing incremental costs versus incremental QALYs. The x-axis represents the health benefit in terms of QALYs. The y-axis represents the cost. After a CEA is conducted, if a technology is found to be beneficial from the perspective of QALYs and cost less than its comparator, it is said to be *dominant* (southeast quadrant). Likewise, a technology found to be less beneficial and more costly than its *comparator* is said to be dominated (northwest quadrant). Such results require only common sense to interpret. Most often, however, CEAs will report that a technology is more beneficial *and* more costly (northeast quadrant) *or* less beneficial and *less costly* (southwest quadrant). The interpretation of such results depends on the perspective of the interpreter. A technology that is marginally better in terms of utility at great cost may not be "cost-effective" if the more important aspect is cost control. On the other hand, a technology that is marginally worse than its comparator but at much less cost may be judged to be cost-effective if cost is the most important aspect of the decision process

At face value, CEA is a relatively simple analysis. There are, after all, only four input categories: (1) cost of the medical technology of interest, (2) cost of the comparator medical technology, (3) health utility associated with the new technology, and (4) health utility associated with the comparator medical technology.

13.3 Establishing Health Utilities or What Is a QALY?

QALYs are a unique outcome measure because they represent a composite measure of quality and quantity of life. It was first used to evaluate the effectiveness of hypertension medications [4]. QALYs are derived from health utilities multiplied by time (typically years). This is important to understand because not all QALYs are created equal (see Fig. 13.2). For example, one full year of life in perfect health represents one QALY (Fig. 13.2). Similarly, one full year of life in a health state valued at 0.5 (half as good as perfect health) represents 0.5 QALY (Fig. 13.2). Figure 13.2 provides a demonstration of two very different scenarios in which there are equal QALY values.

Health utilities are assigned using preference-based health state questionnaires in which populations respond to questionnaires developed to inquire about a number of functional domains. Some commonly used health state questionnaires are the EuroQol-5D, HUI2 and HUI3, etc. The EQ-5D, for example, has 243 possible health states, each with a unique utility value. Utilities for each health state are obtained by asking a general population to rate a sample set of those 243 health states (mathematical modeling was used for the remainder). Instruments such as the HUI2 and HUI3 have even more possible states of health (requiring even more mathematical modeling).

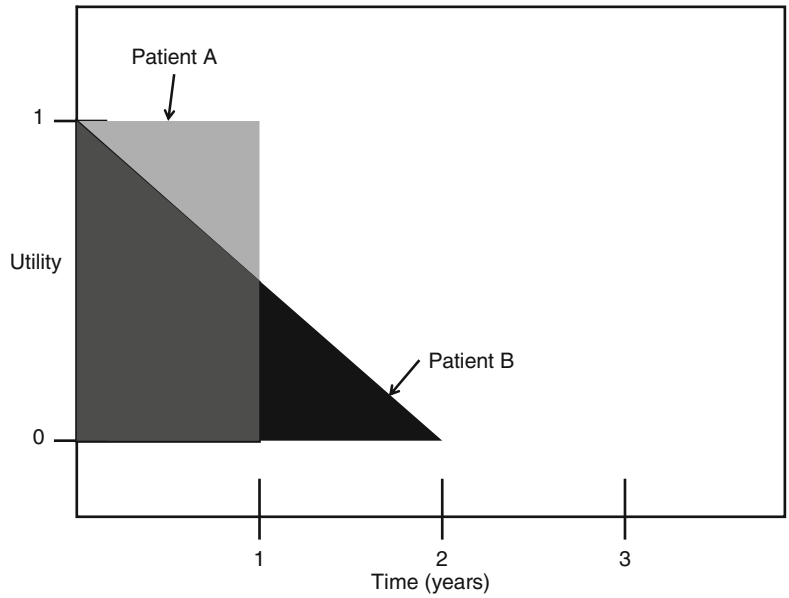

Fig. 13.2 Time, measured in years, is on the *x-axis*. Health utility is measured on the *y-axis* with a value of 1 representing perfect health and 0 representing death. Note that there is space for utilities valued below 0 reserved for health states valued as worse than death. In graphical format, the number of QALYs is equal to the total shaded area. In the case of patient A, one half-year of life was spent in a state of health valued at 0.5 followed by sudden death, resulting in a total of 0.5 QALY. Patient B, on the other hand, experiences a gradual decrement in health state utility until death at 1 year. This also translates into 0.5 QALY. While QALYs represent a way to reduce benefits across patients and interventions into a comparable number, it is important to understand that two very different life courses can represent the exact same number of QALYs

There are a number of important questions to consider that affect the generalizability of CEA results. First, the assignment of health state utilities is biased based on the group providing the ratings. In the case of the EQ-5D, the utilities were derived based on the preferences of the general British population. Since its initial inception, there have been a number of other utility value sets derived for American, Danish, German, and many other populations. However, if a study uses a health state questionnaire that has not been validated in a particular study population, then the health utilities and thus QALYs derived from these questionnaires should be viewed critically. Second, many important considerations (economic, social, etc.) are omitted due to complexity, insufficient data, or limitations of the perspective used for the study [5,6]. If the economic benefits of return to work or the ability to maintain a higher level of employment, for example, is not considered, then the reported QALY may be understated. Lastly, it is also important to recognize that much of the available data comes from carefully designed clinical trials designed to answer one or maybe two hypotheses. Very little *pragmatic* data is included in these trials. Much like the narrowly defined randomized control trial, the generalizability of a CEA study that uses this design is often not generalizable to many clinical situations. Like other aspects of CEAs discussed above, rather than invalidating CEA results, knowledge of such limitations helps inform each reader's final interpretation.

13.4 Establishing Cost

At first glance, cost seems like the simplest aspect of a CEA. Currency is much easier to understand than utility. Yet, significant heterogeneity exists from hospital to hospital and clinic to clinic clouding the "true cost" of a good. Additionally, confusion over the origins and accuracy of hospital charges makes determining the true cost even more difficult [7]. Finally, there are often costs that are not included in studies. These can include the cost of missing work, not only to the patient but to the company; the cost of the time family members and friends spend providing "free" or informal care to patients; the cost to society of diverting resources that could have been used elsewhere to health care instead. Most frequently these are the costs of informal care, but may also include many other aspects that go into the "true cost" of health care.

13.5 Establishing Comparison Technologies

A CEA involves comparison between two existing technologies. The important detail, however, is that one is not free to choose *any* existing technology as a baseline. Instead, the comparator (i.e., the technology serving as the baseline) to which the new technology is being compared *must* be the next best treatment that remains cost-effective. For example, in evaluating new methods to promote fusion in spinal surgery, it is not acceptable to compare each new intervention to medical therapy alone; rather, the comparison must be between the new technology and the standard surgical fusion procedure (see example below). This has two implications. First, in designing a CEA, it is important to choose a baseline technology that is not already known to be *dominated* (i.e., more effective at less cost, Fig. 13.3a). Second, inappropriate choice of comparators can lead to calculation of an extremely misleading value known as the average cost-effectiveness ratio (ACER) rather than the ICER (Fig. 13.3c).

Drawing conclusions from the CEA literature requires a true understanding of this concept. For example, in 2012, Virk et al. [8] set out to determine the cost-effectiveness of the various options available for fusion grafts. The question is simple enough: in patients undergoing L4–L5 fusion for degenerative spondylolisthesis, which bone graft option (iliac crest bone graft (ICBG), local bone graft (LBG) only, corticocancellous chips (CCC) plus LBG, recombinant human bone morphogenetic protein (RhBMP) plus LBG, demineralized bone matrix (DBM) plus LBG) is the most cost-effective in the treatment of these patients? The

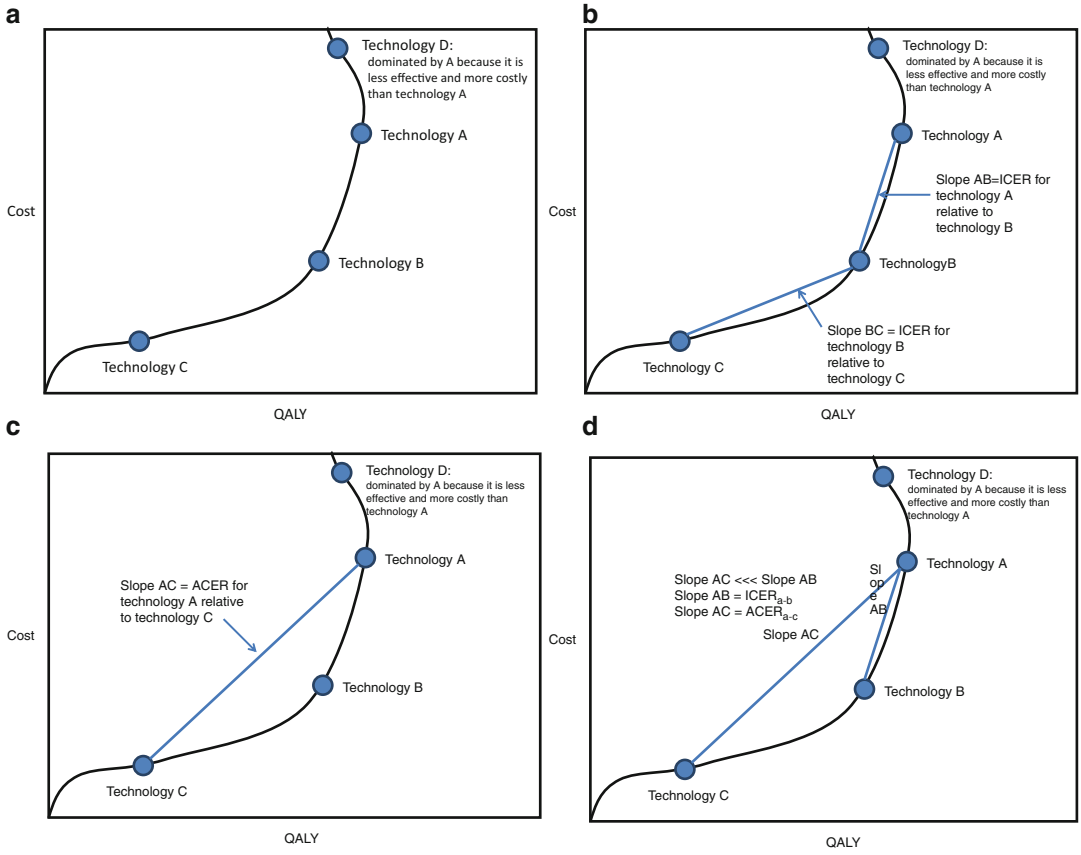

Fig. 13.3 (**a**) A standard cost-effectiveness curve with health effect, often reported as QALYs, on the x-axis and cost on the y-axis. Four different technologies are represented here representing four different treatments for the same disease. Technology D is both more costly and less effective than technology A. This is the definition of dominance, and therefore, technology D would be referred to as being dominated by technology A (sometimes this concept is reported as a negative ICER). Therefore, there is no sense in conducting a CEA for technology D versus any of the other technologies because there is already an alternative that is better in terms of cost and health effect. (**b**) Lines connecting technology A to technology B and technology B to technology C have been drawn. These lines are a graphical representation of what is measured in a CEA, i.e., the difference in cost compared to the difference in health effect. The slopes of these lines, referred to as Slope AB and Slope BC, respectively, represent the ICERs of technology A compared to technology B and technology B compared to technology C. Remember that the slope of a line on an *xy-axis* is the amount of change in vertical units (*y-axis* units) for an increase of one horizontal unit (*x-axis* units). In this case, Slope AB and Slope BC represent the cost of A relative to B and B relative to C for each increase of one QALY. This is otherwise known as the ICER. (**c**) In this case, technology A is compared directly to technology C. The line connecting technology A to technology C has a slope designated "Slope AC." Note that even though technology B derives some benefit for patients relative to technology C, a comparison such as this ascribes *all* of the health benefits to technology A. This is despite the fact that technology A adds very little benefit on top of technology B at a significantly higher cost. (**d**) The effect of inappropriately choosing a comparator that is not the next-best non-dominated alternative. If a CEA analysis were performed comparing technology A to technology C, ignoring technology B, the result would be reported as an ICER equal to the slope of the line connecting technology A to technology C, denoted here as slope AC. This is in contrast to Slope AB referring to the slope of the line connecting technology A to technology B. A more horizontal line represents a lesser slope, and therefore, Slope AC is much less than Slope AB. If only slope AC was reported, technology A would appear to be much more cost-effective than it really is. Therefore, understanding the alternatives available and choosing the appropriate alternative technology for comparison are crucial in conducting CEAs and are critical points that must be understood and examined when interpreting a CEA

paper concludes resoundingly that LBG + RhBMP is the most cost-effective method of fusion with an ICER of $16,595/QALY.

The paper falls short in its methodological integrity in its designation of "no surgical intervention" as the comparator for each of the other types of fusion (p. E206). In this study, it is clear that the purpose is to determine the most cost-effective mode of fusion. With "no surgical intervention" as the comparator, the only possible comparison for this paper is "one type of fusion versus nothing". Rather, LBG + DMB, +CCA, and +BMP should each have been compared ONLY to the LBG group. Likewise, ICBG and LBG should have been compared to each other. In each case, these would have been a comparison between a medical technology and its next-best, non-dominated alternative. This choice of comparator limits cost calculations in this paper to ACERs only, taking away any ability to make true cost-effectiveness comparisons with this data.

13.6 How Much Should a QALY Cost? It Depends

An additional question to consider is in regard to how to interpret an ICER. After all, the ICER is simply a value stating the cost of one additional QALY. The question remains, "How much *should* a QALY cost?" Basic economics states that, in a free market, the cost of a QALY should be equal to the opportunity cost of treatment. The opportunity cost is the value of the benefits that would have been gained had another alternative been selected. For example, an employed patient choosing to undergo surgery loses earnings as a result of required time off work. Unfortunately, because health care in the USA is far from a free market, tolerable cost-per-QALY values are often arbitrarily assigned. In the USA, a value of $50,000 has been the predominant figure and can be traced back to the amount Medicare was willing to pay for patients with end-stage renal disease on renal dialysis in a year in the mid-1980s [9]. Why this value was chosen is not clear. Regardless, the arbitrary nature of this figure is best illustrated by the fact that it has not changed since its inception [10]. Some have suggested that true US societal preferences have upper and lower bounds of $264,000 and $183,000, respectively [11]. The UK National Institute for Health and Care Excellence (NICE) has never explicitly stated an appropriate ICER value but in general has always accepted interventions with an ICER less than £20,000, evaluated those with an ICER between £20,000 and £100,000 lb on a case-by-case basis, and rejected those with ICERs greater than £100,000 [11].

The appropriate value for an ICER might also change based on the identity of the decision-maker. A perfectly healthy 87-year-old widower in a nursing home who has lost independence due to financial stress may not be willing to pay much for one additional QALY. A young male in his 30s with children may have a completely different threshold regarding his willingness to pay for one additional QALY. What value is appropriate for the hospital administrator trying to provide the best care at the least cost? What about the insurance executive responsible to shareholders and not the patient?

13.7 Sensitivity Analysis

CEA results are often dependent on values that represent a range rather than a single definite value. Sensitivity analysis represents a method to evaluate the effect of such variability, parameter by parameter. Because CEAs typically depend on some type of model with different events, outcomes, probabilities, costs, and utilities, they are dependent on decisions made by the researchers conducting the study and by the available evidence. These decisions are more frequently than not subject to significant debate and controversy. While discussion of the details of this topic is beyond the scope of this chapter, any true CEA should include such a section.

13.8 Examples of CEA in Spinal Surgery

This first study is an example of a retrospective analysis that only takes into account hospital costs. Using CEA Angevine et al. [1] wanted to

figure out what the benefit was using allograft versus autograft and/or using a plate following anterior cervical diskectomy [12]. The authors determined the estimated cost by reviewing the hospital bills for 78 patients who had undergone treatment for single-level degenerative cervical disease at one institution. Results are reported as cost per QALY gained. The incremental cost-effectiveness ratio (ICER) was $496 comparing ACDF with autograft to ACDF with allograft. When a plate was added, the ICER increased to $32,560.

This marked increase in cost can be misleading. This is not the cost of the surgery and hospitalization, roughly $11,290 for the ACDF with allograft group and $12,690 for the ACDF with plate group. This is a ratio of difference in cost of these two groups over incremental change in QALY. In this instance, that is, $1,400/0.043, QALY = $32,560 per QALY.

The study showed that short-term costs of anterior cervical diskectomy and fusion with plating might be higher than those associated with ACDF with autograft or allograft and that the 5-year cost-effectiveness of the procedures is similar. This study did not include post discharge costs, lost wages, or return to work into its model. Therefore, although all of the patients seem to do well in the short term and long term from their symptoms, the proposed underlying benefits to using instrumentation, faster return to work and life and no need for external orthosis, are not reflected in the results. If such factors were considered, a lower ICER for plate fixation would be expected.

One of the most common procedures in lumbar spine surgery is the treatment of herniated lumbar disks (HLD). Hansson and Hansson performed a cost-effectiveness analysis in 2006 evaluating operative intervention versus conservative management in patients with HLD [13]. This was a cohort study of 184 individuals in Sweden with a 2-year follow-up. Each person from the surgery group was matched to a similar person in the nonsurgery group with the same age, gender, distribution of pain, intensity, and diagnosis with a total of 92 patients per group. Among other variables the EuroQol-5D questionnaire provided a measure of overall health-related quality of life. The data from this questionnaire was used to establish a QALY for the cohort. Costs were estimated using both direct (e.g., surgical costs) and indirect costs (e.g., absenteeism from work). The surgical group cost was $43,119 and the nonsurgical was $44,638 for the 2-year follow-up. Patients reported a benefit from surgery of 0.327 QALY. The direct cost for improvement of 1 QALY or incremental cost-effectiveness ratio (ICER) was -$4,648 for the surgical group.

In this situation the negative ICER is a good thing. In cost-effective speak the surgical treatment is said to be "dominant." This means that in this study surgery increases QALYs at less cost than conservative treatment.

Soegaard et al. used cost-effectiveness analysis to evaluate circumferential lumbar fusion versus posterolateral fusion [14]. This study included a total of 148 patients from a single center, randomized, prospective clinical trial in Denmark with a 9-year follow-up. The study was taken from the perspective of societal viewpoint; therefore, all possible resources and activity occurring in relation to the treatment contribute to the overall cost estimates. This study included the cost of surgery reoperations and rehospitalizations, primary care service utilization, medications, patient costs, and productivity costs. All costs were expressed in 2004 US dollars. The study had the unexpected result of finding that circumferential fusion costs are roughly $50,000 less per QALY than posterolateral fusion and again "dominates." One explanatory variable for this finding may be the lower rate of reoperations seen in the circumferential group. Also important were the costs of primary care, ancillary care (PT/rehab/chiropractors) and patient out-of-pocket expenses in the follow-up period.

13.9 Using CEA to Improve Practice

It comes as no surprise that the majority of CEAs originate in countries with socialized health care where the question is how to allocate resources

that have already been appropriated. These studies are used to provide a basis for prioritizing treatments within national healthcare budgets. When applied to health care in the USA, CEAs are of much more questionable value. Despite this, CEAs are increasingly being used by hospitals, payers, and providers to justify or deny coverage of procedures.

Polly et al. [15] provided an example of the potential for CEAs to allow comparison across treatment. In their retrospective study of 1,826 lumbar spine fusion patients, the authors compared lumbar fusion surgery to total knee arthroplasty (TKA), total hip arthroplasty (THA), and coronary artery bypass graft (CABG). The outcome measure was clinically significant improvement on the SF-36 (5.42 points) vs. hospital reimbursement. The cost for lumbar fusion was $7,300, TKA $6,600, THR $4,500, and CABG $22,000. While this study is flawed because of its retrospective nature, heterogeneous cohorts, and unclear demonstration of meaningful benefit, it does provide some data comparing "cost-effective" surgical treatments within our society with lumbar fusion surgery.

Studying cost-effectiveness is of little utility when comparing interventions with different outcomes, but when the outcomes are reduced to a comparable measure, i.e., QALYs, CEAs may be able to act as a tiebreaker to help determine which treatment may be of benefit. For example, does PEEK offer any benefit for ACDF compared to allograft? From the clinician's point of view, it is important to carefully inspect all CEAs. Assumptions made can drastically influence the outcome. Concepts such as sensitivity and dealing with uncertainty are not even discussed here. Sensitivity analysis and other concepts such as discounting and extended dominance are beyond this chapter's scope.

The bottom line is this: perfectly conducted CEAs are subject to many significant problems. Many of these are subjective judgments that are necessitated by a lack of data on the exact topic of investigation. Whether or not a clinician agrees with the assumptions made greatly influences the applicability of the paper's findings to a clinician's own patient. Given this limitation, CEAs can only be recommended as an additional tool for clinicians to use in deciding upon a treatment. In countries such as the USA where the healthcare system is fragmented with significant heterogeneity in treatment decisions, CEAs are only likely to be the deciding factor in treatment decisions where everything else is equal. Such situations are understandably rare.

In other countries, where health care is administered within a predetermined budget, the use of CEAs differs. The National Institute for Health and Care Excellence (NICE) in the UK has an entire program dedicated to the development of comprehensive CEAs which represent a crucial component used by the UK's National Health Service in making determinations of which treatments to cover. The true value of a CEA depends almost entirely on the context in which it is being used.

13.10 Final Word

CEAs can be both extremely valuable and extremely misleading. The above discussion sheds light on many of the issues that go into CEAs. At the end of the day, the value of each study depends on whom one is talking to. Much of the data is objective, but decisions about which data to include and exclude are often subjective. In some cases, even the data has an element of subjectivity to it (expert opinion). As should be obvious, CEAs are objective measures reliant upon subjective data. This chapter provides only a cursory introduction to some of the issues that surround the interpretation of CEAs. It is critical to understand that the ICERs generated by these studies represent only one piece of information that should be considered when making policy decisions.

The purpose of this chapter was twofold. First, it is intended to introduce some of the most basic concepts in CEAs. Second, it underscores the subjectivity inherent in many of these studies. Ultimately, CEAs are only one more piece of information rather than *the* answer. In other words, economic evaluation is necessary but not sufficient for medical decision-making.

Consideration of all of these limitations requires the reader to insert his/her own judgments as to whether decisions made by the investigators were appropriate. Interpretation of such studies requires significant subjective judgments on the part of the reader. Just as when reading a spine film or performing a procedure, algorithms are helpful.

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Outcome Measures for Spinal Surgery

14

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Abbreviations

CER	Comparative Effectiveness Research
Cost/QALY	Cost per Quality-Adjusted Life Year Gained
EQ-5D	European Quality of Life-5 Dimensions
HRQOL	Health-Related Quality of Life
ICER	Incremental Cost-Effectiveness Ratio
MCID	Minimum Clinically Important Difference
NDI	Neck Disability Index
ODI	Oswestry Disability Index
PRO	Patient Reported Outcome
QALY	Quality-Adjusted Life Year
RMDQ	Roland-Morris Disability Questionnaire
SCB	Substantial Clinical Benefit
SF-12	Short Form-12
SF-36	Short Form-36
SF-6D	Short Form-6 Dimensions
SPORT	Spine Outcomes Research Trial
SRS-22R	Scoliosis Research Society-22 Revised
VAS	Visual Analogue Scale

14.1 Introduction

The past two decades have seen major advancements in the use of an evidence-based approach to medical treatment, including in the field of spinal surgery. Historically, there has been a lack of patient-reported outcomes (PRO) data to guide surgical decision making. Prior parameters of success in spinal surgery—such as fusion rates, physician assessment, and complications—did not necessarily correlate with clinical outcomes [1–3].

More recently functional outcomes, patient satisfaction, and healthcare costs have become the major focus of spinal surgery research. Newer PRO measures are at the forefront and provide valid data that better reflects the change in overall health status of an individual after treatment. By quantifying health-related quality of life (HRQOL) changes experienced by the patient, these outcome measures allow for a more relevant assessment of treatment effectiveness.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_14

14.2 Outcome Measures Categories

Health-related quality of life (HRQOL) measures assess, through self-reported means, how a patient's physical and mental health is affected over time by a disease process or disability. They can also quantify response to treatment for the specific disease or disability. There are several types of HRQOL measures. These include generic measures, disease-specific measures, pain scales, and health utility scales.

14.2.1 Generic Measures

Generic measures apply to a variety of disease and treatment groups and seek to evaluate multidimensional aspects of health-related function [4]. Originally described by Ware in 1992 to survey health status in the Medical Outcomes Study (MOS) [5], the Medical Outcomes Short Form-36 (SF-36) is the most well known and widely used of these generic outcomes tools. The SF-36 is a 36-item self-administered questionnaire that explores physical and mental health through eight health concepts or domains. These domains include physical functioning, social functioning, general health, mental health, role emotional, role physical, bodily pain, and vitality. From the SF-36 two summary scores can be measured: a physical composite summary score (PCS) and a mental composite summary score (MCS). Using norm-based scoring, all domain scales have a mean of 50 and a standard deviation of 10 based on the general 1998 US population [5]. The SF-36 has been found to be a valid and reliable measure in different disease states, including patients with low back pain [6, 7]. In contrast to other surveys, the SF-36 presents a considerable respondent burden. There are shorter versions available, such as the SF-12 [8] and SF-8 [9], but all items must be answered in order to calculate the PCS and MCS. In addition, the shorter versions do not provide scores across the eight health domains. Lastly, the SF-36, SF-12, and SF-8 require a license to administer and cannot be easily scored in clinic.

Although generic measures translate the effects of treatments across multiple diseases and populations into a numerical value, they do have some limitations. A major disadvantage is that they can miss important components of health evaluation as related to specific diseases or treatments.

14.2.2 Disease-Specific Measures

Disease-specific measures focus on the effects on HRQOL associated with a specific medical condition. Therefore, these disease-specific measures are more likely to detect the effects of a specific intervention on a disease process. The Oswestry Disability Index (ODI) [10, 11], Roland-Morris Disability Questionnaire (RMDQ) [12], Neck Disability Index (NDI) [13], and Scoliosis Research Society-22R (SRS-22R) [14–17] are examples of spine-specific measures.

The ODI is a self-administered survey measuring "low back-specific function" on a ten-item scale with six response categories each [10, 11, 18]. Each item is scored from 0 to 5 and then transformed into a 0–100-point scale with the higher the score signifying a greater disability experienced by the patient. Patients scoring between 0 and 20 have minimal disability, between 21 and 40 have moderate disability, between 41 and 60 have severe disability, between 61 and 80 are crippled, and between 81 and 100 are bed-bound or exaggerating their symptoms. Relative to RMDQ, it has less of a floor effect and is better used in populations with more severe disability [12]. ODI can be easily administered, scored, and interpreted in the clinic. This allows it to help guide treatment decisions.

The RMDQ is a measure of function and daily activity limitations. There are 12 items answerable by yes or no, giving a score ranging from 0 to 24. A higher score reflects greater disability. Relative to ODI, it has less of a ceiling effect and is better used in evaluating populations with lesser disability [12, 19].

The NDI is a ten-item self-administered survey measuring disability in patients with

neck pain. Each item is scored from 0 to 5 for a maximum score of 50 [13]. Similar to ODI and RMDQ, a higher score is associated with a greater disability. Some authors may use a percentage score when one section is missed or is not applicable to what is studied, in which case the range of scores would be from 0 to 100 %.

The SRS-22R is a 22-item questionnaire with five domains, including self-image, pain, activity, mental, and satisfaction, measuring disability specific to scoliosis patients [14, 16, 17]. Each domain is scored from 1 to 5, with higher scores indicating improved outcomes. For patients with either adolescent idiopathic scoliosis or adult spinal deformity, the SRS-22R is the most widely used outcome instrument to measure disease burden and the effect of treatment [20–22].

14.2.3 Pain Scales

The visual analogue scale (VAS) [23–26] and numeric rating scales [27, 28] are commonly used pain scales in which the patient subjectively interprets the pain experience and assigns a value to the measurement scale. The VAS is a 100-mm-long horizontal line anchored on the left with "no pain" and on the right with "worst pain experience." Patients mark on the line the point that they feel best represents their current level of pain. The score is determined by measuring in millimeters from the left-hand side of the line to the point that the patient marks. Numeric rating scales are a variant of the VAS and ask patients to rate their pain levels using numeric values, such as from 0 being no pain at all to 10 being the worst pain imaginable [27]. Advantages of pain scales include a low respondent burden, ease of administration, and a universally accepted tool. Limitations include the difficulty in interpreting objectively the subjective nature of the measurement. Pain scales are also difficult to translate when patients' pain is in flux and changes depending on the time of day, level of activity, or other extrinsic factors.

14.3 Health Utility Scales

Health utilities measure the impact of a disease on society by quantifying health status, or change in health status, weighted for societal preference. Societal impact could theoretically be evaluated by valuing change in SF-36 PCS or ODI score. However, these outcome measures do not give a value that can be directly used in economic analysis.

Utilities or health state values are measured using a single index score for each state of health. Scores range from 0 for death to 1 for perfect health. They are weighted for the relative desirability of the health state. Utility scores are combined with life years for use in economic analysis.

Standards for economic evaluations recommend using societal values (utilities or preferences) [29]. There are two common approaches to obtaining "societal health states values," direct and indirect [30, 31]. Direct measurement of value for health states of a representative sample of the population uses methods such as standard gamble, time-trade-off, and visual analogue scale ratings [30]. In standard gamble, the subject is asked to choose between remaining in a state of ill health for a period of time, or undergoing a medical intervention with the gamble that it will either restore them to normal health or lead to death. As implied by the name, time-trade-off method asks respondents to choose between remaining in a state of ill health for a period of time or being restored to normal health but also having a shorter life expectancy. Visual analogue scale asks respondents to rate a state of ill health on a scale from 0 to 100, with 0 being dead and 100 being perfect health. Indirect measurement uses preference-based measurement systems such as the Quality of Well-Being Scale [32], the EuroQol EQ-5D [33], SF-6D [34], or the Health Utilities Index (HUI) [35].

14.3.1 EQ-5D

Established in 1987 by the EuroQol Group, the EQ-5D has two parts. The first part assesses five

dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension receives a score based upon patterns of response. From these responses, a simple descriptive profile is created. In addition, from this data set a health index score is made by assigning a value to the health states from a set of population-based preference weights. The second part of EQ-5D is a 20-cm visual analog scale where patients rate their own health status.

14.3.2 SF-6D

Derived from a selection of SF-36 items as a means of economic evaluation, the SF-6D estimates a preference-based health measure and describes 18,000 health states. It was constructed using a selection of 11 items from six of the eight SF-36 health dimensions. A representative sample of the UK general population ($n=611$) were asked to value a subset of 249 SF-6D states using the valuation technique of standard gamble. Regression models were used to estimate health state values for the full range of SF-6D health states. The resultant algorithm can be used to convert SF-36 data at the individual level to societal health state values or preference scores.

14.3.3 Health Utility Score Uses

The value of health utility scores derives from their ability to be converted to a standard measure across populations and diseases through utility weighting and in turn be used to determine cost utility or value.

The most commonly used measure of cost-effectiveness is the cost per QALY gained (cost/QALY). In general, when an intervention cost/QALY is in the range of $50,000–$100,000, the intervention is considered cost-effective [36]. To take into account the local financial situation, some researchers have suggested a cost/QALY of less than the local GDP as a means to define an intervention as cost-effective in that region [37].

Although health utilities have been widely utilized in Europe, there is limited data from other countries with regard to spinal disorders. Fortunately, it has been shown that standard disease-specific measures for spinal disorders—NDI [38], ODI [39], Cervical Spine Outcomes Questionnaire (CSOQ) [40], and the SRS-22R [41] —have been shown to accurately predict SF-6D scores and therefore can be used to determine cost utility and QALY values. With the use of these data transformations [42, 43], utility scores can be created from prior studies and provide a means for cost-effectiveness research.

Healthcare economists and health outcomes researchers use QALYs as a means of communication. Universally, healthcare costs have skyrocketed. Along with these increases has come the importance of cost in healthcare decision making to both the patient and society.

14.4 Relevant Outcomes Measures

Researchers in spinal disorders have been at the forefront of measuring outcomes based on health and cost utility. In the mid-1990s, clinical researchers studied generic measures such as SF-36 to evaluate surgical intervention for common spinal disorders [44, 45]. With HRQOL measures clearly proving to be important, both generic and disease-specific measures—ODI, SF-36, back, and leg pain scores—became the benchmark of clinical outcomes research in spine surgery. However, for most surgeons the observed changes in HRQOL measures do not clearly convey an intrinsic value of the treatment.

Another limitation of outcomes research has stemmed from interpretation of statistical significance. Previously, clinical relevance came from a change in outcome that reached statistical significance. However, as more study sample sizes have become larger and therefore better powered, small changes in outcome may reach statistical significance. These statistically significant differences identified do not always lead to clinically relevant differences. Therefore, thresholds of clinical relevance must be established. Many studies today only report group means or the mean change for a group. This may have some

relevance, but a small number of patients who do very well or very poorly may distort the interpretation. Authors should also report on proportion of patients who improve, remain the same, and deteriorate in order to provide the entire story.

14.5 Current and Future Outcomes

With an unclear interpretation of HRQOL measure changes and reaching statistical significance, there has been an increase in use of thresholds to define clinical relevance; the most widely used being the minimum clinically important difference (MCID) [46, 47]. MCID is defined as the smallest change or level of improvement a patient can reproducibly identify as a clinically relevant change [46–49]. The MCID can be thought of as *change above the statistical noise*. Unlike thresholds that report the group means, MCID reports a distribution of patients who achieve the MCID. While MCID's strength comes from providing a measureable clinical change, its weakness comes from not necessarily providing a worthwhile clinical improvement. The MCID threshold is less than an optimal surgical result. It is more appropriate as a floor value, rather than a goal for defining clinical success [50].

Substantial clinical benefit (SCB)—a threshold for commonly used HRQOL measures in lumbar spine function correlated to a patient's perception of major clinical improvement in outcome—has been suggested as an alternate for MCID. SCB values typically are between 50 and 100 % higher than MCID values for most commonly used HRQOL measures [50]. SCBs are a more optimal surgical result in comparison to MCIDs. SCB provides an important tool to evaluate clinical outcomes based on our expectation and patients' expectation for substantial benefit with interventional treatment.

The future of spine surgery relies upon the community to generate comprehensive and valuable data that provides the appropriate information for clinical analysis. However, the data collection must not be overly burdensome for patients or physicians. As the cost of healthcare rises, the evaluation of cost versus benefit for treatments becomes more and more critical. The cost per HRQOL score improvement or more likely cost per QALY gained are ways of translating HRQOL to a financial value. The comprehensive and valuable data must include spine-specific measures along with generic measures or health utilities, which permit the assessment of value to society. The ODI, back/leg pain scores, and EQ-5D would provide a core data set for lumbar disorders while simultaneously minimizing respondent burden. This data in turn would provide information on both HRQOL and cost-effectiveness, thereby facilitating societal valuation of clinical outcomes.

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Lumbar Degenerative Disk Disease: Workup and Conservative Treatment

15

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Low back pain (LBP) is a common complaint, with over 80 % of the population experiencing an episode of LBP during their lifetime [1]. Recent data from the Centers for Disease Control and Prevention found that 29 % of interviewees had experienced LBP pain at some point during the previous 3 months [2]. Usually, the clinical course is benign and most patients recover within a few months. It has been reported that over 90 % of patients will recover within 3–6 months [1, 3].

Identifying the pain generator of low back pain is often challenging. Several structures have been implicated as possible pain progenitors in chronic low back pain, including the intervertebral disks, zygapophyseal joints, bone, ligaments, fascia, and muscles of the lumbar spine. Axial pain that is thought to originate from the disk is termed "diskogenic" pain. The etiology of low back pain is often controversial, but multiple studies suggest that the intervertebral disk is the most common source of chronic LBP [4–6].

Lumbar degenerative disk disease is a common imaging finding. This finding increases with age and typically does not correlate with pain. However, studies have shown that a degenerative disk can be symptomatic, specifically those degenerative disks with outer annular tears. These tears are chemically sensitized with annular granulation tissue and have nerve fibers containing nociceptive neurotransmitters such as substance P [7, 8].

Degenerative disk disease (DDD) can be seen as early as the second decade of life and is closely linked to age [9]. With progression of degenerative changes of the spine, intervertebral disks transition from hydrated and pliable to dessicated with internal disruption, narrowing of the disk, annular bulging, and changes of the biochemical composition. Degenerative changes are usually observed in the surrounding structures, resulting in osteophyte formation, zygapophyseal joint arthrosis, vertebral endplate changes, and loss of disk interspace height. After the age of 50, degenerative changes are radiographically evident in nearly all individuals [10]. This chapter explores the pathophysiology of these changes and explores the clinical presentation, radiographic correlations, and conservative management for disk-related low back pain.

15.1 The Degenerated Disk: Anatomy and Pathophysiology

The disk morphology is composed of the central nucleus pulposus and the outer annulus fibrosis. The vertebral end plates are the top and bottom portions of the vertebrae that interface with the disk.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_15

15.1.1 Nucleus Pulposus

The nucleus pulposus is composed of collagen, proteoglycans, and glycoproteins. Aggrecan, the major structural proteoglycan with the disk, maintains tissue hydration. The strong negative charges of the constituent glycosaminoglycan chains attract and bind water. This water composes 90 % of the composition of the disk and provides the viscoelastic properties of the disk and allows compressive forces [10–13]. The nucleus pulposus is also prevented from deforming while loaded by the cartilaginous end plates, located between the intervertebral disk and the adjacent vertebral body. The end plate is composed primarily of hyaline cartilage [14].

15.1.2 Annulus Fibrosis

The integrity of the annulus is critical to maintaining disk structure. A normal annulus is comprised of concentric sheets of fibrocartilage, called lamellae, separated by layers of ground substance. The tensile strength of the peripheral annulus is due to the lamellae of collagen fibers which are predominately type I collagen. Type I collagen is the primary type of collage found in tendons elsewhere in the body [14].

15.1.3 Disk Innervation

Degenerative changes that occur with aging are difficult to differentiate from those that are pathological. The lack of a clear understanding of the nociceptive source of low back is partially to blame. Initially histological studies were unable to demonstrate that the intervertebral disk was even innervated [15–17]. Improved histological techniques using immunohistochemistry have demonstrated that the innervation of the human intervertebral disk is by the sinuvertebral nerve [16, 17]. In a healthy disk, only the outer annulus is innervated with nerve fibers penetrating as deep as 3 mm into the superficial annulus [18]. However, as part of the degenerative process, the nerve fibers extend deeper into the inner annulus and nucleus pulposus. Freemont et al. demonstrated nerve growth into the inner third of the annulus and into the nucleus, 46 and 22 % of cases, respectively, in patients with chronic LBP who underwent spinal fusion [19].

This more extensive innervation with penetration deeper into the disk is a potential source of pain. Disk tissue is biologically active, and a mechanical insult will result in a proinflammatory cascade. Inflammatory cytokines, such as tumor necrosis factor alpha and interleukin-1, perpetuate the inflammatory cascade [20]. The ingrowth of small nonmyelinated nerve fibers can expose the nociceptive fibers to inflammatory cytokines and potentially trigger symptomatic DDD [13, 17, 18, 21–23].

15.2 The Degenerated Disk: Clinical Presentation

15.2.1 History

The importance of taking a good history cannot be overemphasized. This is the most important part of the outpatient visit and can help a clinician in determining an accurate diagnosis as well as directing treatment. There are specific findings on history that can predict pain from a disk etiology, also known as “diskogenic pain.” Certain characteristics in the patient’s history, such as age, body mass index, gender, to name a few, can better predict diskogenic pain. These characteristics will be reviewed in detail in the following paragraphs.

15.2.1.1 Screening Questions

General screening questions for LBP include characteristics of pain, such as onset, location, quality, severity, duration, progression, aggravating factors, alleviating factors, and associated symptoms. A pain drawing can be a helpful tool [24]. It is important to screen for the so-called red flag symptoms that may suggest a more serious issue. This can include back pain with unexplained weight loss (malignancy), fevers (infection), and progressive neurological changes including weakness, bladder dysfunction, bowel

dysfunction, or saddle anesthesia (cauda equina syndrome). Past and ongoing medical issues are important to include. For example, it would be important to know about prior malignancies, systemic steroid use, history of intravenous drug abuse, or an immunocompromised status [25].

15.2.1.2 Location of Pain

Identifying the location of pain is helpful in determining an etiology. Diskogenic LBP is generally axial. Alternatively a disk herniation can lead to radicular symptoms or a combination of axial and radicular symptoms. Regardless, in this context, we are referring to primarily axial pain. It should be noted that the most common location for diskogenic pain is in the lower lumbar region. DePalma reported the most common levels for diskogenic pain were L5–S1 (40 %) followed by L4–L5 (30 %) [26].

The presence of midline low back pain, defined by pain over the spinous process, has been reported as a good indicator for a diskogenic source of pain. If a patient reports midline LBP, the reported positive predictive value for diskogenic pain is 73 %. A patient who does not report midline LBP has 96 % chance of not having diskogenic LBP. This is in comparison to those who report paramidline pain, which is defined by pain more than one fingerbreadth lateral to the midline. Paramidline pain is more often associated with facet joint pain (FJP) or sacroiliac joint pain (SIJP). Therefore, the presence of midline pain can be used as a tool that increases the probability of diskogenic pain and decreases the probability of a facet or sacroiliac joint pain [26].

It has been reported that the "centralization" phenomenon is a predictor of diskogenic pain and further correlates with the idea of a midline component of pain. This phenomenon is the movement of pain away from radicular and more centrally towards midline in response to repeated lumbar movements (McKenzie assessment).

15.2.1.3 Age

As stated, the radiographic finding of a degenerative disk becomes more common as a person ages. However, a symptomatic painful disk is more common in the younger age group. Thus, increases in age are associated with a decreased likelihood of diskogenic pain but an increased likelihood of facet or sacroiliac joint pain, as seen in Fig. 15.1 [27, 28].

Young adults (age 20–35 years) are reported to be more likely to have diskogenic pain as the source of chronic low back pain (70–98 %) regardless of gender or BMI. By age 50, diskogenic pain was still the most likely source of pain (40–65 %), except for women with low BMIs (average 18.5 kg/m2) in which sacroiliac pain was more likely (49 %). By age 65, men, regardless of BMI, were more likely to have a facet pain (30–54 %), while only women with BMI greater than 30 were more likely to have facet pain (46–64 %) [29].

15.2.1.4 Aggravating and Alleviating Factors

The literature suggests that that diskogenic LBP is worse with sitting, flexion, and rotational forces. Additionally, it has been reported that increasing intrathoracic pressure (coughing, sneezing, bearing down for a bowel movement, etc.) may ultimately transfer forces to a sensitized disk and aggravate diskogenic pain. Diskogenic pain may be alleviated with lying or standing, which correlates with Nachemson's classical study looking at disk pressures in various positions (Fig. 15.2) [30–32].

By measuring intradiscal pressures, Nachemson's landmark study has provided clinicians with a fundamental understanding of postural changes and its effect on intradiscal pressure. There is a linear relationship between the applied external load and the measured intradiscal pressure, with the highest strains occurring in the posterolateral region of the annulus fibrosus. Compared with pressures in the upright position, reclining reduces intradiscal pressure by 50–80 %, unsupported sitting increases the pressure by 40 %, forward flexion and weight lifting increases the pressure by 100 %, while forward flexion combined with rotation increases pressure by 400 % [30]. Figure 15.2 further shows the various positions and exercises and their corresponding disk pressures [33]. The greatest risk for annular strain is a combination of flexion, axial rotation, and

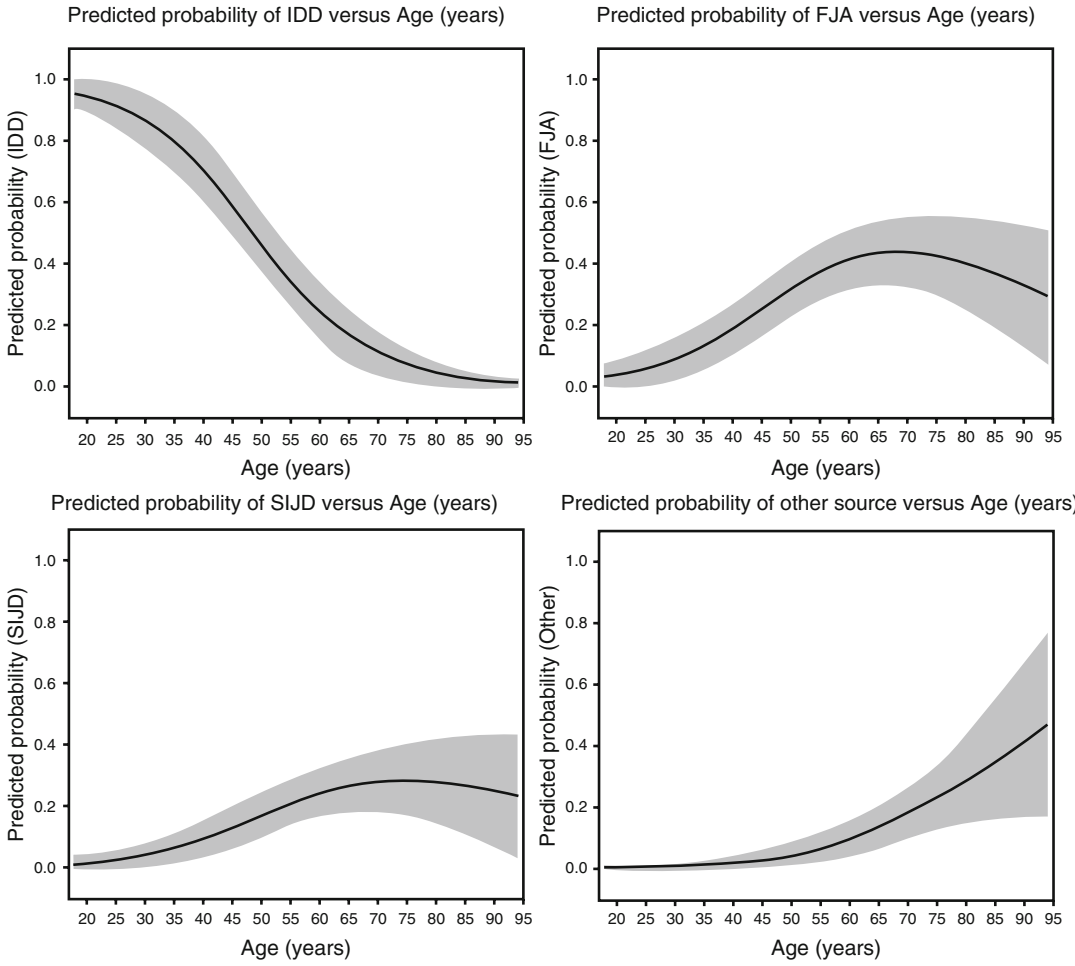

Fig. 15.1 Predicted probabilities and 95 % confidence intervals for internal disk disruption (*IDD*), facet joint pain (*FJP*), sacroiliac joint pain (*SIJP*), and other sources of low back pain (*LBP*) as a function of age (Adapted from DePalma et al. [27]; with permission)

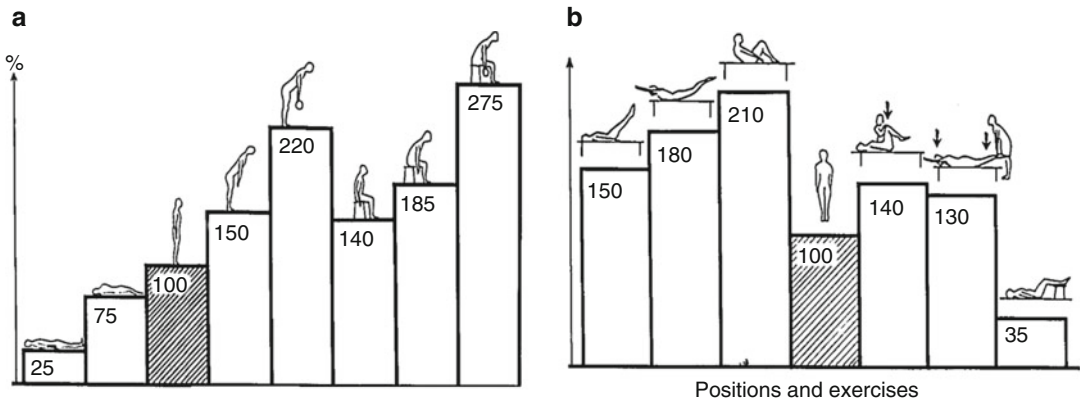

Fig. 15.2 (**a**) Relative change in pressure (or load) in the third lumbar disk in various positions in living subjects. (**b**) Relative change in pressure (or load) in the third lumbar disk in various muscle-strengthening exercises in living subjects (Adapted from Nachemson [30])

compression forces, placing the most pressure in the posterolateral inner annular zone. These asymmetrical loads on the spine are believed to be the source of chronic mechanical overload and may explain why lumbar disk herniations tend to occur in the posterolateral region of the annulus fibrosis [31].

Additionally, it has been reported that aggravation of pain when rising from a seated position correlates with a probable positive diskogram and diskogenic pain. With zygapophyseal joint pain, there is no provocation of pain when rising from sitting position. SI joint pain on the other hand was associated with rising from sitting but is more unilateral and lacks a midline pain component [34]. Unfortunately, the side of a symptomatic annular tear on imaging does not correlate with the side of a patient's back pain [35].

15.2.1.5 BMI

An elevated body mass index is associated with lumbar degenerative disk disease seen on lumbar MRI [36]. However, as noted previously, radiographic changes are not always associated with clinically painful disks [37, 38]. A recent study has indicated that a higher BMI does not correlate with diskogenic low back pain, but rather facet or sacroiliac joint pain [[39]].

15.2.1.6 Gender

Gender differences also correlate with the source of LBP. Women, when adjusting for age and BMI, had increased odds of sacroiliac joint pain compared to diskogenic pain or facet joint pain. Younger men were more likely to have diskogenic pain as their source for chronic pain.

15.2.1.7 Surgical History

Unfortunately, a history of prior back surgeries can increase an individual's likelihood for chronic LBP. Diskogenic pain is the most common reason for chronic LBP after a lumbar diskectomy (Table 15.1). Although radicular pain usually improves after a diskectomy, some have residual low back pain. It has been shown that the most common etiology in this situation is diskogenic pain (82 %) [40]. Conversely, if there has been a lumbar fusion especially when fused to the sacrum, sacroiliac joint pain is the most likely source of low back pain followed by diskogenic pain, facetogenic pain, and soft tissue irritation due to fusion hardware.

Table 15.1 Predictors of diskogenic pain

Midline pain
Young age
Male gender
Smoker
Pain aggravated with seated position or sit to stand
Pain alleviated with supine or standing
History of prior lumbar diskectomy

15.2.1.8 Psychosocial Considerations

Since pain is a subjective experience, it is also important to explore the psychosocial issues. Evidence of psychosocial stressors can often amplify or prolong the pain response. Factors including emotional stress, anxiety, depression, occupational factors such as poor job satisfaction, involvement in litigation, number of failed previous treatments, poor sleep, avoidance behaviors, and catastrophic thinking all contribute to a better understanding of the patient's condition, diagnosis, and therapy plan and also provide some prognostic value [41, 42]. These psychosocial factors are valuable tools in discriminating between symptomatic and asymptomatic disk herniation [43]. Additionally, it is important to inquire about health habits such as smoking and alcohol and drug use. Smoking has been associated with LBP and degenerative disk findings on imaging studies [44].

15.2.2 Physical Examination

The pertinent physical examination findings generally can be found on the focused exam of the lumbar spine. On general inspection, it is not uncommon to see some loss of lumbar lordosis, especially if there is secondary muscle guarding. Range-of-motion (ROM) testing can be utilized. As mentioned before, the presence of midline low back pain over the spinous process has been reported to be a good indicator for diskogenic pain. Thus, important information can be gathered by palpating over the spinous process.

Table 15.2 Waddell signs

Signs	Description
Distraction	Inconsistent findings of pain when patient is distracted. An example would be radicular pain with a positive straight leg raise, but when distracted there is no pain on seated straight leg raise
Overreaction	Inappropriate, disproportionate reactions to a request. This may manifest with exaggerated verbalization, facial expression, tremors, or collapsing
Regionalization	Motor or sensory abnormalities without anatomic basis. Diffuse give away weakness could go along with this
Simulation	Lumbar pain with a light axial load on the head. Lumbar pain with simultaneous pelvis and shoulder rotation in unison
Tenderness	Exaggerated sensitivity or dramatic reproduction of pain with light touch of the soft tissue or with skin rolling

Conversely, if there is tenderness over the paramidline region, this may suggest facet or sacroiliac pain [26, 34]. In addition, paramidline pain can reflect myofascial pain.

With diskogenic low back pain that is axial in location, there generally should not be any associated neurological deficits. Still, it is always prudent on an initial evaluation to evaluate manual motor testing, sensory testing, and reflex exam. These are primarily used to rule out other more concerning issues.

Lastly, some patients may have secondary gain issues. They may present with symptom magnification or malingering. Waddell signs have been described as a way to screen for such patients (Table 15.2). However, some studies have suggested that Waddell signs are not a reliable method to discriminate from organic pain [45].

15.3 The Degenerated Disk: Imaging

The high prevalence of degenerative findings on MRI in asymptomatic individuals has led the clinical relevance of these findings to be questioned [46–48].

Still, imaging for chronic LBP is used and plain radiographs are typically the initial imaging choice. MRI is felt to be more helpful in the evaluation of diskogenic LBP [49]. Diskography has been considered by many to be the gold standard, not without controversy. Imaging findings are eloquently discussed elsewhere in this book; thus, they will only be briefly discussed here.

Some studies have shown a positive association between low back pain and reduced signal intensity and/or reduced disk height [50–52]. The relationship between degenerative findings on imaging and low back pain remains controversial, with conflicting conclusions in the literature. Many studies fail to show any association between structural abnormalities and symptoms [53–55]. In addition, abnormal structural findings are not predictive of the future development of low back pain [51].

In a patient with diskogenic pain, one would expect that there would be at least some disk desiccation on T2-weighted images (T2WI). The likelihood of diskogenic pain is unlikely if the disk appears well hydrated with normal architecture on MRI.

Annular fissures have been associated with diskogenic pain. These appear as high intensity zones (HIZs) on T2WI (Fig. 15.3). These were first described by April and Bogduk in 1992; the presence of an HIZ was found to be highly specific for a concordant reproduction of pain on diskography [56]. Other studies found the correlation between HIZ and reproduction of pain on diskography to be low [57–59]. The discrepancy in the literature has led the accuracy and reliability of HIZ as a sign of diskogenic pain to be questioned. A number of studies have described a high prevalence of HIZ in asymptomatic patients, ranging from 24 to 50 % in different studies [60, 61]. It is clear from the high prevalence of HIZs in the asymptomatic population that not all annular tears are painful. Aprill, who first described HIZs, has suggested that true symptomatic annular tears tend to be larger and not the commonly seen small HIZs.

Vertebral body endplate signal changes on MRI were first described by Modic et al. in 1988, when he correlated endplate changes on MRI with histopathological findings [62]. Modic et al.

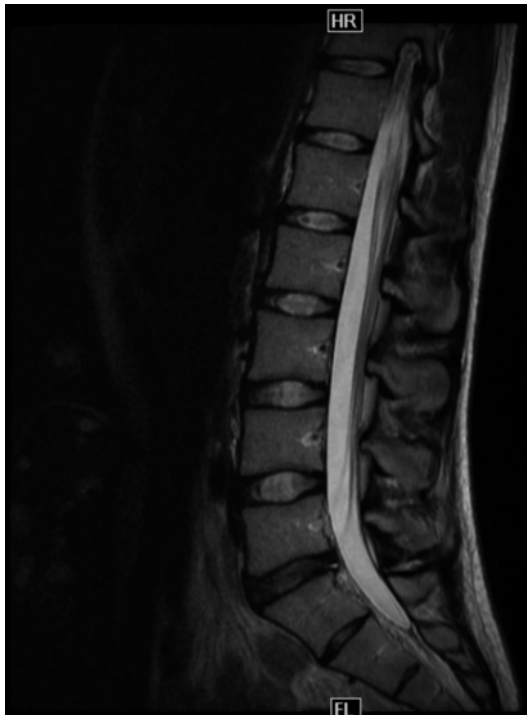

Fig. 15.3 L5/S1 posterior disk high-intensity zone

described three distinct subchondral bone marrow changes, or Modic changes. Type I changes appear edematous (dark on T1WI, bright on T2WI), type II have a fatty appearance (bright on both T1WI and T2WI), and type III changes appear sclerotic (dark on both T1WI and T2WI). Modic changes appear dynamic and are likely different stages of the same pathological process.

Modic changes have been associated with low back pain. Type I changes are more commonly associated with pain. There have been studies suggesting that type I Modic correlates with LBP 20–73 % of the time and has been associated with the reproduction of low back pain with diskography [53, 62–66]. More severe Modic changes, extending over 25 % of the vertebral height, had a 100 % concordance with pain on diskography in one study [58]. The presence of Modic changes in addition to other degenerative findings (loss of disk height and a reduction of disk signal) increased the specificity for positive diskography from 79 to 97 % [66]. Other studies have failed to demonstrate a statistically significant association between Modic changes and concordant pain on diskography [67–69].

Diskography is thought by many to be the gold standard for diagnosing diskogenic low back pain, although there is controversy. Diskography is considered positive when there is reproduction of concordant pain, outer annular tear (confirmed on post diskography CT scan), low pressure provocation, and normal control disk(s). Numerous studies have confirmed these criteria, suggesting this is a valid and reliable test [70]. However, intense debate continues. Recently, a published study suggested that diskography may cause accelerated progression of degenerative findings. Many clinicians have questioned these findings. Nevertheless, such findings do raise concerns [71].

15.4 The Degenerated Disk: Conservative Treatment

There are a variety of treatment options for diskogenic low back pain. Most treatments are focused on conservative options including physical activity, physical therapy, medications, lifestyle changes, complementary medicine, and injections. These treatments often have limitations in diskogenic low back pain. However, there are other interventions like biological injections that have shown promise for the future.

15.4.1 Physical Activity

Physical activity is a frequently used modality to address those with diskogenic low back pain. There is evidence to suggest that activity is better than inactivity in dealing with low back pain. Studies have shown that exercise improves pain, global well-being, and physical function [72]. It also produces multiple other health benefits compared to those who are sedentary and decreases risk of long-term disability [73]. Providers should encourage patients to start slow and advance to regular daily exercise. To remain engaged and continuously challenged, patients should be encouraged to vary the types of activity and set personal goals [73, 74]. Although bed rest had traditionally been the treatment for acute low back pain, this theory has been refuted. Patients with acute low back pain who were asked to

avoid bed rest fared better than those who were asked to rest in bed for 48 h. By day 7, those who had remained active had more fully recovered compared to the bed rest group. Furthermore, there were no adverse outcomes in the non-bed rest group [75]. It should be emphasized to the patient that light activity can actually enhance the repair process and, conversely, fear avoidance behaviors can lead to a vicious cycle of chronic pain as an outcome [76].

15.4.2 Physical Therapy

Physical therapy has been shown to be helpful for those with nonspecific chronic low back pain, both in adult and pediatric populations [77, 78]. Active exercise is generally preferred to passive modalities. There are a number of exercise programs including activity as usual, aerobic activity (e.g., walking, cycling), aquatic activity (pool rehabilitation), directional preference (McKenzie method), flexibility training (e.g., yoga), proprioception/coordination (stability ball, wobble board), stabilization training (e.g., low load exercise targeting abdominal, pelvic, and spinal truck muscles), and strengthen training. There is some data that suggests lumbar strengthening and proper mechanics can increase stability and decrease stress and strain on the spine. In theory, this should help with pain [76].

15.4.3 Medications

Medications are commonly used for the management of low back pain. Acetaminophen (paracetamol), nonsteroidal antiinflammatory agents (NSAIDs), muscle relaxants, antidepressants, and pain medication are some of the more commonly prescribed medications for low back pain. A number of systematic reviews in the literature provide good evidence regarding the efficacy of these medications [79].

A number of studies have assessed the effectiveness of acetaminophen (paracetamol) for nonspecific low back pain. These studies suggest that it is helpful and that it is comparable or slightly inferior to NSAID use [79–84]. Acetaminophen has an excellent safety profile when administered in proper therapeutic doses (less than 4000 mg per day), but hepatotoxicity can occur with misuse and overdose. In the United States, acetaminophen toxicity has replaced viral hepatitis as the most common cause of acute hepatic failure and is the second most common cause of liver failure requiring transplantation. In response to this, the FDA in January 2014 issued a statement that combination prescription pain relievers that contain more than 325 mg of acetaminophen per tablet, capsule, or other dosage unit should no longer be prescribed because of a risk of liver damage.

NSAIDs are among the most commonly used medications for pain. They have been shown to be helpful for acute and chronic low back pain [79–81, 85]. There is currently insufficient evidence for aspirin (acetylsalicylic acid) use for low back pain. The mechanism of action of NSAIDs is the blockage of cyclooxygenase activity which converts arachidonic acid to prostaglandin H2, the precursor of prostanoids. COX exists as two isoforms: COX-1, which I is responsible for the hemostatic prostanoid synthesis, and COX-2, which is responsible for proinflammatory prostanoid production. COX-1 is constitutive within platelets and is associated with the production of thromboxane, which strongly promotes platelet aggregation.

NSAIDs have well-documented GI, renal, and cardiovascular side effects. COX-2 medications have less GI side effects, but both nonselective and COX-2 NSAIDs affect the kidney. Some COX-2 medications have been taken off the market because of increased atherothrombotic vascular events [86, 87]. More recent studies have suggested that all NSAIDs have a cardiovascular risk, with naproxen having the least risk [88]. Thus, it is recommended that NSAIDs be used with caution, especially in those with GI, renal, and cardiovascular risks. Additionally, as a person ages, NSAIDs become more risky. In general, NSAIDs should be used for the shortest time period possible.

The U.S. Food and Drug Administration requires that the summaries of product characteristics of all

NSAIDs carry a boxed warning about the risks of cardiovascular disease, whereas the European Medicines Agency's Committee for Medicinal Products for Human Use decided that coxibs (but not NSAIDs) should be contraindicated in patients with coronary heart disease or stroke and used with caution in patients with risk factors for coronary heart disease [89–91].

Muscle relaxants are occasionally used, as well. A Cochrane Review found that these medications are moderately superior to placebo for short-term relief in acute low back pain [92, 93]. There is a lack of evidence in chronic low back pain [82, 94, 95]. This whole class of medication is well known to cause sedation, although serious complications are quite rare.

Antidepressants are also frequently used for low back pain. Two high-quality systematic reviews found antidepressants to be more effective than placebo for pain relief. However, effects on pain were not consistent across antidepressants. Tricyclic antidepressants (TCAs) were slightly to moderately more effective than placebo [95, 96]. Selective serotonin reuptake inhibitors (SSRIs) have not been shown to be effective for pain relief. But serotonin and norepinephrine reuptake inhibitors (SNRIs) have been used for pain relief. In the United States, duloxetine is the only FDA-approved medication for chronic musculoskeletal pain and chronic low back pain.

Common side effects of TCAs include drowsiness, dry mouth, dizziness, and constipation. The common side effects of SSRIs and SNRIs are nausea, sexual side effects, and depression. There is a black box warning of suicidality with these medications. In addition, the SNRIs affect on norepinephrine can potentially elevate blood pressure.

Opioid medications are also used for low back pain. There is moderate evidence for short-term benefit. There is a lack of evidence for long-term use in chronic low back pain [79]. The most common side effects with these medications include dizziness, drowsiness, nausea, constipation, rash, and at high doses respiratory suppression. Yet other issues plague this class of medication. The risk for abuse and misuse poses a problem. The use of opioids has skyrocketed in many countries. For example, the most commonly prescribed medication in the United States is hydrocodone. Further concerns have been raised concerning opioid-induced hyperalgesia (increased sensitivity to pain) in chronic opioid use especially at higher doses [97, 98]. Additionally, opioids are known to affect the hormone system including testosterone, estrogen, thyroid hormones, growth hormones, ACTH/cortisol, and vasopressin [99–103]. Again, these have generally been documented at higher doses.

15.4.4 Lifestyle Modifications

Lifestyle modifications including smoking cessation, weight loss, and diet are considered an essential part of the comprehensive treatment for chronic low back pain. Multiple studies have demonstrated the association between smoking with low back pain and disk degeneration [104–107]. Smoking increases the risk of circulatory proinflammatory cytokines and affects healing. Smoking also compromises blood vessel integrity to spinal structures leading to degeneration of disks [105, 107]. Current and former smokers have a higher prevalence and incidence of low back pain compared to those who have never smoked. This association was stronger in adolescents compared to adults showing the importance of avoiding smoking early in life [105].

Obesity is an independent risk factor for development of low back pain [104, 108]. It is believed to have harmful effects on the lumbar spine by creating a biomechanics disadvantage leading to increased load bearing, excessive wear, and early degeneration. There is a positive relationship between body mass index (BMI) and low back pain. Those with BMIs >29 were 1.7 times more likely to have back pain compared to those with BMIs in the lowest 20 % of the population. Furthermore, a prospective cohort study found that patients with BMIs greater than 30 are at increased risk of developing chronic low back pain after an 11-year period compared to those who had BMIs less than 25 [108]. Having a healthy body weight is key for long-term treatment of chronic low back pain and is an addressable risk factor.

Diet is also a modifiable risk factor for the development of degenerative disk disease. Atherosclerotic disease from a typical western diet has been associated with degenerative disk disease in the spine. Postmortem studies have shown that DDD is seen more common when atherosclerotic disease is present in the arteries that supply the specific intervertebral disk. Specifically, aortic calcification and stenosis of the lumbar arteries were both associated with low back pain. Nutrition to the lumbar intervertebral disks is supplied by the lumbar arteries which originate from the abdominal aorta. Arterial occlusion is believed to decrease the vascular supply leading to the degeneration of disk [109, 110]. Other cardiac modifiable risk factors include hypertension, elevated LDL cholesterol, and hypertriglyceridemia [109]. A healthy diet has been shown to decrease the risk of atherosclerotic disease in a number of studies. Lifestyle modifications are an essential step in the treatment and management of chronic low back pain and must be addressed with all patients for optimal management.

15.4.5 Complementary Medicine

There is mixed evidence for the use of complementary and alternative therapies in the treatment of chronic low back pain. These therapies can include traction, osteopathic or chiropractic manipulation, acupuncture, herbs, vitamins, minerals, and homeopathic supplements.

Traction has been used historically to treat spine disorders. Multiple theories have been proposed to explain the benefits of traction including changing the disk nerve interface, decreasing nucleus pulposus pressure, and increasing foraminal area; however, the evidence is not clear. A systematic review on four randomized control trials shows that sustained lumbar traction with 30–50 % body weight is no better than low-dose sham traction, mineral baths, underwater massage, or traditional physical therapy for low back pain of greater than 4 weeks' duration [111].

Spinal manipulation and mobilization also dates as far back as 2700 BC in China for the treatment of low back pain [112]. Spinal manipulation therapy is the use of high-velocity, low-amplitude manual thrusts to the spinal joints slightly beyond the passive range of joint motion, while spinal mobilization is the use of manual force to the spinal joints within the passive range of joint motion that does not involve a thrust [113]. There continues to be mixed evidence regarding efficacy. In a large meta-analysis of randomized clinical trials, there was no evidence to show that spinal manipulation was superior to standard treatment such as general practitioner care, analgesics, physical therapy, exercises, or back school [114]. Another study showed moderate evidence that spinal manipulation is similar in effect to a combination of NSAIDS and exercise in both the short and long term [112]. Given that they are at least as effective as other methods diskussed above, this may be another treatment option for patients.

Another tool to help alleviate low back pain may be acupuncture. Although the precise mechanisms of acupuncture for the treatment of chronic low back pain are not fully understood, it is hypothesized that it stimulates the production of endorphins and inhibits the central nervous system via the gait control theory. There is some evidence from short-term follow-up that suggests when compared to no treatment at all, there is some benefit in pain relief and functional improvement immediately after a series of treatment sessions [115].

Massage, another historical tool for the treatment of pain, can also help in the treatment of nonspecific low back pain, especially in combination with exercise [116].

Transcutaneous electrical stimulation (TENs) is commonly used in the treatment of nonspecific low back pain. However, a 2010 review of the evidence showed no benefit for these devices. As of 2012, Medicare no longer provides coverage for such TENs units for diagnosis codes of low back pain or degenerative disk disease [117].

There are a vast number of herbs and supplements that are not a part of conventional medicine but may help in the management of chronic low back pain. As an example, in a randomized control trial, turmeric (active ingredient

curcumin) was compared to ibuprofen for osteoarthritis pain and did equal to slightly better than ibuprofen [118]. With these alternative treatments, there can be side effects that are not always well appreciated. For example, turmeric at higher doses can increase urinary oxalate levels and increase the risk for kidney stones. In general, these alternative treatments have potential benefit but have not been well validated.

15.4.6 Spinal Injections and Interventions

There is limited evidence for the use of epidural steroid injections (ESIs) for the management of diskogenic low back pain. There is better evidence for epidurals with radicular pain. Still, epidurals are sometimes used in the treatment of back pain, and there is some literature present on this practice.

One study noted a reduction in chronic back pain after caudal ESI in patients with chronic diskogenic pain without herniation or radiculitis. This was a randomized, double-blinded, controlled trial, which showed significant reduction in pain (defined as > 50 % improvement) and functional status at 1-year follow-up with caudal epidural injections using fluoroscopic guidance. Fifty-five percent of patients who received caudal epidural injections experienced significant pain relief with local anesthetic compared to 68 % of patients who received a combination of local anesthetic and steroid [119]. A similar study using the lumbar interlaminar approach via fluoroscopic guidance at 2-year follow-up also showed significant pain relief and functional status improvement in 72 % receiving local anesthetic alone compared to 67 % receiving a combination of steroid and local anesthetic [120]. These results have not been replicated, and also these studies were limited by the lack of a true placebo control group.

There are a few intradiscal thermal procedures that have been looked at for treatment of diskogenic low back pain. These procedures include intradiscal electrothermal therapy (IDET), discTRODE, and biacuplasty. The evidence is not overly convincing for any of these procedures at this point [121]. Although a recent randomized placebo-controlled trial of 64 subjects with biacuplasty showed statistically significant improvements in physical function, pain, and disability compared to the placebo group at 6-month follow-up [122]. Still, there is no overwhelming evidence in support of these procedures.

The most promising of treatments are biological agents including growth factors, cell therapy, use of gene transfer, and tissue engineering to repair the damaged disk and reduce the nociceptive input. There are many features involved in the interplay of diskogenic pain that continue to be poorly understood including oxygen tension, pH, Modic changes, and disk hydration [123].

15.4.7 Other Interventions

Other interventions have shown promise as a potential treatment for the future. Protein factors such as bone morphogenetic protein (BMP) 2, BMP 7 (osteogenic protein-1, OP-1), and BMP 14 (growth differentiation factor 5, GDF-5), transforming growth factor beta (TGF-B), insulinlike growth factor, fibrin sealant, platelet-rich plasma, and gene therapy can all hypothetically stimulate matrix production. There have been preclinical animal studies with many of these that show promise with disk restoration [123].

One human study that has shown promise to date has been a stem cell study looking at the intradiscal injection of mesenchymal precursor cells (MPCs) for diskogenic low back pain. This was a double-blinded randomized control of 100 patients. There were two treatment groups that included high- and low-dose MPCs which received 18 million and 6 million MPCs, respectively. The control groups received either an injection of saline or hyaluronic acid into the disk. At 1 year out, mean VAS decreased from 72 to 32 in the high-dose and 70 to 33 in the low-dose MPCs. The high dose was statistically significant compared to the control groups. At 12 months, the 62 % of the high-dose group and 69 % of the low-dose group had >50 % relief of pain with $p < 0.05$ for both groups compared to

control groups. Finally, 52 % of the low dose and 42 % of the high dose had pain scores <20 on the VAS (p 0.05 and 0.01, respectively, vs. control) [124].

Gene therapy also has the potential to promote endogenous synthesis of therapeutic proteins via viral or nonviral vectors. Currently, studies have only been done in animal models. Direct intradiscal injections of BMP-2 complementary deoxyribonucleic acid (cDNA) carried by recombinant adenovirus vector resulted in restoration of disk height in animal models. Cell-based delivery of genes that promote the growth of proteoglycan and collagen production has been shown to be successful in rat models. The safety concerns regarding these methods are still not fully understood; however, gene therapy may be a potential treatment option in the future to restore internal disk disruptions [123].

Unfortunately, there is no gold standard in the treatment of diskogenic low back pain. Conservative measures include physical activity, physical therapy, medications, lifestyle modifications, and educational strategies. If conservative measures fail, a comprehensive multidisciplinary approach along with interventional procedures can be attempted. Further research is required for a variety of treatment methods; however, there is optimism regarding the future of diskogenic treatment, especially with the advances in biological agents.

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Facet Joint Pain: Presentation and Treatment, Is It a Myth?

16

Stephan Klessinger

16.1 Introduction

This chapter on facet joints is included in a book that is actually dedicated to the intervertebral disk, because there are some correlations between the disk and the facet joints. Together with the intervertebral disk, the facet joints form a functional spine unit. Indeed, the contemplation of the joints is an important aspect when looking at the disk, so this chapter deserves its inclusion in part III of this book.

The nomenclature of the small joints of the vertebral spine is inconsistent. *Facet joint* is commonly used in North American literature to describe paired synovial joints between the posterior elements of adjacent vertebrae. The joints are also known as *zygapophysial joints*, *zygapophyseal joints*, *apophysial joints*, or *posterior intervertebral joints*. Because a facet is simply a small articular surface and, as such, pertains to any small joint, in this chapter the term *zygapophysial joint* is used. The term *zygapophysial* stems from the Greek roots *zygos*, meaning "yoke"; *apo,* meaning "away"; and *physis*, meaning "process." The facet joints bridge the vertebrae behind the vertebral foramina.

The existence of pain deriving from the zygapophysial joints is discussed controversially. The importance of the zygapophysial joints is often underestimated. The existing literature does not support the existence of a *facet syndrome*. There are no typical examination findings or diagnostic proofs to justify the term *syndrome*. Is zygapophysial joint pain therefore a myth? In the section about anatomy, it is shown that zygapophysial joints are typical synovial joints. We know pain not only from bigger joints like those in the knee or hip but also from the small joints in the fingers. So why should the zygapophysial joints not be a source of pain?

Zygapophysial joint pain is defined as pain originating from any structure integral to both the function and configuration of the lumbar facet joints, including the fibrous capsule, synovial membrane, hyaline cartilage surfaces, and bony articulations [1]. Regardless, some postulates must be satisfied for any structure to be deemed a cause of back pain [2]: (1) The structure should have nerve supply; (2) the structure should be capable of causing pain, ideally demonstrated in normal volunteers; (3) the structure should be susceptible to diseases or injuries that are known to be painful; and (4) the structure should have been shown to be a source of pain in patients.

This chapter investigates if these postulates are met. Zygapophysial joint pain remains a

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_16

misunderstood, misdiagnosed, and improperly treated medical condition. Therefore, an overview is provided about the clinical presentation and treatment of zygapophysial joint pain where the significance of zygapophysial joints as a pain source is highlighted.

16.1.1 History

The proposition that the lumbar zygapophysial joints might be a source of back pain had initially been articulated more than 100 years ago by Goldthwait in 1911 [3]. Sixteen years later, after anatomical dissections, Putti [4] suggested that local inflammation and degenerative changes in lumbar facet joints could result in sciatica from the irritation of nerve roots. In 1933, the term *facet joint syndrome* was introduced [5]. Badgley [6] emphasized in 1941 the significance of the zygapophysial joints as a pain source. According to him, 80 % of all back pain and referred pain were caused by the joints. With the implementation of successful operations of herniated disks by Mixter and Barr in 1934 [7], the focus was directed away from the zygapophysial joints and to the intervertebral disks.

The first description of a method to treat particular pain arising from zygapophysial joints was published in 1971 [8]. Rees attempted to sever the articular nerves using a special scalpel to make longitudinal incisions through the back muscles. The procedure was called *rhizolysis* [9, 10]. However, the articular nerves did not run where Rees had depicted [11]. Inspired by the success for the treatment of trigeminal neuralgia with radiofrequency of White and Sweet in 1969 [12, 13], Shealy (1974–1976) modified the intervention using radiofrequency electrodes to coagulate the articular nerve [14–17]. This procedure was known as *facet denervation*. However, again, the nerves were not located where Shealy described placing his electrodes [18, 19].

More detailed anatomical knowledge was necessary to correct the surgical anatomy. The targets for denervating zygapophysial joints were the medial branches of the dorsal rami. This procedure was named *medial branch neurotomy* to distinguish it from *facet denervation* [8, 18, 19]. For several years, the procedure became controversial, and no further studies appeared. The impetus for new studies and for comparative or placebo-controlled trials for lumbar and cervical radiofrequency came when cervical radiofrequency neurotomy was shown to be efficacious in a randomized placebo-controlled trial in 1996 [20].

A different approach, cryolesioning, was subsequently introduced. The scientific groundwork for this therapeutic option was laid between 30 and 40 years ago, and although the primary target of this technology was the treatment of tumors, it has been used successfully in the treatment of a wide range of peripheral pain syndromes [21–25]. Lloyd et al. [26] coined the term *cryoanalgesia* for its use in pain management. He proposed that this technique was superior to other methods of peripheral nerve destruction (e.g., alcohol, phenol, or surgical lesions), because it is not followed by neuritis or neuralgia [27]. Barnard and colleagues [28–30] popularized cryoneuroablation in the early 1980s, but relatively little has been written on the technique since.

16.2 Anatomy

16.2.1 Joint

The smallest functional motion unit is called *functional spine unit* or *motion segment*. It consists of the vertebrae, all adjoining ligaments between them, and three joints. The most prominent component of this unit is the interbody joint which consists of the intervertebral disk and the vertebral endplates. The other two joints are the paired zygapophysial joints, which are formed by the articulation of the inferior articular processes of one lumbar vertebra with the superior articular processes of the next vertebra.

Although the zygapophysial joints are small, they exhibit the features typical of synovial joints [31]. This means the facets are enclosed by a capsule. The surface of the facets is covered by cartilage, a typical synovium, and even a meniscoid exists. The joint space is capable of accommodating between 1 and 1.5 mL of fluid [32].

16.2.1.1 Articular Facets

The articular facets of the lumbar vertebrae are ovoid in shape, measuring some 16 mm in height and 14 mm in width and having a surface area of about 160 mm^2 [33].

Viewed from behind (Fig. 16.1), the articular facets of the lumbar zygapophysial joints appear as straight surfaces in the longitudinal direction. However, viewed from above, the articular facets vary both in the shape of their articular surfaces and in the general direction they face. In the transverse plane, the articular facets may be flat or planar, or they may be curved to varying extents (Fig. 16.2). In the upper lumbar spine, approximately 80 % of the facet joints are curved, and 20 % are flat. In the lower lumbar spine, these numbers are reversed [34].

The orientation of a lumbar zygapophysial joint is, by convention, defined by the angle made by the average plane of the joint with respect to the sagittal plane (Fig. 16.2) [31]. Smaller angles (less than 45°) are found more often in the upper lumbar spine. The levels L3–4 to L5–S1 usually show angles about 45–50° [34]. The extent to which a joint can resist forward displacement or rotatory displacement depends on the shape and orientation of the joint. The smaller the angle and the closer the joint is orientated toward the sagittal plane, the less the vertebra can resist forward displacement [31].

In the case of joints with curved articular surfaces, particular portions of the surface are involved in resisting different movements. During rotation the entire articular surface is in contact. Therefore, rotation is well resisted [31].

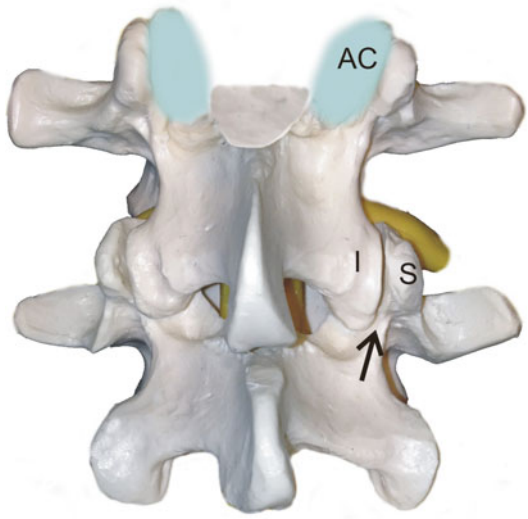

Fig. 16.1 Posterior view of the L3–L4 zygapophysial joints. (*Arrow*) straight surface of the right joint, (*AC*) articular cartilage, (*I*) inferior articular process L3, (*S*) superior articular process L4

16.2.1.2 Capsule

Each lumbar zygapophysial joint is enclosed by a fibrous capsule that is about 1 mm thick. At the superior and inferior ends of the joint, the capsule is long and relatively lax and attaches somewhat away from the articular margin [31, 34]. Its laxity accommodates the superior and inferior displacements of the articular process during flexion of the lumbar spine (Fig. 16.3). In a joint in its neutral position, this lax capsule creates subcapsular recesses that extend over the surface of the articular process, at the superior and inferior poles of the joint. In some patients, the anterior synovial recess may extend into the ligamentum flavum. The posterior synovial recess of the lumbar zygapophysial joint often extends beyond the articulating surfaces of the lumbar facets into the posterior fibrous capsule [35]. In both the superior and inferior parts of the capsule, there is a tiny hole that permits the passage of fat during movements of the joint [31]. Anteriorly, the fibrous capsule is replaced by the ligamentum flavum [36].

16.2.1.3 Intra-articular Structures

Articular cartilage assumes the same concave or convex curvature as the underlying facet. It is thickest over the center of each facet, rising to a height of about 2 mm [31, 37]. The articular cartilage rests on a thickened layer of bone known as the subchondral bone. Age changes and degenerative changes affect the articular cartilage and also the subchondral bone.

There are no particular features of the synovium of the lumbar zygapophysial joints that distinguish it from the synovium of any typical synovial joint. It attaches along the entire peripheral margin of the articular cartilage on one facet and extends across the joint to attach to the margin of the opposite articular cartilage [31].

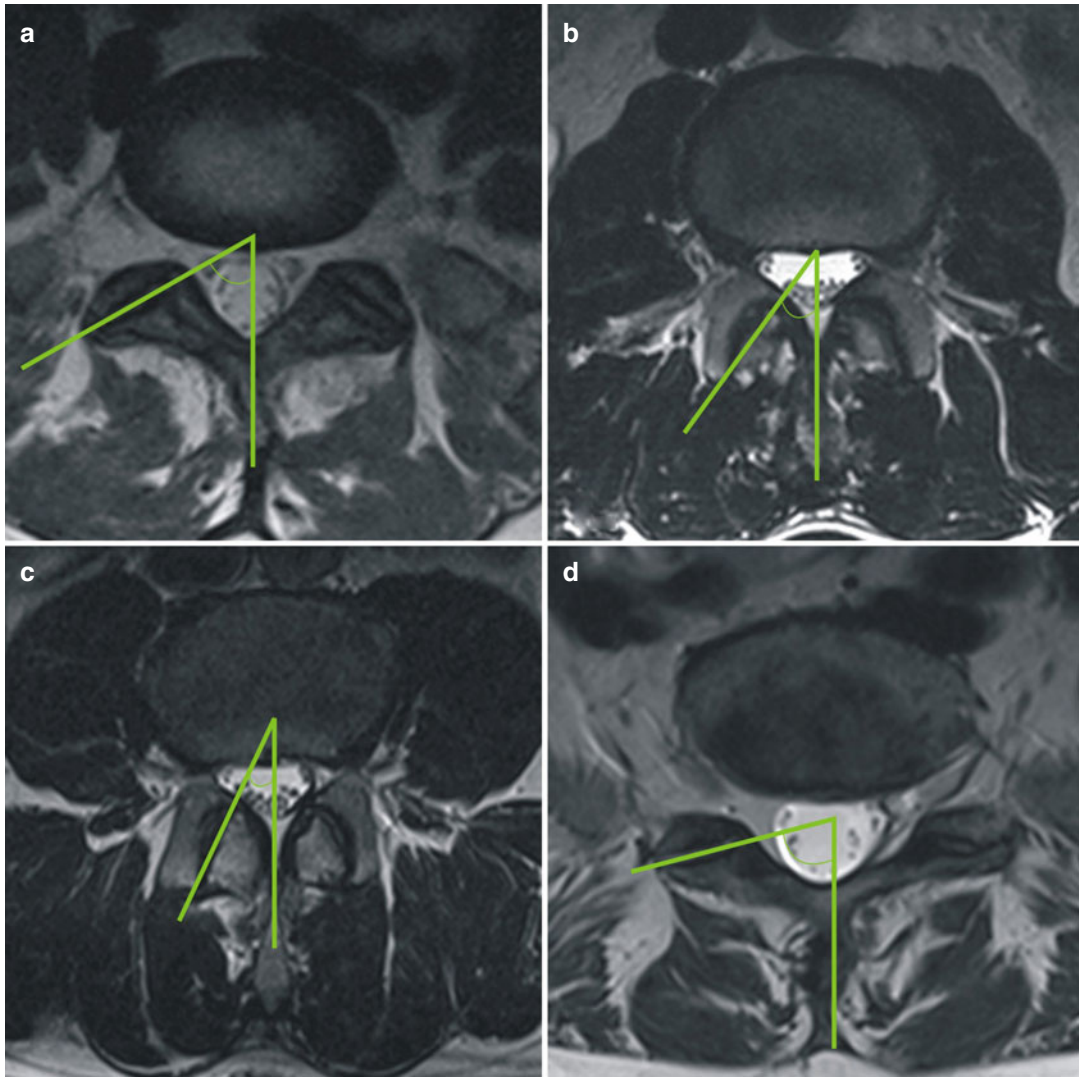

Fig. 16.2 Varieties of orientation and curvature of the lumbar zygapophysial joints. (**a**) Flat joint orientated 60° (L3–L4), (**b**) curved joint (C shaped) orientated 30° (L2–L3), (**c**) flat joint orientated 25° (L3–L4), (**d**) flat joint orientated 75° (L5–S1)

Two more intra-articular structures are present. These are fat and a structure referred to as *meniscoid*. The fat fills all leftover space underneath the capsule. It communicates with the fat outside the joint through the foramen in the capsule [31]. From their histology, it is clear that meniscoids are not comparable to a meniscus in the knee. They resemble more the intra-articular structures found in the small joints of the hand [38, 39]. There have been many different interpretations of the meniscoid structures. The most comprehensive study identifies three types [31, 40, 41]. The smallest structure is the connective tissue rim, a thickening of the internal surface of the capsule. The second type of structure is an adipose tissue pad (Fig. 17.3), consisting of a fold of synovium, fat, and blood vessels. The largest structure is fibroadipose meniscoids which also consist of synovium, fat collagen, and blood vessels. The adipose tissue pads and the fibroadipose meniscoids have been interpreted as serving a protective function [31, 40].

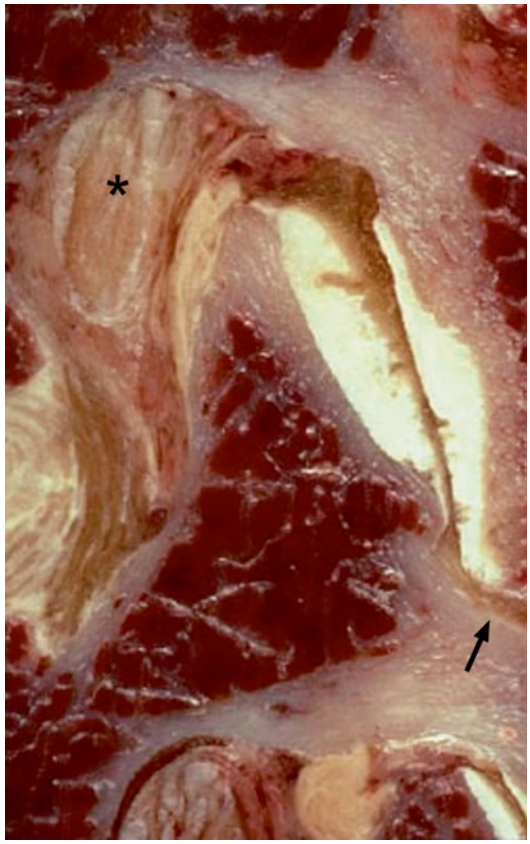

Fig. 16.3 L4–L5 zygapophysial joint in a spine in an intact cadaver and frozen in situ. The extension causes the tip of the inferior articular process to come in contact with the pars interarticularis of L5 (*arrow*). The joint capsule is elongated and severely compressed against the pars interarticularis. A richly vascularized meniscoid (*) is projecting into the opening of the superior joint space (Courtesy of W. Rauschning)

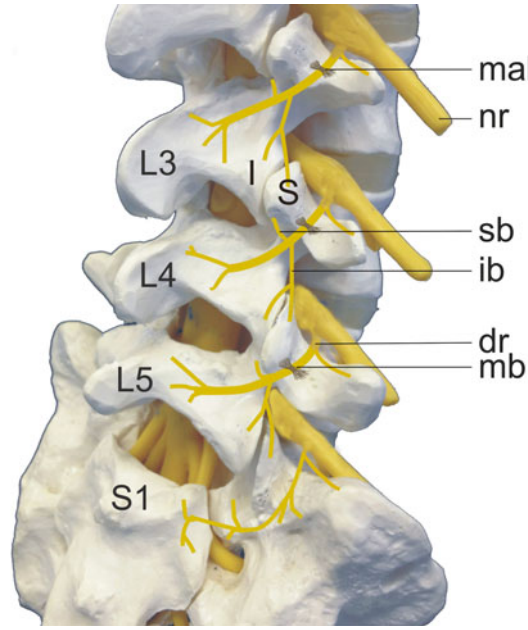

Fig. 16.4 Lumbar medial branch anatomy. Left anterior oblique illustration. (*L3–S1*) spinous processes, (*mal*) mamillo-accessory ligament, (*nr*) nerve root, (*I*) inferior articular process, (*S*) superior articular process, (*sb*) superior branch from medial branch, (*ib*) inferior branch of medial branch, (*dr*) dorsal ramus, (*mb*) medial branch (Reproduced from Klessinger [42])

16.2.2 Innervation

The zygapophysial joints of the lumbar spine have a dual nerve supply from the medial branches of the dorsal rami of the spinal nerves at the same level and from the level above. The numbering of the spinal nerve and the bone that it crosses is different. The spinal nerve of a particular segment issues from below the vertebra with the same segmental number as the spinal nerve, but the spinal nerve then crosses the superior articular process of the next vertebra.

The medial branch of the dorsal ramus in the lumbar spine courses over the base of the transverse process at the junction of the superior articulating process (Fig. 16.4) [18]. The lumbar dorsal rami carry the same segmental number as the vertebra from which they originate. In their subsequent course, these nerves cross structures and innervate joints below their segment of origin [43]. The course of the medial branches L1–L4 is similar. Each nerve runs in the groove formed by the junction of the transverse process and the superior articular process. Subsequently, each medial branch runs under the mamillo-accessory ligament [44]. This ligament is responsible for the reliable location. It can be large and sometimes ossified, particularly at lower levels [44]. Beyond the ligament, the medial branch sends branches to innervate the zygapophysial joint, multifidus muscle, interspinal muscles, and the interspinous ligaments [45]. There are three branches of the medial branch. The proximal branch hooks around the articular process to supply the facet above. The medial descending

branch courses in inferomedial manner to innervate the superior and medial portions of the capsule below plus muscle and skin. The ascending branch supplies the joint above [46]. As a consequence, each zygapophysial joint has a dual nerve supply. For example, the L2 and L3 medial branches innervate the L3–L4 joint. In addition to the joints, the medial branch also innervates the multifidus muscle, the interspinous muscle, and the periosteum [45, 47–49].

The L5 dorsal ramus crosses the ala of the sacrum. There is no medial branch for L5. The target is the dorsal ramus itself. The medial branch does not arise until the dorsal ramus reaches the caudal region of the L5–S1 joint [49].

The joint capsules and the surrounding structures are richly innervated by encapsulated, unencapsulated, and free nerve endings. Nociceptors fire when the capsule is stretched or subjected to compressive forces [47, 50]. The presence of low-threshold, rapidly adapting mechanosensitive neurons suggests that in addition to transmitting nociceptive information, the facet capsule also serves a proprioceptive function [51]. Nerve fibers have also been found in subchondral bone and intra-articular inclusions of zygapophysial joints, signifying that facet-mediated pain may originate in structures other than the joint capsule [52, 53].

16.3 Physiology

The zygapophysial joints are involved in all principal movements of the spine. Possible movements are axial compression/distraction, flexion/extension, axial rotation, and lateral flexion. Horizontal translation does not occur as isolated movement [36].

In the reflection of the joints as a possible pain source, the applied loads and the restriction of movements are particularly important.

16.3.1 Axial Compression/Distraction

The interbody joints (i.e., the intervertebral disks) are designed as the principal weight-bearing components of the spine. The importance of the zygapophysial joints is discussed controversially. Studies reported that all the compressive force is resisted by the disk [54]. Others found that the zygapophysial joints can bear 28 % or more of vertically applied load [55].

Three conditions lead to a remarkable load to the zygapophysial joints: First, with axial load in combination with a backward movement, the articular facets are driven into each other, and load can be transmitted through the joints [36]. Second, with severe or sustained axial compression, the inferior articular processes can be lowered until their tips impact the laminae of the vertebrae below [56]. Axial loads can be transmitted through the inferior articular process to the laminae. Third, in prolonged standing with a lordotic spine, the joints at each segmental level bear an average of some 16 % of the axial load [54, 57].

In contrast, in a neutral position, the articular surfaces run parallel to the direction of axially applied load. Thus, in a neutral position, they cannot sustain the load. Also, in the conditions of erect sitting, the zygapophysial joints are not impacted [36].

Axial distraction has been studied far less. The capsules of the zygapophysial joints are remarkably strong when subjected to longitudinal tension [36]. A single capsule can sustain 600 N before failing [58]. Stretching of the capsule is painful because of the free nerve endings.

16.3.2 Flexion/Extension

Flexion involves a combination of anterior sagittal rotation and anterior translation. Anterior translation is resisted by the impaction of the superior and inferior facets. In curved joints, the load is concentrated on the anteromedial portions of the facets [59], where commonly age changes are seen. The sagittal rotation component involves tension in the joint capsule. The capsules of the joints contribute about 39 % of the resistance during flexion.

Extension involves posterior sagittal rotation and posterior translation together with the downward movement of the inferior articular process

and the spinous process. This movement is limited by bony impaction between the spinous processes [36, 60]. The interspinous ligament buckles and becomes trapped.

16.3.3 Axial Rotation

The zygapophysial joints protect the intervertebral disk from excessive torsion. The inferior articular facets of the upper vertebra will be impacted against its opposing superior articular facet. Because the joint space is quite narrow, the range of movement before impaction occurs is quite small. The capsule of the opposite joint is being stretched. Experimental studies have established that the zygapophysial joints contribute between 42 and 54 % of the torsional stiffness of a segment [36, 61]. The zygapophysial joints provide a substantial buffer during the first 3° of rotation. They must be severely compressed before rotation exceeds the critical range of 3° [36].

16.3.4 Lateral Flexion

Lateral flexion involves a complex and variable combination of lateral bending and rotatory movements [36].

16.3.5 Rotation in Flexion

This is a common movement associated with the onset of back pain. However, studies offer conflicting results and opinions that stem from the complexities of this movement [36].

16.4 Pathological Changes

16.4.1 Degeneration

During life, changes occur to the intervertebral disk and to the zygapophysial joints called spondylosis or osteoarthrosis. These changes are not per se a disease but an expression of the morphological consequences of stress applied to the disk and the joints during life. The incidence of osteoarthrosis is just as great in patients with symptoms as in patients without symptoms [62, 63]. Additional factors must be present to make the zygapophysial joints a pain source.

The degenerative changes are more advanced in the concave superior articular process than in the inferior articular process. It is the backward-facing portion of the facet that resists the forward shear stresses applied to the intervertebral joint during weight-bearing and flexion movements [64]. After the fifth decade, the subchondral bone of the zygapophysial joint gets thinner [65]. The articular cartilage exhibits focal changes. Vertical fibrillation of the cartilage, which reflects the repeated stress, and sclerosis of the subchondral bone plate are common [66]. Severe or repeated pressure may result in erosions and focal thinning of the cartilage (Fig. 16.5). Other regions might exhibit swelling of the cartilage. Where cartilage is lost, fibrofatty intra-articular inclusions may increase in size [66].

Older joints exhibit gross thickening (Fig. 16.6a). The development of osteophytes along the attachment sites of the joint capsule and ligamentum flavum to the superior articular process increases. As a result of repeated stress during rotatory movements, the articular cartilage spreads out to cover and protect the edges of the bony articular process [64].

A progressive decrease of range in movement with age is evident in the entire lumbar spine and in individual intervertebral joints [67, 68].

Zygapophysial joints are frequently affected by osteoarthritis. The arthritis is usually secondary to disk degeneration or spondylosis [69], but in 20 % of cases, it can be totally independent [70]. This condition is believed to be a possible cause of zygapophysial joint pain [71–74].

Inflammatory mediators, such as cytokines, prostaglandins, and neuropeptides, increase within the joint and the dorsal root ganglion in joint inflammation and arthritis [75–77]. Specifically, prostaglandin E2 (PGE2) has been identified as a key mediator of inflammation-induced behavioral sensitivity and increased neuronal excitability [78–80]. Overexpression of

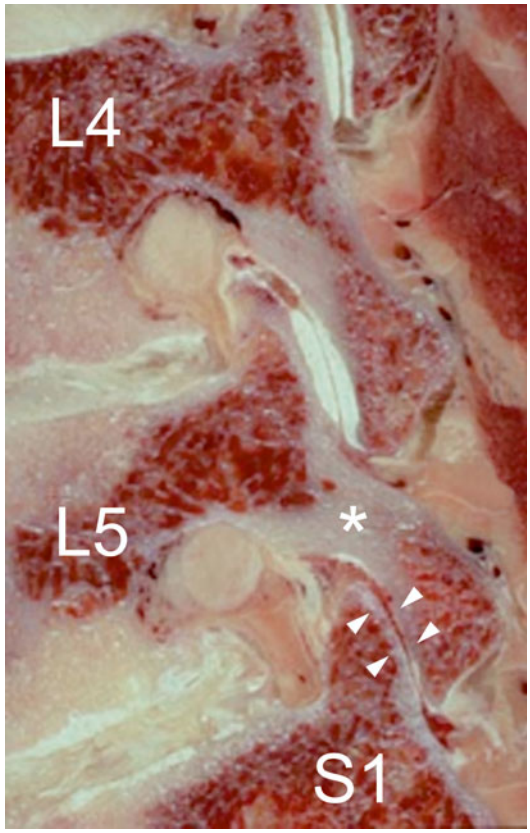

Fig. 16.5 Sagittal section through the neuroforamina of a severely degenerated lower lumbar spine of a 70-year-old man. The zygapophysial joints are in a subluxated position due to the loss of segmental height. The pars interarticularis of L5 is being eroded superiorly by the inferior articular process of L4 and inferiorly by the superior articular process of S1 (*). Such pars erosion is a prerequisite for the development of degenerative spondylolisthesis. There is no cartilage in the L5–S1 zygapophysial joint (*arrow heads*) (Courtesy of W. Rauschning)

MMP-1, induced by interleukin-1β, plays an important role in the inflammatory process of lumbar zygapophysial joint degeneration [81].

16.4.2 Degenerative Disk Disease

The intervertebral disk and the paired zygapophysial joints form a functional unit, and therefore, changes in the disk height are relevant for the load of the zygapophysial joints. The pressure between the facets increases significantly with the narrowing of the disk space [59]. Increased pressure may be a source of pain in patients with reduced disk spaces [59]. Maintenance of disk height is the normal feature of aging. Overt disk narrowing invites the consideration of some process other than aging [64].

One possible process is *internal disk disruption*. It may lead to disk degradation and disk resorption and is independent of degenerative changes [82]. Degradation of the nucleus of the disk is initiated by an endplate fracture that progressively destroys the nucleus pulposus [2]. Less able to bind water, the nucleus is less able to sustain pressure. In time, the annulus buckles under the load, and the disk loses height, which compromises the function of all joints in the affected segment [2]. As a result, reactive changes occur in the form of osteophyte formation in the zygapophysial joints. Disk narrowing may also predispose zygapophysial joint disease. When the disk becomes narrowed, up to 70 % of the compressive force usually applied to the disk is transferred to the zygapophysial joints [54].

Another reason for a loss of disk height is herniation of disk material. The material that is extruded into the spinal canal can no longer contribute to the disk height. In contrast to degenerative changes, the loss of disk material and disk height occurs within a short time. A gradual adaptation of the involved structures to the new situation is hardly possible. In addition, in case of surgery, sometimes not only the extruded disk material but also parts of the annulus and the central portion of the nucleus are removed. Therefore, patients with a herniated disk and compression of the nerve root suffer not only from radicular pain but also often from zygapophysial pain, which can exacerbate after surgery.

Degeneration and loss of structural integrity of the intervertebral disks have been shown to result in concomitant degenerative changes in the zygapophysial joints [83–85]. The reverse is also true. Degeneration and motion abnormalities at the zygapophysial joints can induce and accelerate degeneration of the intervertebral disks [57, 86, 87]. In a magnetic resonance imaging (MRI) study evaluating the relation

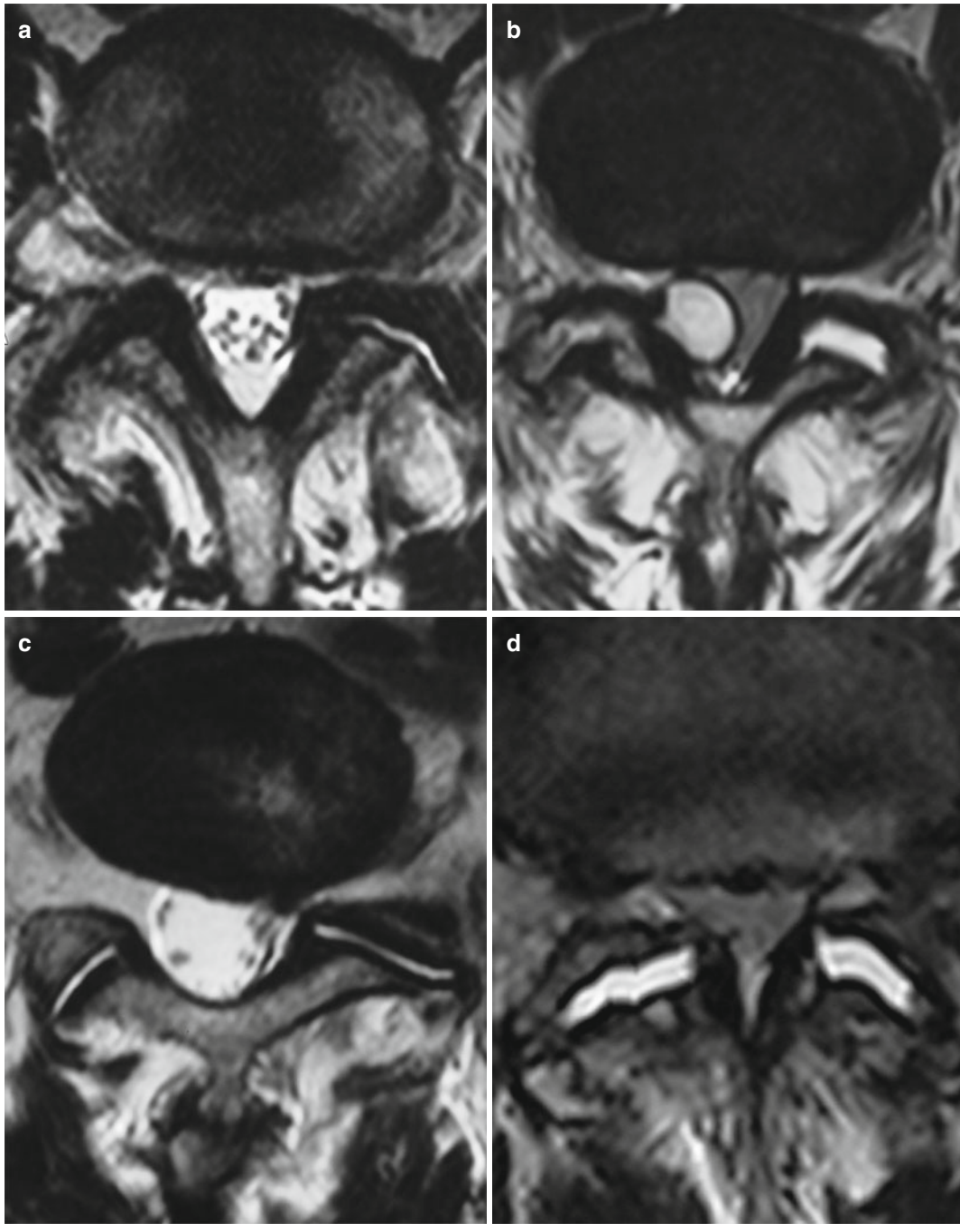

Fig. 16.6 Examples of magnetic resonance imaging findings concerning the zygapophysial joints. (**a**) Degenerative changes, (**b**) synovial cyst of the zygapophysial joint and increased joint volume, (**c**) asymmetric joint gap, (**d**) increased joint volume (Reproduced from Klessinger [42])

between facet joint osteoarthritis and degenerative disk disease, facet joint osteoarthritis was rarely found in the absence of disk degeneration but tended to be most pronounced at spinal levels associated with advanced degenerative disk disease [88].

16.4.3 Synovial Cysts

The term synovial cyst refers to cysts that arise from the zygapophysial joint capsule of the lumbar spine (Fig. 16.6b) [89]. They can be lined with synovium and contain serous, gelatinous, or hemorrhagic fluid [90]. The development is linked to degenerative spondylosis, segmental instability, and perhaps trauma [90, 91]. They are a cause of back pain and radiculopathy, with zygapophysial joint degeneration being the most common cause for cyst formation [81].

Intrafacetal synovial cysts can be a source of pain because of distension and pressure on adjacent pain-generating structures, calcification, and asymmetrical facet hypertrophy [91–95].

16.4.4 Asymmetric Load

A temporary one-sided load is often found in the context of knee or hip problems with appropriate gait disturbance or when walking with crutches. These patients develop often zygapophysial joint pain without structural changes. The reason is unusual strain or overuse of the joint. The treatment prognosis is good.

Facet tropism (asymmetry of the facet angles) may have a relationship to degenerative changes in the spine, either as the cause of degenerative changes or as the result of abnormal forces produced by degeneration [96]. These degenerative changes can be a potential cause of back pain [96]. The clinical significance of facet tropism is not yet well established [96–101]. A difference of facet angles of more than 7° (Fig. 16.6c) is found in 77 % of men and 66 % of women [96]. Facet tropism is a predisposing factor for degenerative changes [102, 103] but does not seem to be associated with zygapophysial joint osteoarthritis [96].

However, there is a positive association between the sagittal orientation of the facets and osteoarthritis [96]. Severe osteoarthritis is associated with back pain, independent of sociodemographics and the narrowing of disk height [104].

Scoliosis is a further condition with asymmetric load. Asymmetric degeneration leads to increased asymmetric load and therefore to a progression of the degeneration and deformity, as either scoliosis or kyphosis. The destruction of zygapophysial joints, joint capsules, disks, and ligaments may create mono- or multisegmental instability and, eventually, spinal canal stenosis [105]. In primary degenerative scoliosis, the degeneration ends up with zygapophysial joint arthritis with hypertrophic capsules, calcification, and osteophytes [105]. The most frequent clinical problem of adult scoliosis is back pain. At the site of the curve, it can be localized either at the apex or in its concavity, and zygapophysial joint pain can be localized in the countercurve from below the curve to above the curve [105].

16.4.5 Spondylolisthesis

Arthritis of the zygapophysial joints with loss of their normal structural support is the major local reason that probably leads to the development of degenerative vertebral slippage [106, 107]. It seems to be evident that morphological abnormalities of zygapophysial joints in the lumbar spine are a significant cause of low back pain and segmental instability and a predisposing factor in the development of degenerative spondylolisthesis [108–110]. One of the most probable sources of pain related to degenerative spondylolisthesis is degenerated and subluxated zygapophysial joints and segmental instability that causes tension in the zygapophysial joint capsule and ligaments [106, 109]. Patients with degenerative spondylolisthesis have more sagittally orientated zygapophysial joints and more significant zygapophysial joint tropism than normal control subjects [109]. The cephalad portion of the zygapophysial joints is more sagittally oriented, and the caudad portion of the zygapophysial joints is more coronally oriented in patients with degenerative spondylolisthesis [111]. Often, an increased joint volume indicates spinal instability [112], or synovial cysts associated with degenerative spondylolisthesis and zygapophysial joint osteoarthritis can be found [113]. Exaggerated fluid in the facets seen on axial MRI (Fig. 16.6d) is significantly suggestive of spondylolisthesis [114].

It is well known, though, that patients with degenerative spondylolisthesis might have sources of pain other than the zygapophysial joints [115]. In particular, the often additionally present spinal canal stenosis causes symptoms. The second pathology often interlinked with degenerative spondylolisthesis is disk degeneration [106, 107].

Spondylolisthesis is a characteristic example of concurrent pain sources in the same patient at the same time. The proportion by which the zygapophysial joints are involved in the complex symptoms is often difficult to diagnose [116].

16.4.6 Injuries

Extension of the spine is limited by the impaction of the inferior articular process on the lamina below. Under this condition, the continued application of an extension force results in a rotation around the impacted articular process and draws the contralateral zygapophysial joint backward. A rupture of the joint capsule is possible [2]. Rotation is also limited by the impaction of the zygapophysial joint. Further rotation also can result in a rupture of the contralateral capsule.

Zygapophysial joint pain is likely to occur with repetitive, chronic strains as might be seen in the elderly or, less frequently, after an acute event such as tearing the joint capsule by stretching it beyond its physiologic limits. This hypothesis is supported by clinical studies indicating a higher prevalence of facet arthropathy in elderly patients [117–119] and numerous cases of lumbar facet arthropathy after high-energy trauma [120]. There are more than two dozen reported cases of lumbar facet dislocation after rapid deceleration injuries [120–123]. The mechanism of injury in these cases is purported to be a combination of hyperflexion, distraction, and rotation [120, 121, 124].

Both in biomechanical studies and in postmortem studies, capsular tears, capsular avulsion, subchondral fractures, intra-articular hemorrhage, and fractures of the articular process have been found [2, 125–129]. Fractures of the zygapophysial joints cannot be detected on plain radiographs and might be too small to be seen in computer tomography (CT) scans [128, 129]. Lesions such as capsular tears cannot be detected by radiography, CT, or MRI. It may be that these lesions underlie zygapophysial joint pain [2].

16.4.7 Other Conditions

These include inflammatory arthritides such as rheumatoid arthritis, ankylosing spondylitis and reactive arthritis [130–132], synovial impingement, meniscoid entrapment, chondromalacia facetae, pseudogout, synovial inflammation, villonodular synovitis, and acute and chronic infection [71, 133–136].

16.5 Symptoms

Pain originating from the zygapophysial joints is a *lumbar spinal pain* [137]. This means that the pain is arising in an area between the lateral borders of the erector spinae at any lumbar level. The pain results from noxious stimulation and is therefore a *somatic pain*. Somatic pain must be distinguished from visceral pain and from neurogenic pain. Neurogenic pain results from damage or irritation of the axons or cell bodies of a peripheral nerve. Radicular pain is a typical example of neurogenic pain. Zygapophysial joint pain is often associated with pain in the buttock or in the leg. However, in this case, it is a *somatic referred pain* and not a radicular pain. Referred pain is perceived in a region innervated by nerves other than those that innervate the actual source of pain [2, 36]. Referred pain occurs because of a misperception of the region of the signal that reaches the brain by a convergent sensory pathway [2]. Somatic referred pain is perceived deeply. It is diffuse and hard to localize and it is aching in quality [138].

The joint capsule seems to be more likely to generate pain than the synovium or articular cartilage. There is considerable overlap between all lumbar facet joints, with the referral pattern being more widespread and variable in patients with chronic pain than in asymptomatic volunteers [1].

The zygapophysial joints meet all requirements that are necessary to be a possible pain source: They are well innervated by the medial branches, and free nerve endings are found in the joint capsules (see Sect. 16.2.2). In both patients and volunteers, mechanical stimulation or chemical stimulation of the joints with injection of hypertonic saline or with a contrast medium produces back pain and referred pain identical to that commonly seen in patients [47, 70, 139]. Pain can be relieved by anesthetizing one or more of the lumbar zygapophysial joints. Therefore, like other synovial joints in the human body, the zygapophysial joints represent a potential pain generator in patients with chronic low back pain.

Often, the patient can localize the center of zygapophysial joint pain at a specific level, unilateral or bilateral. Sometimes tenderness is evident over the affected joint [140]. Additionally, referred pain with diffuse borders is present. It occurs predominantly in the buttock and in the thigh in a nondermatomal distribution. Radiation below the knee can occur, even as far as the foot [70, 141]. All of the lumbar facet joints are capable of producing pain that can be referred into the groin, although this is more common with lower facet joint pathology [1]. Pain emanating from upper facet joints tends to extend into the flank, hip, and upper lateral thigh, whereas pain from the lower facet joints is likely to penetrate deeper into the thigh, usually laterally and/or posteriorly [1].

Pain at the beginning of a movement is typical for pain of joint origin. Therefore, the zygapophysial joints often hurt when moving from a sitting to a standing position or while sleeping when turning from one side to the other. Morning stiffness with difficulty to put on socks in a standing position and pain early in the morning that is relieved during the next hours and with walking will be reported often. The considerations of the normal movements (Sect. 16.3) allow one to form opinions regarding the movements that cause pain. Twisting or rotational movements, extension, and rotation in flexion are more likely to increase pain. Sitting with a round back and a relaxed musculature results in a substantial load for the joints. Also the monotonous seating position in a car might be a strain on the joints.

An acute onset of a sharp, penetrating low back pain with immobilization of the lumbar spine (*acute locked back*) is called *Hexenschuss* (witch's shot) in German. This term illustrates the medieval idea that diseases are inflicted to people through an arrow shot (Fig. 16.7) by supernatural beings (e.g., witches, elves). Even today, the pain sometimes comes so unexpectedly out of a normal movement that an explanation seems to be difficult.

And indeed, the cause remains speculative. However, theories have been advanced involving the concept of meniscal entrapment [2]. Upon flexion, these meniscoid structures (Sect. 16.2.1) are trapped in the subcapsular pockets of the joint [142]. This condition might be amenable to manipulative therapy.

The description of the pathological changes of the zygapophysial joints (Sect. 16.4) makes it clear that zygapophysial joint pain is often only one component of a more complex syndrome. Spinal canal stenosis is often symptomatic with

Fig. 16.7 Illustration of a *Hexenschuss* on a print by Johann Zainer around the year 1489/1490. Woodcut from the *Tractatus von den bösen Weibern, die man Hexen nennt* by Ulrich Molitor

neurogenic claudication and radiculopathy and, at the same time, pain deriving from the zygapophysial joints. However, back pain from the zygapophysial joints can occur together with radicular pain or even with a radiculopathy if the spinal nerve is irritated or compressed by an additional pathology, like a herniated disk, neuroforaminal stenosis, or a synovial cyst.

16.6 Diagnosis

16.6.1 Clinical Findings

No historic or physical examination variables exist to identify a zygapophysial joint as the pain source [143, 144]. Target joints might be identified by the pain pattern, local tenderness over the area, and provocation of pain with deep pressure. The neurological examination is usually normal. When performing the straight leg rise test (Lasègue's sign), the patient often experiences back pain. However, there should be no sciatic pain.

Revel et al. [118] identified seven variables associated with a positive response to facet joint anesthesia: age greater than 65 years and pain not exacerbated by coughing, not worsened by hyperextension, not worsened by forward flexion, not worsened when rising from forward flexion, not worsened by extension-rotation, and well relieved by recumbency. However, subsequent investigations have also failed to corroborate the findings of Revel et al. [118].

Of course, the clinical examination serves to delineate zygapophysial joint pain from other pain sources. As shown above (Sect. 16.5), zygapophysial joint pain appears often in combination with other pathologies (e.g., spinal canal stenosis, spondylolisthesis, or a herniated disk).

16.6.2 Radiologic Findings

The prevalence of abnormal zygapophysial joint changes on radiologic imaging depends on the age and presence of symptoms in the study population, the imaging modality used, and the threshold use for rendering a diagnosis of abnormal. In studies conducted in patients with low back pain, the incidence of degenerative facet disease on computed tomographic scanning ranges from around 40 % in some studies [73, 145] to upward of 85 % in others [146]. MRI is considered to be somewhat less sensitive than CT imaging in detecting degenerative facet changes [146–148], although several studies conducted in chronic low back pain patients found both the sensitivity and specificity of MRI to be more than 90 % compared with those of CT [88, 147].

On plain radiographs, osteoarthrosis (Fig. 16.8) appears as commonly in asymptomatic individuals as in patients with back pain [63, 149]. In addition, CT scans do not have a diagnostic value for lumbar zygapophysial joint pain [150].

Particularly striking results in MRI (Fig. 16.6) can be helpful to identify the level of the pain source. An increased joint volume indicates spinal instability [112].

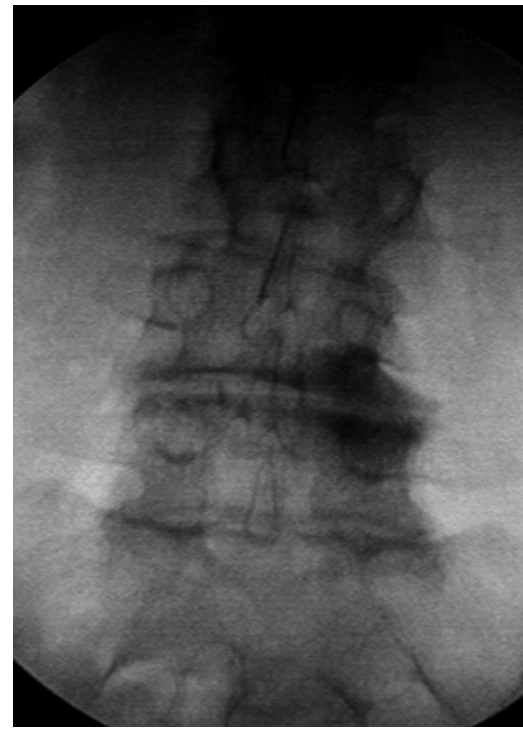

Fig. 16.8 Plain radiography with severe osteoarthrosis L4–L5

In summary, the evidence in the literature does not support the routine use of radiologic imaging to diagnose zygapophysial joint pain.

16.6.3 Medial Branch Blocks

A detailed description of the technique of medial branch blocks (Fig. 16.9), the evaluation of results, and the validity is given in Chap. 33.

Medial branch blocks are a diagnostic tool. They are used to test if the pain stems from a zygapophysial joint because the medial branch innervates the joint. For this reason medial branch blocks are also referred to as zygapophysial joint blocks or facet joint blocks. The fundamental indication for medial branch blocks is the desire to know if the zygapophysial joints are the pain source. Diagnostic lumbar zygapophysial joint nerve blocks are recommended in patients with suspected zygapophysial joint pain. Of course, the response must affect the management. The only validated treatment for pain mediated by the medial branches is radiofrequency neurotomy [152].

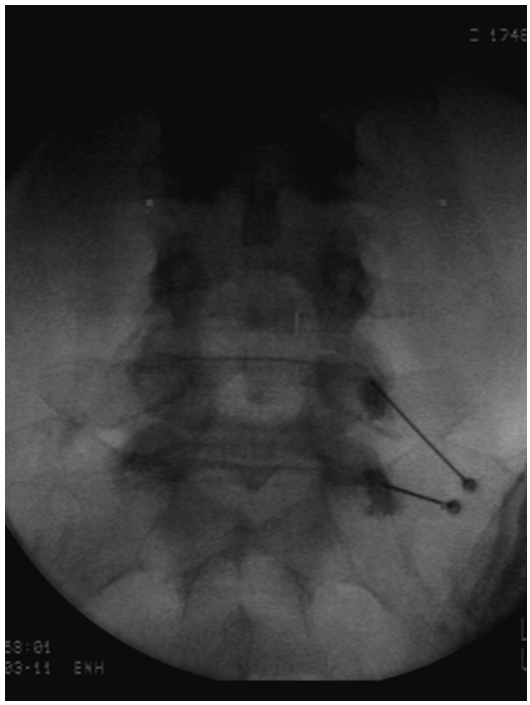

Fig. 16.9 AP view of needles in position for an L4 medial branch block and L5 dorsal ramus block after application of a contrast medium (Reproduced from Klessinger [151])

Because the singular reason for performing diagnostic medial branch blocks is to obtain information, the evaluation of the patient's response is essential. A positive response to a block is complete relief of that part of the pain that the blocks are expected to provide relief for the duration commensurate with the expected duration of the local anesthetic's effect. If more than one pain source is known, only a proportion of the pain will be relieved [151].

Lumbar medial branch blocks are the most thoroughly validated of all spinal interventional procedures [153, 154]. Single diagnostic blocks are not valid because they carry an unacceptable high false-positive rate of 25–45 % [8, 155–159]. In order to reduce the likelihood of responses being false positive, controlled blocks are mandatory [152]. Uncontrolled blocks or intra-articular blocks lack validity [8]. In addition, false-negative results after medial branch blocks are reported [160]. For a detailed discussion on false-positive and false-negative blocks, see Chap. 33.

The degree of relief that should occur after medial branch blocks remains contentious [161]. Ideally, diagnostic blocks should produce complete relief of pain or near-complete relief. This would occur only when the patient's sole or principal source of pain lies in the joints innervated by the nerves blocked. Some investigators, however, use a more liberal criterion, such as >50 % relief of pain. This criterion allows medial branch neurotomy to be used to provide substantial, but not necessarily complete, relief of pain, which is nevertheless clinically worthwhile [8]. Adopting lesser diagnostic criteria admits more patients for treatment, but the outcomes are poorer. The implication is that physicians will be treating more patients but not achieving optimal outcomes. Adopting more stringent diagnostic criteria admits fewer patients for treatment, but the outcomes achieved are of greater quality (see discussion in Chap. 33).

16.6.4 Arthrography

Arthrography is the demonstration of the internal contours of the joint by injecting a contrast medium [162]. Although various interesting features of a zygapophysial joint can be demonstrated, none of these features has been shown to be diagnostic of any disorder, and none has been shown to determine if the joint is a source of pain. Consequently, lumbar zygapophysial arthrography has no established diagnostic value [162].

16.6.5 Intra-articular Blocks

In this procedure, a local anesthetic is injected into the joint. The objective is to test if anesthetizing a particular joint relieves the patient's pain. The validity of intra-articular blocks of the lumbar zygapophysial joints has never been tested and has never been established [8, 163, 164]. For intra-articular blocks, there is no consequent treatment [163].

Moreover, several advantages of medial branch blocks exist [152]: Medial branch blocks are easier to perform. Entering a narrow joint space can be difficult. Sometimes osteophytes or degenerative changes may block the entry. Medial branches are safer because bone prevents overpenetration of the needle and entering the spinal canal. Target nerves can be anesthetized with different agents whose duration of effect is known. If the response to medial blocks is positive, radiofrequency neurotomy is a therapeutic utility with predictive validity [151].

16.7 Therapy

16.7.1 Conservative Treatment

No specific conservative treatment for zygapophysial joint pain exists. Patients with zygapophysial joint pain are treated in the same way as patients with low back pain emerging from a different pain source. There are no clinical studies specifically assessing pharmacotherapy or noninterventional treatment for lumbar arthropathy [1].

The treatment of low back pain (and also of zygapophysial joint pain) consists of a multimodal approach comprising conservative therapy, medical management, procedural interventions, and, if indicated, psychotherapy. Nonsteroidal antiinflammatory drugs are widely considered first-line drugs for the treatment of low back pain, with little evidence to support one particular drug over another [165–167].

16.7.2 Radiofrequency Denervation

Guidelines only exist for radiofrequency denervation of the zygapophysial joints, published by the International Spine Intervention Society [43]. Radiofrequency denervation is the direct consequence after the diagnosis of zygapophysial joint pain was validated by controlled medial branch blocks, and it is the only validated treatment for pain mediated by the medial branches [152].

Percutaneous denervation procedures offer pain relief by denervation of the nerves that innervate painful joints. It is a percutaneous therapeutic procedure in which a radiofrequency electrode is used to coagulate one or more of the medial branches of the lumbar dorsal rami, or the L5 dorsal ramus, in order to relieve back pain mediated by these nerves.

For medial branch neurotomy to be anatomically accurate and effective, the electrodes should be placed parallel to the target nerve. Also, lesions should be placed along the maximal available length of the nerve to optimize duration effect [8]. Therefore, exact anatomic knowledge is essential.

Medial branch neurotomy is performed in patients experiencing pain for at least 3 months and in those who did not respond to conservative treatment. Controlled medial branch blocks are mandatory as a diagnostic test to prove that the target nerve is responsible for the pain. Radiofrequency neurotomy provides good evidence-based results whenever patients have been selected correctly and when anatomically accurate surgical techniques have been used.

Thermal radiofrequency neurotomy is a procedure distinct from pulsed radiofrequency or

dorsal root ganglion radiofrequency. Thermal radiofrequency deliberately produces a lesion in the target nerve by denaturing its constituent proteins at the site at which the electrode is applied. The other procedures do not do so [43].

16.7.2.1 Patient Selection

The optimal patient for medial branch neurotomy is one who has been experiencing pain for at least 3 months and whose pain did not respond to conservative treatment. The patient should have a realistic expectation. Previous surgery does not preclude neurotomy [168, 169]. Repeat radiofrequency neurotomy after recurrence of pain is possible [170]. It is quite safe to coagulate one or two nerves, but it is not known how many more nerves can be coagulated with safety.

For various reasons, medial branch blocks are the only acceptable and validated diagnostic test as an indication for radiofrequency neurotomy [8]. Medial branch blocks have been validated for validity [171], target specificity [172], and construct validity [173]. Patients with positive responses to controlled blocks can expect to have substantial and lasting responses to medial branch neurotomy [173]. Uncontrolled blocks or intra-articular blocks lack validity [8].

Even after cervical or lumbar spine surgery or in patients with spondylolisthesis, pain emerging from zygapophysial joints can be treated with radiofrequency neurotomy [168–170]. In these patients, the zygapophysial joints are often not the only pain source.

16.7.2.2 Contraindications

Absolute contraindications for radiofrequency exist in patients unwilling or unable to consent to the procedure, patients with systemic infection or bleeding diathesis, or those on anticoagulants with a high risk of bleeding and pregnancy. Relative contraindications exist in patients using pacemaker equipment, after immunosuppression, in patients with unrealistic expectations, and in uncooperative patients [43].

16.7.2.3 Technique

For radiofrequency neurotomy, a high-frequency electrical current is alternating between a large surface area on a ground plate and a small area on the uninsulated tip of the electrode. The electrical field becomes denser at the electrode tip, and therefore, charged molecules around the tip start to oscillate [174]. Where the current is strong enough, this oscillation heats the tissues sufficiently to coagulate them. The volume of the tissue assumes the form of a spheroid. Coagulation occurs principally in a radial direction perpendicular to the long axis of the electrode [175, 176]. The dimensions of the lesions generated are proportional to the length and the width of the electrode. As a rule, in the radial direction, tissues up to 1.6 or 2.3 electrode-widths away from the electrode surface are coagulated [43, 175]. For practical implication, it is important to know that the electrode does not reliably coagulate in the distal direction. Therefore, electrodes that are placed perpendicular to the nerve may miss coagulating the nerve. Consequently, the electrode must be placed parallel to the target nerve [175, 176]. Because the lesion size is proportional to the width of the electrode, small-gauge electrodes should be avoided.

The size of the lesion also depends on the temperature and duration of coagulation. Coagulation starts at a temperature of 65 °C [175, 176]. The volume of the lesion expands as the temperature increases to 80 °C. The optimal duration of coagulation lies between 60 and 90 s at 80 °C. During neurotomy, the temperature should be increased slowly [177].

Several ways exist in which radiofrequency neurotomy is currently practiced [178]. In this overview the technique recommended by the International Spine Intervention Society is described [43]. A steep caudocephalad axial tilt of the fluoroscopy beam along with a 20° lateral tilt is used [43]. The cannula can be positioned precisely parallel to the target nerve. However, the appearance of the vertebral structures might be unusual. A spinal needle inserted primarily as a guide might be needed. The distance from skin to the target nerve might be long (Fig. 16.10).

Lumbar medial branch neurotomy is performed as an outpatient procedure. The patient is placed prone on a radiolucent fluoroscopy table. The patient's back is prepared and draped in a

sterile manner. An adhesive grounding pad is placed on the upper back and connected to the radiofrequency generator. Generally, no sedation, systemic analgesia, or premedication is required. The procedure can be performed under local anesthesia.

The technique is analogous in all lumbar levels. Only the terminology is different. The L5 dorsal ramus is itself targeted where it crosses the ala of the sacrum instead of its medial branch. One way to find the medial branch is to perform a medial branch block using a standard technique (Sect. 16.6.3 and Chap. 36) and leave the block needle in place. It can be used for the administration of local anesthetics. The tip of the needle will always be pointing to where the target nerve lies irrespective of the type of fluoroscopic views used. The target point is the lateral surface of the superior articular surface just above its junction with the root of the transverse process. The tip of the electrode must be placed proximally from the mamillo-accessory ligament (Fig. 16.5). At the sacrum, the mamillo-accessory ligament is rudimentary.

At all levels, the electrode needs to be as closely parallel to the nerve as possible. Typically, it needs to be 15–20° oblique to the sagittal plane and it must be inserted somewhere below the target level (Fig. 16.10). Sometimes multiple parallel placements of the electrode are necessary to coagulate the nerve properly. As a larger gauge electrode makes larger lesions, an 18-G electrode with a 10-mm tip is recommended.

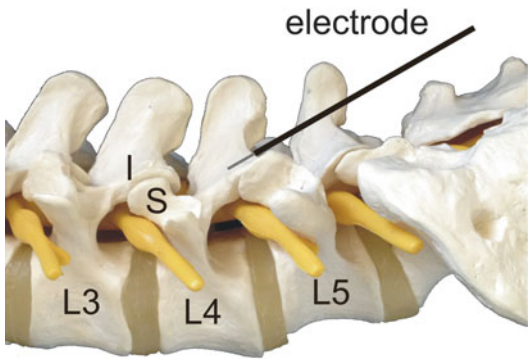

Fig. 16.10 Illustration of a lateral view of the lumbar spine. The optimal trajectory of the electrode with an insertion point below the target area. (*L3–L5*) vertebral body, (*I*) inferior articular process, (*S*) superior articular process (Reproduced from Klessinger [42])

The accurate placement of the needle and the electrode must be documented with hard copy films, images on paper, or digital storage (Fig. 16.11). Now the nerve and the surrounding tissue can be anesthetized. The lesion is made by increasing the temperature slowly until it reaches 80 °C. This temperature is maintained for 60–90 s.

The radiofrequency electrode includes the possibility of nerve stimulation, with sensory and motor capabilities, which allows the precise localization of the target nerve. However, in the guidelines of the International Spine Intervention Society, electrical stimulation is considered unnecessary [43].

For lumbar radiofrequency medial branch neurotomy, several theoretical risks apply. These include hematoma, infection, and allergic reactions to local anesthetics. Provided that the electrodes are placed correctly, they penetrate only the skin and posterior back muscle. The spinal nerve and the ventral ramus lie more anterior. Skin burns should not be a risk when a correct ground plate is used. In the literature, no reports of adverse effects can be found [179, 180]. Examples from medicolegal proceedings are known.

16.7.2.4 Results

A comprehensive narrative review of lumbar medial branch neurotomy was presented by Bogduk et al. [8]. Two main problems in the assessment of studies were described: (1) a technique without parallel needle placement and (2) an inconsistent patient selection [8].

Considering the historical development of radiofrequency neurotomy (Sect. 16.1.1), it is obvious that different techniques were used, which cannot be compared with one another. The position of the electrode plays an essential role. The earliest studies with the technique described by Shealy in 1974–1976 [14–17, 181] claimed good success even if it was not possible to coagulate the nerve with the described technique. In the later study of Leclaire et al. [182], the operative technique was not described. The outcome was

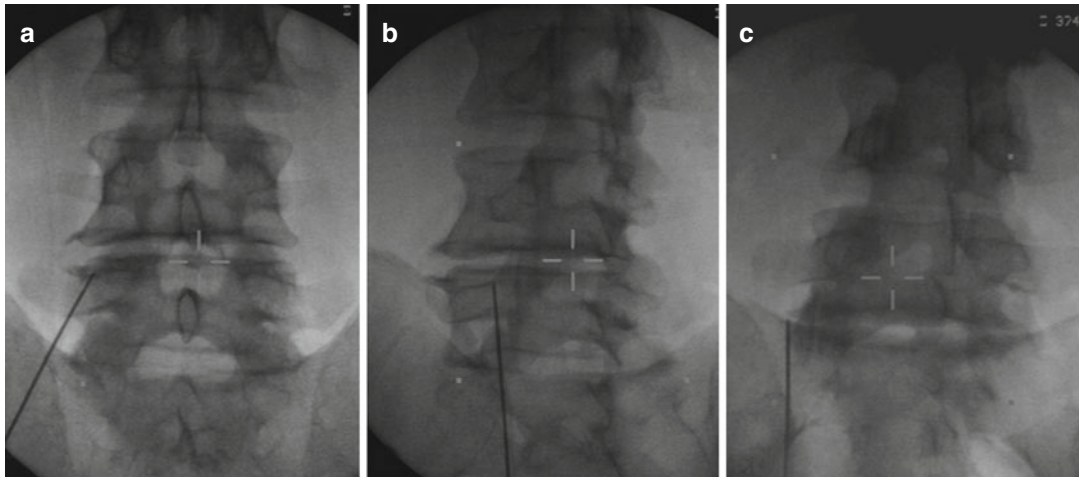

Fig. 16.11 Different views of an electrode placed for an L4 medial branch neurotomy. (**a**) Anteroposterior view, (**b**) corresponding oblique view, (**c**) anteroposterior view of an electrode placed for an L5 medial branch neurotomy

poor. Negative results were also found in the study of van Wijk et al. [183]. Again, an inaccurate surgical technique was used [184].

In other studies, patient selection was questionable. Van Kleef et al. [185] did not select patients on the basis of controlled medial branch blocks but did require 50 % pain relief after single diagnostic blocks. A low success rate with a short duration was the result. Nevertheless, active treatment was superior to placebo treatment. Nath et al. [186] included patients with different pain sources. Controlled blocks and a correct technique were used. Complete and enduring pain relief was not reported because patients still had other sources of persisting pain. However, for the pain for which patients were treated, the study showed significant improvements after radiofrequency neurotomy compared with sham treatment. Another study [187] designed to test pulsed radiofrequency showed that conventional radiofrequency neurotomy was significantly more effective than sham treatment.

The first study with the appropriate selection criteria and correct surgical technique was the descriptive study of Dreyfuss et al. [173]. A total of 60 % of the patients treated with radiofrequency neurotomy achieved 80 % pain relief lasting at least 12 months and 80 % achieved 60 % pain relief. Similar outcomes were found in a study of Gofeld et al. [188]. Approximately 68 % of the patients maintained at least 50 % pain relief lasting between 6 and 24 months. A third descriptive study of Burnham et al. [189] recorded high patient satisfaction.

The evidence shows that radiofrequency treatment fails when patients are wrongly selected or when an inaccurate technique is used [8]. Yet reviews in the past have acknowledged procedurally flawed studies. The reviews of Boswell et al. [190, 191] and Manchikanti et al. [192] provide strong evidence for short-term and moderate evidence for long-term relief. Manchikanti et al. [193] provide a strong recommendation for lumbar radiofrequency neurotomy. The strength of evidence in the review of Datta et al. [194] is II-2 to II-3 with a recommendation of 1B or 1C. Whenever patients have been selected correctly and when anatomically accurate surgical techniques have been used, the expectations of success have been met [8].

The available data vindicate the use of lumbar medial branch neurotomy provided that the correct surgical technique is used and patients are selected rigorously using controlled blocks [43]. There are no data that vindicate any other technique [43]. If the criterion for a positive response to diagnostic blocks is raised to complete relief, some 56 % of patients achieve complete relief of pain [195]. They restore their normal activities, and the need for other health care is eliminated.

16.7.3 Cryoneurolysis

Different methods are used for peripheral nerve destruction (e.g., alcohol, phenol, or surgical lesions). However, there have not been any significant publications or systematic reviews with pulsed radiofrequency, cryoneurolysis, and laser neurotomy [191]. Since cryoneurolysis is established in some regions, it is discussed.

The cold temperature of the cryoprobe is created by passing a gas at a relatively high pressure through a small central channel in the probe. Once the gas reaches the tip of the probe, it enters an expansion chamber, which is at a much lower pressure. The high-pressure gas entering the chamber rapidly expands, causing the cooling of the gas and of the tip of the cryoprobe. Generally, the tips of these probes may be cooled to as low as −70 °C. This extreme cold then causes the tissues nearby to form an ice ball at the tip of the probe. The size of the ice ball is between 3.5 and 6 mm [196]. When close enough to a nerve, the ice ball causes the entrapment of the nerve. The application of cold to tissues creates a conduction block, similar to the effect of local anesthetics. At 10 °C, larger myelinated fibers stop conducting, but all nerve fibers stop conducting at −20 °C. The extent and duration of the effect is therefore a function of the degree of cold obtained and the duration of exposure [197]. Long-term pain relief from nerve freezing occurs because ice crystals create vascular damage to the vasa nervorum, which produces severe endoneural edema. This disrupts the nerve structure and creates Wallerian degeneration but leaves the myelin sheath and endoneurium intact [198].

Brechner [199] studied the effects of percutaneous cryoneuroablation of the zygapophysial joints in patients with neck and low back pain. There was 70 % pain relief after 1 h, but by 3 months, pain had returned to baseline. Schuster [200] studied 52 patients observed for a 13-month period. A total of 90.4 % had significant relief of low back pain after cryoneuroablation. Ross [201] described 21 out of 23 patients with complete relief for a follow-up of 6 months to 2 years. These studies are limited by a lack of certainty that the zygapophysial joint was the sole pain generator. Prognostic blocks, if performed, did not use currently recommended techniques. A current review about cryoanalgesia was presented by Trescot [198].

16.7.4 Therapeutic Zygapophysial Joint Blocks

Medial branch blocks are well known for their diagnostic capability (Sect. 16.7.1 and Chap. 36). However, they have been shown to be effective for long-term therapy. The results in the literature are conflicting. The International Spine Intervention Society does not mention this procedure in its guidelines [43, 152, 162], but the American Society of Interventional Pain Physicians assesses the evidence of therapeutic joint blocks with and without steroid for managing chronic low back pain as fair to good for short- and long-term improvement [202].

Two high-quality randomized trials [203, 204] reported positive results with or without steroids. In one study [204], 85 % of patients receiving local anesthetic and 90 % of patients receiving local anesthetic and steroids were successfully treated with approximately five or six procedures on average over a period of 2 years. The second study compared local anesthetic blocks with radiofrequency neurotomy [203]. At the end of 1 year, 90 % of the patients in the radiofrequency group and 69 % of the patients in the zygapophysial joint block group showed significant improvement. However, they did not use controlled blocks for selection.

The exact mechanism of the therapeutic effect is not known. Lumbar zygapophysial joint blocks may be repeated to reinstate the pain relief.

In other reviews, the indicated level of evidence is level II-1 or II-2 with a strong recommendation (1B or 1C) for the use of therapeutic joint blocks [194] or rather moderate for short-term and long-term pain relief after therapeutic medial branch blocks [190, 191]. In particular a strong recommendation (1B or 1C) is given for the use of therapeutic lumbar zygapophysial joint nerve blocks to provide both short-term and long-term relief in the treatment of chronic zygapophysial joint pain [205].

16.7.5 Intra-articular Steroids

Intra-articular injections are always performed with a therapeutic intention, not for diagnostic reasons.

Several reviews exist about lumbar zygapophysial joint injections with results from moderate evidence [190, 191] for short-term and long-term improvement in low back pain over very weak recommendation [194] to no recommendation for therapeutic blocks [8, 205].

Intra-articular steroids have not been tested in patients with a diagnosis of zygapophysial joint pain proven by controlled diagnostic blocks [162]. Therefore, injection of steroids is speculative. The available evidence argues strongly against intra-articular steroids having any effect greater than that of sham therapy [8, 206].

16.7.6 Treatment of Cysts

Lumbar zygapophysial joint access can be used in the management of synovial cysts of the lumbar zygapophysial joints [162]. The cyst can be distended and ruptured by forceful injection of contrast medium. Or it can simply be aspirated; or steroids can be injected into the joint [207, 208]. Descriptive studies are the sole level of evidence for such procedures. Success rates differ between 46 % [209] and 72 % [208], between 6 and 12 months after treatment.

16.7.7 Radiologic Imaging

16.7.7.1 CT

In the guidelines of the International Spine Intervention Society, fluoroscopy is mandatory [43, 152, 162]. If CT is to be used, multisliced and pulsed CT is necessary to avoid a higher radiation exposure for the patient and the physician. Several images are obtained at one tube rotation. These may be displayed simultaneously or reconstructed. The optimization of new CT protocols has shown a possible effective dose reduction of 85 % compared with standard lumbar spine CT protocol [210]. Usage of CT might be more time-consuming than fluoroscopy. No real-time view of the track of the needle is available. An advantage of CT is that the target and any vulnerable structures, such as soft tissue, are directly visualized with CT rather than inferred from expected relationships to bony landmarks.

Continuous fluoroscopy, during and throughout the injection of a contrast medium, is the best available means of demonstrating intra-arterial flow away from the site of injection [179, 211]. Vascular opacification on CT is a dot or line traceable over multiple axial images. It is present during contrast injection and washes out after cessation of injection [212, 213]. There is no data to demonstrate that CT detects vascular uptake at a rate comparable to fluoroscopy or digital subtraction angiography.

The literature supporting the efficacy of CT-guided spine interventions is sparse and often of poor quality [214, 215].

16.7.7.2 MRI

MRI-guided zygapophysial joint infiltration provides an alternative to CT and fluoroscopy. The advantage is the avoidance of radiation for both the patient and physician, a high tissue contrast, and unrestricted multiplanar imaging capabilities. Clinical outcomes are comparable with conventional fluoroscopy [216].

Disadvantages include limited patient access inside the scanner and the enormous technical and financial expenses. MR-compatible equipment including injection needles is necessary.

16.7.7.3 Ultrasound

Ultrasound injections have a place in interventional pain management. They may render some procedures safer and more effective. However, the best indications for ultrasound injections are not at the spine. Fluoroscopy is still a very strong competitor.

The biggest advantage of ultrasound is not having radiation. It provides continuous imaging and visualization of nearby vulnerable structures and real-time visualization of fluid injection. Smaller volumes of local anesthetic are needed. Ultrasound devices are portable.

Disadvantages include poor needle visualization and ultrasound shadows (no visibility behind

bones and air). Patient-related factors (e.g., body weight) affect visibility. Working under sterile conditions is more complicated. The success very much depends on practitioner's expertise.

In patients with zygapophysial joint pain, ultrasound injections may be an alternative to fluoroscopy for diagnostic blocks. However, there is no chance of seeing the lumbar medial branches or the L5 dorsal ramus [217]. Nevertheless, over 90 % successful needle placements seem possible by experienced practitioners [217]. There is also some evidence for feasibility of ultrasound-guided intra-articular injections, although the joint cleft is difficult to visualize and injected fluid cannot be visualized.

16.7.8 Surgery

Surgery is occasionally performed to treat facet arthropathy despite a lack of evidence supporting fusion for degenerative spinal disorders [218, 219]. Not surprisingly, the results of studies evaluating the use of zygapophysial joint blocks to predict lumbar arthrodesis outcomes are discouraging [220–224].

New methods for percutaneous fusion of the zygapophysial joints are being developed but are not yet sufficiently investigated.

16.8 Prevalence

The prevalence of zygapophysial pain is very difficult to specify. In the literature, studies with different prerequisites are found. Different criteria for success were applied: 50 % relief of pain, 80 % relief of pain, or complete relief of pain was used. To be valid, controlled blocks must be used to obviate false-positive results. However, in some studies, only uncontrolled blocks were used for diagnosis. Furthermore, the patient population, which was investigated in different studies, was unequal. Sometimes only certain age groups or only patients with injuries were included, and patients with degenerative changes were excluded. Almost all studies excluded patients with neurologic signs or symptoms secondary to a herniated disk, and many excluded patients with previous back surgery [1]. Actually, all studies investigate only the presence of isolated zygapophysial joint pain, especially, of course, if 100 % pain relief was used as a diagnostic criterion in medial branch blocks.

Original prevalence studies used 50 % pain relief as a criterion. The patients studied were younger injured workers. The prevalence was 10–20 % [155]. Later studies with 75 % relief as a criterion reported prevalence rates of 27 % [159], 31 % [158], 38 % [156], and 45 % [155]. In elderly patients with no trauma in history and 90 % pain relief as a criterion, the prevalence was 40 % [225]. Using single diagnostic blocks but looking for complete pain relief, the prevalence of zygapophysial joint pain is only 10 % or less if controlled blocks were used [151].

In patients with thigh pain, it was demonstrated that the source of chronic low back pain (internal disk disruption, zygapophysial joint pain, or sacroiliac pain) varies with age. Older age was predictive of zygapophysial joint pain with a predicted probability of more the 50 % in 60-year-old patients and more than 85 % in patients over 80 years old [226].

Especially when considering degenerative diseases, zygapophysial joint pain often comes along with other pain sources (spinal canal stenosis, spondylolisthesis, disk degeneration, etc.). With different pain sources existing simultaneously, it would be great to know which proportion of pain derives from the zygapophysial joints. Unfortunately, no study exists about the prevalence of zygapophysial joint pain in patients with additional painful conditions. Assuming multiple sources of pain are possible at the same time, it is not possible to claim for complete pain relief after medial branch blocks and incomplete pain relief after radiofrequency neurotomy must also be accepted [227].

16.9 Zygapophysial Joint Pain in Selected Patients

Particularly well studied is zygapophysial joint pain in patients without comorbidities. In this group of patients, diagnostic standards

(Sect. 16.6.1) can be applied best and success rates after a specific therapy (Sect. 16.8.1) can be measured. In this chapter, the significance of zygapophysial joint pain is elaborated in patient groups in which zygapophysial joint pain is clinically relevant but does not occur as an isolated and independent disease. It is thus expected that diagnostic and therapeutic methods are only partially successful. For the patients, this can nevertheless make a significant difference in their daily lives.

16.9.1 Elderly Patient

The degenerative changes described in Sect. 16.4 are more common in older age. The joints can be affected by osteoarthritis, which is believed to be a possible cause of zygapophysial joint pain [71–74]. Compared with other sources of low back pain (e.g., diskogenic pain or sacroiliac joint pain), zygapophysial joint pain becomes the most important pain source [226].

However, there is often an image of mixed pain of various causes. Especially in combination with diskogenic changes, spinal canal stenosis, and degenerative spondylolisthesis, several pain sources might exist.

In elderly patients, a common situation is that a surgical solution (e.g., decompression of the spinal canal or stabilization) is not taken into consideration. In this respect, interventional pain therapy is significantly prioritized as an additional treatment method to medication and physical therapy. Each, decrease in pain, however small, or a reduction of pain medicine is a success for the patient and means a relief in daily life.

16.9.2 Spinal Canal Stenosis

In degenerative spinal canal stenosis, we are dealing with elderly patients who, on the one hand, have a symptomatology coming from the stenosis and the compression of the nerves in the dural sac. These symptoms are called *claudicatio spinalis* and are manifested in a restricted walking distance with pain, a sensory disturbance in the legs, or even neurologic deficits.

On the other hand, the most important reason for the development of a spinal canal stenosis is the destruction of the zygapophysial joints [105]. Therefore, patients suffer at the same time from pain deriving from the zygapophysial joints. Radiofrequency denervation might be a useful tool to treat the low back pain deriving from the zygapophysial joints. Of course it cannot be expected that the radiating pain or the claudication will improve. No results are known from literature.

16.9.3 Spondylolisthesis

In degenerative spondylolisthesis, the whole upper vertebra slips relative to the lower vertebra [106] due to degenerative changes in the spine. To treat low back pain in patients with degenerative spondylolisthesis with radiofrequency denervation seems obvious because morphological abnormalities of the lumbar zygapophysial joints are a predisposing factor in the development of degenerative spondylolisthesis [109], pathology of the zygapophysial joints is a significant cause of low back pain within the lumbar spine [108], and radiofrequency neurotomy is the "gold standard" for treating zygapophysial joint pain [144].

A sufficient pain reduction could be achieved in 65 % of the treated patients for a reasonable time [116, 227]. It is known that these patients might have sources of pain other than just the zygapophysial joints [115]. In particular the often additionally present spinal canal stenosis causes symptoms not treated by medial branch neurotomy. The second pathology often interlinked with degenerative spondylolisthesis is disk degeneration [106, 107]. Diskogenic pain also is not treated by medial branch neurotomy.

16.9.4 Failed Back Surgery

The treatment of postsurgery syndrome is difficult. Some patients will not improve with conservative measures, and therapies that are more interventional will be required. The evidence base for these interventions has grown in recent

times [228, 229]. Zygapophysial joints are an important pain source not only in patients with chronic low back pain but also in patients after disk surgery [168, 169]. Therefore, a specific therapy against zygapophysial joint pain is rational. Continued pain following lumbar spine surgery has been hypothesized to be secondary to multiple causes, including epidural fibrosis, acquired stenosis, sacroiliac joint pain, and zygapophysial joint pain [230–232]. It is difficult in postlumbar surgery syndrome to identify pain-generating structures [233]. The prevalence of zygapophysial joint pain in patients with postlumbar laminectomy syndrome is 32 %. In patients after disk surgery, the prevalence of zygapophysial joint pain is 7 % and 28 % in patients with persistent back pain after surgery [169].

The reasons why the zygapophysial joints are involved even if the joint was untouched during the operation might be inflammatory processes, low-level trauma, changes in disk height, or stretching of the joint capsule [144]. The process of degenerative disk disease, particularly when enhanced by a herniated disk or diskectomy, results in progressive loss of intervertebral disk volume and disk height and increased load to the joints, which might be a reason for pain [234].

Zygapophysial joint pain can be identified and treated with a radiofrequency neurotomy with a success rate of 58.8 % [169] in patients after disk surgery.

After spinal fusion, zygapophysial joint pain can occur due to residual mobility in the index segment or in adjacent segments due to overload. Studies on the effectiveness of a specific joint therapy after spinal fusion do not exist.

Conclusions

Zygapophysial joints meet all prerequisites to be a source of pain. They are often involved in back pain and radiating pain and should not be underestimated. The prevalence of isolated zygapophysial joint pain increases with age. In addition, zygapophysial joint pain appears also in combination with other common spine diseases, such as disk degeneration, spinal canal stenosis, and spondylolisthesis.

If the diagnosis is made with controlled medial branch blocks, radiofrequency denervation is the only validated treatment for pain mediated by the medial branches.

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Part IV

Lumbar Disk Herniations

17 Advanced Scientific Considerations for Surgery in Patients with Lumbar Disk Herniation

Wilco C.H. Jacobs and Wilco C. Peul

17.1 Lumbar Disk Herniation

Typically, patients present to their general physician (GP) with complaints of radiating low back pain, which they may or may not have been experiencing for a while. In first instance, in absence of emergency surgical indications, conservative care is prescribed. With persistent complaints, the GP refers to a second-line physician, such as a neurologist, who calls for an MRI. When the MRI shows a concordant disk herniation or nerve root compression, referral to a neurosurgeon often results in disk surgery.

Considerable practice variation exists [1] in the occurrence of spine surgery across geographic locations. The probable cause for this practice variation is inconsistency in the referral patterns as well as differences in treatment decisions. If patient history and diagnostic assessments do not lead to treatment choice in a reliable, reproducible manner, choice for treatment is care provider dependent, while it should be patient dependent, based on disease characteristics and patient preferences. Standardization of these pathways and diagnostic assessments are needed, and once established in guidelines, these should be followed to improve quality of care.

Another aspect of the diagnostic pathway is the utilization of second-line, in-hospital care. The journey through the health-care milieu by patients with disk herniation results in additional diagnostic assessments, leading to extra cost and interventions. Alternatively, a wait and see policy can often perfectly be maintained by the GP and can result in satisfactory, comparable, outcomes in many patients. The spine community should make it a priority that patients are adequately equipped and educated to make a balanced decision. Patients are best informed in the primary care environment, including first-line GPs, physiotherapists, but also second-line neurologists and neurosurgeons. Modern e-health applications can help in this regard.

17.2 Diagnosis

In primary care, patient history and physical examination are the key aspects for diagnosis of the cause of sciatica, either defined as disk herniation or nerve root compression. In this process,

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_17

these compressive causes of sciatica should be distinguished from other causes such as inflammatory irritation of the nerve root, lumbar stenosis, or malignant causes. Either with primary or secondary care, the following considerations are important before a decision for surgery should be considered.

17.2.1 Relevance of History Taking

In a systematic review, "male gender", "pain worse in the leg than in the back", and "non-sudden onset" have been shown to possess prognostic value for the presence of nerve root compression [2]. For the presence of a disk herniation, relevant factors were "BMI<30", "non-sudden onset", and "sensory loss". This information should be considered before requesting further diagnostic tests such as MRI.

17.2.2 Relevance of Clinical Assessments

Physical tests to diagnose disk herniation include usually reflex testing, sensory test, and motor strength tests. These components of the neurological examination, either individually or in combination, are associated with suboptimal clinically relevant accuracy in identifying the level of herniation on an MRI [3]. Physical and neurological examination are especially poor in isolation [4], although this was only studied in surgical populations. Further research is necessary regarding value of combined tests in primary care.

The optimal window for surgical intervention for disk herniation is thought to be between 6 and 8 weeks and 9 months. As a consequence, referral to second-line neurologist, with possibilities for diagnostic imaging such as MRI, is not indicated before 6–8 weeks [5]. Waiting too long might predispose patients for chronic complaints and should also be avoided [6], one of the recommendations from the Choosing Wisely Netherlands campaign (Table 17.1).

Table 17.1 Recommendations from the Choosing Wisely Netherlands campaign

	Recommendation
1	Do not operate in case of isolated low back pain
2	Do not operate with short existence of leg pain (<6 weeks), but also do not wait too long (>9 months)
3	Do not call for an MRI during natural recovery or after disk surgery
4	Do not operate when the compressed nerve does not match the affected dermatome
5	Only apply new surgical techniques and implants in context of research

17.2.3 Interpretation and Consequences of MRI

In patients that are referred to a neurologist for suspicion of a herniated disk, an MRI is a commonly used tool to identify the probability of a disk herniation. MRI was found to be reliable in diagnosing the affected disk levels, the affected nerve roots, and the probability of nerve root compression [7]. However, most MRI findings have a poor correlation with clinical symptoms or outcome [8]. In a conservative group of patients from a randomized trial, 55 patients received delayed surgery due to persistent complaints [9]. MRI at baseline did not predict which of the conservatively treated patients eventually needed delayed surgery [10].

In case of persisting complaints after surgical or conservative treatment of sciatica, a follow-up MRI did not distinguish between favourable outcome and unfavourable outcome [11]. From an economical point of view, it is thus not advised to perform a repeat MRI when confronted with a patient that has persisting complaints after 1 year. This also was adopted by the Choosing Wisely Netherlands campaign (Table 17.1).

To distinguish recurrent herniated disk from scar tissue, contrast-enhanced MRI with gadolinium is often used. This was found to possess slight to fair agreement between observers to identify enhancement. Further there was also no correlation between enhancement and clinical outcome 1 year after the initial surgery [12].

It should be noted that reliability applies to the interpretation of an existing MRI, not for a repeated MRI, which might even show lower reliability.

In conclusion, MRI appears to be mainly useful in identifying and confirming the affected level. For other applications of MRI findings, we certainly need more research.

17.2.4 Prognostic Factors

Little is known about which factors have prognostic value in patients with lumbar disk herniation. In patients indicated for conservative interventions, a recent review [13] only identified leg pain intensity as a prognostic factor for subsequent surgery. Age, body mass index, smoking, and sensory disturbance did not possess prognostic abilities for outcome. Especially when we want to assess the value of published literature, we need to know which factors influence outcome of patients with sciatica at different stages of the disease. More research needs to be done in this area.

17.3 Decision for Surgery

17.3.1 Evidence for Effectiveness of Surgery Compared with Conservative Interventions

There are five trials [9, 14–17] that compare surgical with conservative interventions, either being conservative management (three trials), prolonged conservative management with optional surgery (one trial), or steroid injections (one trial). Unfortunately, these trials are heterogeneous regarding interventions, some have a high risk of bias, and some suffer from poor reporting which prohibits quantitative analysis [18]. The general conclusion after evaluation of these trials does not support either surgery or nonoperative intervention [18]. However, surgery appeared to result in faster recovery in at least two of the trials. This implies that the choice for surgery over continuation of conservative care comprises balancing fast recovery against surgical risks, cost, and burden.

The three studies [14–16] that compared surgery with conservative management showed conflicting results. One older, high risk of bias study including 126 patients [14] demonstrated that diskectomy was significantly better regarding patient and observer ratings than conservative treatment at 1 year. Twenty-four of the 66 patients (36 %) in the conservative care group versus 39 of the 60 patients (65 %) in the surgery group reported a good outcome. This difference disappeared after 4 and 10 years. One high risk of bias trial including 56 patients [15] found no significant differences for leg pain or back pain and subjective disability throughout the 2 years of follow-up. VAS leg pain scores, however, improved more rapidly in the diskectomy group; 6-week score in the surgery group was 12 (SD 20) versus 25 (SD 27) in the conservative group. The per-protocol analysis demonstrated no statistically significant differences. A large low risk of bias trial including 501 patients showed that both the surgery and the conservative treatment group improved substantially over 2 years for all primary and secondary outcome measures [16]. The intention-to-treat analysis showed no statistically significant differences for any of the primary outcome measures. There was considerable crossover: 50 % of the patients randomized to surgery and 30 % of the patients randomized to conservative treatment. After 2 years this was 45 and 40 %.

The sciatica trial randomized 283 patients with severe sciatica for 6–12 weeks to early surgery or prolonged conservative treatment followed by surgery if needed [9]. In this study, crossover was anticipated and offered surgery to patients that did not improve after 6 months. After 2 weeks, 89 % of patients randomized to early surgery underwent micro-diskectomy, while 39 % of patients randomized to conservative treatment underwent surgery after a mean of 19 weeks. Relief of leg pain was faster for patients assigned to early surgery. Intention-to-treat analysis showed statistically significant more leg pain relief was found in favour of early

surgery compared with prolonged conservative care at 3 months (MD −17.70, 95 % CI −23.1 to −12.3). There was no significant overall difference between the two groups regarding disability scores during the first year. The median time to recovery was 4.0 weeks (95 % confidence interval (CI), 3.7–4.4) for early surgery and 12.1 weeks (95 % CI, 9.5–14.9) for prolonged conservative treatment. During the first year, early surgery achieved a faster rate of perceived recovery with a hazard ratio of 1.97 (95 % CI 1.72–2.22, $P<0.001$). At 1 year of follow-up, however, 95 % of patients in both treatment groups had experienced satisfactory recovery, and no subsequent differences were found. This lack of a difference between groups was maintained after 2 years and also after 5 years [19]. The same pattern was found for the subset of 150 patients with a motor deficit [20]. Motor deficit recovered significantly faster in patients randomized to early surgery, but there were no differences found after 1 year.

One high risk of bias trial including 100 patients compared micro-diskectomy with epidural steroid injection [17]. Patients undergoing diskectomy had the most rapid decrease in their symptoms. The decrease in leg pain in the diskectomy group was significantly greater than epidural steroid injection group at 3- and 6-month follow-up intervals, but not beyond 1 year. There were no significant differences between groups for back pain throughout the follow-up. Twenty-seven of 50 patients receiving a steroid injection had a subsequent micro-diskectomy. Outcomes in this crossover group were similar to those of the surgery group.

17.3.2 How Long to Wait Before Indicating Surgery

The current status of evidence does not support a definite choice for conservative or surgery, at least for the indications that were studied in these trials. The general consensus from guidelines is to wait for at least 6–8 weeks before considering surgery [5]. Also, some of the choosing wisely initiatives provide definitive advice not to proceed with surgery too early but also not to wait too long (more than 9 months) [21]. Between these margins, choice for either surgery or conservative intervention should be based on preferences of well-informed patients (Fig. 17.1). Only if the patients have information about the advantages and disadvantages of surgery on the short term and the equivalent outlook of both interventions on the longer term, an informed choice can be made [9]. Decision tools can guide these decisions [22].

17.4 Surgical Techniques

Once the need and preference for disk surgery are established, preoperative planning can begin and the choice for surgical approach can be made. Several techniques are available and they differ in invasiveness, approach, extent of disk resection, and use of co-interventions such as preventive measures of scar tissue.

17.4.1 Evidence for Effectiveness for Different Surgical Techniques

The most common type of surgery is microscopic diskectomy, which is defined as the surgical removal of part of the disk, performed with the use of an operating microscope or other magnifying tools. Most studies refer to Caspar [23], Yasargil [24], and Williams [25] when diskectomy is performed with microscope and to Foley and Smith [26] or Greiner-Perth et al. [27] when diskectomy is performed with tubular, muscle-splitting, retractor systems and endoscope. However, some have returned to using a microscope while retaining the less invasive muscle-splitting approach of Foley and Smith [26]. The result is an array of surgical approaches for which it is difficult to acquire sufficient evidence from randomized trials comparing all techniques.

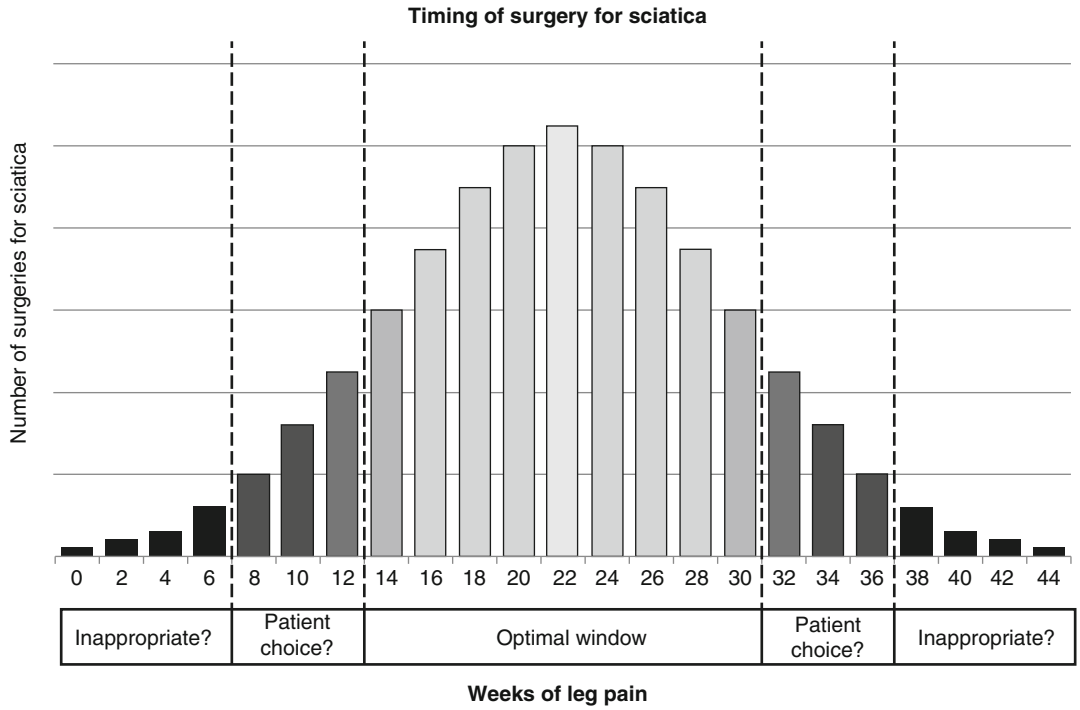

Fig. 17.1 The optimal window for surgery for lumbar disk herniation. Before 6–8 weeks and after 9 months (36 weeks) can be regarded inappropriate care. Note that complaints of over 9 months are not a contraindication for surgery but that one should have treated the majority of these patients earlier

17.4.2 Open Versus Microscopic Diskectomy

There are eight trials that have compared open diskectomy with minimal invasive techniques, including microscopic diskectomy, video-assisted microscopic diskectomy, automated percutaneous micro-diskectomy, or micro-endoscopic diskectomy.

Six trials compared the classical open diskectomy, also called standard diskectomy or macrodiskectomy, with microscopic diskectomy [28–33]. There is a consistent finding in these studies that microscopic diskectomy leads to an increased operating time with a pooled effect of 12 min (95 % CI 2.20–22.3; $p=0.02$; moderate quality of evidence). No differences were found for length of stay, which was only reported in five studies with a total of 452 patients. The mean difference was 0.18 days in favour of open diskectomy (95 % CI −0.09 to +0.45 days; $p=0.47$; moderate quality of evidence). Blood loss was reported in two studies; in one study with 119 patients, microscopic diskectomy resulted in less blood loss [31], while in the other study with 60 patients, there was no difference [28]. The quality of evidence for blood loss was "very low". The length of incision was reported in three studies with together 353 patients and found to be shorter for microscopic diskectomy in two studies [30, 33]. The quality of evidence for incision was "low". Leg pain was reported in four studies with together 453 patients and was significantly less for microscopic diskectomy by 2.01 mm (95 % CI 0.57–3.44; $p=0.006$; moderate quality of evidence), while this can hardly be regarded as a clinical relevant difference. Further outcomes (pain, return to work) were found to be comparable, except for a higher return to work at 4 weeks for microscopic diskectomy [33] in one study with 114 patients where two other studies with together 140 patients found no difference at 10.4 weeks [28] and 14.9 months [29]. It should

be noted that all but one of these trials was associated with a high risk of bias.

Two trials compared open diskectomy with micro-endoscopic diskectomy [32, 34]. Huang et al. [34] reported results of a very small, high risk of bias, trial with only 22 patients. The micro-endoscopic diskectomy group had shorter postoperative hospital stay and less intraoperative blood loss compared with the open diskectomy group, but duration of the operation was longer. There were no differences in pain severity and MacNab criteria between the groups. Teli et al. [32] showed in a larger trial including 220 patients that the micro-endoscopic group compared to open and microscopic diskectomy suffered more dural tears (7 %, 3 %, 3 %, respectively), root injuries (3 %, 0 %, 0 %, respectively), and a recurrent herniation (7 %, 4 %, 3 %, respectively).

One low risk of bias trial with 60 patients found that patients who had received video-assisted arthroscopic micro-diskectomy had similar satisfactory outcomes compared with open laminotomy and diskectomy, but patients who had had an arthroscopic micro-diskectomy had a shorter duration of postoperative disability and used narcotics for a shorter period [35].

17.4.3 Different Minimally Invasive Techniques

There is evidence on the comparative effectiveness of the different minimal invasive techniques for diskectomy such as endoscopic diskectomy, video-assisted diskectomy, percutaneous transforaminal diskectomy, etc.

Eight trials with an accumulative 1047 patients evaluated different approaches for less invasive diskectomy, such as micro-endoscopic diskectomy, tubular microscopic diskectomy, microscopic-assisted percutaneous nucleotomy, minimal access trocar/microsurgical micro-diskectomy, percutaneous endoscopic diskectomy, or sequestrectomy. We analysed the comparisons between these techniques, keeping the differences muscle damage and differences in use of microscope or endoscope in mind. The results of these trials are given in Table 17.1.

Seven (six high risk of bias) trials with 923 patients compared tubular diskectomy with conventional microscopic diskectomy [32, 36–41]. Of these, four used an endoscope [32, 36, 37, 39]. There was low to moderate quality of evidence for incision length and this was consistently shorter for tubular diskectomy in all three studies ($n=260$) that reported this outcome [32, 36, 39]. However, results could not be pooled due to sparse data on variation (SD). The quality of evidence for the remaining outcome parameters was "low' to "very low", so no further meta-analyses could be performed. Inconsistent results were found for operative morbidity. Two studies ($n=368$) of the six studies ($n=718$) reporting operative time found a longer duration for tubular diskectomy [32, 36], while one study ($n=100$) found a shorter duration [38]. No differences were found for blood loss in three studies. Length of stay was longer (2 h) for conventional microscopic diskectomy in only one of four studies [36]. One study found a faster improvement in pain scores for tubular diskectomy before discharge [37], while the only low risk of bias study found a slightly better pain score for conventional diskectomy at 2 years [41]. All other outcomes for pain as measured with VAS, for Oswestry or Roland-Morris score, or for SF36 scores were not significantly different between the two surgical techniques. For Shin et al. [37], baseline values for back pain were not comparable. In one trial, the postoperative analgesic consumption was significantly less in the tubular diskectomy group [40].

One high risk of bias trial [42] with 40 patients compared percutaneous endoscopic diskectomy (cannula inserted into the central disk) with microscopic diskectomy. This trial showed comparable clinical outcomes after the two procedures but contained a small sample size.

17.4.4 Techniques to Prevent Scarring

Evidence regarding techniques that are applied for the prevention of scar tissue is relatively sparse. Recent trials of an interposition gel covering the dural sheet, fat, preservation of the liga-

mentum flavum, and use of a drain show promising effects in reducing epidural scar formation, but no effect on clinical outcomes.

Thirteen studies considered the effect of different techniques to prevent formation of intraspinal scarring following diskectomy, as assessed by magnetic resonance imaging or enhanced computerized tomography. Ten studies evaluated the use of an interposition membrane. The types of membrane used are autologous free fat graft or commercially available gels. The results of these trials are given in Table 17.1.

Four high risk of bias studies compared the use of fat graft versus no fat graft [43–46]. These studies failed to show any improvement in clinical outcomes following use of fat. Three studies evaluated fibrous tissue formation on CT or MRI, two found a decrease for fat graft [44, 46], and one small subsample of MacKay et al. [43] found no difference. The pooled effect with a moderate quality of evidence yielded a significant decrease in scar tissue for fat graft (OR 0.22 (95 % CI 0.08–0.62). One study reported a lesser number of painful episodes 1 year after surgery [46], but this was evaluated by the surgeon.

The synthetic gels in the studies consist of bioresorbable carbohydrate polymer gels (Adcon-L, derived from porcine collagen and dextran sulphate), polytetrafluoroethylene (Prelude), polyethylene oxide with carboxymethylcellulose (Oxiplex/SP), or polyethylene glycol (DuraSeal Xact). There are three trials of ADCON-L [47–49]. Two of these studies [47, 48] show conflicting results. Twelve-month results are reported from a pilot study of Oxiplex/SP gel [50]. Although there is a trend suggesting that treatment diminishes leg pain severity and lower limb weakness, the study was very small and the results reported are not statistically significant. Fransen et al. [51] compared DuraSeal Xact with no gel in a small, double-blinded low risk of bias study. One small, high risk of bias, study [52] did not find a difference on any of the clinical outcomes or on scar volume between ADCON-L and Preclude Spinal Membrane (PSM). The third arm of MacKay et al. [43] included gelfoam and also found no differences for this additional group.

Three studies evaluated the effect of other approaches, namely, the use of antibiotics, drains, or preservation of ligamentum flavum. One low risk of bias study assessed the effect of locally applied mitomycin C on peridural fibrosis during lumbar micro-diskectomy [53] ($N=60$). Mitomycin C is isolated from *Streptomyces caespitosus* and is purported to suppress fibroblast proliferation. At a median follow-up of 18 months, there were no differences between the group with or without mitomycin C on postoperative evaluation of the MR images, pain scores, and neurological function. One small high risk of bias study compared micro-diskectomy with preservation of the ligamentum flavum with usual micro-diskectomy [54]. There were no differences in clinical outcomes (pain, functional status, and straight leg raising), but the group with preserved ligamentum flavum had less epidural fibrosis as assessed with MRI at 6-month follow-up compared with the usual micro-diskectomy group. However, this study had an inadequate randomization procedure, was not blinded, and only included 20 patients. One high risk of bias study compared micro-diskectomy with a drain aimed at reducing postoperative epidural hematoma with usual micro-diskectomy [55]. The study found no differences in clinical outcomes after 6 months. The group with a drain had statistically significant less postoperative epidural hematoma. After 6 months there was less epidural fibrosis in the drain group, but this difference was not statistically significant. The study had an inadequate method of randomization.

17.4.5 Considerations on the Extent of Disk Removal

One low risk of bias trial [56] with 84 patients compared clinical outcomes and recurrence rates after sequestrectomy (removal of only the sequestration while leaving the remaining disk intact) and standard micro-diskectomy (removing the herniated material and resection of disk tissue from the intervertebral space). There were no statistically significant differences in back and leg pain and quality of life up to 2 years of follow-up [57].

17.5 Methodological Considerations

The evaluation of surgical interventions for sciatica suffers from a number of challenges. Surgical performance is likely to be surgeon dependent, the timing of surgery differs, there is a big placebo effect from surgery, the surgical evolution of techniques and medical devices is highly technology driven, and relevant follow-up assessments are in the very far future. Especially comparing conservative and surgery is difficult, as conservative intervention would normally imply continuation of an already ineffective treatment from the patient point of view.

17.5.1 Randomized Trials

There are apparent methodological problems in randomized trials in comparing surgery with nonsurgical interventions. First, there is considerable crossover in all of these trials. An intention-to-treat analysis is confounded by this crossover, but also by re-interventions. The intention-to-treat analysis should be interpreted as a treatment strategy analysis, except that there were no real-life treatment strategies compared as interventions are likely to have been applied different from usual care in the context of the trial. As an alternative, the per-protocol analysis will not provide insight in patient outcomes for a specific choice of treatment strategy, let alone specific interventions. Second, blinding is impossible for patients and care providers and difficult for outcome assessors. Lack of blinding for patients could result in disappointment when no surgical intervention is offered. Third, as many care providers and patients are hesitant to participate in these trials, external validity is compromised. These problems limit the applicability of randomized trials in these comparisons.

Nevertheless, randomized trials still hold value and likely we should make use of all research designs and decide for the best design for each question at hand. Randomized trials are mainly applicable, within spinal surgery, for comparisons between surgical techniques.

17.5.2 Alternatives

Alternatives to randomized trials include the use of the opt-out strategy, where patients are included in an experimental study, unless they object. This has however some serious ethical problems. Another approach is the use of clinical equipoise, where a patient is included in an observational study when a team of care providers decides (independently) that there is no consensus about the most appropriate treatment [58].

17.5.3 Spine Registries

The evolving spine registries will provide an opportunity for additional analyses, which will be more representative of usual care, with a higher patient participation and better representativeness. The best current examples of such registries are in the Scandinavian countries (SweSpine in Sweden, NorSpine in Norway, and DaneSpine in Denmark), as well as the Netherlands, the United States, Spain, and Switzerland. New initiatives are to be expected in Canada, Australia, Russia, Turkey, and Singapore.

Spine Tango from the Spine Society of Europe serves individual clinics around the world. This approach could result in a selected inclusion of patients when participating clinics differ from the average clinic in a country. On the other hand, also the national registries are not yet obligatory in all countries.

Most of these registries are initiated for surgical interventions, while others focus on conservative interventions such as the Spanish registry. For a comprehensive view on the patient with lumbar disk herniation, we will need to assess the patients through the whole pathway of care, from first-line general practitioner, to second-line neurologist, and if applicable to neurosurgeon. Only then we can evaluate which patients need which treatments at which point in their disease.

A recent important step has been the global consensus on the outcome parameters that need to be assessed in these registries and assessment timing [59], in order to facilitate global benchmark and comparisons between interventions. A

global group of spine specialists agreed on using the Oswestry Disability Index (version 2.1a), NRS for leg and back pain, and EQ5D as outcome measures along with a series of other measures for assessing complications, reoperation, need for medication, and work status. The existing registries as well as the new registries will hopefully adopt this guidance.

The identification and assessment of relevant prognostic factors are essential for a valid analysis of observational data. This is necessary for proper case mix adjustment of other advanced analysis methods such as propensity score modelling. Most registries now collect age, gender, marital status, duration of complaints, baseline pain and function scores, analgesic use, work absenteeism, and educational level. For example, the patient selection in the Spine Tango registry should be evaluated for these variables. Additional research is still needed to identify the relevant prognostic factors.

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Surgery for Lumbar Disk Herniations

18

Luca Papavero

18.1 When to Operate?

> As you leave the OR after an apparently successful microdiscectomy, remember that a successful surgical outcome depends 90 % on patient selection and only 10 % on technique. John A. McCulloch [1]

> Up to 15-fold variation in regional lumbar diskectomy rates in the United States [2] and lower rates internationally raise questions regarding the appropriateness of some of these surgeries [3, 4]. James N. Weinstein, SPORT [5]

18.2 How to Operate?

18.2.1 Microsurgical Versus Non-microsurgical Surgical Techniques

The spectrum of open surgical treatment of lumbar disk herniations (DHs) ranges from conventional technique without optical magnification to the use of loupes or microscope. Although there is a still ongoing debate about the benefits of the use of microscope for diskectomy for the medium- and long-term outcome, the short-term advantages include less damage to the paravertebral muscles, decreased blood loss, and reduced postoperative morbidity and by far outweigh the relative disadvantages such as the learning curve [6–9]. In our experience, once this hurdle has been overcome, there is no reason to operate without the aid of a microscope. The surgical techniques described in this chapter are best performed with the aid of the microscope, although they are feasible also with loupes.

18.2.2 Fragmentectomy Versus Diskectomy

When symptoms are caused by an extruded disk fragment, the disk space should not be cleared. The removal of disk material from the disk space does not lower the recurrence rate but may increase the postsurgical back pain due to segmental instability [10, 11]. Furthermore, the mean operation time is shorter in the fragmentectomy group and there is no risk of abdominal vascular and visceral injuries [12].

18.2.3 Subperiosteal Versus Transmuscular Approach

The subperiosteal approach requires the incision or retraction of the ligamentous insertions of the paravertebral muscles from the spinous processes.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_18

The intraoperative injury of the posterior supporting structures of the lumbar spine may lead to increased postoperative back pain [13–15].

The micro-endoscopic diskectomy (MED) was introduced by Foley and Smith [16]. It was the first technique that addressed the shortcomings of the conventional subperiosteal approach. Many investigators have reported that MED is associated with less postoperative pain, a shorter hospital stay, and more rapid return to work [17–19]. However, MED has some limitations related to a small operation field, visualized through a cylindrical tubular retractor [20].

The paraspinal muscle-splitting or "Wiltse" approach along the natural cleavage planes of the paraspinal muscles has shown to cause less damage and retraction of the paraspinal muscles compared to the subperiosteal approach [21]. This leads to decreased back pain and less postoperative analgesic consumption during the early postoperative period [15]. The choice of the transmuscular approach may be left to the surgeon's preference in patients with fatty degenerated muscles. It is recommended whenever minimizing muscle traumatization becomes an issue.

18.2.4 Retractors: Tubular Versus Conventional

The introduction of transmuscular approaches via tubular or miniaturized speculum retractors has prompted the development of miniaturized surgical tools which are sized between the conventional microsurgical instruments and the endoscopic ones. Their design facilitates the intraoperative view of the surgical target area (Fig. 18.1). Surgical times are comparable to open conventional techniques.

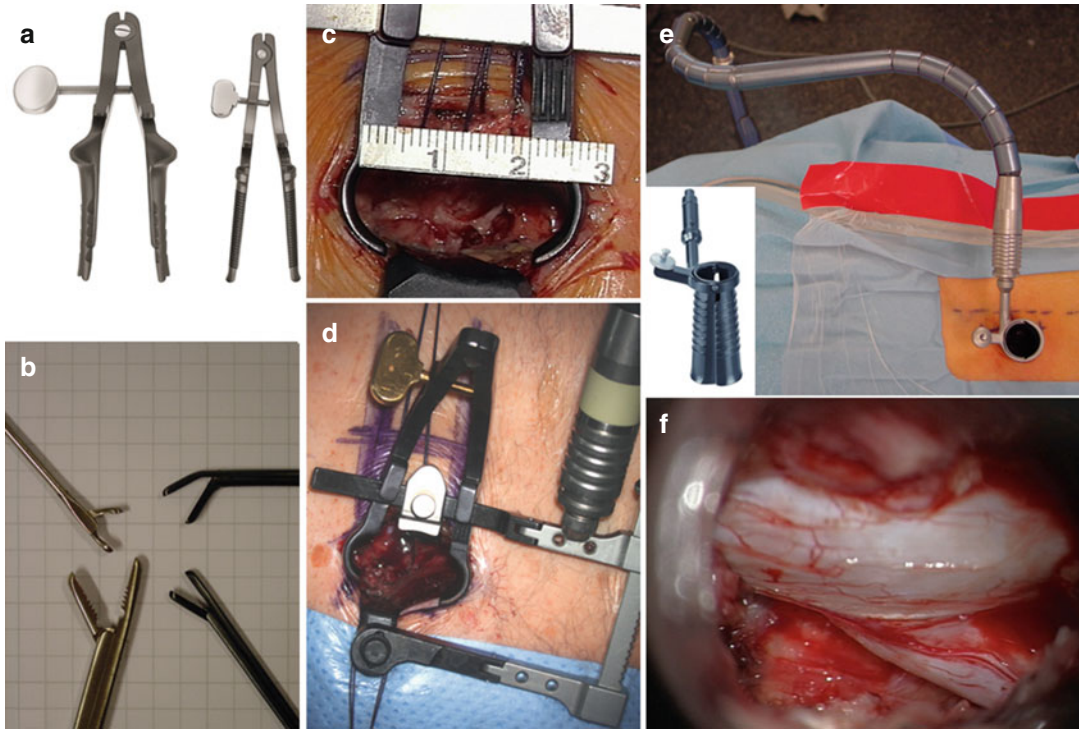

Fig. 18.1 (**a**) Conventional vs. modified minimally invasive speculum retractor; (**b**) conventional (*bottom left*) vs. miniaturized rongeurs; (**c**) miniaturized speculum retractor in situ; (**d**) the speculum-counter-retractor system can be docked to a self-holding arm; (**e**) expandable tubular retractor with holding arm; (**f**) close-up view of an exiting nerve root through the tubular retractor

18.3 Surgical Techniques

18.3.1 Primary Disk Herniations

18.3.1.1 Interlaminar Approach [22, 23]

Indications

- All contained disk herniations (DHs) and extruded fragments between the midline and the medial border of the pedicle. In relation to the disk space, the fragments may be caudally or cranially extruded. In the latter case, the translaminar approach is preferred.
- DH combined with central/recess stenosis or with asymptomatic segmental instability.
- Recurrent DH.

Contraindications

- Foraminal or far lateral DHs which are located lateral to the lateral border of the pedicle

Preoperative Planning

- *Biplanar plain radiographs*
  Optional in first surgery cases, provided that the MRI investigation encloses a coronal slice (scoliosis!). Mandatory (1) in recurrent DHs cases to evaluate bony defects and (2) whenever MRI leads to suspect a bony abnormality (spina bifida, pars interarticularis defects)
- *MRI*
  Sagittal slices: Contained disk herniation (DH) or extruded fragment? Caudal or cranial (suitable for translaminar approach) fragment dislocation? Mid-vertebral body herniation (halfway between two disk spaces)? *Foraminal slice*: Black neuroforamen? *Extraforaminal slice*: Disk fragment still apparent? *Axial slices*: Axillary disk fragment? How much of the DH is underneath the thecal sac, intraforaminal or extraforaminal (Fig. 18.2)? Pseudomeningocele in recurrent disk surgery? *Coronal slices*: Which approach for combined intra- and extraforaminal DH? *Gadolinium-enhanced slices*: Amount of scar tissue on the way to and into the spinal canal? Differentiation between recurrent DH and scar tissue?
- *CT scan*
  Second choice whenever MRI contraindicated or not available. *Disko-CT* (diskography + CT): helpful in suspected extraforaminal DH. *CM-enhanced CT*: indicated for recurrent disk and differentiation between intraforaminal DH and neurinoma

Positioning

We recognize that several positioning could provide good clinical results, especially with experienced operating room personnel (ORP). The features of our preferred positioning technique are described below:

- The patient is placed prone on the Wilson frame. Advantages: Hip and knee joints are only moderately flexed, especially important in obese patients. The lordosis of the lumbar spine should be reduced as required by increasing the height of the arches. The distance between the laminae can be adjusted according to the size of the patient in order to allow a free-hanging abdomen to reduce bleeding (Fig. 18.3).
- The head is positioned into a ProneView mask (Manufacturer: Dupaco Inc, Oceanside, California, USA). Eyes, nose, and chin are protected: The anesthesiologist is able to check them intraoperatively by use of a mirror (Fig. 18.3).
- For safety reasons the patient is secured with a belt on the gluteal area: This becomes helpful when the OR table has to be tilted away from the surgeon, e.g., in dealing with extraforaminal or far lateral disk herniations (EFDHs).
- The OR table is tilted until the lumbar spine is parallel to the floor.
- X-ray localization: A 2 cm skin incision does not allow a "seek and find" surgery. Therefore the correct X-ray localization of the surgical target area is of paramount importance. The needle is always inserted contralateral to the intended surgical side in order to avoid subcutaneous or intramuscular hematoma and off the midline in order to prevent inadvertent CSF leakage. The needle is perpendicular to

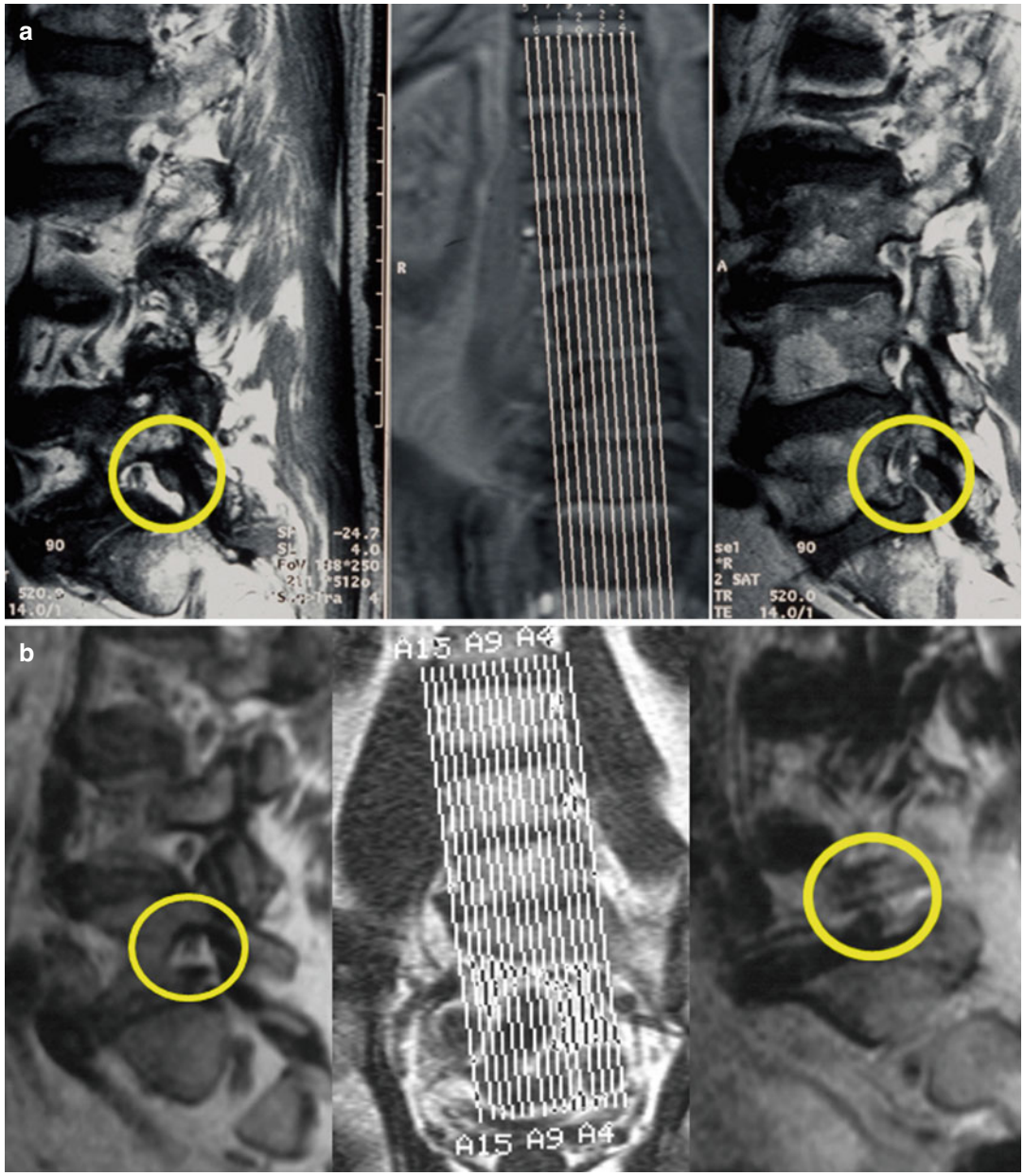

Fig. 18.2 Teaching case: A 64-year-old lady presented with mild low back pain and severe left-sided L5 pain requiring opioids since 3 weeks. The examination demonstrated a left-sided foot dorsiflexion weakness. (**a**) Because the sagittal MRI slices were not performed lateral enough, the L5/S1 disk was reported as normal. Conservative therapy was advised. (**b**) MRI was repeated with appropriate lateral slicing. The small intraforaminal disk herniation squeezing the left-sided L5 root (*bottom right*) was removed surgically

the target area (and to the floor): Soft tissue dissection is easier straightforward down. Even small oblique deviations can lead to the wrong level, especially in obese patients. The needle should point to the equator of the target disk. With increasing experience, the surgical field may be narrowed further to only the extruded disk fragment.

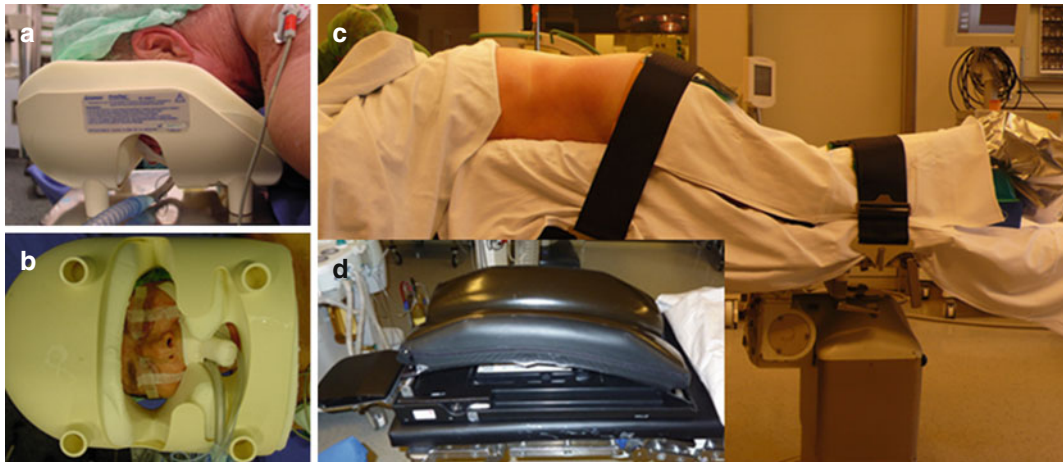

Fig. 18.3 Positioning for open lumbar disk surgery: (**a**) The face is embedded in anatomically tailored foam. (**b**) The mirror enables a continuous monitoring of the eyes and of the tube. (**c**) The lumbar spine is parallel to the floor. The belts secure the patient during tilting the table 30° away from the surgeon, as required in extraforaminal disk surgery. (**d**) The Wilson frame can be adjusted according to the size of the patient and may open up the interlaminar window by decreasing the lumbar lordosis

Soft-Tissue Approach

The interlaminar space can be approached via a subperiosteal (SP) or a transmuscular or paramedian (TM) route. Although the use of the microscope "from skin to skin" is optional, its advantages will be appreciated in dealing with a miniaturized surgical corridor. The most relevant steps are described below:

- Prophylactic antibiotic coverage (e.g., cephazoline 2 g) 30 min before skin incision
- *Skin*: 2 cm incision, 5 mm (SP), or 10 mm (TM) off the midline
- *Fascia*: (SP) Slightly semicircular incision toward the midline. Five holding sutures on the medial lip secured to a clamp with weights. (TM) Straight incision with one holding suture on each side.
- *Muscle*: (SP) Paramedian retraction of the paravertebral muscles from the interspinous ligament. Sharp dissection of the rotators from the lower rim of the superior lamina and from the facet joint capsule. Insertion of a miniaturized speculum-counter-retractor system (Fig. 18.1c; manufacturer: Medicon, Tuttlingen, Germany).
  (TM) Blunt splitting with the index finger until the lamino-facet junction can be palpated. Opening of the muscular corridor with miniaturized muscle retractors or with a dilator. Insertion of an expandable tubular retractor (Fig. 18.1e; manufacturer: Medicon, Tuttlingen, Germany) of 15 mm or 18 mm diameter. Both the speculum and the tube may be secured to the OR table with a self-holding arm nicknamed the "snake" (Fig. 18.1e).
- *Interlaminar space*: From this step onward, the surgical technique is identical. The lower rim of the cranial lamina, the medial border of the facet joint, and the yellow ligament are the area of interest. Radiographic confirmation of the level is performed. Following a lateral flavectomy or flavotomy with suspension sutures, the epidural fat is exposed. The medial border of the inferior articular process is undercut or drilled off until the shoulder of the root is palpated.
- *Epidural dissection*: Up-down dissection of the epidural fat performed with a microdissector and a flat sucker along with careful bipolar coagulation of veins which opens access to the root-DH complex.

Exposure of the Herniated Disk

- *Management of the DH*: The local anatomy will dictate the necessary steps. Usually, a gentle

dissection between root and disk material is accomplished first. In our experience the root retraction is performed intermittently with a flat sucker rather than with a conventional root retractor. Free disk fragments are removed with miniaturized forceps (Fig. 18.1b, manufacturer: Medicon, Tuttlingen, Germany). If indicated, the annulus is split bluntly with the dissector or with a scalpel and further disk material is removed. In the authors' experience, additional diskectomy is performed in 20–30 % of the cases.

Closure

- The disk space, when opened, is rinsed with normal saline. The opening of the annulus is closed with a collagen sponge coated with fibrinogen and thrombin (Tachosil®, manufacturer: Behring, Marburg, Germany). The epidural fat is mobilized in order to cover the root. Careful hemostasis goes along with closure by layers.

18.3.1.2 Translaminar Approach [24–28]

Indications

- Cranially extruded disk fragments pushing the exiting root against the lower rim of the pedicle. Usually they are located within the root canal between two lines marking the medial and lateral border of the superior facet.
- Recurrent cranially extruded disk fragments of DH previously removed via an interlaminar approach.

Contraindication

- Lack of an adequate bony lamina, e.g., severe spinal canal stenosis and spina bifida

Preoperative Planning

- *MRI* (*sagittal slices*): Measure the distance between the upper border of the disk space and the lower rim of the cephalad pedicle. The translaminar hole will be centered on the halfway of this distance. *Axial slices*: Look at how much of the bulk of the DH is underneath the thecal sac and how much is lateral of it or even intraforaminal. The translaminar hole is centered on the lateral border of the dural sac.

Positioning

- Basically the same as for the interlaminar approach.
- Important: The target lamina should be parallel to the floor! This may require the surgeon to tilt the OR table in a reverse-Trendelenburg position. The advantages of a horizontal target lamina are twofold: The placement of the retractor blade and the drilling of the hole become easier (see Figs. 18.6 and 18.7).
- Radiographic localization: The needle should point to the largest portion of the DH which is usually halfway between the upper border of the target disk and the lower rim of the cranial pedicle. At the beginning of the learning curve, these landmarks may be labeled on the skin incision centered in between.

Soft-Tissue Approach

- The lamina can be approached via a subperiosteal (SP) or a transmuscular (TM) route. The soft tissue approach mirrors the interlaminar approach. Remember: The width and the overlapping of the lamina in relation to the disk space increase in the caudal-cranial direction, whereas the width of the isthmus decreases. This means that the translaminar hole will be more medially and more oval-shaped in the upper lumbar levels (Figs. 18.4 and 18.5).
- *Lamina*: Irrespective of the type of retractor used, the lateral border of the lamina should be visible underneath the retractor valve. A dissector is placed onto the lamina where the bulk of the DH is suspected and a fluoroscopic localization is performed. At this point the lamina should have been tilted parallel to the floor, so that the high-speed cutting burr can be held easily perpendicular to the lamina. With slow circular movements, a round (L5) or oval-shaped (L4 and cranially) hole of about 10 mm in diameter is performed (Figs. 18.6 and 18.7). Three layers "white" (outer cortical bone), "red" (spongy bone), and "white" (inner cortical bone) will be

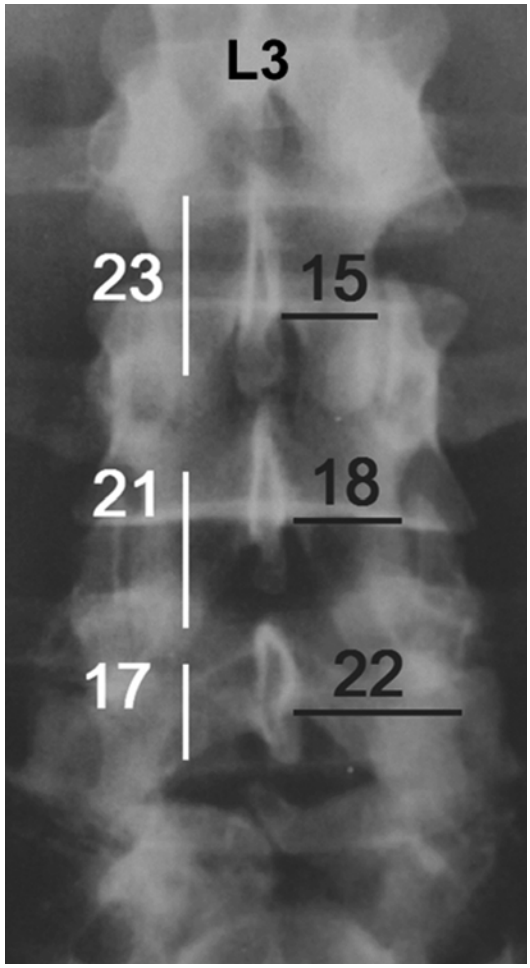

Fig. 18.4 The up-down length of the lamina (*white figures*) increases, whereas the width of the isthmus (*black figures* in mm) decreases in the caudal-cranial direction. That means that the overlap of the disk by the lamina increases also in the upper lumbar levels. Furthermore, there the translaminar hole becomes more paramedian and oval-shaped

drilled off. For the sake of safety, the inner cortical bone should be drilled with a diamond burr. Remarks: (1) At least 3 mm of the lateral border should be spared in order to avoid a fracture of the pars interarticularis (Fig. 18.6); (2) usually the translaminar hole is located just cephalad to the cranial insertion of the yellow ligament. So, after removal of the thin shell of inner cortical bone with small patches, epidural fat will appear.

- Epidural dissection: Up and down dissection of the fat along the lateral border of the dura. That should be continued cranial up to the axilla of the exiting root.

Exposure of the Herniated Disk

Usually an extruded or subligamentous disk fragment(s) can be mobilized. After decompression, the root slips caudally into the visible field (Fig. 18.7). The foramen is then probed with a double-angled hook or blunt probe. If an extensive annular perforation is detected, the disk space should be cleared. In our experience that was required in merely 20 % of the cases. The rate of recurrence was 7 %.

Closure

- Gelfoam soaked with a long-acting steroid to fill in the hole is optional, but should be avoided if the disk space has been cleared.

18.3.1.3 Extraforaminal or Far-Lateral Approach [29–31]

Indication

- DH whose bulk is located at least two-thirds lateral to the pedicle

Contraindication

- Foraminal DH located more than two-thirds inside the root canal

Preoperative Planning

- MRI – *sagittal slices*: Usually scans are not lateral enough, i.e., lateral to the root canal, and may miss the extraforaminal disk herniation (EFDH). *Axial slices*: Compare the amount and distribution of the extraforaminal fat tissue on both sites. *Coronal slices*: Although rarely performed, they are of invaluable assistance to show the spatial relationship between the exiting root, root canal, and extraforaminal compartment.

Positioning

- Basically the same as for the interlaminar approach.
- For safety reasons the patient should be belted on the gluteal region: The OR table has to be tilted 20–30° away from the surgeon in order

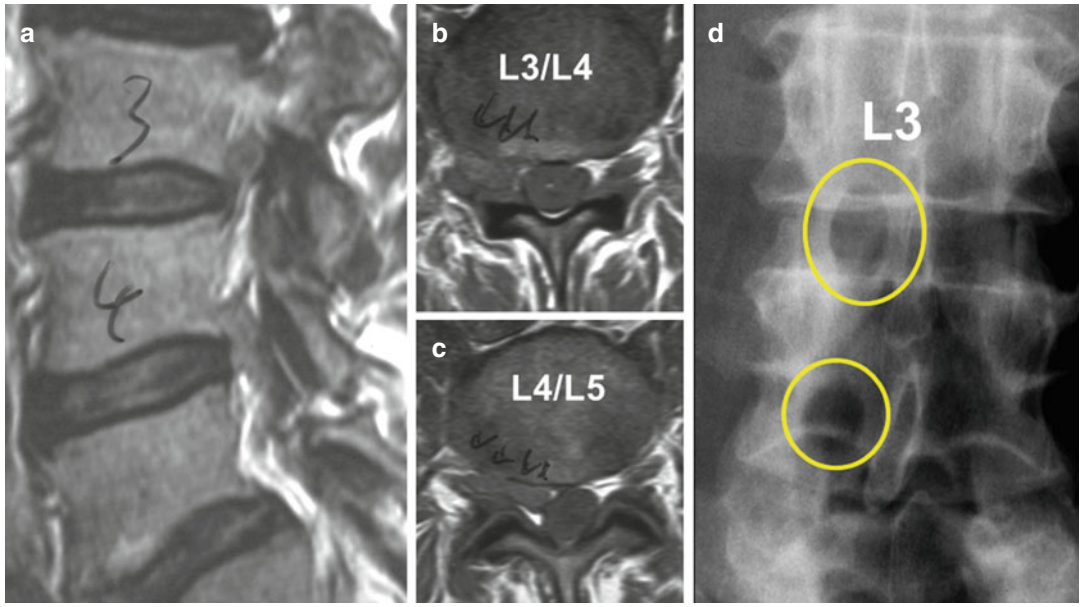

Fig. 18.5 Clinical case: (**a**) The sagittal MRI shows cranially extruded disk herniations at the level L3/l4 and L4/L5. (**b**) The DH encroaches the root L3 and (**c**) L4 on the right side. (**d**) Because the 28-year-old lady complained about a three-fifth weakness of the m. quadriceps, both DHs were removed via translaminar holes. Note that the L3 hole is more medial and more oval-shaped due to the narrower pars. Clearing of the disk spaces was not necessary

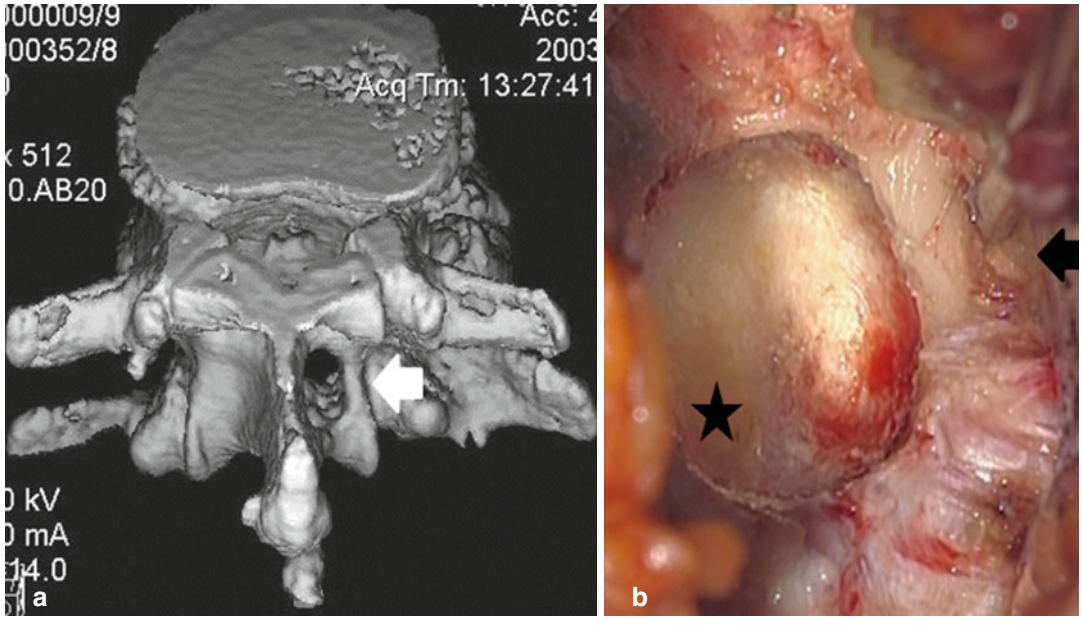

Fig. 18.6 (**a**) The 3-D CT shows a translaminar hole at L3 on the left side. Note: The facet joint L3/L4 is intact and a sufficient lateral rim (5 mm, *arrow*) of the pars is maintained where the bone is strongest. (**b**) Intraoperative view: The internal lamina is drilled off inferomedially where the upper rim of the yellow ligament (*star*) appears. The lateral rim of the pars (*arrow*) is the lateral boundary

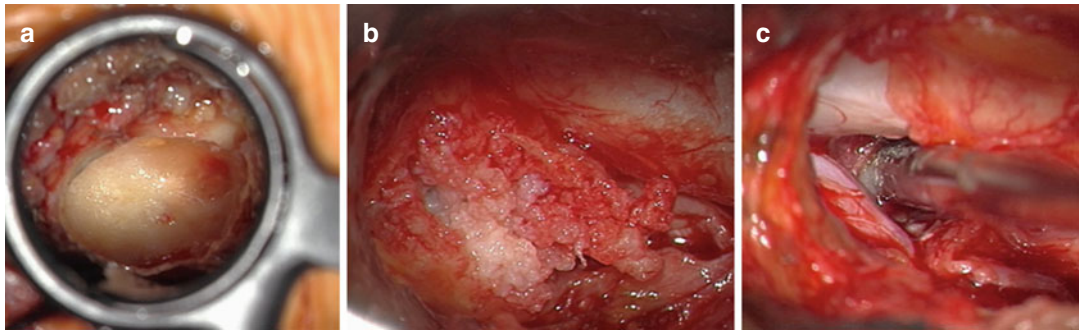

Fig. 18.7 (**a**) A right-sided 10 mm translaminar hole at L4 with an intact inner cortical bone is seen through the expandable tubular retractor (15 mm Ø); (**b**) following dissection of the epidural fat, a large extruded disk fragment appears in the axilla of the exiting L4 nerve root; (**c**) after the removal of the disk fragments, the L4 nerve root slips back into the visible field

to get a better oblique view of the extraforaminal compartment. Morbidly obese patients may risk to "roll over" on to their abdomen.

- Radiographic localization – *lateral view*: Insert a spinal needle one finger's breadth lateral to the spinous process, perpendicular to the skin and projecting toward the affected disk space. Draw a horizontal line at this level (Fig. 18.8a, DS).
- *AP view*: Two horizontal lines are drawn, (1) the affected disk (DS) and (2) the lower border of the transverse process above the affected disk (TP). Two vertical lines are also drawn: (1) the midline (row of the spinous processes, M, and (2) a line about 4 cm off to the midline, marking the lateral boundary of the pedicle above and below the affected disk. The distance between the two horizontal lines (SI) is the skin incision and will be 3 cm in length and about 4 cm paramedian (Fig. 18.8a).

Soft-Tissue Approach

The paraspinal transmuscular blunt-splitting approach to EFDH at the level L4/L5 or more cranially can be performed with an expandable tubular retractor or with a miniaturized speculum combined with medial and lateral counter-retractor blades (Fig. 18.8). At the level L5/S1, the author recommends the use of two counter-retractors inserted perpendicular to each other. That allows to choose four blades of different lengths matching with the following structures: facet joint (medial), transverse plane (lateral), transverse process (cranial), and ala (caudal) (Fig. 18.9). Furthermore, the use of the microscope "from skin to skin" is advised.

- *Skin*: 3 cm in length 4 cm off the midline.
- *Transmuscular route*: After incision of the fascia of m. erector spinae, the muscle is dissected bluntly using the index finger along the cleavage plane between the multifidus and the longissimus muscle (Fig. 18.8b). If this intermuscular plane cannot be palpated, the muscle is split downward to the medial third of the transverse processes. The selected retractor is then introduced so that the tips rest firmly on the lower half of the upper transverse process and on the upper half of the lower one. The lateral surface of the pars interarticularis represents the medial border of the surgical exposure. Fluoroscopic confirmation at this point of the procedure is essential (Fig. 18.8d).
- *Extraforaminal approach*: Tilting the OR table by 20–30° away from the surgeon gives a better view of the area lateral to the pedicle. Drilling off bone is usually not necessary, except in the case of an extremely hypertrophied facet joint or at the L5/S1 level. The medial half of the intertransverse muscle is incised and pushed laterally, thereby exposing the intertransverse membrane, also called the "intertransverse ligament." Use of bipolar cautery is essential to maintain hemostasis and blood-free surgical field. After incision of the membrane, the fat surrounding the nerve appears. Because of

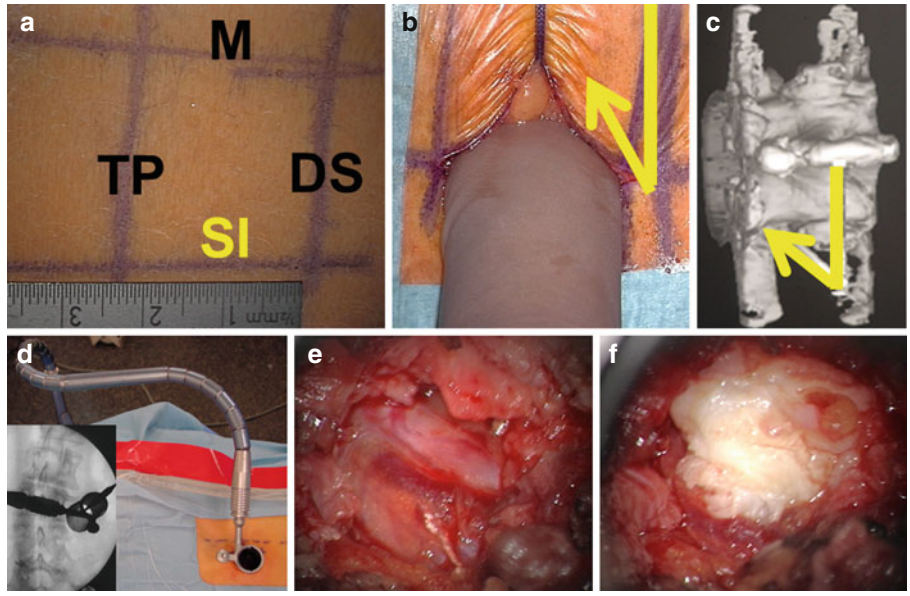

Fig. 18.8 (**a**) Preoperative labeling for a left-sided paraspinal approach at L3/L4: midline (*M*), disk space (*DS*), transverse process (*TP*), and skin incision. (**b**) The blunt muscle-splitting approach uses a cleft between the multifidus muscle (medially) and the thoracic longissimus muscle (laterally). (**c**) The index finger palpates the junction between the medial part of the transverse process L3 and the ascending facet joint (*yellow arrow*). The 3-D CT shows the target point. (**d**) The expandable tubular retractor points to the extraforaminal area. (**e**) The L3 nerve is displaced laterally, cranially, and superficially by (**f**) the underlying extruded disk fragment

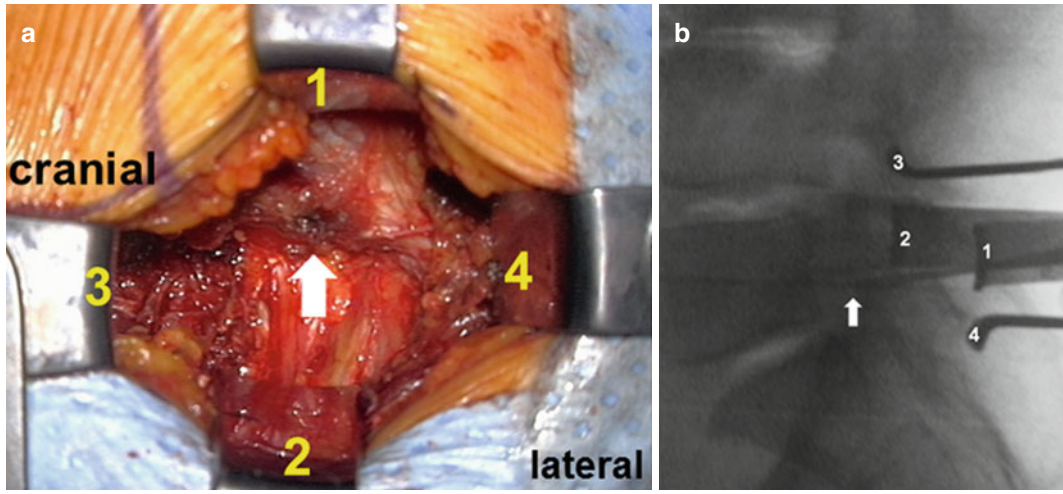

Fig. 18.9 (**a**) Operative site of a left-sided paraspinal approach L5/S1: four slim retractor blades of different lengths are inserted. (*1*) Ascending facet (medial); (*2*) thoracic longissimus muscle (lateral); (*3*) transverse process L5 (cranial); (*4*) ala sacri (caudal); the *white arrow* shows the point where the nerve L5 is to be expected; (**b**) intraoperative fluoroscopic check: The dissector points to the target point (*white arrow*)

the proximity of the nerve, the accompanying vessels, and DH, the sucker should also be used as a nerve retractor. However, beware of an excessive retraction of the dorsal root ganglion in order to minimize the incidence of postoperative burning dysesthesias which

should be counseled to the patient preoperatively. Branches of the radicular artery should be dissected carefully and spared whenever possible. The accompanying veins can be cauterized, if they hinder the access to the disk fragment.

Exposure of the Herniated Disk

Management of the DH: Typically, we find the nerve and the ganglion pushed laterally and cranially by the free disk fragment (Fig. 18.8c). Usually, removal of the fragment alone is sufficient. If an extensive perforation of the annulus is evident, clearing of the disk space should be considered. After probing the root canal with a double-angled blunt hook for residual fragments, the nerve may be covered with a gelfoam soaked with crystalline steroid.

Closure

- Placing a drain is optional and in our experience seldom necessary. Muscles do not require suturing.
- *Special considerations for the L5/S1 level*: Because of the particular anatomical relationship between disk space, transverse process L5, and ala, the microsurgical muscle-splitting approach at the lumbosacral level should be practiced by a surgeon who is already familiar with the technique at the more cranial levels. Repeated intraoperative fluoroscopic checks may also be necessary. If difficulties should arise, switching to the conventional macro-approach should be considered.

18.3.2 Recurrent Disk Herniation [32, 33]

A prevalence of 7–10 % recurrent herniations is reported in the literature independently from the surgical technique used. To deal with a recurrent DH usually does not mean to perform a "redo surgery" identical to the first procedure. The peculiarities of surgery for recurrent DH will be addressed.

18.3.2.1 Preoperative Planning

- The use of the microscope in our view is a must as it facilitates the differentiation between scar tissue and the thecal sac.
- Bypassing most of the scar tissue is imperative. This can be achieved either by using a wider approach than the previous one exposing the lower edge of the upper lamina or the medial wall of the pedicle where unscarred dura can be found. The translaminar approach of a recurrent cranially extruded disk fragment can be used via a virgin translaminar route instead of dissecting the interlaminar scar tissue.
- Preoperative radiographs show the amount of previously resected bone. This is of paramount importance if previous surgery has been performed elsewhere. If doubts persist, CT scan shows the bony landmarks which will guide the surgical approach.
- Gadolinium-enhanced MRI shows the relationship between scar tissue and true recurrent disk material and may differentiate the two. However, this holds true if the recurrent disk herniation occurs roughly within 3 years after the first surgery. Furthermore, endplate Modic – lesions and CSF collections – should be also be closely examined.

18.3.2.2 Positioning

- The same as performing first-time surgery

18.3.2.3 Soft-Tissue Approach

- Fluoroscopic labeling of the target area is mandatory as the scar of the skin may slip depending on the positioning and on the amount of subcutaneous tissue.
- Cautious sharp subperiosteal dissection is recommended to the interlaminar window. The lower border of the cranial lamina, the medial border of the remnant facet joint, and the upper border of the caudal lamina should be clearly visible.
- Drilling off bone with a diamond-coated burr is the most commonly used entry point in the area between the cranial border of the epidural scar and the virgin dura. If this approach should fail, the area between the medial border

of the pedicle and the shoulder of the traversing root is an alternative option.

18.3.2.4 Exposure of the Herniated Disk

- A generous decompression of the root in the lateral recess should precede the mobilization of the nerve from the annulus or from the extruded disk fragment. An intraoperative single shot of steroids may be helpful at this stage of the procedure.
- "Peeling" of the fibrous tissue from the nerve carries a high risk of injuring the dura and does not provide a better clinical outcome. Before biting with the Kerrison punch, a light tug may show the scarred dura jump: a sentinel sign of imminent dural tear!
- The disk space can be entered laterally from the border of the dural sac and cleared. This reduces the pressure on the extruded disk material. Repeated flushing with saline within the disk space may bring further disk material to the surface. We do not recommend to curette the endplates. The fibrous pocket containing the extruded disk material is opened and its content removed bluntly with straight/angled probes of different length. A tiny fibrous shell is left adherent to the dural sac. There is no evidence that forced "neurolysis" provides a better clinical outcome.

18.4 Postoperative Care [34]

18.4.1 Uncomplicated Surgery

The patient is encouraged to leave the bed 6 h after surgery. Sitting is allowed starting from the first postoperative day. Physiotherapy starts the morning after surgery. Hospital staying is usually 1–3 days.

18.4.2 Standard Dural Repair

Forty-eight hours of bed rest with the head in slightly Trendelenburg position (head down). If intraoperative loss of CSF was significant, the patient is treated with intravenous hydration + promethazine + analgesic regimen.

18.4.3 Very Difficult Dural Repair Not Watertight at the Time of Wound Closure

Closed subarachnoid drainage obtained by puncture at one level above the dural opening and the catheter placed at the thoracic-lumbar junction. The amount of CSF can be controlled by the level of the collection bag relative to the lumbar spine. CSF drainage can be continued up to 1 week and should cause mild headache.

18.5 Complications

The literature lists several "generic" complications such as deep vein thrombosis, pulmonary embolism, and urinary infections which are fortunately rare. Retroperitoneal major vessel injuries and postoperative visual disturbances (risk factors: diabetes mellitus, long operation time) are even more rare.

Microsurgical diskectomies have significantly less severe intraoperative complications as compared to non-microsurgical diskectomies [35]. Experienced surgeons have significantly less complications (2.2 %) than beginners (10.7 %) [36]. Recurrent surgeries are burdened with a higher incidence of complications [37].

The most common complications of even refined microsurgical techniques are: wrong-level surgery, dural opening/CSF leakage (2–7 %), root injury (0.06 %), and spondylodiskitis (0.4–1 %). Some remarks about the first two pitfalls are as follows:

18.5.1 Wrong-Level Surgery

- The surgical target area should be as much parallel to the floor as possible.
- Use a spinal needle (for CSF tap: more expensive, but also more radiopaque, especially in adipose patients) perpendicular to the back, one finger's breadth off the midline, down to

the lamina, contralateral to the intended surgical approach, and pointing to the upper rim of the disk space.
- Label the corresponding horizontal line, the midline, and the skin incision.
- Drape the C-arm (lateral view) and park it conveniently in the surgical suite.
- Time-out procedure: Confirm the correct level and side of surgery
- Repeat the trajectory of the cannula inserting the retractor. Remember: In overweight patients, a minimal oblique trajectory can lead a surgeon to the wrong level.
- C-arm – Check of the level before drilling off bone.
- Do not rely on scars in recurrent surgery; mark the skin incision with the aid of radiographic localization.
- The intraoperative threshold for obtaining a fluoroscopic confirmation should be low.

18.5.2 Dural Opening

Each dural opening requires a specific treatment depending on location, shape, and size of the lesion, potential concomitant injury of the cauda fibers, and microsurgical skills of the surgeon – just to mention the most important factors.

The following acronym "Bird Mc Dove" may aid in remembering a sequence of steps (Fig. 18.10):

1. *B*one removal until you see the whole dural tear.
2. *I*ntradural look.
3. *R*epone the fibers, if necessary.
4. *D*o an inside patch (e.g.,Tachosil® with the yellow surface to the dura).
5. *D*ural closure, at best by suturing.
6. *O*utside patch (the same as step 4).
7. *V*alsalva maneuver (e.g., 40 cm $H_2O \times 30$ s).

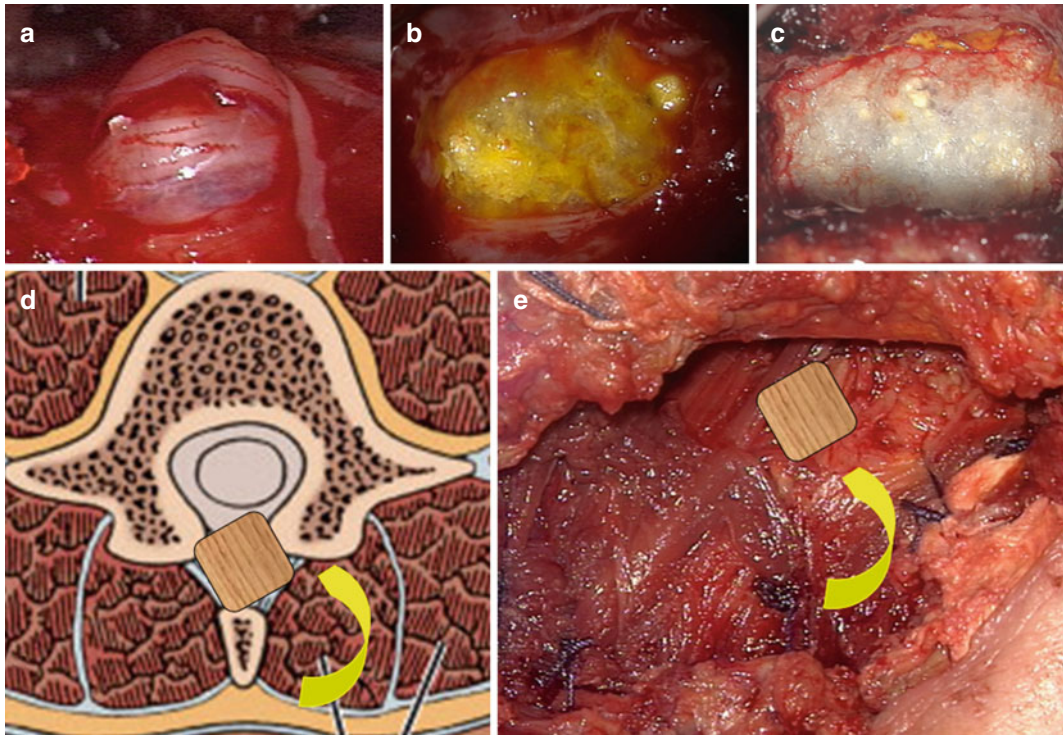

Fig. 18.10 (**a**) Large dural defect not suitable for direct repair. (**b**) The opening has been closed from the inside with haemostatic (*yellow surface*) collagen fleece (Tachosil®). (**c**) The same has been done from the epidural side with the haemostatic yellow surface inward (sandwich technique). (**d**) A tension-free pedicled epidural muscle flap has been swung to fill the epidural space (drawing). (**e**) Intraoperative site seen from the left. The *brown square* points to the epidural space

8. *E*pidural pedicled muscle flap (from the paraspinal muscles in order to fill the epidural dead space).
9. *M*ultilayer closure (muscle layer anchored to the spinous process also in the depth).
10. *C*SF drainage, if necessary.

Of course not all of the abovementioned steps are necessary every time. The first goal is to get a watertight closure of the dura (5). Should that fail, then three steps became mandatory: to seal the dural opening (4+6), to achieve a watertight wound closure (9), and to lower the postoperative CSF pressure (10) [34].

18.6 Critical Evaluation

> But successful lumbar disk microsurgery is also based on the surgeon's appreciation of the facts that microsurgery is not seek-and-find surgery, and that the microscope does not do the surgery. [23]

The first half of the citation stresses the importance of preoperative planning: the careful evaluation of location, size, and shape of the disk herniation and its relationship to the disk space, to the exiting and to the traversing root, to the lateral recess, and to the root or spinal canal require excellent MRI-imaging and dictate the soft tissue approach and the intraspinal handling of the pathology. A surgical plan tailored for the individual disk herniation becomes necessary. At that point, the short skin incision, the reduced muscle traumatization, the conservative bone drilling, and the plain removal of the offending disk fragment become the practical implementation of the microsurgical philosophy.

The second half of the citation points out that, although "small is beautiful," it should never be an end in itself. Especially at the beginning of the microsurgical learning curve, switching to a larger approach should be considered whenever problems arise. However, with increased experience, all difficult situations will be addressed even more effectively with the aid of the microscope.

The gap which has been bridged between macro- and microsurgery is going to be overcome by the latter and endoscopic spinal techniques. Robotic nano-surgery is waiting behind the corner in the future. The goals do not change: to get a good clinical result with the least iatrogenic trauma.

18.7 Key Points

1. Even though this chapter has dealt with technical aspects of the surgical treatment of lumbar disk herniations, proper indications with the right technique at the right moment is the most important factor influencing the clinical outcome.
2. The use of the microscope provides many advantages.
3. The most important aspect of the microsurgical philosophy which supports minimally invasive surgery is the "mental planning" of the procedure beforehand.
4. The assumption that one approach fits all subgroups of lumbar disk herniations has been substituted by the conviction that tailored approaches such as the interlaminar, translaminar, and paraspinal approaches address the different pathologies in a less traumatizing manner.
5. The use of a paramedian muscle-splitting approach and use of tubular retractors when available have even further reduced the approach morbidity, especially in obese patients.

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Lumbar Disk Revision Surgery

19

Christoph Mehren and H. Michael Mayer

19.1 Introduction

With the increasing numbers of lumbar disk surgeries, the quantity of revision cases is increasing as well. Especially recurrent disk herniations or diskogenic restenosis of the spinal canal generates challenges in spinal microsurgery.

Primary lumbar diskectomy or fragmentectomy is performed with minimally invasive surgical techniques. Microsurgical or endoscopic removal of lumbar disk herniations have become international standards. However, irrespective of the surgical technique, the incidence of recurrent disk herniation still varies in the literature from 1 up to 38 % [1–8].

The huge range of these figures is explainable by different follow-up times and by the method of detecting the recurrent herniation. If the patient is asymptomatic, a postoperative MRI is usually not performed. However in routinely performed MRIs 2 years after diskectomy, 56 % of the patients had asymptomatic disk reherniations [3].

Recurrences of a disk herniation are multifactorial. In a number of studies, potential risk factors have been identified. Gender (male), smoking, and heavy work seem to be independent risk factors [9–11]. But it is most probably the genetic predisposition with ongoing or accelerated degeneration which predominantly influences the recurrence rate. Disk height index and sagittal range of motion show a correlation with higher recurrence rates [9]. Additionally, the competence of the disk annulus and the type of herniation can predict the postoperative clinical outcome following lumbar diskectomy. The lowest rates of reherniation and reoperation (1 %) with the best clinical result can be expected for sequestrated herniations with a small annular defect followed by contained, fragmented disk herniations also with a small annular tear (10 %). In patients with extruded fragments and massive posterior annular loss recurrent herniation can occur in up to 27 % and the reoperation rate can reach 21 %. In case of contained non-fragmented herniations, 38 % of the patients had recurrent or persistent sciatica [7].

19.2 Surgical Techniques at Primary Surgery

The role of different surgical techniques for the risk of developing a recurrent disk herniation is not clear. The epidemiologic data, suggesting that recurrence rates following closed endoscopic diskectomy seem to be somewhat higher when compared to “open” microsurgical techniques,

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_19

have not been substantiated by sound randomized controlled trials.

The same is true for the question whether limited versus more aggressive disk removal diminishes the risk of recurrence. Randomized controlled trials have suggested that the clinical results seem to be comparable; however, the morphology of the annulus defect as well as the amount of preserved disk height might play a more dominant role [5, 12, 13].

This seems to be supported by Carragee's study [4]. The clinical outcome – regarding low back pain – and the recurrence rate are competing with each other with reverse results. It was shown that the incidence of a recurrent disk herniation was lower in the diskectomy group, but in the 2-year follow-up, the clinical outcome regarding low back pain was 2–2.5-fold worse than in the limited disk removal group [2, 4, 5].

Thus, so far general recommendations cannot be established according to scientific data. There is however agreement that patients with higher disk heights and large annular defects seem to have higher risk of recurrencies.

19.3 Diagnostic Considerations

MRI with/without contrast enhancement is the primary diagnostic tool for recurrent disk herniations as it defines precise location of the recurrent disk herniation for accurate planning of the approach. MRI also allows to distinguish disk material from fibrotic tissue and provides information about the amount of intraspinal fibrosis (Figs. 19.1, 19.2, and 19.3).

Should there be contraindications for an MRI (e.g., pacemaker, prosthetic heart valve, clips, etc.), CT scan and myelo-CT are alternative options. CT scan allows the evaluation of the amount of bony defect created by the first surgery.

This can also be assessed with preoperative radiographs in standing position as well as flexion/extension x-rays. The alignment of the segment, the global sagittal balance, and the presence of gross instabilities can be evaluated with radiographs.

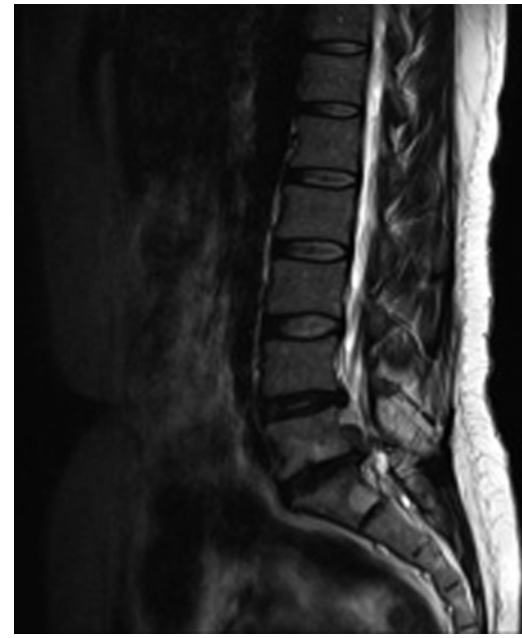

Fig. 19.1 Sagittal lumbar spine MR T2-weighted image depicts a cranially sequestered recurrent disk herniation

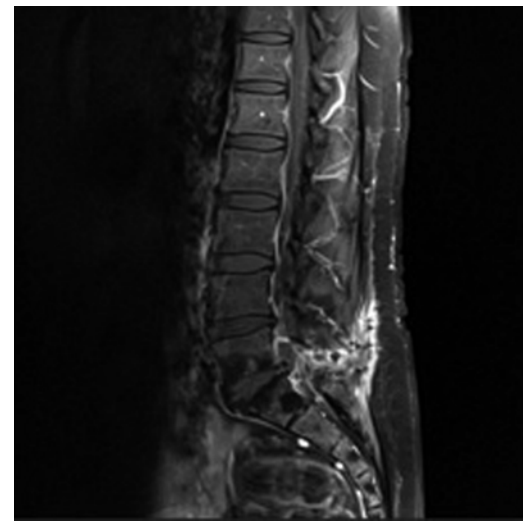

Fig. 19.2 The disk material does not show an enhancement of contrast media and is therefore distinguishable from scar tissue in doubtful cases

19.4 Indication for Surgery

The chances of a successful conservative therapy in case of recurrent disk herniations are lower as compared to primary disk herniations.

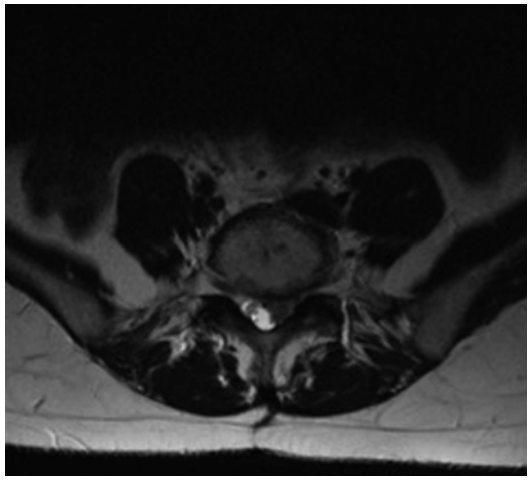

Fig. 19.3 The axial MR T2-weighted image clearly demonstrates nerve root compression of S1 on the left side due to herniated disk material

This can be explained by the fact that the neural structures are less "mobile" in the spinal canal due to adhesions or scar tissue without the possibility to "give way." On the other hand, it was shown that a high percentage of the recurrent disk herniations include endplate disk material, with harder consistency and less ability to shrink than "pure" nucleus material [14].

Indication for surgery as well as the choice for different types of surgical techniques follows the clinical symptoms of the patient.

If signs of nerve root compression are paramount, the primary surgical option is the decompression/re-diskectomy. Unless functional factors such as gross instability or leading back pain are predominant, there is no need to consider additional stabilization.

The options for surgical treatment range from endoscopic or microsurgical re-sequestrectomy/diskectomy to a fusion/reconstruction procedure. Besides the natural process of degeneration of the functional spinal unit, the technique of the previous surgery plays an important role regarding a segmental instability with consecutive narrowing of the spinal canal. Laminectomy, extensive resection of the facet joint and iatrogenic discontinuation of the pars interarticularis are predictable factors of a postoperative segmental instability [15, 16]. In other words minimally invasive techniques like endoscopic or microsurgical procedures are able to prevent postoperative instability due to less resection of bony structures [17]. Therefore the surgeon has the option for minimally invasive techniques in revision surgery as well.

In the setting of a clinically dominant sciatica, the solitary revision of the spinal canal is indicated, irrespective of the type of a previous surgery. If the pathology leading to nerve root compression is caused by a segmental instability, additional reconstruction of the functional spinal unit for the purpose of spinal fusion is necessary. Most of the time, the patients report also significant back pain.

Up to now there is a lack of clear algorithms regarding the treatment of recurrent disk herniations. A survey among neurological and orthopedic spine surgeons in the USA concerning the surgical treatment patterns of one- and two-time recurrent lumbar disk herniations revealed significantly different opinions. The surgical treatment options were revision microdiskectomy, revision microdiskectomy with in situ fusion, posterolateral fusion using pedicle screws, and PLIF/TLIF or ALIF procedures in combination with posterior instrumentation. Experienced surgeons with more than 15 years of practice were more likely to select just microdiskectomy in contrast to surgeons with fewer years who were more likely to select the microdiskectomy in combination with PLIF/TLIF. Overall, the probability that two randomly selected spine surgeons would disagree on the surgical procedure of two-time recurrent disk herniation was 69 % [18].

19.5 Surgical Technique

The previous surgical technique influences the revision surgery strategy. In contrast to the first operation, the surgeon is faced with scar tissue and altered anatomical landmarks in terms of bony defects. In principle all operative techniques (endoscopic, microsurgical, and macrosurgical with and without fusion procedures) are also evaluated in revision surgery. The selection

of the appropriate technique should be adapted to the surgeon's experience. The steps of microsurgical re-diskectomy/re-decompression will be described.

The exact localization of the recurrent disk herniation should be known as well as its topographic relation to the nerve root and/or scar tissue. This can be best achieved with an MRI with contrast media. The bony landmarks (e.g., medial facet border, lamina border, isthmus) can be seen on the x-rays. If necessary a CT scan can give detailed information about the extension of the previous laminotomy, hemilaminectomy, facetectomy, etc. It also provides data concerning potential ossification of the herniated disk (Fig. 19.4).

The disk space height is localized under fluoroscopic control and a 2 cm skin incision is placed centered over the disk space or over the maximum extension of the recurrence. Sharp subperiostal dissection is done preferably from the remaining superior lamina down to the transition zone of the superior lamina and the inferior facet. The reliable exposure of the bony "edges" is essential. The scar tissue must be safely detached from the bony rim of the lamina and the medial border of the inferior facet. Extreme care has to be taken if MRI shows a bulging dura dorsal to the lamina border. With a small blunt dissector or a diamond drill, the caudal border of the superior lamina is undercut until untouched ligamentum flavum or healthy dura is exposed under the lamina. Once healthy dura is identified, dissection of the scar tissue is started along the medial border of the inferior facet until the rim of the superior facet is identified.

Blunt dissection is performed between bone and scar tissue until the exposure of the lateral border of the exiting nerve root is achieved. This is followed by the decompression along the shoulder of the nerve root until the caudal pedicle. If significant fibrosis is found, a layer of scar tissue may be left on the nerve root, respectively, on the dural sac to avoid dural tear.

The exposure of the lateral dural margin, respectively, of the lateral nerve root margin is followed by a careful mobilization of the nerve root to the middle. There are often adherences of the nerve with the disk space. In these cases it is advisable to leave the nerve in place and open the scar tissue lateral to the nerve to get a safe access to the recurrent herniation. The herniated disk can then be mobilized carefully with a blunt dissector or with a small nerve hook.

At the end of the operation, the neural structures, especially the dura, are checked again for integrity and sufficient decompression. Careful hemostasis and irrigation of the approach and the epidural space finalize the intervention. A drainage is not needed in most of the cases; the patients are allowed to stand up immediately after they regained circulatory stability and consciousness. If there may be high risk for a recurrent disk

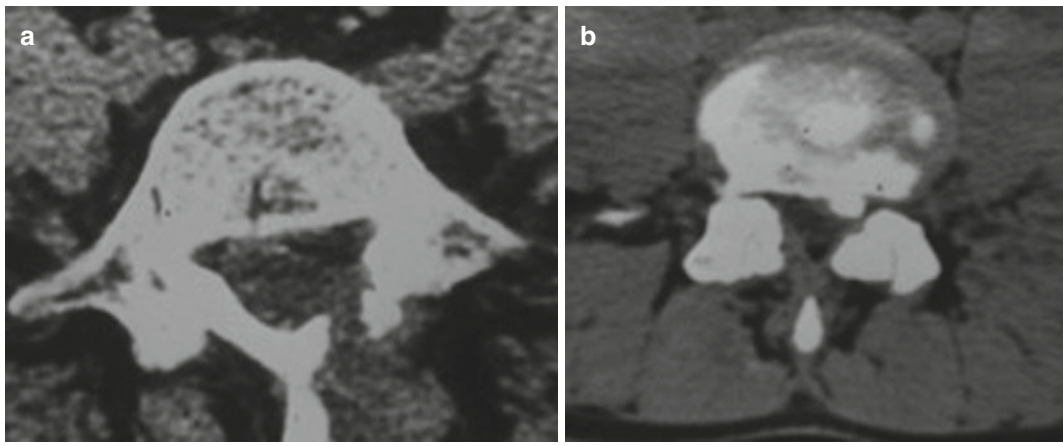

Fig. 19.4 (**a**) Bony defect in the lamina on the left side. (**b**) Calcified disk material in the lateral recess on the left side

herniation, the use of a soft brace for 4–6 weeks postoperatively is advised.

19.6 When Is Additional Stabilization Necessary?

If the patient is suffering from significant low back pain prior to the planned operation or if there is radiologically proven severe instability of the functional spinal unit, microsurgical decompression of the spinal canal should be combined with a stabilizing procedure.

The pedicle screw-rod system allows the physiologic alignment of the vertebral bodies to be restored. The decompression of the neurological structures takes place in an analogous microsurgical technique. Due to stability reasons, the 360° fusion may be favored, through a PLIF or TLIF fusion, as well as for a very high disk space or for severe instabilities via an anterior retroperitoneal approach with an ALIF procedure. From the aforementioned issues concerning nerve root dissection from fibrotic tissue, a posterior intervertebral fusion procedure is obvious. Especially in the presence of severe epidural fibrosis, the feasibility to mobilize the dura is limited. The technical option to choose an access into the disk space lateral of the dura – like the TLIF procedure – may reduce the risk of dural tears or nerve root irritation postoperatively. The additional anterior fusion (ALIF) ensures a higher primary stability and a higher fusion ability [19] (Figs. 19.5, 19.6, 19.7, and 19.8).

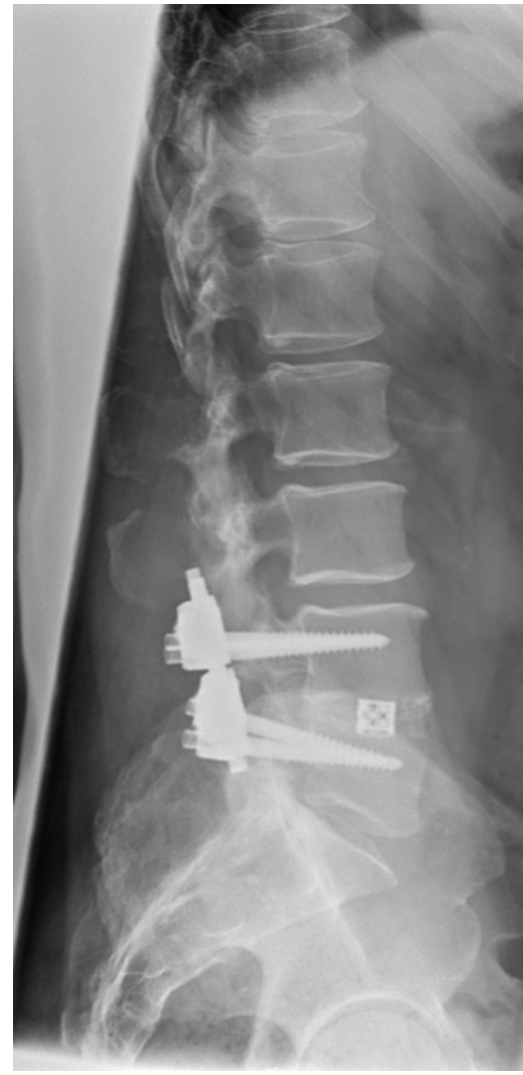

Fig. 19.5 Lateral x-ray at the time of microsurgical diskectomy L3/4. Status after fusion L4/5 8 years ago

19.7 Prevention

The decision-making concerning disk removal whether to clear the disk space with a diskectomy and its possible adverse effects like accelerated disk degeneration and likely low back pain or to just perform a sequestrectomy with potential higher recurrence rate is an individual challenge each time. It is up to the surgeon's consideration and estimation if the patient benefits more from the one or the other technique. Trails to prevent a recurrent disk herniation with the aid of special techniques (annulus suture) or implants to close the defect in the dorsal annulus (e.g., Barricaid®) did not yet show a significant improvement in the postoperative outcome in the actual literature especially due to the fact that long-term results are lacking [20, 21]. For interspinous spacer, the database regarding recurrent herniation is negligible. There is rather a general tendency so far that these modalities of implant are not able to prevent a recurrent disk herniation [22, 23].

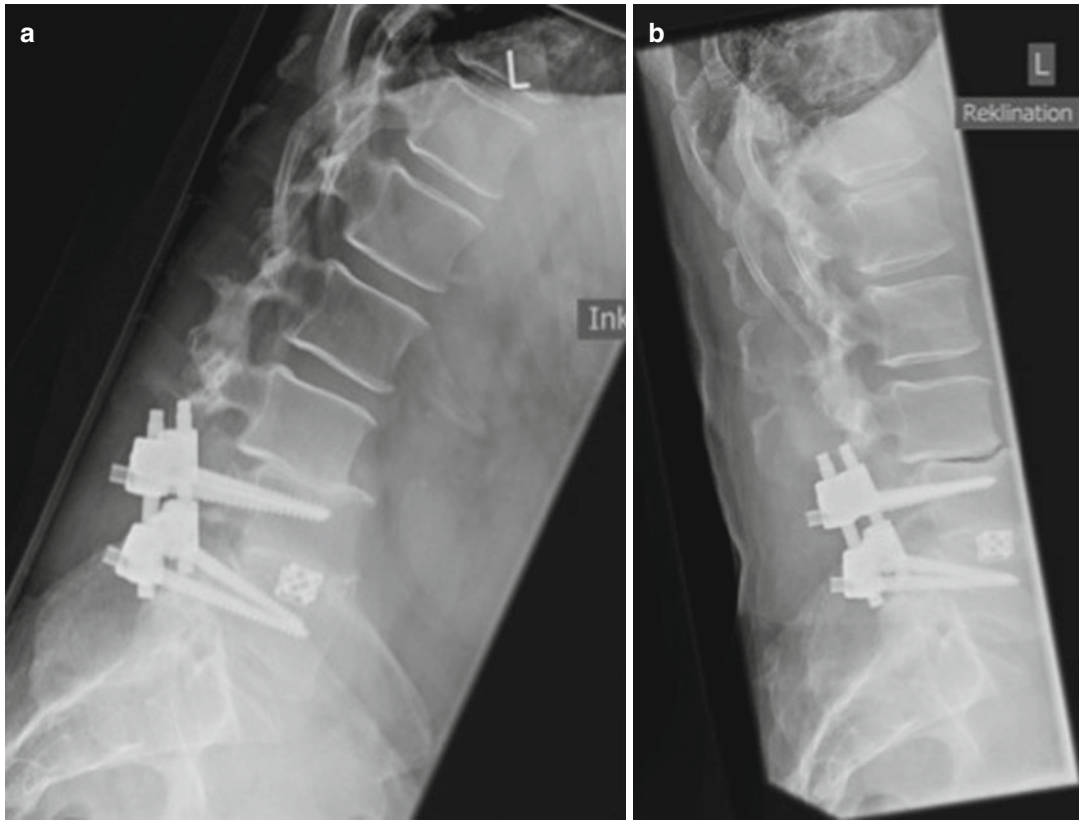

Fig. 19.6 X-Ray in flexion (**a**) and extension (**b**) 3 years after the diskectomy at the level L3/4

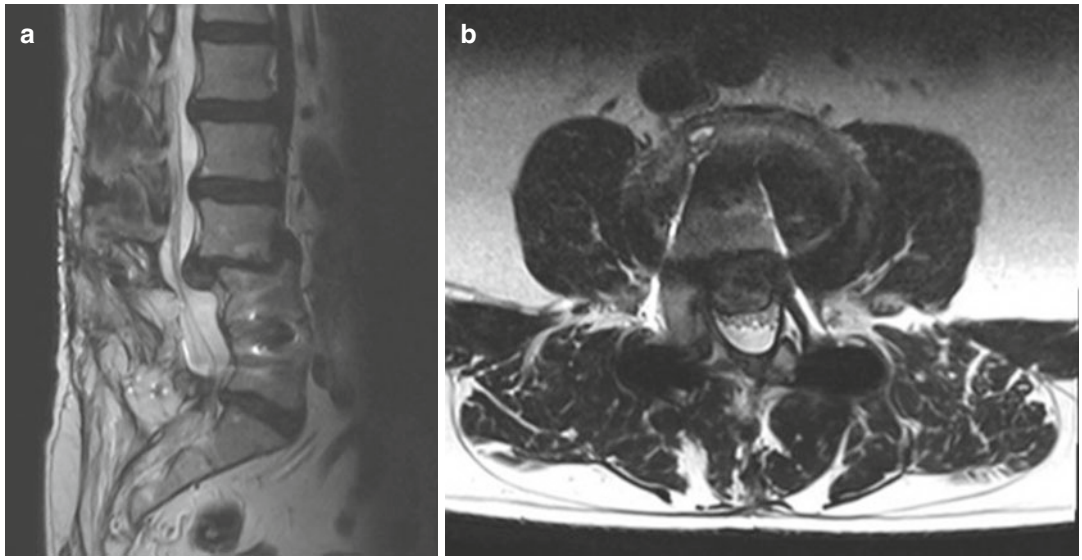

Fig. 19.7 The MRI of the lumbar spine is showing a huge recurrent disk herniation (**a**) and a severe segmental instability (**b**) at the level L3/4

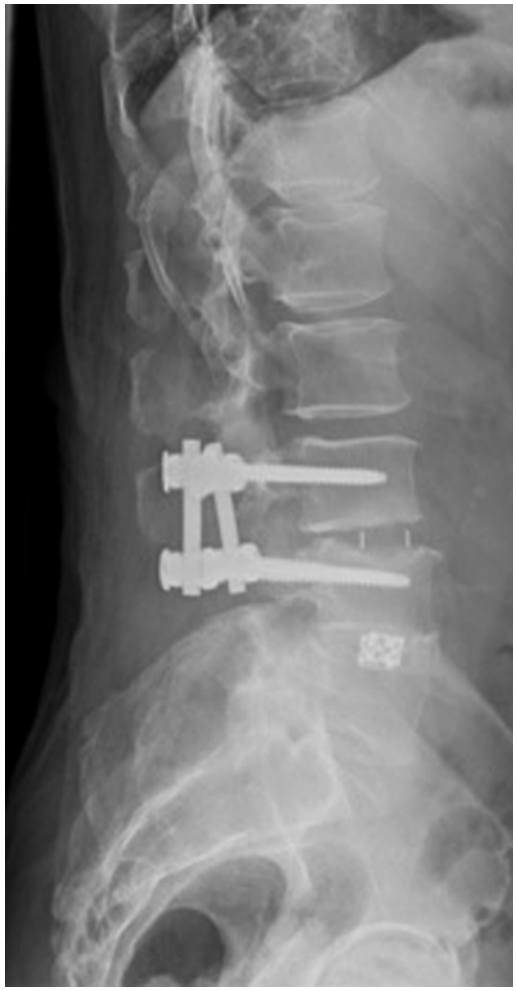

Fig. 19.8 Lateral x-ray following a re-diskectomy and dorsoventral fusion at the level L3/4

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Part V

Surgical Treatment of Lumbar Degenerative Disk Disease: Doubts, Decisions, and Techniques

The Decision to Operate: Advanced Concepts

20

James P. Lawrence and Todd J. Albert

20.1 Introduction

Low back pain continues to be a vexing and disabling problem affecting the vast majority of the population at some point in their lives [1]. A small subset of this large segment of the back pain population will continue to suffer chronic disabling pain from degenerative disk disease (DDD) requiring treatment, and this care consumes large resources for patients, payors, and providers [2]. The traditional methods for treatment of the patient with symptomatic degenerative disk disease of the lumbar spine involves "conservative treatment," consisting of analgesic and anti-inflammatory medications, limitations of activity or "behavioral modification," and active muscle exercise to recondition and train the truncal musculature. Although there has been progress in the understanding of the pathology underlying DDD and its correlation with pain, the commonality of degenerative changes in the population at large and the still indeterminate nature of the "pain generator" in DDD obscure the clarity of the disease as well as the pathway toward treatment recommendations. Assessment of patient pathology is of course critical in the recommendation of a surgical option, and the decision to operate should represent the best understanding of the underlying pathology and its consequences, the belief that operative treatment will be efficacious in itself, and the knowledge that the choice of procedure will be preferable to other treatment alternatives for that patient. An appropriately thorough history and physical examination, assessment of imaging modalities, and tailoring of preoperative patient care should provide the most informed body of information on which to base appropriate patient selection for surgery in the setting of symptomatic DDD. However, appropriate patient selection remains a difficult endeavor that reflects both the art and science of medicine. While the surgical options for DDD have expanded to include diskectomy and fusion, arthroplasty, posterior dynamic stabilization, nucleus replacement, and other alternatives, the identification of the appropriate patient (or patients) for these procedures remains a challenging process.

20.2 Pathology of DDD

The challenging aspects of DDD that affect the difficulty in recommending surgery stem from the fact that the radiographic changes resulting

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_20

from the very same findings can occur frequently in asymptomatic patients [3]. Particularly as it concerns an older population, the disk space narrowing, endplate sclerosis, formation of osteophytes, and other radiographic changes characteristic of DDD can occur typically as part of the aging process. It is critical, therefore, that pathologic findings on imaging are distinguished from normal findings and correlated with patient symptoms.

20.3 Patient Evaluation

20.3.1 History

Beyond the identification of patients with symptomatic DDD unresponsive to conservative care, there are numerous aspects of the patient history and course that are predictive of favorable and unfavorable outcomes with surgical intervention. The patient evaluation should provide not only a comprehensive history but should also serve to alert the physician to other items on the differential diagnosis and provide insight into the potential for recovery. Furthermore, the history should serve to eliminate any issues relating to secondary gain.

As many as 3 % of patients with low back pain presenting to the musculoskeletal specialist have a non-spinal cause requiring identification and medical evaluation [4]. Gastric ulceration, abdominal aortic aneurysm, renal disorders, and pancreatitis can all present with back pain and will require attention from appropriate specialists. Red flags for a more extensive generalized patient workup include unexpected weight loss, nocturnal sweating, fevers, or generalized malaise. Any history of previous surgery involving the abdomen or lumbar region should be reviewed.

The patient's previous treatment and treatment response should be carefully delineated. Previous therapeutic modalities including medical treatment, physical therapy, and injections (including facet and medial bundle branch blocks, selective nerve root blocks, and epidurals) should be documented. Notes describing the specific nature of these procedures thus not relying only on patient recollection are extremely helpful. The response to these interventions can reflect patient compliance to prescribed treatments and may serve to estimate the likelihood of improvement with surgery.

20.3.2 Examination

A thorough examination should be performed to identify areas of pain, assess patient ROM, identify areas of neurologic impairment indicative of compressive pathology, and help rule out other disease entities which may result in similar complaints (sacroiliac disease, hip osteoarthritis).

Patients with symptomatic DDD generally have a relatively nonspecific examination devoid of focal posterior tenderness, although muscle spasm may be present. Generally, there is a reduction in flexion-extension, rotation, and lateral bending motion limited by pain. Motor, sensory, and reflex changes are not typically seen. Tension signs are typically negative. Waddell's criteria [5], involving a series of tests designed to indicate nonorganic causes of low back pain, are also helpful to identify.

The patient with neurologic impairment (radicular or myelopathic) involving motor weakness, sensory impairment, or gait instability requires a well-documented examination and comprehensive imaging to localize and define ongoing compressive pathology and differentiate from isolated intradiskal pathology unlikely to result in neurologic impairment.

Based on observational studies, favorable predictors of success with spinal surgery include a high degree of motivation, an absence of active psychopathology, lack of workmen's compensation status, and an absence of tobacco and narcotic use [6, 7]. The patient's psychological profile, although a significant determinant of outcome [8, 9], can be difficult to correlate with surgical outcomes, even using appropriate psychological testing such as the Minnesota Multiphasic Personality Inventory (MMPI) index [10].

20.4 Diagnostic Imaging

Pathologic characteristics identifiable on imaging that predispose to a favorable surgical outcomes include focal disease at one or two levels, significant disk collapse, the presence of Modic changes, and a positive provocative diskogram with negative surrounding control levels.

20.4.1 Radiographs

The initial imaging modality used in the patient with low back pain who fails to demonstrate improvement by approximately 6 weeks are standing plain radiographs. These radiographs serve to define the sagittal and coronal alignment of the lumbar spine, assess the functional disk height, and identify visible pathology such as spondylolysis (Fig. 20.1), spondylolisthesis (Fig. 20.2), or chronic degenerative changes (vertebral body osteophytes, Modic changes). For the patient under consideration for surgery (in particular for interbody arthroplasty), the radiographs should also be examined to assess morphology of the vertebral endplates, as the contour of the endplates may affect the implant bone interface and predispose to or malalignment or subsidence if surgery is contemplated. Flexion-extension radiographs have not been shown to readily identify pathology not recognizable on plain films if employed routinely for patients with isolated lumbar complaints [11]. However, they are useful in the evaluation of patients with risk factors for segmental instability (i.e., prior trauma, prior posterior decompression, congenital anomalies, or inflammatory disease such as rheumatoid arthritis) and in providing detailed quantitative information on the motion segment in the preoperative patient (Fig. 20.3).

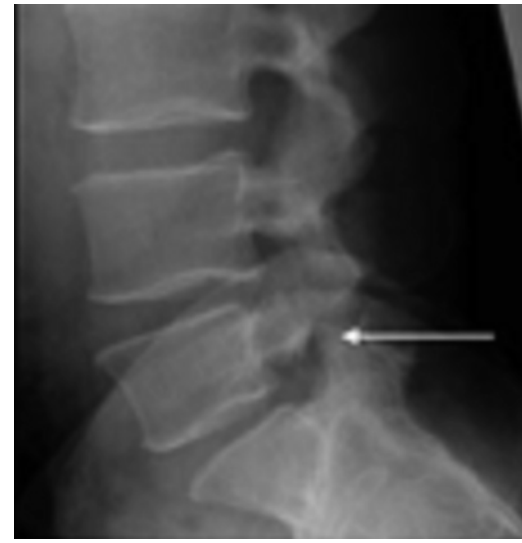

Fig. 20.1 Lateral radiograph demonstrating defect of the pars interarticularis (*arrow*) (spondylolysis)

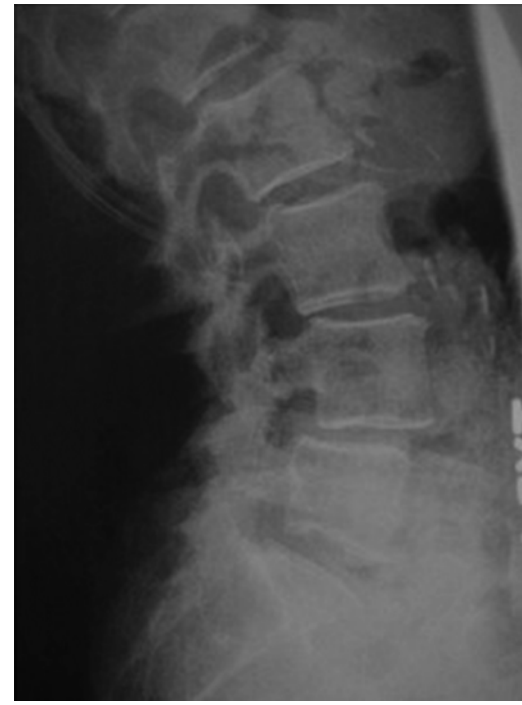

Fig. 20.2 Lateral radiograph demonstrating a degenerative spondylolisthesis

20.4.2 Computed Tomography

CT scans, although also not employed as part of the routine evaluation of the patient with isolated lumbar complaints, provide useful information in the preoperative assessment of the patient with recalcitrant DDD. The excellent osseous imaging capacity of CT is most useful in illustrating the

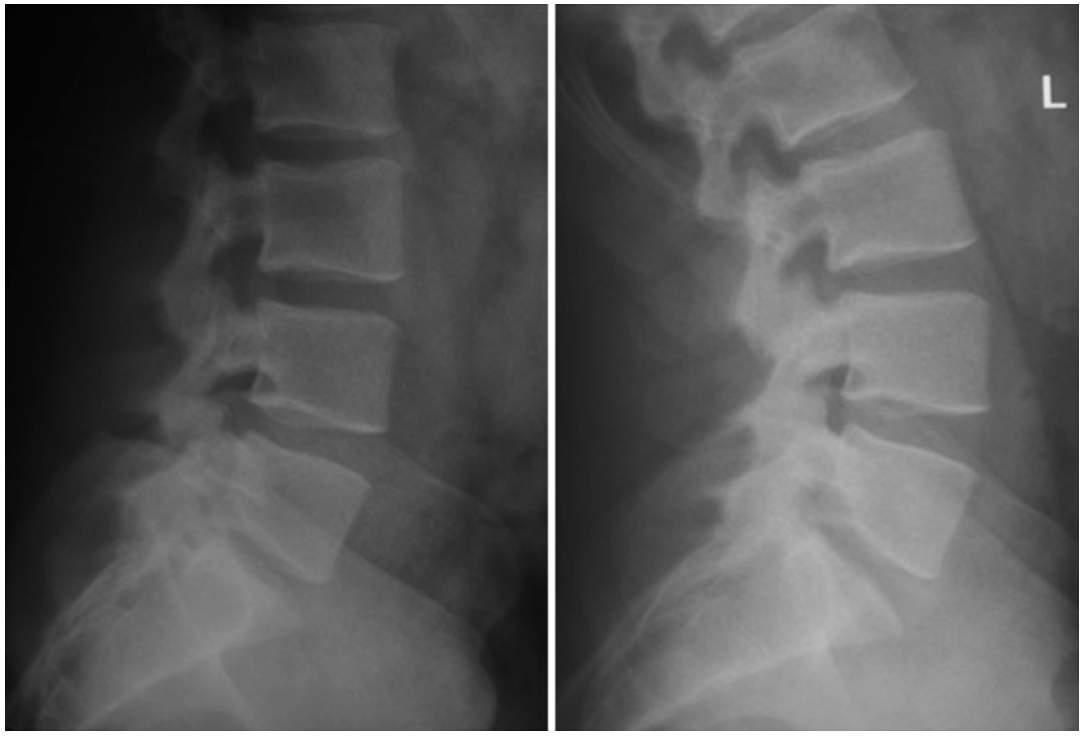

Fig. 20.3 Flexion-extension lateral radiographs in a patient with chronic LBP. Note the disk collapse and loss of height at L5–S1 in the absence of segmental instability

presence of facet joint degeneration (Fig. 20.4) and fractures of the pars interarticularis (Fig. 20.5), which can compromise the use of anterior-based motion-sparing procedures. Furthermore, CT scanning can provide an indirect assessment of bone density as well as provide detailed measurements of the bony anatomy for implant sizing (vertebral body and pedicular anatomy). Quantitative CT may serve as an alternative to bone scintigraphy in the assessment of bone density, although there is a larger dose of radiation imparted to the patient.

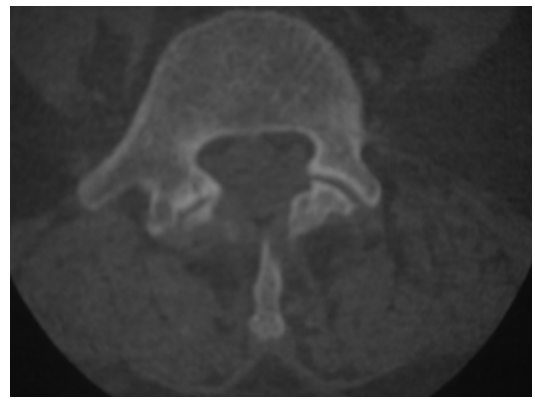

Fig. 20.4 Axial CT scan demonstrating L4–5 facet joint arthritis on the right side

20.4.3 MRI

MRI provides great imaging detail on both normal anatomic and abnormal pathologic entities that can affect decision-making (Fig. 20.6). The identification of diskal pathology (herniation, annular tears, dehydration), degenerative changes (vertebral endplate edema, facet joint degenerative pathology), or other compressive pathologies (ligamentum flavum infolding, facet hypertrophy) has all been greatly enhanced by the routine use of MRI. As detailed by Boden et al. [3], however, abnormal findings on MRI (such as disk degeneration, annular fissures, small protrusions, and

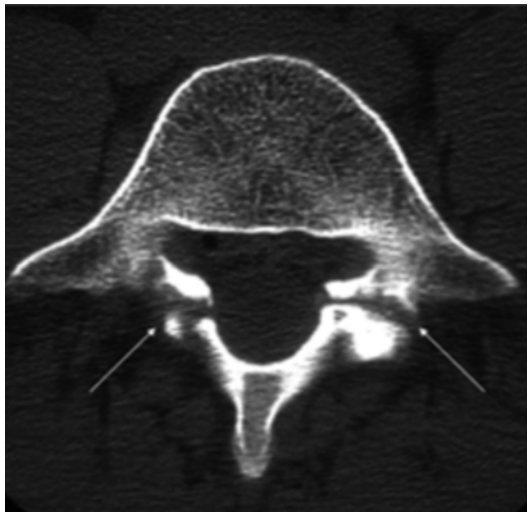

Fig. 20.5 Axial CT scan demonstrating bilateral fractures of the pars interarticularis (*arrows*)

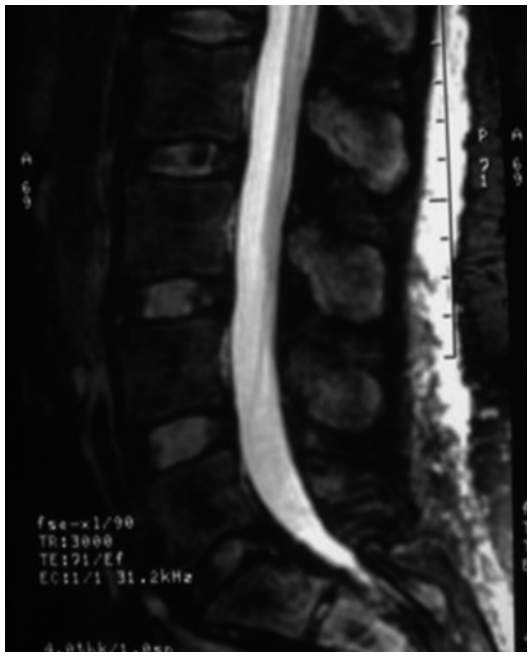

Fig. 20.6 Sagittal T2-weighted MRI demonstrating the characteristic dehydration and loss of disk height seen with degenerative disk disease, seen here at L5–S1

facet arthritis) can be commonly identified in asymptomatic patients. This phenomenon requires that a measured evaluation of MR imaging occurs in light of the patient's history, exam, age, and suspected cause of symptoms. The primary advantages of MRI in the evaluation of the lumbar patient lie in the evaluation of compressive pathology, the staging of disk degeneration, and the evaluation of facet joint degenerative changes. No validated staging system exists, however, for degenerative disk disease using MR imaging.

20.4.4 Bone Scintigraphy

Bone scanning using either dual-energy X-ray absorptiometry (DEXA), dual photon absorptiometry (DPA), or quantitative CT should be performed in all patients suspected of osteopenia or osteoporosis, particularly postmenopausal women, men over age 50, and chronic smokers. DEXA scan has become the standard modality used for this purpose due to its relative low cost and lower dose of imparted radiation versus the alternatives.

20.4.5 Diskography

As discussed in an earlier chapter, the usefulness of diskography is primarily as an adjunct to the clinical and diagnostic imaging evaluation. The current limited recommendations for diskography include the definition of the symptomatic level in the patient with multilevel pathology and in distinguishing between spinal and extraspinal causes of pain. Although numerous studies have questioned the positive predictive value of diskography [12–14], it remains the sole modality to permit identification of an intradiskal pain generator, and it can allow for the determination of the symptomatic level in a patient with multilevel pathology. It is important to note that the adequate pressurization of the disk requires annular competency, and an incompetent annulus may result in false-negative results using diskography. More recent data has demonstrated that even using modern administration techniques, diskography has deleterious consequences to the nuclear cells, the annulus, and the disk itself [15]. And although the mechanical insult of the needle introduction and pressurization alone have been shown to contribute

to the insult, both radiocontrast and local anesthetics have been shown to have markedly adverse consequences for the diskal environment [16, 17], While the highest yield for diskography may be in the symptomatic back pain patient who has undergone all methods of conservative treatment without relief and has evidence of isolated degenerative disk disease in the absence of other pathology, the risks of the procedure, its limited diagnostic yield, and its known side effects have largely relegated it to the historical realm.

20.4.6 Pain Management for Diagnostic and Therapeutic Purposes

Lumbar facet blocks (both with and without steroids), medial branch blocks, and radiofrequency ablation are techniques employed for both the diagnosis and treatment of disorders attributable to the zygapophyseal joints resulting in low back pain. Furthermore, these techniques have been expanded to attempt pain relief of low back pain attributable to the sacroiliac joints as well. Historical data have shown that facet blocks (both intra-articular and medial branch) provide adequate accuracy, reproducibility and safety in the diagnosis, and management of facet-mediated pain [18]. Interestingly, the addition of steroids may not add to the efficacy of this modality [19]. Based on a Cochrane-style review of the literature, diagnostic anesthetic blocks were given a level-1 recommendation, with level-II values associated with therapeutic medial branch blocks and radiofrequency ablation [20].

A successful diagnostic or therapeutic injection does not appear to accurately predict a successful surgical outcome, however [21]. In fact, one historical study appears to indicate that pain relief with temporary external fixation seems to offer better a better prediction of surgical success when compared with other modalities [22]. This is historical data, surely, but the conclusion is that despite their efficacy in diagnosis and treatment, pain management modalities cannot currently be said to predict surgical success.

20.4.7 Spinal Cord Stimulation (SCS)

SCS has emerged as a valuable technique for the management of chronic back and leg pain and unresolved symptoms after thoracolumbar spine surgery, the termed "failed back surgery syndrome" [23, 24]. Patients suffering from complex regional pain syndrome (CRPS) also may benefit from this technology [25]. The data to support its use for the patient with predominantly low back pain as a result of DDD, however, remains lacking. Leg pain as the predominant symptom has been the main if not the only predictor of positive outcomes following SCS to this point [26].

20.5 Clinical Data on Surgery

Clinical data that can be considered concerning surgery for DDD consists of randomized controlled trials (RCT) comparing arthrodesis with conservative care and RCTs comparing various procedures with arthrodesis as the control. Although there are many case series of emerging techniques and devices for diskogenic pain, there is not an existing evidence basis to support posterior interspinous devices or nucleus replacement for the treatment of diskogenic back pain.

The landmark paper published by Fritzell et al. in 2001 was the first to compare surgical treatment with nonoperative treatment of chronic low back pain in a well-matched randomized trial. This study was notable for the improved low back pain outcomes seen in the surgical group (33 %) versus the control (9 %) at 2-year follow-up. Criticisms of this trial include the indeterminate nature of the causative entity of the low back pain seen in the control patients. Diagnosis was made on the basis of history, physical examination, and radiographs alone, and MRI and diskography were not employed. Furthermore, the patients randomized to the surgical group were treated with three different fusion options: posterolateral uninstrumented, posterolateral instrumented with pedicle screws, and circumferential (360°) fusion. Also, for the patients treated conservatively, there was considerable variability in the nonoperative care. No

formal physiotherapy protocol was defined, and the use of injections and other pain modalities (acupuncture) was not standardized [27]. This paper was followed by an RCT from Norway by Brox et al. comparing posterolateral arthrodesis with cognitive intervention and exercise for chronic low back pain [28]. The authors used a more defined nonoperative treatment evaluation employing patient education, range of motion exercises, and intensive physiotherapy. At 1-year follow-up, there were no noted differences in improvement in low back pain or in disability as measured using the Oswestry Disability Index (ODI). Fairbank and colleagues performed a similar RCT comparing surgery with conservative treatment and found reductions in disability in both groups 2 years after treatment, but minimal differences using the ODI and a shuttle walking test [29]. A systematic review of these trials was performed in 2007 by Mirza et al. The authors noted that surgery, when compared with cognitive-behavioral therapy and a highly structured rehabilitation protocol for "diskogenic" back pain, resulted in only a modest improvement in back-specific disability [30]. In 2013, Mannion et al. reported long-term follow-up of three randomized trials comparing surgery and nonoperative treatment (multidisciplinary cognitive-behavioral and exercise rehabilitation) for chronic low back pain and found no differences in patient-reported outcomes at an average of 11 years [31].

Numerous RCTs have been performed to assess the efficacy of lumbar arthroplasty for the treatment of diskogenic low back pain, in each case using arthrodesis as a control. In general, the clinical results comparing disk arthroplasty with lumbar fusion have failed to demonstrate significant differences between the interventions in terms of functional outcomes, pain, use of medication, or occupational disability [32–34], with the exception of the investigational device exception (IDE) trial examining the ProDisc-L, which demonstrated marginal superiority of arthroplasty results on the VAS, ODI, and return to employment. However, although the treatment alternatives have been demonstrated to be comparable in this patient population, approximately half of the clinical trial patients, despite the stringent eligibility criteria, appear to not meet the criteria for clinical success. Furthermore, when following the criteria used for the FDA studies, it becomes apparent that the contraindications to this procedure are common when considering the surgical population in a spine practice, as was demonstrated in a review by Huang et al. [35].

When considering outcomes following any surgical intervention (using health-related quality of life, or HRQOL, instruments), it is important to gauge the magnitude and clinical significance of the score difference and not only the presence of a statistically measurable difference. Using functional scoring scales such as the ODI, for example, the degree of change in the ODI (or ODI delta) may be a more accurate predictor of the functional impact of the intervention. The "minimal clinically important difference" (MCID) has also been described in order to clarify the minimum amount of necessary change in an outcome score to suggest a tangible clinical benefit to the patient [36]. For the ODI, the MCID has been defined variously as ranging from 5.2 to 16.3 historically [37, 38]. Copay, Glassman, et al. performed a prospective study of patients gathered from the Lumbar Spine Study Group and determined the MCID for patients as assessed by the ODI to be 12.8 points for patients undergoing lumbar spinal surgery [39].

It is in this context, then, that the more recent trials for lumbar surgery, including trials examining surgery for DDD, should be viewed. Weinstein et al., in the degenerative spondylolisthesis arm of the SPORT (Spine Patient Outcomes Research Trial) trial, reported a mean improvement in the ODI of −24.2 in the surgery group at 2 years, versus −7.5 in the nonoperative group, for a treatment effect of −16.7 (in light of a MCID of 12.8). In the larger trials of lumbar arthroplasty, the ODI has served as a critical tool in the functional outcome assessment and as a statistical piece of the overall assessment of clinical success. The degree of the clinical effect, however, remains an issue of discussion. In the pivotal trial of the Charite prosthesis, Blumenthal et al. [34] noted changes in the arthroplasty group from a mean preoperative ODI score of 50.6–37.7 (−12.9), 29.9 (−20.7), 27.5

(−23.1), 26(−24.6), and 26.3(−24.3) at 6 weeks and 3, 6, 9, 12, and 24 months, respectively. In the pivotal trial of the ProDisc-L implant, Zigler et al. also used the ODI as part of functional outcome assessment the FDA IDE study [40]. The investigational group had a mean initial ODI of 63.4 (reflecting use of an alternative ODI scale, which can result in a higher disability core), 25.3 % higher than in the Charite trial. At intervals of 6 weeks, 3 months, and 6 months, the authors reported statistically significant differences from control in the ODI and a trend toward significance at 24 months. Versus the baseline values, although precise data were not published, it appears that the range of mean ODI following arthroplasty was between 34.5 and 47, with a value (34.5) provided at 24 months. From baseline ODI, this value reflects a −28.9 point change (46.1 %). The FDA criteria for outcomes were specified to include a decrease of 15 % on the ODI for "ODI success." Although there was a significant decrease following arthroplasty (and fusion, which resulted in a mean ODI of 39.8 at 24 months, for a change of −22.9 points, or 36 %), the patients remained with some degree of disability as reflected by an ODI of 34.5 at 24 months in the investigational group. Furthermore, the differences in the initial disability between the two trials demonstrate that the administration of functional scoring scales has some inherent variability depending on the content and application of the instrument. These data would suggest that the procedure (and the control), although they meet the statistical criteria, the specified FDA criteria, and MCID criteria for success of the intervention (and the control), results in improvement with a remnant of continued functional disability (mean ODI of 26.3 in the Charite trial and 34.5 in the ProDisc trial).

20.6 Summary

Patient selection for the surgical treatment of degenerative disk disease involves an appropriate and thorough evaluation, an understanding of the pathology and pathoanatomy, a recognition of responsiveness to previous treatments and motivation, a discussion of the appropriate operative course, and a clarification of the expectations following surgery both for the surgeon and the patient.

As previously described, degenerative changes of the intervertebral disk or the finding on MR imaging of a so-called black disk can simply be a feature of normal aging in the asymptomatic patient [3] or can represent a pathologic entity capable of causing disabling pain and dysfunction. The keys in the differentiation between these populations involve the detailed history, exam, appropriate imaging, and the judicious usage of targeted pain management procedures. Diskography appears to have been largely invalidated. Ultimately, there is no definable role for invasive procedures in the patient with a "black disk" in the absence of a correlative history, exam, and unsuccessful conservative care. Rather, a combination of the pathoanatomy-based approach (seeking the pain generator) and the psychosocial approach (including the psychosocial components that contribute to LBP) should be included in the evaluation of the disabled low back pain patient. In general terms, surgery should not be considered unless there is significant functional disability, a prolonged period of pain (>6 months), and a failure of improvement after a significant period of conservative treatment. The history, physical examination, patient course, and imaging modalities should reflect the suspected disease cause, and other causes of pain should be eliminated. Issues of secondary gain, active psychological or psychiatric disease, low motivation, workmen's compensation status, or a history of tobacco/narcotic use are less likely to result in positive outcomes with surgery. Once the decision has been made to explore a surgical option, diskography, targeted injections, and a careful assessment of the imaging to identify pathoanatomy unsuitable for motion-sparing procedures (facet arthrosis, spondylolysis, endplate disease, or segmental instability) can assist in the decision among surgical alternatives: diskectomy with arthrodesis, intradiskal techniques, or a motion-sparing alternative. An understanding of the evidence basis for surgical treatment and the factors predisposing to favorable and unfavorable outcomes can be critical in improving patient

selection and future outcomes, and over time more information should become available to assist both patient and surgeon in this regard. Currently, the clinical data suggests that the outcomes of all surgical treatment for degenerative disk disease are less than optimal. It appears that even in the mostly rigorously controlled trials of surgery for the best indications, the outcomes result in functional improvement yet a resultant degree of functional impairment. Therefore, caution should be maintained in the consideration of surgery for degenerative disk disease. Lastly, surgeons should be cognizant of their particular skill set and present options to the patient accordingly.

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To Fuse or Not to Fuse: That's the Question

21

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21.1 Introduction

Over the last few decades, significant advances have been made with regard to fusion technologies in the lumbar spine. The advent of pedicle screw fixation, lateral interbody grafting techniques, recombinant human bone morphogenetic proteins, and minimally invasive surgical approaches has resulted in a significant increase in the number of fusion procedures annually [1–4]. As an aging, active population continues to expand, more patients seek appropriate therapies to alleviate pain, restore function, and maintain their active lifestyles [5]. While the technologies and techniques available to the spine surgeon have improved and expanded, the debate continues over the appropriate indications for fusion in the setting of lumbar degenerative disk disease [4, 6]. The purpose of this chapter is to review current evidence for lumbar spinal fusion procedures and provide recommendations for evaluation, clinical workup, and surgical decision making in this challenging patient population.

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21.2 Overview

Lumbar degenerative disease can present with a multitude of symptoms, so it is important to distinguish between various pathologic processes. An appropriate trial of nonoperative therapy should always be attempted before consideration of surgical intervention. If the patient's symptoms persist, imaging studies as well as other diagnostic testing must be carefully reviewed prior to formulating a surgical plan.

Lumbar degenerative disease clinically manifests in five basic forms: axial low back pain, spinal stenosis, radiculopathy, degenerative spondylolisthesis, and degenerative scoliosis. These conditions may occur alone or in combination with one another. Surgical decision making, with regard to the need for fusion, for any of these entities depends upon multiple factors, which will be discussed in relation to each disease process.

21.3 Axial Low Back Pain

Chronic axial low back pain has a high socioeconomic impact, with a lifetime prevalence of 30–50 % for moderate and severe back pain [7]. Pure axial low back pain without deformity is successfully treated nonsurgically in the vast

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_21

majority of cases [8]. Nonoperative modalities include medications, short-term bed rest, physical therapy, and chiropractic therapy. Medications include nonsteroidal anti-inflammatories (NSAIDs), acetaminophen, muscle relaxants, and short durations of narcotics.

After an initial trial with one of the above treatments, epidural and/or facet injections may be useful. In patients with symptoms refractory to nonoperative management for greater than 6 months, fusion may be indicated. However, there is a lack of consensus regarding the efficacy of fusion for discogenic axial back pain [9]. Multiple studies have demonstrated only marginal improvement in back pain following fusion [10–14]. Because of these less than optimal results, many surgeons advocate diagnostic testing to attempt to isolate the pain generator prior to surgical intervention [15]. Provocative discography is the most common test utilized in this scenario, although there is debate in the literature over whether it actually predicts outcomes of spinal fusion [16–19].

In a 2006 comparison of single-level fusion patients with axial low back pain and concordant discogram to a matched control group of patients with unstable spondylolisthesis, Carragee et al. reported a dismal 43 % satisfactory outcome in the discography group at 2 years compared to 92 % in the controls [19].

In a recent systematic review, no subset of patient with chronic back pain could be identified for whom spinal fusion is a predictable and effective treatment. They concluded best evidence does not support the use of provocative discography for patient selection in clinical practice [20]. Clearly, there is lack of agreement upon whether concordant discography can predict the outcome of a fusion for axial low back pain. Due to this fact, it is important to keep in mind that discography is merely one diagnostic component to consider when developing a treatment plan for this challenging problem.

We consider all the factors in the axial low back pain patient's case and, in this subset of patients, would only recommend fusion after failure of a minimum of 6 months nonoperative therapy. We utilize provocative discography, performed by an experienced pain management specialist, in patient who have failed this regimen and have radiographic evidence of single-level degenerative disease. We offer surgery only if a concordant disk correlates with MRI findings and adjacent disks are non-concordant [21].

21.4 Lumbar Spinal Stenosis

Unlike axial low back pain, the question of whether to fuse in cases of lumbar spinal stenosis (LSS) is somewhat more straightforward. If nonoperative measures fail to relieve symptoms in this subset of patients, most obtain meaningful relief of symptoms from surgical decompression [22–24]. Patients with pure stenosis in the absence of degenerative spondylolisthesis or scoliosis may be treated with decompression alone. Numerous studies have shown excellent outcomes in this patient population with regard to relief of leg pain and paresthesias, lower extremity weakness, and walking tolerance [22–24].

LSS patients who demonstrate radiographic evidence of instability should be strongly considered for a fusion procedure [25, 26]. Gross instability may be detected on plain lateral radiographs in the form of spondylolisthesis that translates with active flexion or extension. Additionally, lateral listhesis seen on AP images may also indicate instability. Finally, excessive facet joint fluid seen on T2-weighted trans-axial MRI images is a sign of a more subtle, but clinically significant, instability. Patients with such instability, who undergo decompression alone, are more likely to experience worsening instability and back pain secondary to the loss of posterior stabilizing elements including the supraspinous ligament, intra-spinous ligament, ligamentum flavum, and varying amounts of the facet joints and pars interarticularis. Even in patients without preoperative instability, removal of greater than 50 % of the facet joint or pars interarticularis can lead to iatrogenic instability resulting in poor outcomes and potential need for further surgery [27].

One recent study evaluated nationwide trends in the surgical management of patients with lumbar spinal stenosis (LSS) with and without coexisting spondylolisthesis and scoliosis from 2004 to 2009. They demonstrated simple fusion surgery has increased for treatment of LSS compared with decompression only [4].

As previously mentioned, a clinician must take into account multiple patient factors, including obesity, which has been shown to negatively impact lumbar surgery. One study demonstrated inferior results of surgery for lumbar stenosis, [28] while another demonstrated longer operative times and an increased rate of infection [29].

In today's era of advanced imaging studies, it is important to remember to obtain good anteroposterior, lateral, and flexion/extension lumbar spine radiographs to rule out degenerative scoliosis or spondylolisthesis. Both of these entities can easily be missed if only an MRI is examined during preoperative planning. If scoliosis or spondylolisthesis is identified in a patient with symptomatic spinal stenosis who has failed nonoperative treatment, it is our typical practice to recommend decompression and fusion in addition to at the scoliotic or unstable levels. Patients undergoing this procedure should be extensively counseled that the purpose of the procedure is to relieve lower extremity symptoms and that relief of back pain is less predictable.

21.5 Lumbar Radiculopathy

If nonoperative management fails, radiculopathy secondary to herniated nucleus pulposus with or without coexisting stenosis is reliably treated with decompression through laminoforaminotomy and excision of the disk fragment [30]. As with symptomatic lumbar stenosis, we recommend fusion for patients with lumbar radiculopathy only in the setting of degenerative scoliosis or spondylolisthesis.

Some spine surgeons believe that fusion is necessary for treating disk reherniation. As repeated diskectomy for either ipsilateral or contralateral recurrence requires the removal of more disk material and posterior elements, such as lamina or facet joint, further invasion at the same surgical level can increase the risk of segmental instability [31]. A recent study evaluated the treatment patterns for recurrent lumbar disk herniation among US spine surgeons. The study highlighted the lack of consensus with regard to treatment plan, as some surgeons preferred repeat microdiskectomy, while others preferred microdiskectomy with posterior lumbar interbody fusion/transforaminal lumbar interbody fusion (PLIF/TLIF) [32].

Rarely, patients with lumbar radiculopathy may also have a significant component of low back pain. In these patients, if there is clear evidence via discography or single-level disk degeneration on MRI that the back pain may be referable to the same level as the source of radiculopathy, concomitant fusion may be contemplated. However, it should be noted that studies have shown that such back pain often resolves with diskectomy alone [30, 33].

Among patients with radiculopathy who have a degenerative spondylolisthesis or degenerative scoliosis on imaging studies, decompression with fusion should be strongly considered, regardless of whether or not a significant back pain component is present. Failure to identify these instability patterns and address them at time of surgery may lead to progressive instability and pain.

21.6 Degenerative Spondylolisthesis

Surgical treatment, consisting of decompression and fusion with or without instrumentation, has been shown to be an effective treatment of symptomatic degenerative spondylolisthesis [25, 34, 35]. Numerous retrospective and prospective studies have demonstrated satisfactory results with a variety of fusion techniques [35]. Standing flexion and extension radiographs may be the key images necessary to identify this diagnosis as it is often a dynamic rather than a static process and may be missed with MRI alone. Advanced imaging studies should be obtained to identify any areas of stenosis to ensure an adequate decompression and fusion may then be limited to the levels demonstrating instability.

21.7 Degenerative Scoliosis

With an aging population in the United States and an increased attention to quality of life versus cost issues, degenerative scoliosis has become a considerable health concern [36, 37]. Many female patients with mechanical low back pain over the age of 60 will have a degenerative form of lumbar scoliosis. Most of these patients do not have significant radicular or claudication symptoms; therefore surgical treatment is not indicated. However, when these patients present with symptoms of stenosis or radiculopathy unresponsive management, decompression with instrumented fusion is appropriate. In addition to the scoliosis, advanced imaging studies will usually reveal disk degeneration, foraminal stenosis, and nerve root compression. Many of these patients will have a rotatory component to their deformity that may also be addressed with reduction maneuvers utilizing a pedicle screw construct. If there are a large rotatory component and significant lateral listhesis causing a broad curve across several levels, these authors will sometimes recommend a circumferential fusion technique to restore anterior column integrity, obtain better curve correction, and hopefully improve long-term outcomes [38–42].

Despite the risks of scoliotic surgery, there is an increasing demand for operative intervention in this population [43–45]. A recent systemic review analyzed 16 studies including 553 patients with DS and reported that despite an overall 49.0 % complication rate and 15.3 % rate of repeat procedures, surgery is still an effective and reasonable treatment option for DS [46].

Conclusions

In the absence of scoliosis or spondylolisthesis, fusion is typically not indicated in the treatment of degenerative disease in the lumbar spine. In the rare case of single-level degeneration with concordant discography, many surgeons would consider fusion. Patients with recurrent disk herniations above L5–S1 may also benefit from fusion at reoperation, although no literature exists to support this theory. Finally, numerous studies have shown that fusion in patients with degenerative scoliosis or spondylolisthesis is not only beneficial from an outcomes standpoint but usually required to prevent further instability and deformity.

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Biomechanics of the Lumbar Degenerative Intervertebral Disk

22

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22.1 Introduction

Degenerative lumbar disk disease is one of the most common causes of low back pain and disability in patients above 45 years of age [1, 2]. Diagnosis and treatment of lumbar herniated disks remain perplexing at times. Magnetic resonance imaging (MRI) is the imaging study of choice for the identification of herniated lumbar disks; however, there remains only a moderate correlation between imaging findings and patients symptoms [2]. Disk degeneration is a broad term that includes a variety of changes noted in gross specimens and radiographs from patients with clinical dysfunction. These changes may lead to derangement of the normal biomechanics of the lumbar spine, such as pathological and dysfunctional intervertebral motion – with a commensurate clinical response.

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22.2 Structure of the Intervertebral Disk

The human spine contains 23 intervertebral disks (6 cervical, 12 thoracic, and 5 lumbar); there are no disks between the atlas (C1) and axis (C2) or in the sacrum and coccyx. Each intervertebral disk lies between adjacent vertebrae. Cartilaginous endplates surround each disk superiorly and inferiorly; the anterior longitudinal ligament is ventral to each disk and the posterior longitudinal ligament is dorsal. The disk contains fibroblasts, cartilage cells, and few notochord cells and is composed of the nucleus pulposus centrally, annulus fibrosus radially, and annular epiphysis cranially and caudally.

The nucleus pulposus is composed of proteoglycan loosely held together by an unorganized matrix of type II collagen and elastin fibers. The proteoglycan component, mainly aggrecan, is highly anionic and provides a colloid osmotic pressure that pulls water into the nucleus. This is crucial for shock absorption, as the hydrostatic pressure generated from osmotic swelling resists spinal compression [3].

The annulus fibrosus is composed of bands of collagen type I fibers arranged in parallel. The orientations of these fibers are at 30° from the cartilaginous endplates and are reversed in each successive lamella so that in each adjacent lamella, fibers are at 120° angles. The peripheral lamellae are tightly adhered to the ring epiphysis of the

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_22

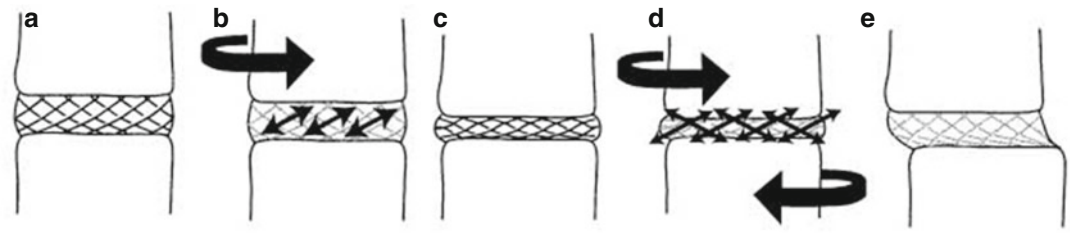

Fig. 22.1 Annular fibers are oriented in a 30° orientation with the endplate (**a**). This permits a significant torsion prevention potential (*arrows*) (**b**). In fact, they are more optimally oriented for torsion prevention than for distraction (or compression) prevention. If the annular fibers are lax (**c**), torsion resistance diminishes (*arrows*) (**d**). Chronic instability and mechanical pain may result. Lax annular ligaments also predispose to the more commonly observed imaging correlate of chronic instability and subluxation (**e**)

vertebral bodies by Sharpey's fibers. This oblique laminated fiber pattern helps resist axial rotation by acting like tendons resisting force along their longitudinal orientation (Fig. 22.1). Transverse and radial annular tears have been shown to disrupt this tendon-like longitudinal force resistance and allow for greater axial rotation [4].

The rostral and caudal endplates are composed largely of hyaline cartilage and are firmly attached to the adjacent vertebral bodies by calcified cartilage. The endplates act as a semipermeable barrier *between* the vascular medullary portion of the vertebral bodies and the disk. Disks in adults and children are avascular and nutrients must enter through the adjacent endplates or capillaries into the annulus fibrosis [5]. In contrast, infant's disk spaces are vascular and therefore nutrients enter the annulus via arteries or arterioles.

22.3 Function of the Intervertebral Disk Space

The intervertebral disk space composes 20–25 % of the vertebral column height. In axial loading the disk acts as shock absorber for the relatively incompressible vertebral body. The disk is exposed to variable compression loads throughout the day. The effects of position on the hydrostatic disk have been measured and confirmed by various authors [6–8]. As body weight increases with aging or when one rises from a supine position, the load on the disk space increases, predominantly in lower lumbar levels [5]. In the supine position with knees bent and supported, the lumbar spine is relaxed in a slightly less lordotic posture. The disk pressure in this position is the least and is primarily produced by surrounding ligaments and musculature. As a standing position is taken, the pressure in the disk increases as it takes on more of the axial load of the body. In a resting standing position, the majority of the pressure is borne in the center of the disk and is fourfold greater than that of being supine. As the nucleus pulposus compresses under axial loading, it bulges out laterally and is contained by the annulus fibrosus. The collagen fibers of the annulus are placed under tension and thus act as a capsule to contain nucleus pulposus. With bending, the nucleus migrates away from the increased force and the annulus bulges in the direction of the concavity of the curve. For instance, bending forward produces more kyphosis in the lumbar spine. In this position, the pressure in the ventral annulus is increased and the nucleus pulposus moves dorsally, where the pressure is less. This dorsal displacement places the dorsal annulus under tension as the nucleus pushes against it (Fig. 22.2).

With asymmetric loading of the spine, the intervertebral disk provides a measure of stiffness that is augmented by extra-discal structures such as spinal ligaments, muscles, and facet joints [7, 9]. To achieve both stability and motion, each of the components of the intervertebral disk plays different yet critical roles.

Under compression, the nucleus pulposus plays an important role in maintaining equal pressure along the endplates and maintaining

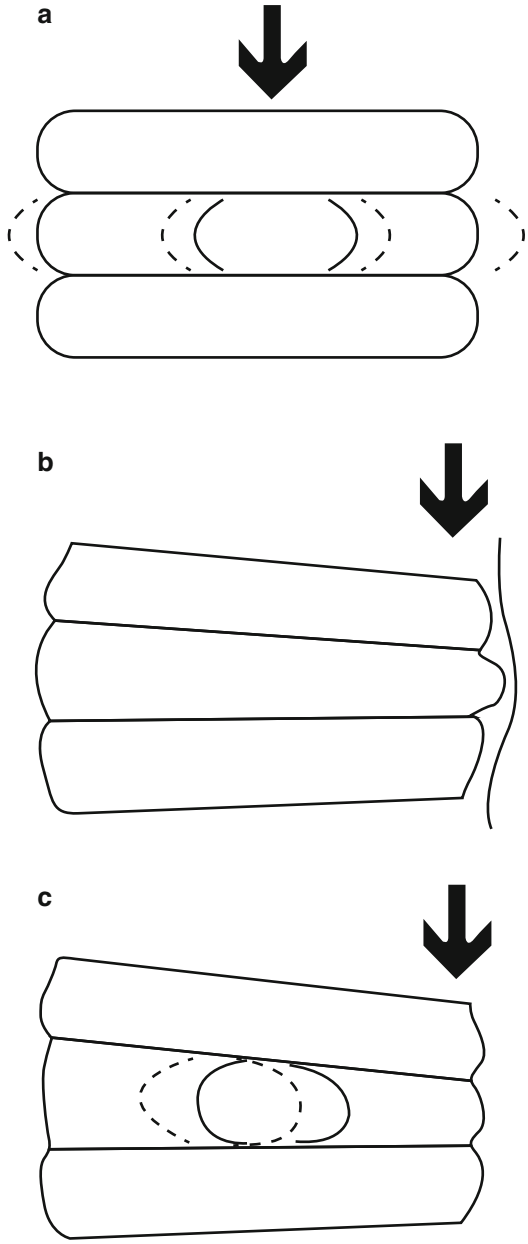

Fig. 22.2 An axial load causes an equally distributed force application to the disk (**a**). An eccentric force application results in annulus fibrosus bulging on the side of the greatest force application (i.e., the concave side of the bend) (**b**). The nucleus pulposus moves in the opposite direction. *Dashed lines* indicate the positions of structures during force application (**c**)

intervertebral disk height. The osmotic properties of the intervertebral disk space are crucial regarding these roles. This osmotic system is centered about the hydration of the nucleus pulposus and abilities of the annulus fibrosus and the cartilaginous endplates to act as semipermeable membranes through which water moves.

The movement of water is governed by several factors. The forces that keep water within the disk are the extra-discal hydrostatic pressure and the oncotic pressure of the nucleus ground substance. The forces that drive water out of the disk are the extra-discal oncotic pressure and the intra-discal hydrostatic pressure. The semipermeable barriers through which water moves are the endplates and the annulus fibrosus. As axial loading increases, the intra-discal hydrostatic pressure increases, driving fluid out of the disk. As fluid leaves, the anionic charge of the mucoid ground substance becomes more concentrated and thus pulls fluid back into the disk so that the following equilibrium is maintained: intra-discal hydrostatic pressure + extra-discal oncotic pressure = extra-discal hydrostatic pressure + intra-discal oncotic pressure. With changes in compressive forces (i.e., position changes during the day), fluid shifts between the intra-discal substance and medullary bone to maintain this equilibrium [6, 7, 10]. These fluid shifts facilitate the transport of nutrients and wastes and may be important for the overall health of the disk.

As previously noted, the vertebral endplates act as firm surfaces that transfer axial loads to the intervertebral disk. They also act as semipermeable membranes that allow not only water but also nutrients to diffuse through from the vascular medullary bone of the vertebral bodies into the relatively avascular disk space. Disruption of the vertebral endplates is linked with disk degeneration and is discussed in further detail later.

22.4 Degenerative Changes in the Intervertebral Disk Space

Many events can occur to weaken the main components of the intervertebral disk leading to degenerative changes. The most common level of disk degeneration is at L4/5 and degeneration is more common at multiple levels as compared

to a single level [1]. Degeneration results in decreased nuclear energy dissipation, swelling pressure, and compressive modulus relative to a normal nucleus; additionally, the annulus has a higher compressive stiffness and matrix function of the disk undergoes breakdown weakening biomechanical behavior [3]. Imaging findings that are associated with degeneration include: diminished disk height, facet narrowing, endplate spondylophytes and sclerosis, canal stenosis, lateral recess narrowing, desiccation, fibrosis or diffuse bulging of the annulus beyond disk space, fissuring or mucinous degeneration of annulus, defects or sclerosis of endplates, and osteophytes at vertebral apophyses [1, 11]. Mechanical behavior of the disk is related to biphasic-swelling properties as well as individual components: annulus, nucleus pulposus, and cartilaginous endplates [12].

The degenerated disk displays several interrelated changes. Annular tears develop as chondrocytes and fibroblasts are no longer able to produce quality fibers that can resist the expansile pressure of mobile central disk [5]. These tears are seen as early as the second generation of life and are present primarily in three different patterns: circumferential, transverse, and radial tears [13]. Transverse and radial tears are of greater clinical importance in degeneration as they have been shown to increase segmental motion markedly in rotation as well as moderately in flexion and extension but not significantly in lateral bending [4]. It has also been proposed that transverse tears in the posterior annulus act as a conduit for nucleus pulposus to herniate and cause nerve root compression. Though if the external layer of annulus fibrosus remains intact, there exists a possibility the protruded disk matter can return to its original position [5].

Decreased water content has also been noted in disk degeneration and has been linked to proteoglycan degradation. It is greatest in the nucleus pulposus [1]. Up to 70 % reduction in hydration is observed, resulting in desiccation of both the nucleus pulposus and other components of the disk [1]. The decrease of hydrostatic pressure of nucleus in disk degeneration has been noted both in vivo and in vitro studies [10, 14, 15]. This loss of water decreases the ability of the nucleus to weight bear. This progressively leads to increased weight bearing by the annulus and thus degeneration over time.

Weakening of the endplates may result from trabecular micro-damage and are identified on MRI as disk bulging into the vertebral bodies [16, 17]. With complete endplate disruption, herniation of nucleus fragments into vertebral bodies may occur. These are termed Schmörl's nodes when they become calcified. The loss of the endplate's ability to provide a firm surface for translation of compressive forces leads to the loss of the hydrostatic nucleus to weight bear in compression. The resultant compressive forces are then passed to the annulus and the developing fibrocartilaginous scar that forms peripherally. Further calcification of ligaments that span the intervertebral space can result in added fixation of the spinal segment [5]. With increased compressive stress, buckling of the annulus inward into the decompressed nucleus and outward beyond the margins of the vertebral endplates may occur and lead to a further decrease in disk height.

Disk height plays an important role in reducing compressive loads to the articular surface of the facet joints. With decreased height, load bearing in neural arch may increase to up to 50 % of the total compressive forces [18]. With this increased stress on the articular surface, facet joints undergo osteoarthritic changes that lead to facet injury and hypertrophy.

22.5 Spinal Instability

Instability of a vertebral motion segment may be defined as pathological or as increased motion of a joint [19]. Kirkaldy-Willis and Farfan argued against using this term alone, as there may be increased motion in asymptomatic individuals. For this reason, they adopted the term clinical instability and defined it as increased abnormal joint motion that produces a clinical response, such as pain or deformity [20]. The intervertebral disk is the main motion segment of the spine [5]. When the disk space is compromised by degeneration,

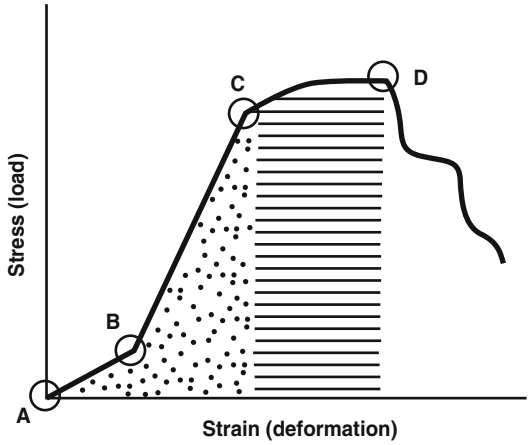

Fig. 22.3 A typical stress/strain curve for a biological tissue, such as a ligament. (*AB*) The neutral zone. (*BC*) The elastic zone. When the elastic limit (yield point) (*C*) is reached, permanent deformation can occur (permanent set). (*CD*) The plastic zone where a permanent set occurs. Past (*D*), failure occurs, and the load diminishes. *Hashed* plus *dotted areas* quantitatively represent strength, whereas the *dotted area* represents resilience

injury, or diskectomy, instability can occur and cause further degeneration of the spine [5].

The assessment of mechanical instability in the degenerated lumbar disk obligates the consideration of several additional concepts. Krismer, in 1997, defined instability as being associated with the following mechanical abnormalities: excessive dorsoventral transitional movement, pathological accompanying movements, enlarged neutral zone (NZ), and pathological center of rotation [5, 21]. The instantaneous axis of rotation (IAR) is the point around which a moment arm causes rotation in any given plane. The NZ is the component of motion in which the joint moves in response to an applied force with minimal internal resistance. The limit or "end" of the NZ is the point at which substantial resistance to motion is first exhibited [15]. As joint motion passes the limits of the neutral zone, it enters the elastic zone. This is the zone in which greater resistance to an applied force is observed, and motion is linearly related to the applied force. At the extreme of the elastic zone, a point is reached that results in permanent deformation in response to the applied force or injury to the affected structure (Fig. 22.3) [22]. Therefore, the summation of the NZ and elastic zone gives rise to the full range of motion (ROM) of a joint. The neutral zone ratio (NZR) has been defined as NZ/ROM and is used as a mechanical index of instability [15, 23]. A high NZR is associated with a clinical situation in which a joint was excessively lax (or unstable). Lastly, as degenerative disk disease progresses, ROM, NZ, and NXR all increase [19].

Clinical and radiographic observations of lumbar disk degeneration have led to numerous in vitro and in vivo studies that were designed to determine how disruption of one or more of the functional structures of the disk may result in instability [8, 24]. However, the link of disk degeneration to overt instability is not clear. Kirkaldy-Willis and Farfan postulated that there are three stages in lumbar disk degeneration: (1) temporary dysfunction, (2) unstable, and (3) stabilization [20].

The temporary dysfunction stage may be initiated in younger patients by an inciting damage, such as trauma, or functional changes (slackening of disks) resulting in degeneration. Intradiscal tissue displacement and disk protrusion can produce pain without radiographic correlate [5]. The unstable phase generally occurs in middle-aged patients in whom mechanical pain is accompanied by instability, loss of disk height, and/or arthritic joint changes [5]. The stabilization phase, most commonly observed in the elderly, is defined by re-stabilization of the joints as the vertebral joints stiffen with age.

Using cadaver models, several authors have investigated the role of physiologic compressive forces on the lumbar spine and the resulting changes in the motion segment [14]. In these studies, endplate damage was commonly noted and resulted in a rapid decompression of the nucleus. This, in turn, caused increased load bearing by the annulus. Zhao and colleagues evaluated the role of decreased water content and resulting endplate disruption in the lumbar motion segment [15]. They found increased NZRs in flexion and lateral bending, as well as a decreased bending stiffness, when the water content was decreased. These changes were greater when endplate disruption occurred. Furthermore, horizontal

translation was also noted to increase when the disks were subjected to compressive forces. The coupling of horizontal translation with angular rotation may have resulted in the observed increased translocation of the IAR toward the direction of rotation. Of note, in extension, the IAR moved toward the inferior facet. This phenomenon correlates with the observation of increased load bearing by the facet joints in extension. These results suggest that with initial dysfunction, the joint becomes more lax in flexion and lateral bending. With further damage or inadequate healing, the joints may enter an unstable phase that is characterized by increased abnormal segment motion. This, in turn, may produce mechanical low back pain.

Cadaver studies, however, do not reveal the cellular mechanism of healing. Traction vertebral osteophytes, facet hypertrophy, and the healing of annular tears via scarring are reactive changes noted with increasing age and disk degeneration [13, 25]. These changes usually lead to a stiffer, albeit altered, motion segment. With further reactive changes, the motion segment may enter the stabilization phase, in which the previously lax motion segment becomes progressively stiffer.

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23 Adjacent Segment Disease: Natural History of Lumbar Degeneration or Consequence of Fusion?

Mark P. Coseo, Nelson S. Saldua, Eric B. Harris, and Alan Hilibrand

23.1 Introduction

Spinal arthrodesis is the surgical gold standard treatment for symptomatic lumbar degenerative disk disease. Over the last decade, the number of lumbar fusion procedures in the United States has risen dramatically [1, 2]. However, there is significant concern over the potential affects lumbar fusion procedures have on the health of adjacent segments. Loss of a lumbar motion segment has been shown to alter lumbar mechanics and increase disk pressures and loading of endplates and facet joints [3–5]. Long-term follow-up studies have shown rates of adjacent segment degeneration after lumbar fusion procedures over 80 % [6–8]. The question remains as to whether adjacent segment degeneration and subsequent disease are a result of lumbar fusion procedures or the result of natural history of progression of lumbar disk disease.

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23.2 Adjacent Segment Disease: Definitions

Adjacent segment disease is symptomatic degenerative changes of an adjacent level following surgical intervention, whereas adjacent segment degeneration is the presence of abnormal imaging findings in the adjacent level following a surgical intervention at the index level that is asymptomatic. While there is no classification system for adjacent segment disease, it constitutes a myriad of signs and symptoms including axial low back pain, instability, stenosis, and radiculopathy of the cranial or caudal adjacent segment [9, 10].

23.3 Natural History of Lumbar Degeneration

The lumbar spine is susceptible to arthritic changes with age. Under pure compression, healthy lumbar disks demonstrate near uniform stress distribution. Physiologic forces are generally distributed equally along the endplate [11]. As a disk degenerates, stress concentrations shift to the annulus, progressing to disk bulges and protrusions. In addition, the posterior elements encounter greater transmission of forces. The affected segment becomes more susceptible to shear forces and less able to transfer load appropriately [12]. With moderate disk degeneration, there is greater translation under compression as

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_23

the instantaneous axis of rotation of the spinal functional unit moves inferiorly and has a wider range toward the periphery [13, 14]. This results in an increase in motion of the spinal functional unit with moderate degeneration. However, as degenerative changes progress, motion decreases [12]. These degenerative changes occur most frequently at the L5–S1 level, followed by L4–L5, and then L3–L4 [15] and occur in asymptomatic patients. Multiple studies have shown a disconnect between imaging findings of degeneration and symptom profile. MRI studies of asymptomatic patients have demonstrated abnormalities in the lumbar spine in greater than 50 % of patients over 60 [15]. Even in asymptomatic patients, lumbar degeneration has been shown to progress over time. In a 2002 study, Elfering et al. examined 41 asymptomatic individuals with MRI studies over a 5-year period. The investigators found 41 % of patients had evidence of progression of lumbar disk degeneration over the 5-year span [16]. However, there was no statistically significant correlation of progression of degenerative change to development of symptoms.

If the progression of lumbar degeneration is a result of natural history as these studies indicate, are certain patient populations at higher risk? Multiple studies have shown there is a likely genetic predisposition to lumbar degenerative disease [17, 18–22]. Much of this evidence has been the result of twin studies. Battie et al. published on the results of MRI studies of 116 pairs of monozygotic Finnish twins. The investigators found familial and genetic influences accounted for variance in disk degeneration for 61 % in the upper lumbar region and 34 % in the lower lumbar region [19]. Another classic twin study, from Sambrook et al., reviewed lumbar MRI studies of 172 monozygotic and 154 dizygotic twins. They showed 64 % heritability for severe disease in the lumbar spine and overall heritability of lumbar degenerative disease of 74 % (95 % CI 64–81 %) [17]. A follow-on twin study of monozygotic and dizygotic Finnish twins by Battie et al. supported the high rate of genetic influence in lumbar degenerative disk disease. They estimated heritability ranging from 29 to 54 % depending on lumbar level and phenotype [23]. The higher concordance rate seen in the monozygotic twin populations has clearly shown there is a genetic predisposition to the development of lumbar degenerative disk disease.

However, it is also clear there is no signal gene responsible for this increased risk. Progress has been made on delineating possible candidate genes yielding the greatest influence on lumbar degeneration. Polymorphisms of the genes coding proinflammatory cytokines and matrix metalloproteinases leading to overexpression in the intervertebral disk have been hypothesized to be a contributing factor. Of particular concern is overexpression of MMP-2, MMP-3, and IL-1 leading to increased inflammatory response and increased susceptibility to lumbar disk degeneration [24–27]. In addition, healthy disks contain high concentrations of aggrecan and collagen-9. Certain polymorphisms in the genes encoding both these proteins have also been shown to be associated with increased risk of lumbar degenerative change [28–31]. Asporin is a leucine-rich repeat protein found in extracellular matrix. Overrepresentation of the D-14 allele of the asporin gene has been associated with increased risk of osteoarthritis and lumbar degeneration [32–34].

While progress has been made and certain gene alleles have been identified that are associated with lumbar degeneration, there is still much that is unknown. As gene sequencing becomes faster and computing power increases, genome-wide studies across multiple populations will become more feasible. This will not only help delineate the genotypes most at risk for developing lumbar degenerative disease but also may identify genetic profiles that are more resistant to disease progression. While the entire genomic influence in lumbar degenerative disease is unclear, it is evident from available studies there are populations that are more susceptible. This lends credence to the belief adjacent segment disease may be progression of natural history, rather than as a result of surgical intervention in the lumbar spine.

23.4 Patient Factors in Adjacent Segment Disease

In addition to genetic predisposition, certain patient factors have been hypothesized to increase risk of adjacent segment disease after fusion. There is evidence to suggest facet tropism and laminar inclination could predispose toward disease [35–38]. Okuda et al. reviewed 87 patients who underwent PLIF for L4 degenerative spondylolisthesis and found that facet tropism at L3–4 and horizontal lamina at L3 correlated with increased rate of degenerative change at L3–4 after L4–5 posterior lumbar interbody fusion [36]. The investigators hypothesized that facet joint asymmetry and increased lamina inclination angle resulted in abnormal motion of the spinal unit with increased intradiscal pressures and subsequent degradation [36]. In a follow-on study of this population, investigators found patients undergoing reoperation rates for adjacent segment disease had higher rates of facet tropism and lamina horizontalization in the cranial level to the fused segment [39].

Patient age is also thought to be a risk factor for adjacent segment disease [6, 9]. In a retrospective review of 3188 patients undergoing lumbar fusion procedures, Ahn et al. found a correlation between increasing age at index procedure and need for a reoperation on adjacent segments [6]. Interestingly, the study also found males were more at risk for reoperation [6]. Harrop et al. found similar conclusions in another retrospective review. Older age was associated with development of adjacent segment disease [9].

Finally, it has been hypothesized that obesity and history of smoking play a role in adjacent segment degeneration, while some studies reported no evidence of increased risk with higher BMI or nicotine intake [6, 9, 36, 40, 41]. Cho et al. reviewed 154 patients in a retrospective study and found age, BMI, and preoperative existing degenerative changes at the cranial level had the most significant risk for requiring repeat operative procedures for adjacent segment disease [42].

23.5 Prevalence of Adjacent Segment Disease

Many long-term studies have shown the progression of radiographic evidence of degenerative changes on adjacent segments following surgical intervention. While adjacent segment degeneration is common, rates of adjacent segment disease are much lower. A recent meta-analysis reviewed 94 studies with 34,716 patients included. In subgroup analysis, investigators found pooled prevalence rates for adjacent segment degeneration from 21.8 to 37.4 % and rates of 3.2–12.1 % of adjacent segment disease [43]. Harrop et al. in a meta-analysis found similar rates of adjacent segment degeneration and disease. The investigators reported rates of adjacent segment degeneration of 34 % (314/926) and disease rate of 14 % (173/1216) [9]. There is good evidence showing adjacent segment disease is more prevalent in the levels proximal to surgical intervention [9, 43–45]. Celestre et al. found in patients undergoing L4–5 fusion, 75 % developed adjacent segment degeneration at L3–4, while only 25 % had similar progression at L5–S1 [44]. The study found in all cases of adjacent segment disease the cranial levels were affected 90 % of the time [44].

The conclusions from these meta-analyses must be interpreted with caution due to their retrospective nature, differences in symptom evaluation, follow-up time, and imaging studies. However, our best available evidence does show a significant rate of adjacent segment degeneration and disease following lumbar fusion. The literature also shows cranial levels are at highest risk of development.

23.6 Is Fusion a Risk Factor?

Lumbar spinal motion is complex, as the functional spinal unit does not have a fixed center of rotation. It is inherently difficult to study given lumbar kinematic behavior is nonlinear. The lumbar spine is viscoelastic and motion coupling

occurs in vivo [46]. This makes in vitro studies of lumbar spinal motion following arthrodesis difficult. However, multiple in vitro models have been developed to study the effect fusion has on adjacent levels [5, 47–49]. In a cadaveric study, Weinhoffer et al. measured intradiscal pressures in uninstrumented, single-level bilateral instrumented L5–S1 and multiple-level bilateral instrumented (L4–S1) models [48]. The investigators found intradiscal pressures were increased in the levels above the instrumentation and more significantly increased as more levels were instrumented [48]. The findings of this study were corroborated by a similar cadaveric study by Chow et al., in 1996. Single-level instrumentation at L4–5 increased intradiscal pressures in the cranial segment. Double-level instrumentation from L4–S1 resulted in marked increase in intradiscal pressure of the cranial segments [5]. This study also measured mobility of the cadaveric spines prior to and following instrumentation. They found one- and two-level instrumentation resulted in increased motion of the unfused segments closer to the extremes of their functional range [5]. Similar results have also been seen in in vitro studies of calf lumbosacral spine specimens. Shono et al. used this model to study the differences in motion following one-, two-, and three-level instrumentation in flexion, extension, lateral bending, and rotation [47]. As levels of instrumentation increased, the motion of the segments proximal to the construct had greater increases in motion [47]. This finding has also been seen in vivo. Axelsson et al. utilized roentgen stereophotogrammetric analysis of six patients undergoing fusion for low-grade spondylolisthesis to study the mobility of pre-fused and fused lumbar segments. Mobility of L4–5 and L5–S1 segments was measured preoperatively and after fusion. They found increased mobility of the proximal segment following fusion procedure [49]. While the results of these studies show concerning effects of loss of a motion segment, they must be interpreted critically. Current in vitro studies do not fully recreate the complexities of in vivo spinal motion, and available in vivo studies are limited by sample size. Improvements are needed in in vitro studies, and progress has been made to develop models that more accurately replicate spinal motion in vivo for bench studies [50].

It is very plausible biomechanical changes to the lumbar spine secondary to fusion result in abnormal forces on the adjacent segments and subsequent disease. However, does surgical intervention alone without fusion increase this risk? Some hypothesize decompressive laminectomy alone without fusion may alter lumbar mechanics and predispose to disease [51]. Biomechanical studies have shown posterior element excision in laminectomy produces increased motion of the surgical segment in flexion, extension, and rotation [52]. Using comprehensive national data from Sweden, Jansson et al. examined a 10-year follow-up on 9664 patients who underwent decompressive laminectomy for spinal stenosis [53]. They found progression of symptoms and need for reoperation in 11 % of patients on 10-year follow-up [53]. The results of this study and those like it show that fusion alone is not the sole risk for developing adjacent segment disease. The process of degeneration proceeds with non-fusion procedures as well.

While available data does show there is an increase in intradiscal pressures and motion in the levels surrounding a fusion mass, the question still remains if this change increases risk of adjacent segment disease. Models that more accurately represent spinal motion may provide insight if changes following loss of motion segments in the lumbar spine are well compensated in vivo or if they lead to symptomatic degeneration. Adjacent segment disease occurs after spinal fusion; however, there is no definitive evidence in the literature to date proving this phenomenon occurs as a result of the fusion.

23.7 Surgical Intervention: Does Method of Fusion Matter?

It is clear there are multiple methods to achieve fusion of a functional unit in the lumbar spine. However, it is still unclear if approach and fusion method utilized affects risk of adjacent segment disease. Some believe posterior approaches and

pedicle screw-based instrumentation may predispose adjacent segment disease over anterior-based techniques [52, 54, 55]. Chen et al., in 2008, utilized CT scans following pedicle screw fixation for lumbar fusions to assess the rate of superior segment facet joint violation. Of this study cohort, 47 % of patients had evidence of superior facet joint violation after instrumentation [54]. It is possible that violation of the facets at the fusion interface may increase the risk of degeneration. If posterior approaches and instrumentation increase the risk of adjacent segment disease, it would follow then that anterior lumbar interbody fusion procedures would have lower rates of reoperation for adjacent disease. There is some level IV data to support this hypothesis. While not examining adjacent segment disease directly, Strube et al. found a significant difference in patient satisfaction, Oswestry disability index, and visual analog scale in patients undergoing anterior lumbar interbody fusion (ALIF) alone versus anteroposterior lumbar fusion [56]. Wai et al. performed MRI studies on 39 patients after ALIF with a minimum of 20-year follow-up. Only three patients in this group required additional surgery. The investigators also found 30.7 % of patients had advanced degeneration, but of that group, 17.9 % had preservation of the adjacent segment. They concluded the rates in their study were similar to unfused patients [8]. A study by Min et al. compared 48 patients who had undergone either L4–5 ALIF or PLIF for degenerative spondylolisthesis. They reported rates of adjacent segment degeneration of 44 % in the ALIF group and 82.6 % in the PLIF group. However, there was no significant difference in adjacent segment disease rate [57]. It is difficult to ascertain the clinical significance of the differential finding in adjacent segment degeneration in these two groups. Though likely, it is more consistent with progression of natural history of the degenerative spine rather than fusion related. Finally, while these studies may show a benefit to stand-alone anterior lumbar interbody fusion in association with development of adjacent segment disease, there is also evidence fusion method has no effect. Analyzing outcomes from the SPORT trial, Abdu et al. found no significant difference in 4-year outcomes comparing posterolateral in situ fusion, posterolateral instrumented fusion, and 360° fusion [58]. Given the disparity in the literature, there is no definitive answer as to the effect the method of fusion has on the development of adjacent segment disease.

Finally, potentially avoidable surgical results have been associated with increased risk of adjacent segment disease. Over distraction at time of fusion is hypothesized to pathologically load the posterior elements resulting in earlier degeneration [59]. In a study of 85 patients after posterior lumbar interbody fusion at L4–5, Kaito et al. found 13 out of 85 patients developed adjacent segment disease at 2-year follow-up. In the group developing adjacent segment disease, there was an average distraction of 6.1 mm at L4–5, while in the asymptomatic group, there was an average distraction of 3.1 mm [59]. There is also evidence to suggest the importance of maintaining near anatomic sagittal balance following fusion [60–63]. Keorochana et al. reviewed MRI findings of 430 patients with low back pain and found the patients with hyperlordosis (>50°) and hypolordosis (<20°) had increased disk degeneration compared to those with normal lordosis [63]. Djurasovic et al. corroborated these findings, where they found hypolordosis at the fused lumbar segment correlated with adjacent segment degeneration [62]. These results clearly show the importance of good surgical technique when performing lumbar fusion procedures. Particular attention must be paid in avoiding over-distraction and changes in postoperative sagittal alignment.

23.8 Motion-Sparing Surgery: Is Arthroplasty the Answer?

Concern of adjacent segment disease has helped lead to the development of disk and spinal functional unit arthroplasties of the lumbar spine. The goals of motion-preserving surgical interventions are to replace the diseased segment and remove the pain generator while maintaining as close to normal spinal kinematics and motion. It is thought this would help limit the risk fusion has on the development of adjacent segment disease.

There is literature to support this claim. In a recent meta-analysis, Harrop et al. included 27 retrospective studies to compare the development of adjacent segment degeneration and disease in patients who had undergone lumbar arthrodesis versus arthroplasty. They found rate of adjacent segment disease in the arthrodesis cohort to be 14 % (173/1216) and a rate in the arthroplasty group to be 1 % (7/595) [9]. Another recent meta-analysis of 1584 patients at 2-year follow-up found a significant improvement in ODI and VAS scores of patients following lumbar disk arthroplasty compared to those after fusion [64]. These results appear promising in support of motion-sparing technology; however, they must be interpreted with caution given the nature of studies included in the meta-analysis. In addition, there is relatively little data on the long-term survivability of lumbar disk arthroplasty. The longest follow-up data is available from case series out of Europe [65, 66]. David reported on 106 patients with mean 13.2-year follow-up after one-level lumbar disk arthroplasty. In this case series, 82.1 % reported good to excellent outcomes, 90.6 % were still mobile with mean flexion and extension range of 10.1°, and only three cases (2.8 %) of adjacent segment disease [66]. Huang et al. reported on 42 patients at a mean of 8.7 years following lumbar disk arthroplasty. They found an adjacent segment degeneration rate of 24 % but noted no adjacent segment degeneration developed in patients with motion greater than 5° at their arthroplasty site [67]. Siepe et al. performed MRI studies on 93 patients at a mean of 53.4 months following lumbar disk arthroplasty and found an incidence of adjacent level degeneration of 10.2 % but characterized the level of degeneration as mild in all cases [68]. Comparing motion at adjacent segments following fusion versus arthroplasty suggests there is less change in postoperative range of motion following disk replacement [69, 70]. Berg et al. compared 72 patients following arthrodesis and 80 patients after total disk arthroplasty at 2-year follow-up and found significant difference in preservation of preoperative mobility of the adjacent segments in the arthroplasty group [70].

Compared to arthroplasty in other joints, lumbar arthroplasty is in its infancy. The data available is promising in the preservation of adjacent segments following surgery. However, there is still concern of abnormal forces on the posterior elements of the involved segment following disk replacement. This has continued to lead to development of more optimal arthroplasty techniques, including total lumbar functional unit arthroplasty. As this technology develops, continued research is needed to elucidate if lumbar arthroplasty is more effective in preventing adjacent segment disease over fusion.

Conclusion

The best available evidence to date suggests that adjacent segment disease is a multifactorial process. There are populations of patients more prone to lumbar degenerative disease from a combination of underlying genetic risk factors and environmental factors. However, there is also good evidence to suggest surgical intervention plays a role in its development. Fusion procedures of the lumbar spine likely hasten the progression of natural degeneration in the lumbar spine. Good surgical technique, limited dissection of the posterior elements, and maintenance of sagittal alignment have been shown to be crucial in helping prevent this condition. As lumbar arthroplasty technology continues to develop, it may prove to be superior to current fusion methods in treating pain generators of the lumbar spine without progression of adjacent segment disease.

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How to Obtain the Best Lumbar Lordosis

24

Jean-Paul Steib and Yann Philippe Charles

Instrumented lumbar fusion is a common operation worldwide. Nevertheless, lumbar lordosis is not always restored [1]. Lumbar lordosis, however, is essential for standing and ambulation in a balanced position [2]. During growth, for a child to stand, the human spine develops a lumbar lordosis. This lordosis changes during daily activities and with position (sitting, laying, or standing) [3]. It also changes over time, when degenerative changes occur in the lumbar spine [4]. Back pain can affect lordosis [5]. The best way to assess lumbar lordosis is via measurement on a lateral standing radiograph. Other imaging studies, such as CT or MRI, are not able to provide a good assessment of lordosis since this parameter should be assessed in the erect position. However, its measurement remains controversial [6]. It seems that global lordosis is the most realistic measurement. Lumbar lordosis is the key to sagittal balance of the spine. Lordosis is individual but significantly correlates with pelvic incidence [7]. After surgery, a lack of lordosis disturbs normal gait, imbalances the spine and is compensated by hyperlordosis at the adjacent level, which in turn may lead to a new degenerative disease – adjacent segment degeneration [8, 9]. Therefore, a proper establishment of lordosis is important when considering lumbar fusion. The purposes of a spine fusion may be to restore lordosis, with instrumentation, and to fuse the spine in a proper position. As two thirds of the lumbar lordosis occurs at L4–S1 [10] and two thirds of lumbar fusions address this region, the ability to achieve a good lordosis of the lumbosacral spine represents the basis of surgery. Today, total lumbar disk replacement remains a popular strategy for treating lumbar disk degeneration. The prosthesis is a tool, which allows the patient to find the optimal lordosis during different daily activities. In this chapter, we describe the strategies to achieve optimal lordosis during lumbar spine during surgery.

24.1 Patient Positioning on the Operating Table

The position of the patient on the table is the first step for a successful surgery.

- In prone position

  The knee-chest position decreases lumbar lordosis. It is useful for non-instrumented spinal canal decompression or microdiskectomy, since it enlarges the interlaminar space. However, this position should be avoided for

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_24

instrumented fusion of the lumbar spine. The best position is flat on the table without flexion of the hips. This neutral position allows a natural lordotic posture and makes additional internal correction maneuvers possible that facilitate the acquisition of optimal lordosis through the instrumentation.

- In supine position

  A roll placed under the patient's back or bending the operating table enables to increase lordosis in supine position. This position facilitates the correction and setting of segmental lordosis in anterior approaches. On the other hand, it can complicate the surgery by stretching the iliac vessels, thus making the exposition of the disks difficult and dangerous. Therefore, a flat patient positioning on the table is certainly the most reasonable option for the anterior access to the lumbar spine.

24.2 Release of the Spine

- Opening of facet joints

  The purpose of posterior instrumented fusion is to obtain an arthrodesis of the lumbar spine in a lordotic position. Opening the facet joints during the posterior approach represents a useful method of releasing the lumbar spine, which in turn allows increasing lordosis and further grafting of the facets. This release can be performed using chisels or a saw by resecting the inferior articular process (the cranial part of the facet joint). This bilateral release enhances segmental mobility, especially in case of severe osteoarthritis with major osteophytes. Posterior compression maneuvers lead to shortening of resected posterior elements and open up the anterior intersomatic disk space, which might eventually be addressed with an additional cage.
- Section of the disks

  The opening of the disks can be achieved either by anterior, posterior, or combined approaches. The posterior approach uses posterior cages (PLIF or TLIF) to maintain the intersomatic height with additional fusion between vertebral bodies. In anterior approaches using stand-alone cages (ALIF) with a primary stabilization system, the release of the anterior longitudinal ligament and the major part of the disk allows progressive dilatation of the intervertebral space and segmental lordosis restoration. In combined approaches, it can be very useful to release the disk by anterior approach first, prior to posterior deformity correction (kyphoscoliosis or posttraumatic malunion). The anterior approach can be minimal invasive video assisted. It is important to cut at least two thirds of the annulus and to decorticate the superior and inferior endplates. The rib, harvested during the anterior approach, can be used as a graft (Fig. 24.1). It is inserted as an onlay or a strut graft. The remaining intervertebral space is then filled with cancellous bone from the vertebral body. A postopera-

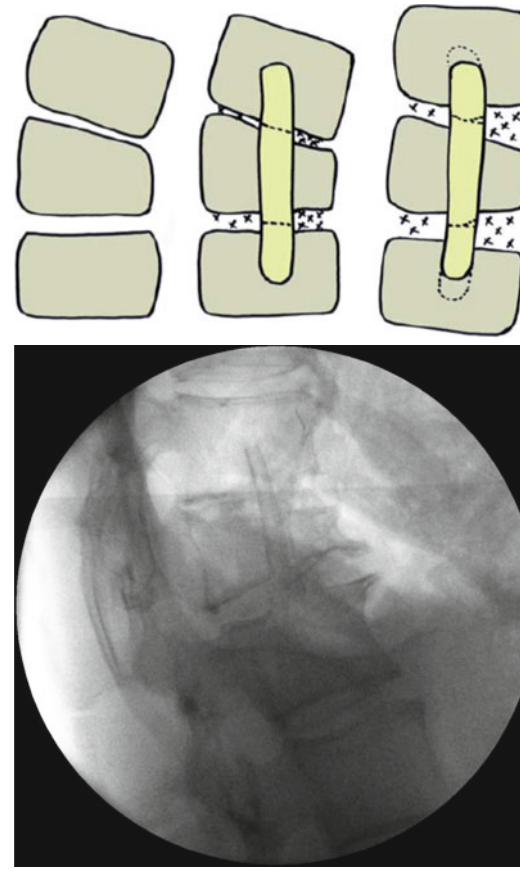

Fig. 24.1 Rib used as an inlay or a strut graft

tive CT analysis has demonstrated that this rib graft mixed with cancellous bone leads to massive fusion in the anterior column [11]. With this technique, the malleable bone graft allows the mobility during posterior reduction maneuvers and facilitates lordosis correction in combined approaches of the thoracolumbar spine [12].

- Osteotomies

  A bony fusion between two vertebrae represents an obstacle to allow a good surgical lordosis restoration.

  – The Smith-Petersen osteotomy is the easiest manner to obtain a mobilization of the spine when the anterior column is still mobile. We start the osteotomy by a Farcy's osteotomy (Fig. 24.2), which is achieved by removing the superior articular process (the caudal part of the facet joint). After exposure of the superior articular process, a curette is passed along the lateral part of the facet joint in order to cut all soft tissues adherent to it and to separate the isthmic vessels from the bone. A saw is then used to cut the superior articular process straight ahead: the blade of the saw is set perpendicular to the facet in the transversal plane, adjacent to the cranial edge of the transverse process. The osteotomy is then completed using the chisel to ensure a safe separation of the facet towards the intervertebral foramen. Once the facet is cut, it is removed using a curette inserted in the articular cavity. The last insertions of the flavum ligament attached to the facet are removed. The same procedure is performed bilaterally. It is important to avoid electrocoagulation at the recessus and the foramen.

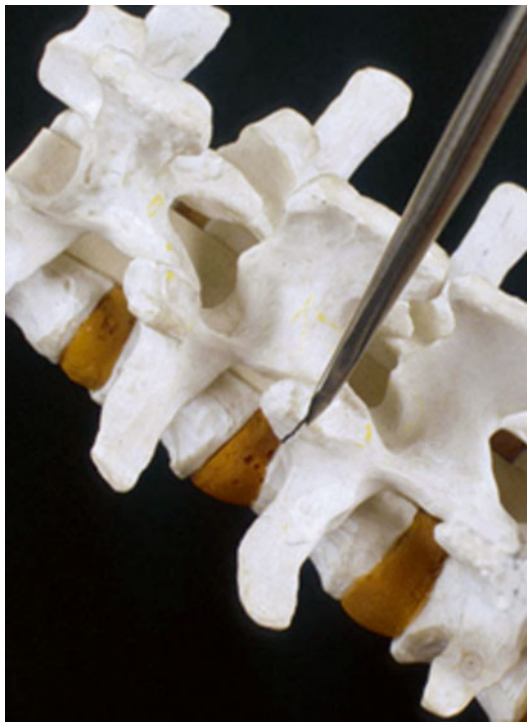

Fig. 24.2 Farcy's osteotomy

24.3 Instrumentation

- Hooks or pedicle screws are implants that facilitate lordosis reduction and fixation of the spine.

  Hooks provide a posterior anchoring of the vertebrae. Compression on hooks at posterior spinal elements induces lordosis. On the other hand, posterior distraction has a kyphosing effect at the level of the disk. In the lumbar spine, hooks can only be used on the laminae. Hooks cannot be placed in a neutral position: a tension between the hook and the bone is required to ensure implant stability. For that reason, lamina hooks are used in claws bridging two adjacent vertebrae. Pedicle screws provide an anchoring in the three columns of the vertebra. As opposed to hooks, screws can be placed in a neutral position. Today, indications for hooks in lumbar spine are very restricted. Special situations and difficulties during pedicle screw placement may however require the use of hooks as a backup option.
- Rods

  It seems obvious that a rod in lumbar spine should be lordotic according to physiological sagittal curvatures of the spine. Therefore, it is not usually appropriate to use a straight rod in a curved spine. The shape of the rod and the amount of bending represent key factors

in order to achieve the best possible lumbar lordosis. A rod that follows the spinal curvature is always better than a rod bridging the spine when low profile instrumentations are used.

24.4 Reduction

- Compression
  - Hooks: As previously mentioned, the use of hooks required tension and posterior compression to achieve lordosis (Fig. 24.3). Compression of posterior vertebral elements induces a posterior narrowing of the intervertebral space and an anterior elevation of the superior vertebra.
  - Screws: The anchorage of the screws is posterior and anterior at each vertebra. Compression on monoaxial screws does not create or induce lordosis if the shape of the rods is straight or curved (Fig. 24.4). Therefore, a lordotic bending of the rods is mandatory to achieve sagittal alignment correction. The center of rotation is posterior with a rod-screw construct if the orientation is 90° between the rod and the monoaxial screw. Polyaxial screws work like hooks: a posterior compression on the screws induces a lordosis on the anterior column by distraction at the level of the disk (Fig. 24.5).

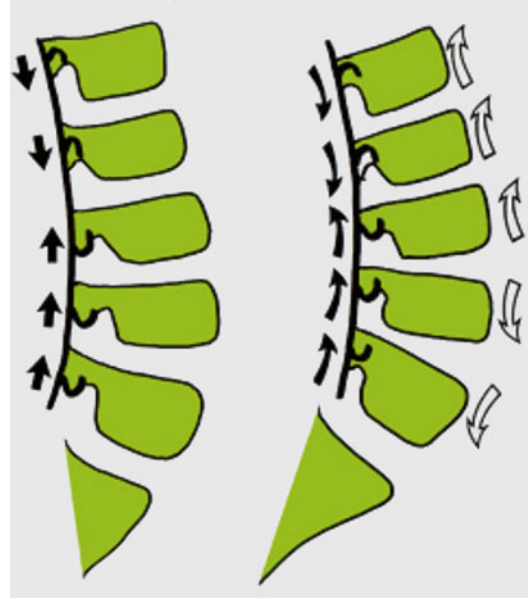

Fig. 24.3 Posterior compression using hooks

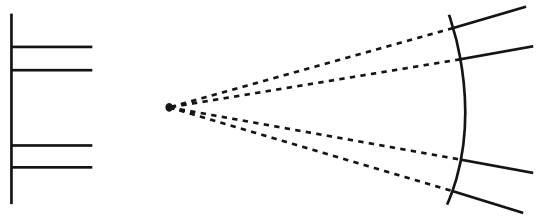

Fig. 24.4 Posterior compression using lordotic rod and monoaxial screws

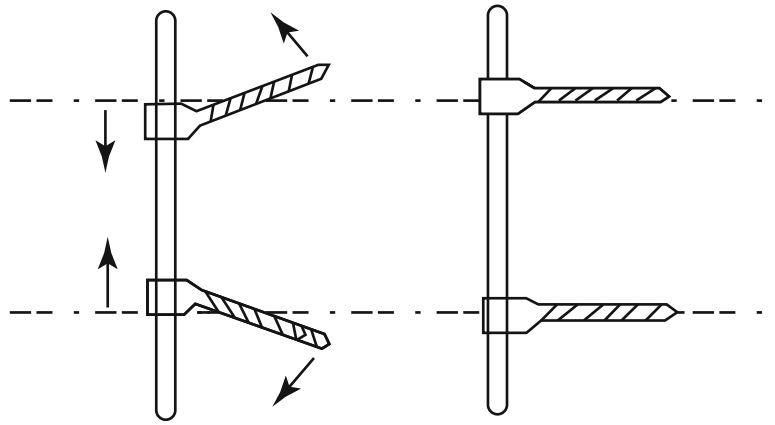

Fig. 24.5 Posterior compression on polyaxial screws induce anterior distraction and segmental lordosis of the lumbar spine

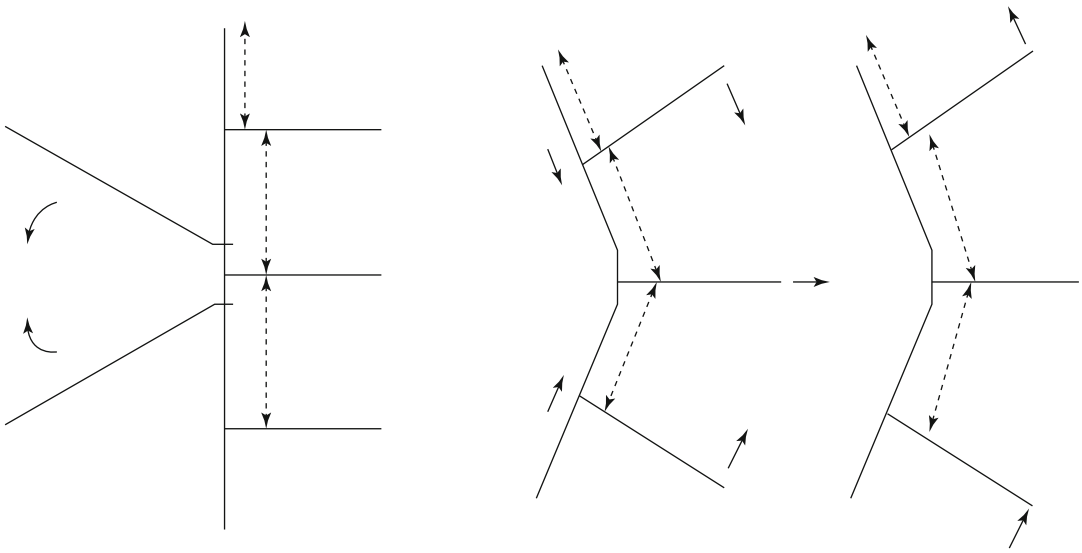

Fig. 24.6 Bending of the rod pushing the screws forward

- Translation

  Translation (approximation) is very popular today with instrumentations using persuader systems of the rod. This technique is used on a regular base with percutaneous instrumentation in MIS. With this practice, care should be taken that the vertebrae are not pulled backward to the rod, which might happen if the shape of the rod is too flat. It is mandatory to pull back the end vertebrae of the lordotic construct and to push the apical vertebrae anteriorly. Accurate bending of the rod is mandatory and is achieved by giving a lordotic shape to the rod prior translation and rotation of the apical vertebrae in the sagittal plane. Polyaxial screws facilitate the rod-screw connection with multilevel persuaders. However, the screws must be in line in the sagittal plane to allow lordotic opening of the spine by pushing the curved rod into the screws with the persuaders.
- In situ bending

  The principle is to mimic the shape of the spine and then to make the spine follow the shape of the rod. Instead making the vertebra following a prebent rod as with the approximation technique, the rod is inserted without any stress onto the uncorrected (flat) spine. The screws are closed but not locked once the rod is in place. Bending irons are set on the two rods, right and left symmetrically, and the rods are then bent inside the patient by pushing the bending irons together. This maneuver applied to the rod induces a movement of the screws, and subsequently of the vertebra, which are pushed anteriorly into a lordotic alignment. This maneuver is not dangerous while the screw is pushed anterior and not pulled back (Fig. 24.6). Bending has to be repeated along the rod, by little forces given in many times. The reduction is easily obtained by a 90° rod-screw connection with monoaxial screws, thus giving the spine the shape of the rod (Fig. 24.7).

24.5 Bone Graft

The bone graft is used to maintain the lordosis at long term. The purpose of the instrumentation is to obtain and to maintain the correction until the spine is fused. The absence of fusion or pseudarthrosis is mechanically associated with micro movement, followed by macro movement, mobilization of the implants with bony lysis around the pedicle screws (radiologic evidence of halo), and finally rod breakage. The consequence is back pain and loss of lordotic correction. The site of grafting

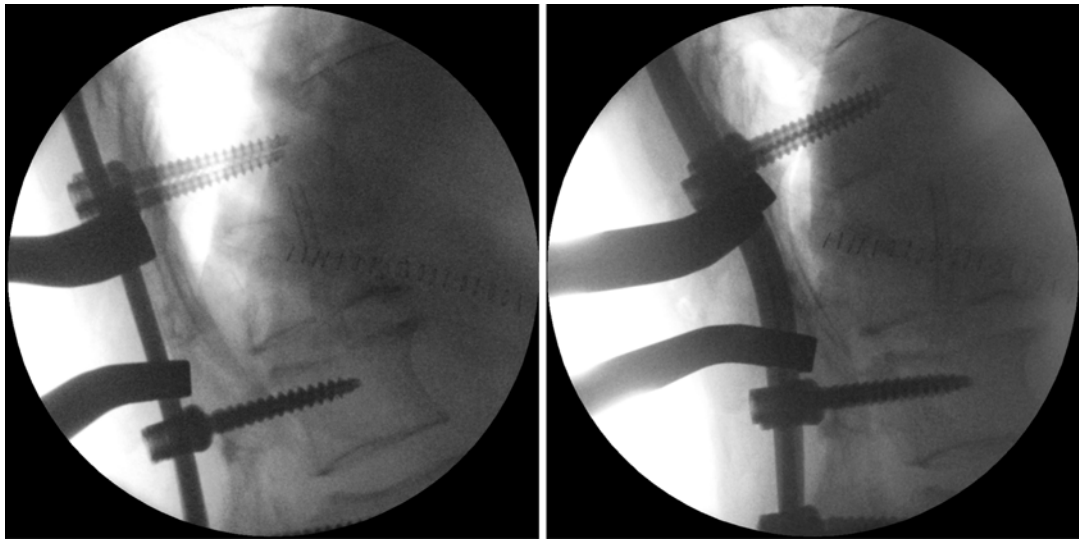

Fig. 24.7 Example of correction obtained by in situ bending

(anterior, posterior, or 360° fusion) can be relevant for the success of fusion. In the case of suspected non-fusion during follow-up, it is important to verify the consolidation of the graft using radiographs (measurement of segmental lordosis, screw, or rod breakage), CT scan (evidence of fusion between the vertebrae), and isotopic CT (hyper- or hypo-fixation). The combination of CT and isotopic CT is useful to determine the exact area of non-fusion.

- Fusion material
  - Autologous bone

    Iliac crest remains the gold standard and the best way of obtaining fusion. The incidence of pain caused by graft harvesting (donor-site morbidity) is closely related to the surgical technique. Cancellous bone should be preferably harvested without cracking the cortex and damaging the sacroiliac joint. Furthermore, a good reconstruction of the iliac crest is mandatory to avoid a painful traction on the gluteus medius. The iliac crest can be used as bone chips or as a tricortical bone block.
  - Pieces of osteotomies

    In some cases, the amount of bony resection from the vertebrae is sufficient to allow bone grafting. Soft tissues need to be entirely stripped from the bone to avoid the risk of pseudarthrosis. The harvested bone should not be mixed with cartilage from the facet joints or necrotic bone from vertebral bodies.
  - Bone substitutes

    There is no evidence or clear consensus on the possibility of obtaining a bony fusion with bone substitutes. They are used to induce or to facilitate fusion after preparation of bone surfaces on the spine
- Posterior fusion
  - Posterior fusion at the level of the posterior arch is not able to maintain lordosis because of a certain amount of remaining elasticity at the anterior column. This graft works in tension and is in bad position to keep the correction.
  - Posterolateral fusion is located between the transverse processes, at the level of the posterior wall and the vertebral bodies. This type of fusion is closer to the axis of rotation in flexion-extension. Therefore, posterolateral fusion is in neutral position and leads to a better resistance, thus maintaining the lordotic correction.
  - Articular fusion is optimal because it is in line with the two posterior columns of the spine, at the level of movement through the facet joints. A continuous fusion through all facet joints leads to adequate stability.

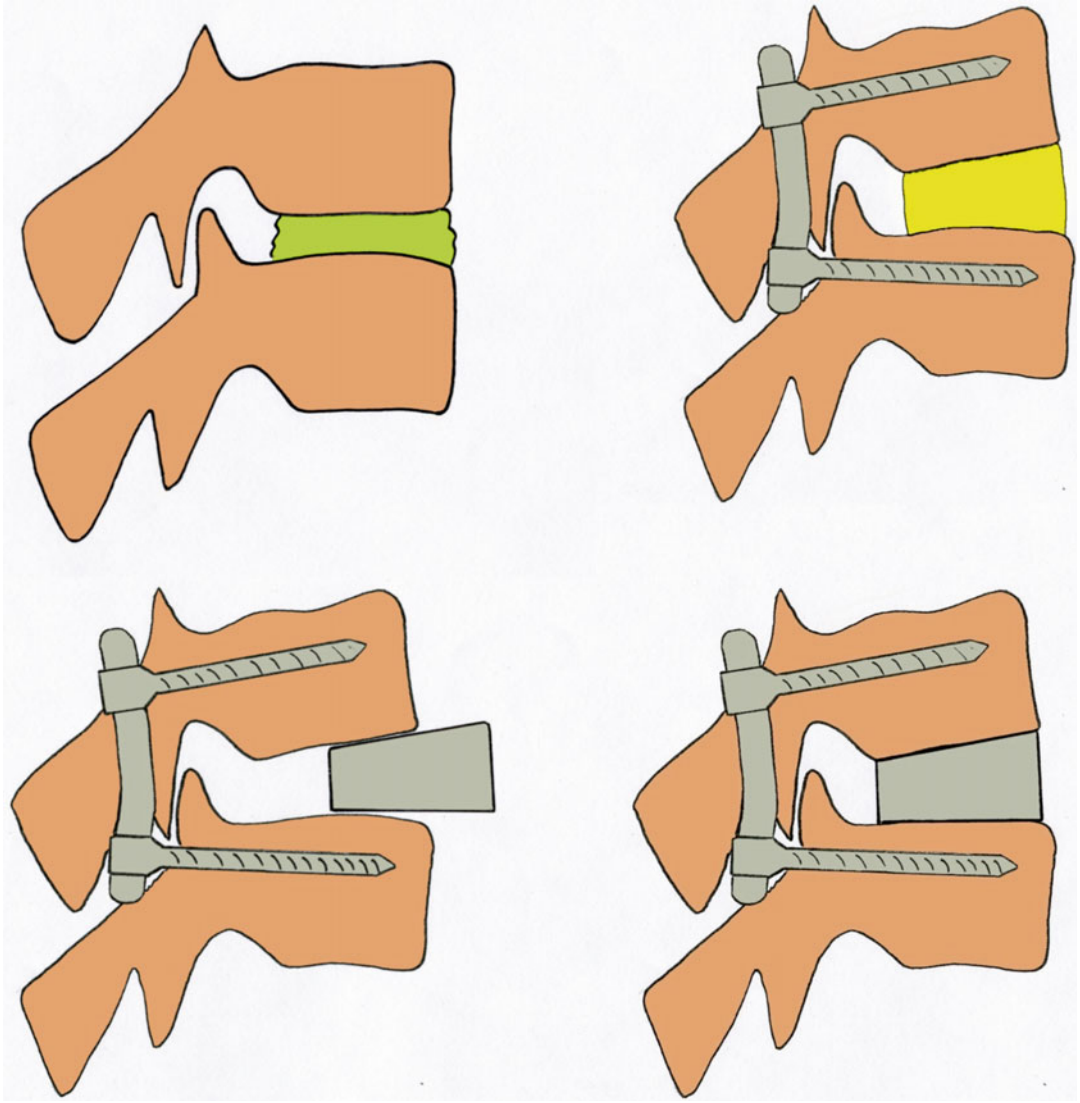

Fig. 24.8 Cage closing the anterior gap between the two anterior endplates

- Anterior fusion
  - PLIF, TLIF, ALIF, XLIF, and other cages are currently used today. The method of placing the cages followed an evolution with time. The main purpose of using a cage is to add an anterior support and to close the anterior gap between the two endplates of the intervertebral space (Figs. 24.8 and 24.9). Mechanically, an interbody fusion offers the best support to keep segmental lordosis. It is important to avoid the complications related to the specific approaches of each cage: nerve root stretching, destabilization of the spine by large arthrectomy, and vascular or femoral nerve injury.
  - An anterior parallel distraction of the disk does not provide lordosis and the endplates should not stay parallel once the cage is inserted. The segmental lordosis of the spine is triggered by the lordosis of the cage. The anterior support helps to keep the anterior opening of the disk. An anterior bone graft seems necessary when the operated disk is narrow preoperatively and elevated after surgery. A gap between two endplates after posterior segmental lordosis

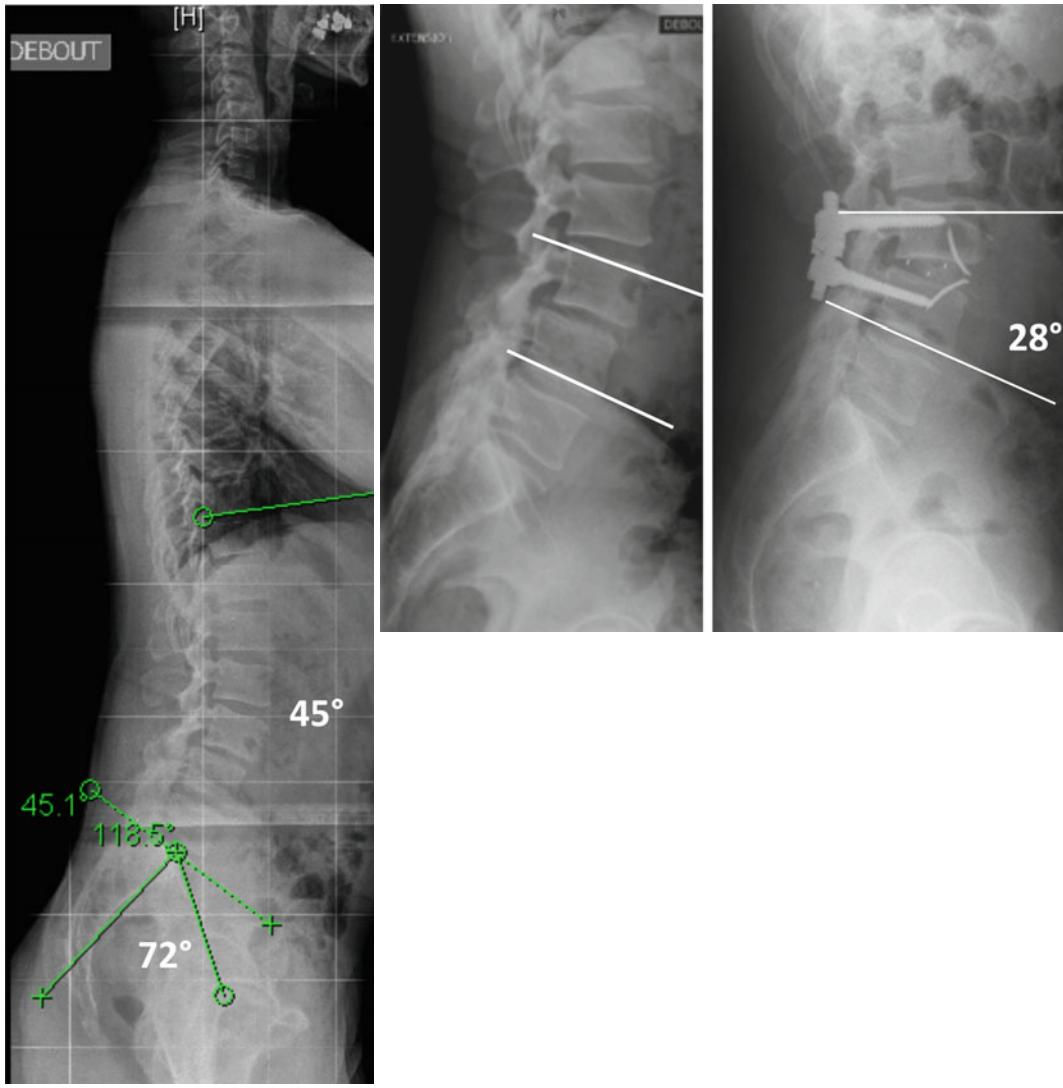

Fig. 24.9 Example of result obtained with an anterior cage

correction will be a weak point in the construct and needs to be filled by an anterior support.

24.6 Total Lumbar Disk Replacement

Obviously, the difference with fusion is the movement, thus allowing changes of segmental lordosis, during positional changes. The surgeon does not set the spine into fixed lordosis, but the implant allows the patient to adapt his own lordosis depending on his position. The patient is operated in supine position: flat on the table. There is no lordosis in supine position. The extension of the lumbar spine stretches the vessels and may complicate the anterior access to the disk. Once the disk is exposed, it is largely opened anteriorly. The intervertebral space is progressively distracted while disk material is removed. Overdistraction is not recommended to avoid a possible painful decompensation at the level of the facet joints. The posterior longitudinal ligament is usually retracted in the degenerative lumbar spine. In order to

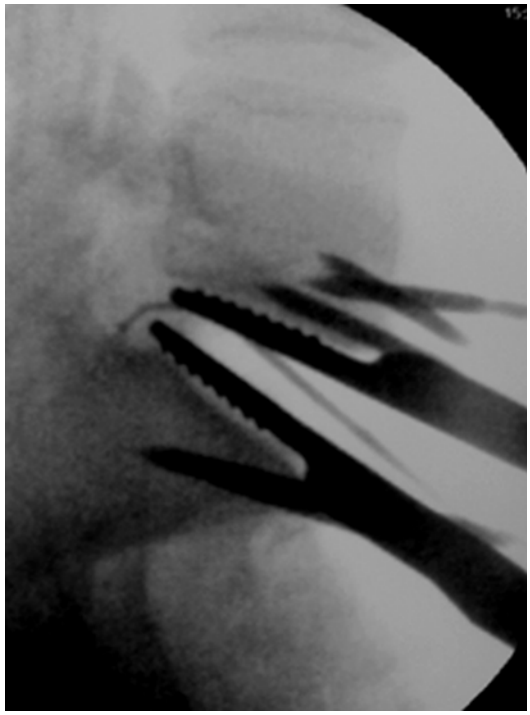

Fig. 24.10 To achieve a parallel distraction of both endplates and adequate prosthesis placement, it is recommended to release the posterior longitudinal ligament

achieve a parallel distraction of both endplates and adequate prosthesis placement, it is recommended to release this ligament (Fig. 24.10). The artificial disk has to be inserted while maintaining the endplates parallel intraoperatively. The posterior ligament release will further allow the automatic lordotic setting of the prosthesis and enhance range of motion during flexion of the spine. Total disk replacement is not recommended when the pelvic incidence is too high since the segmental lordosis is relatively high at L4–L5 and L5–S1, thus preventing proper functioning of the prosthesis. Segmental instability in flexion-extension and associated facet degeneration represent two other main contraindications for total disk replacement.

Conclusion

Lumbar lordosis represents a key factor that needs to be considered and restored during lumbar surgery. The role of the surgeon is to position the spine of his patient to obtain and to keep the best possible sagittal angle depending on the amount of pelvic incidence. One of the main drawbacks of lumbar surgery is the lack of lordosis, which will lead to adjacent segment degeneration and possibly a bad clinical result at short or midterm. We described some technical aspects of lumbar surgery including some tricks that may allow successful lumbar lordosis acquisition.

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Bone Substitutes

25

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25.1 Introduction

Spinal fusion is a common surgical procedure and is often considered for degenerative pathologies as well as deformity, trauma, or tumor indications. Approximately 200,000–250,000 patients in the USA annually undergo a spinal fusion procedure, the majority of which are lumbar spinal fusions [1, 2]. Spinal fusion constitutes over half of all bone graft procedures each year [1]. Spinal arthrodesis eliminates motion between segments with the aim of decreasing instability, maintaining alignment, and protecting the neural elements. Fusion is a biologic event in which bridging bone forms between adjacent motion segments.

In order to promote biologic fusion, spinal segments can be immobilized with or without instrumentation. Spinal arthrodesis with internal fixation hardware provides transient stability to the spinal segments that can facilitate fusion. However, if biologic fusion is not realized over time, hardware failure will generally occur.

Autologous bone remains the "gold standard" graft material for spinal fusion and is most often obtained from the iliac crest or from bone local to the fusion/decompression site. Autologous bone graft may be limited in its supply and often requires a second surgical site with the associated additional risks. Due to these considerations, the use of iliac crest bone autograft (ICBG) has decreased over the past decade, and the use of bone graft substitutes and bone graft extenders has increased.

As a result of the above considerations, there has been significant work to develop alternative graft materials to supplement or even replace autogenous bone graft. This chapter will discuss the biological processes underlying spinal fusion and the mechanisms by which these graft materials serve to facilitate arthrodesis.

25.2 The Biology of Spinal Fusion

Spinal fusion consists of a tightly controlled series of cellular and molecular events that are dependent upon the biologic conditions of the fusion environment. There are three main cellular components that must be present for bone formation to occur. Osteogenic cells are precursors that populate the fusion site and can be induced to differentiate into osteoblasts (bone-forming cells).

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_25

Osteoinductive factors are proteins that induce the recruitment and differentiation of the osteogenic cells. Finally, osteoconductive matrices serve as a scaffold onto which bone formation and neovascularization can occur.

The process of bone formation at a spinal fusion site starts with inflammation, continues with reparative processes, and then finishes by remodeling [3]. Overall, this is a cascade that mirrors fracture healing. During the inflammatory phase, there is a hematoma that surrounds the fusion site with inflammatory cells and allows for neovascularization and the recruitment of cells with osteogenic potential. Next, in the reparative phase, the soft hematoma begins to solidify into new bone via intramembranous and endochondral bone formation while the graft bone is gradually resorbed [4]. Finally, during the remodeling phase, there is organization of the new bone and continued resorption of the graft bone.

There are a myriad of systemic factors that may compromise a patient's ability to achieve a fusion. Issues can be with the local fusion environment, the mechanical stability at the fusion site, or systemic host factors.

In terms of the local fusion environment, the preparation of the fusion site is believed to be critical. The bony surfaces to be fused need to be decorticated. This allows for delivery of local osteogenic cells and provides for a local blood supply to the fusion site. Maximizing the area of decorticated bone increases the surface area available for fusion. Minimizing trauma to adjacent anatomic structures, and allowing for vascularity of surrounding structures, such as muscle edges, allows for or access of further precursor cells and blood supply.

In terms of mechanical stability at the fusion site, this is needed to allow for bone formation. Often, this is achieved with instrumentation, but bracing or immobilization can help achieve this as well [5]. As the newly formed bone is loaded, it matures according to Wolff's law of bone formation. This explains why bone is found to form more easily under compression than tension. It is for this reason that anterior column interbody constructs are thought to have an advantage [6, 7].

In terms of systemic host factors, examples such as nicotine, nutrition, and others can affect bone formation [6]. For example, individuals who smoke have consistently demonstrated higher rates of pseudarthrosis because nicotine use interferes with angiogenesis, bone metabolism, and regeneration [8–12]. Similarly, drugs that inhibit the systemic inflammatory cascade such as nonsteroidal anti-inflammatory have been shown to inhibit new bone formation [13, 14]. Additionally, decreased thyroid and/or growth hormone function can increase the risk of delayed union. Others have demonstrated that nutritional status can influence bone healing as well [15].

Lumbar fusion is the most commonly performed spinal fusion procedure. Traditionally, posterolateral fusion is the most common approach and seeks to achieve bone formation between adjacent transverse processes. Historic nonunion rates for uninstrumented posterolateral fusions have been reported to be between 40 and 60 % [16, 17]. In order to minimize motion, decrease the reliance on bracing, and facilitate biologic fusion, instrumentation has become the standard.

Interbody fusion has been developed to directly support the anterior column of the lumbar spine. This technique is used to increase the surface areas for fusion and decrease the biomechanical forces on posterior constructs, especially when considering the limited posterior bony surface area when applying posterior minimally invasive techniques [18].

Autologous corticocancellous bone was the first and initially only option that spinal surgeons used for bone graft and it remains the gold standard. Its widespread utility stems from the fact that it is the only single material that contributes all of the elements required for bone regeneration (i.e., osteogenic cells, osteoinductive signaling molecules, and an osteoconductive matrix). However, as discussed earlier, there are reasons to strive to avoid autograft and this has fueled the desire for bone graft supplements and substitutes.

Commonly used bone graft substitutes include allograft products, recombinant osteoinductive factors, and ceramics.

25.3 Mineralized Allograft

Allogeneic bone is one of the most commonly transplanted tissues among humans, and it has been used for numerous orthopedic applications including spinal fusion [19]. Bone allografts are obtained from a deceased donors, are readily available, and thus do not face the same supply limitations as autograft. Mineralized allograft (fresh frozen and freeze-dried) is considered non-osteogenic, osteoconductive, and very mildly osteoinductive [20].

Allograft can consist of cortical bone, cancellous bone, or a corticocancellous mixture. The cortical allograft bone provides better structural support through its ability to resist compressive forces but is slower to incorporate and resorb. Cancellous allograft bone has limited ability to resist compressive forces and resorbs more quickly but provides a more intricate framework for osteoconduction.

Allograft bone is processed either by freezing (fresh frozen) or lyophilization (freeze-drying) after it is harvested from a human cadaver in a manner that avoids infectious agents, decreases its antigenicity, and preserves the grafts for storage. This sterilization process can biomechanically weaken the bone (compared to fresh allograft), significantly decreases any osteoinductive potential, and eliminates osteogenic cells [21].

There is the underlying question of allograft being capable of transferring disease, such as human immunodeficiency virus (HIV). HIV transmission has been documented in non-spinal fresh-frozen allografts, but not documented in freeze-dried allograft cases [22].

When structural allograft is implanted under compression in the anterior column, it is associated with relatively high fusion rates, both in the cervical and the thoracolumbar spine [23, 24]. Fusion rates for single-level ACDF with allograft are similar to those with autograft, but the union rate decreases for allograft more so than autograft when used in multilevel ACDFs. As mentioned earlier, this is in accordance with Wolff's law of bone formation.

Cancellous allograft is preferred to cortical allograft for posterior spinal fusion as it allows for better vascular ingrowth and has better osteoinductive properties. Cortical bone isn't needed for structural support because the compressive forces are sufficiently low. When nonstructural allograft bone is placed under tension, as in the posterior spine, it incorporates at a slower rate than similarly positioned autograft and leads to lower rates of fusion when used alone [25, 26]. Thus, for posterior spinal applications, allograft is often employed as a bone graft extender in combination with autograft rather than as a substitute for autograft.

An exception to this is in the pediatric scoliosis population, where allograft alone appears to be a reasonable alternative to autograft for posterolateral fusions. In these patients, the use of allograft resulted in similar rates of arthrodesis compared to autograft, with far less morbidity [27–29].

25.4 Demineralized Bone Matrix Allograft

Demineralized bone matrix (DBM) was introduced in the early 1990s. DBMs are also derived from cadaveric bone, have lesser osteoconductive properties, and have some low-level osteoinductive properties.

The donor bone is decalcified (removal of calcium and phosphate) by acid extraction, exposing the extracellular matrix and a composite of type I collagen and noncollagenous proteins, including low concentrations of bone morphogenetic proteins (BMPs) and other constitutively expressed growth factors [24]. There are many proprietary-processing techniques, but they all have the above-described process in common. Once extracted, these products are combined with carriers to improve product and handling properties (e.g., pastes, putty, chips, and gels) [2].

Research has shown that there is variability in the osteoinductive activities of commercial DBMs both when comparing different company brands and within a single company's brand [30, 31]. In one study comparing the osteoinductive properties of several commercially available DBM products, the fusion rates of athymic rats

ranged from 0 to 80 %, in part demonstrating the great deal of variability between the different DBM formulations [32]. This is thought to be due to the varying quantity and composition of osteoinductive factors in various DBM preparations [33].

DBMs have been used successfully as autograft extenders in several animal studies [34, 35]. Animal studies have also shown that posterolateral arthrodesis rates were significantly improved with a composite graft consisting of DBM and allograft bone compared to allograft alone [36, 37].

In a multicenter, prospective equivalency trial with each patient serving as his/her own control, researchers compared Grafton DBM gel/autograft on one side vs. iliac crest autograft on the contralateral side of the patient's instrumented posterolateral lumbar spine [38]. Of 120 patients followed up at 24 months, fusion was found for 42 cases (52 %) on the Grafton DBM (Osteotech Inc., Eatontown, NJ)/autograft side and in 44 cases (54 %) on the autograft side. The authors concluded that the Grafton DBM gel allowed them to use less ICBG.

Another prospective, multicenter randomized clinical trial assigned 46 patients undergoing a single-level instrumented posterior lumbar fusion to receive Grafton DMB/local bone or only iliac crest bone autograft [39]. At 2 years, no statistical difference was noted in the radiographic fusion rate of the Grafton (86 %) vs. the ICBG (92 %) groups ($p=0.23$). The authors concluded that for this application, Grafton combined with local bone is not different than ICBG.

One study compared one- and two-level posterolateral fusions using lamina autograft (i.e., local bone graft) and demineralized bone matrix (Osteofil/ICM, Sofamor Danek, Memphis, TN) in a 50:50 mix. Based on dynamic radiograph assessment, the study found the one-level fusion rate to be 98 % and the two-level fusion rate to be 96 % with similarly improved SF-36 clinical outcomes 1-year after surgery [40].

In a separate study of posterolateral uninstrumented lumbar fusions, 79 patients underwent an average of 4.9-level lumbar laminectomies with an average 2.0-level non-instrumented posterolateral fusions using lamina autograft and DBM [41]. Six months postoperatively, 17.3 % patients were found to have radiograph (computed tomography and dynamic x-ray) confirmed pseudarthrosis. Only 1 of the 13 patients diagnosed with pseudarthrosis had persistent clinical symptoms that lead to reoperation.

These studies support the use of demineralized bone matrix in the posterior lumbar spine for reducing the amount of autograft needed to achieve similar fusion rates. The studies found similar results in both posterior and posterolateral fusions as well as single- and two-level fusions.

There is minimal clinical data on the use of DBM for anterior lumbar interbody fusion (ALIF). A study by Thalgott et al. retrospectively studied 50 patients who received DBM combined with coralline hydroxyapatite, a synthetic bone graft material, in an anterior cage and an instrumented posterior fusion [42]. Their intention was to assess the utility of coralline hydroxyapatite in the anterior spine. Ninety-six percent of patients achieved radiographic fusion at 3–5 years after surgery. The authors concluded that the combination of titanium mesh cages, coralline hydroxyapatite, and demineralized bone matrix is effective for anterior interbody fusion of the lumbar spine when used as part of a rigidly instrumented circumferential fusion.

The relatively fewer clinical studies utilizing demineralized bone matrix in the anterior lumbar spine may reflect the anterior spinal column's better fusion environment relative to the posterior spinal column.

25.5 Synthetics

Another alternative to autograft for spinal fusion is a synthetic osteoconductive scaffold, such as ceramic. Examples of synthetic ceramic materials that facilitate new bony ingrowth include beta-tricalcium phosphate, hydroxyapatite, and calcium sulfate.

These products do not function well by themselves because they only provide an osteoconductive matrix. It is for this reason that they must be used as a bone graft extender in conjunction

with other materials that provide the osteoinductive and osteogenic characteristics.

These synthetic bone graft extenders have been frequently used in part based on their inability to cause an immunogenic response, no risk of human disease transmission, and ample supply. One of the inherent disadvantages of ceramics is that most are relatively weak and brittle. When ceramics are introduced into the anterior spinal column, they must be protected from the significant compressive forces by internal fixation until the graft is incorporated into the new bone growth [24]. Like allograft, ceramics are also inferior to autogenous bone when placed under tension, as in the posterior spine [43, 44].

Other biologically active materials such as DBM, osteoinductive growth factors, or ions (e.g., silicate, magnesium) may be combined with a ceramic osteoconductive matrices to form a composite graft that can then lead to increased amounts of bone formation [45, 46]. Silicate and other bioactive ions are reported to play a role in bone metabolism via stimulation of osteocytes as well as angiogenesis [47]. One animal study on magnesium didn't show a difference in the rate of bone fusion vs. controls but did show an improvement of the bone fusion quality by histological and scanning electron microscopy assessment [48].

Concerns about ceramics include their ability to withstand compressive loads, particularly those seen in the anterior spinal column, their ability to deliver osteogenic and osteoinductive factors, and their resorption rates. Ceramic biomechanics involves a trade-off in porosity and resorption rates [49]. As porosity increases, so does surface area, which allows for increased interaction between the ceramic and the local bone fusion environment. Less porous materials can have slower resorption rates which if long enough can lead to the implant being semipermanent [50]. This is not ideal as it can cause a foreign body reaction and is a potential nidus for infection.

In a clinical study, a non-randomized retrospective review of 1- or 2-level lumbar degenerative disorders assessed the impact of silicate on an instrumented posterolateral bone fusion. Using silicate hydroxyapatite ceramic as a bone graft substitute, without the addition of iliac crest bone graft, researchers showed CT confirmed successful lumbar posterolateral fusion rates of 77 % in patients with 2-year follow-up [49].

As mentioned, Thalgott et al. set out to assess the clinical and arthrodesis efficacy of coralline hydroxyapatite as a synthetic osteoconductive bone graft substitute in the anterior lumbar spine in addition to a posterolateral fusion [42]. The coralline hydroxyapatite's porosity is similar to that of cancellous bone. A prospective case series involving 50 patients (including 14 smokers and 29 revision lumbar surgeries) who received 1- and 2-level lumbar interbody fusions as well as a posterolateral fusion procedure, reported a 96 % success rate after implanting titanium mesh cages packed with a DBM and a coralline hydroxyapatite carrier [42].

25.6 Bone Morphogenetic Proteins and Osteoinductive Growth Factors

The discovery of bone morphogenetic proteins (BMPs) is attributed to Urist and colleagues in the 1960s [51–55]. BMPs are osteoinductive in nature and operate by inducing pluripotent mesenchymal stem cells to become bone-forming cells. With the use of recombinant gene technology, large quantities of osteoinductive growth factors can now be produced in a purified form for clinical use. Multiple strongly positive animal studies supported the continued research on rhBMP-2 in clinical trials [56–58]. The efficacy of these recombinant human bone morphogenetic proteins (rhBMPs), including rhBMP-2 and rhBMP-7 (also known as osteogenic protein-1, or OP-1), has been studied in a number of clinical studies [59–61].

In a multicenter, prospective, randomized trial, 279 patients with lumbar degenerative disk disease underwent ALIF with lumbar-tapered fusion devices (LT-CAGE, Medtronic) filled with either rhBMP-2 (1.5 mg/mL) on an absorbable collagen sponge carrier or autogenous iliac crest bone graft [59]. The radiographic fusion rate of

the patients receiving rhBMP-2 was 94.5 % and that of the ICBG patients was 88.7 % at 24 months. The authors concluded that rhBMP-2 in combination with the LT-CAGE for this surgical indication and approach was an appropriate bone graft substitute. As a result of this and other studies, the FDA approved the combination of rhBMP-2 with an absorbable collagen sponge (INFUSE, Medtronic Sofamor Danek, Memphis, TN) for use with threaded fusion devices in the anterior lumbar spine in the treatment of degenerative disk disease at one level from L4 to S1.

Other uses of INFUSE have also been studied. Some of these have been in off-label cohort studies (such as the cervical spine) and others have been in randomized trials (such as a higher dose in posterolateral, called AMPLIFY).

After encouraging results from a pilot study [62], Dimar et al. carried out a randomized prospective study, which was also part of the Food and Drug Administration (FDA) Investigational Drug Exemption (IDE) for rhBMP-2. The researchers looked at 463 patients treated with single-level instrumented posterolateral fusion [63]. The authors compared iliac crest bone autograft to an rhBMP-2 matrix. The matrix was a 20-cm^3 block of bovine type I collagen carrier containing 15 % hydroxyapatite and 85 % β-tricalcium phosphate particles to create a compression-resistant graft. All patients had symptomatic single-level lumbosacral degenerative disease (with no greater than grade one spondylolisthesis). In addition to showing that the rhBMP-2 group had statistically significant shorter operative times and decreased blood loss, the authors noted that at 24 months, fusion was evident in 96 % of the patients in the recombinant human bone morphogenetic protein-2 matrix group compared with 89 % in the iliac crest bone graft group ($p=0.014$).

Regarding cancer risk related to rhBMP-2, Dimar et al. noted that at 24 months the rate of all cancers in the investigational arm of this AMPLIFY study was 3.3 % vs. 0.9 % in the control arm ($p=0.107$) [63, 64]. Follow-up data submitted to the FDA at 60 months showed the cancer incidence in the same subjects to be 5.0–6.3 % for the rhBMP-2 arm versus 2.2 % for the ICBG arm (no p-value is given). In 2011, based in part on data that lead to the question of associating rhBMP-2 with an increased cancer rate, the FDA rejected Medtronic's application for approval of rhBMP-2 at the higher dose (AMPLIFY) for use in posterolateral lumbar fusion.

In a retrospective study comparing off-label use of rhBMP-2 with local bone graft (LBG) in 70 patients undergoing primary one- or two-level posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF), the authors found similar rates of radiographic fusion (89.5 % LBG vs. 94.1 % rhBMP-2, $p=0.61$) but a higher complication rate for the rhBMP-2 (41.2 % vs. 10.5 %, $P=0.05$) [65]. These complications included radiculopathy, radiculitis, adjacent segment disease, development of ectopic bone, and vertebral osteolysis.

In recent years, with the increasing on- and off-label use of INFUSE as well as reported clinical complications, the efficacy and safety of INFUSE has come under scrutiny. This was somewhat unexpected given that the 13 original industry-associated BMP-2 studies did identify several surgical complications but ultimately reported no (0 %) device-/BMP-2-related or unanticipated adverse events.

Carragee et al. compared the published data from 13 industry-associated trials on rhBMP-2 covering 780 patients and compared this with "available FDA data summaries, follow-up publications, and administrative and organizational database analyses" [66]. The authors concluded that rhBMP-2 was associated with adverse events 10–50 % of the time.

Carragee et al. found that ALIF was associated with higher rates of "implant displacement, subsidence, infection, urogenital events, and retrograde ejaculation" compared to controls.

Further, they noted that PLIF was "associated with radiculitis, ectopic bone formation, osteolysis, and poorer global outcomes" at higher rates than controls. The authors ultimately questioned the methodology and reporting of biases of the original rhBMP-2 trials.

Faced with several questions regarding the complications of INFUSE [67–72], Medtronic

(Minneapolis, Minnesota) voluntarily submitted all the INFUSE clinical trial individual participant level data as well as supplied funding for analysis to the Yale University Open Data Access (YODA) Project in 2011. The YODA Project then commissioned two outside academic groups to independently analyze the individual participant data and report their conclusions [73, 74].

Fu et al. concluded that INFUSE was similarly effective to ICBG for lumbar ALIF and PLIF. They found that INFUSE was associated with increased risk of complications (adverse events, wound complications, dysphagia or dysphonia) when used for anterior cervical spine fusion, an increased risk of cancer (all approaches and levels grouped together), and associated with a reporting bias that failed to give sufficient attention to the risks of its use [73]. They state that an earlier, more complete reporting of the data would have been helpful to clinicians and patients.

Simmonds et al. concluded that INFUSE did improve the rate of bony fusion when compared with ICBG but they found that this was not associated with less post-fusion pain [74]. Further, they found that the data was suggestive of a higher rate of adverse events but stopped short of making firm conclusions regarding the true rate of adverse events associated with rhBMP-2 given the small sample size and numerous non-randomized studies that were used in the analysis. Consistent with other study findings, Simmonds et al. found that the rate of cancer was "nearly double" that of ICBG. They concluded that despite this, the absolute rate of cancer was low for both, and it is unclear if the risk is clinically significant [74].

Of historical interest but not clinically approved for lumbar fusion by the FDA at this time is BMP-7 also known as osteogenic protein-1 (OP-1). The OP-1 gene was identified in the 1980s, approved for long bone fractures in 2001 under a Humanitarian Device Exemption (HDE), and in 2004, the FDA approved OP-1 Putty (Stryker and subsequently Olympus) under an HDE for performing revision posterolateral lumbar spinal fusion based on several positive animal and early clinical studies [16, 75–80]. Based on a clinical trial [81] that failed to show non-inferiority, in 2009, an advisory panel to the FDA rejected Premarket Approval (PMA) for OP-1 Putty for instrumented posterolateral lumbar spine fusion.

25.7 Gene Therapy: Intracellular Signaling Proteins

The benefits of gene therapy are thought to be twofold: first, using current replication techniques producing complimentary deoxyribonucleic acid (cDNA) is cheaper than producing an osteoinductive protein and second, delivery of the DNA rather than the protein may allow for a more prolonged delivery of the final osteoinductive protein through activation of the cascade [1].

Importantly, gene therapy requires a vector to deliver the intracellular proteins. In one experiment, the cDNA was delivered via an adenovirus. Alternatively, a plasmid was used but the transfection rate was lower than hoped for [82, 83]. As the cellular and molecular mechanisms underlying these novel osteoinductive signaling proteins continue to be elucidated, the clinical indications may expand to include them as alternatives to autogenous bone for spinal fusion and numerous other orthopedic applications.

Several cell signaling proteins, such as LMP-1, NELL-1, and rhGDF-5, have been studied for their use in ex vivo gene therapy. LIM mineralization protein-1 (LMP-1) is an osteoinductive growth factor that potentiates the cellular response to exogenous BMPs [82–88]. NEL-like molecule-1 (NELL-1) is a protein expressed predominantly in neural tissue that encodes epidermal growth factors in cells of the osteochondral lineage; it was first noted to be overexpressed in patients with craniosynostosis [89, 90]. Recombinant human growth and differentiation factor-5 (rhGDF-5) is another example of another type of signaling molecule that has earned some attention from the scientific community [86, 87].

Gene therapy techniques may allow for the sustained local release of these molecules at more physiologic levels. The hope is that these techniques would result in a more potent

osteoinductive signal to the surrounding tissues. Presently, however, the safety and efficacy of gene therapy techniques have not yet been sufficiently established to justify its widespread use in a clinical setting.

25.8 Autologous Stem Cells

Autologous bone marrow represents another source of osteogenic cells and osteoinductive material for spinal fusion. The most significant advantage of this technique is that aspiration of bone marrow has much less morbidity than the procurement of iliac crest autograft. When used in combination with an osteoconductive matrix, bone marrow aspirate forms a composite graft that may be an effective alternative to autogenous bone.

In one animal study, aspirates were used as bone graft extenders and were found to significantly increase the rate of arthrodesis for posterolateral fusions in rabbits [91]. The major limitation to this technique is that unfractionated bone marrow has only moderate osteogenic potential. There is a low concentration of mesenchymal stem cells in the graft harvest – 1 in 10,000 cells. However, adipose tissue has been noted to have a higher concentration of these stem cells (1 in 4000 cells). With this as a foundation, Zuk et al. were able to use the BMP signaling cascade on human adipose-derived stem cells to induce cellular differentiation into the osteoblastic lineage [92]. Moreover, Hsu et al. used these stem cells, transfected with AdBMP-2 (adenoviral vector containing BMP-2), to achieve posterolateral spine fusion in an athymic rat model [93].

To further address the problem of limited stem cell availability, attempts have been made to increase the effective concentration of osteoprogenitor cells in these aspirates by selectively retaining these cells within an osteoconductive matrix or by expanding the number of these mesenchymal stem cells in cell culture before transferring them to the matrix [91].

In a prospective randomized study, 24 patients undergoing one-, two-, or three-level lumbar fusions were randomized to receive autologous bone marrow concentrate (from the iliac crest) combined with allograft on one side of their spinal fusion and then iliac crest bone autograft on the other side of their spinal fusion [94]. The authors concluded that there was no difference in the radiographic fusion rate for autogenous bone marrow concentrate combined with allograft as compared to autologous iliac crest bone graft in the lumbar spine.

Bone graft substitutes utilizing stem cell options are continuing to be the focus of significant research. As of yet, there is insufficient evidence to conclude whether bone marrow aspirates or bone graft substitutes will serve only as bone graft extenders or if they will be true alternatives to autogenous bone.

Conclusion

The development of bone graft alternatives has progressed rapidly over recent years, with several options now available for various clinical applications. Iliac crest autograft is still recognized as the gold standard graft material for spinal fusion, because it is the only graft option that contains osteogenic cells, osteoinductive growth factors, and an osteoconductive matrix.

Since no other single method to date provides all of these elements necessary for bone formation, the future of bone graft research will likely be focused on creating new composite grafts. These composite grafts will consist of multiple biologically active materials implanted together and acting synergistically to enhance spinal fusion. Further advances in the understanding of the intricate cascade of molecular and cellular events underlying spinal fusion will allow for continued refining and development of new grafting techniques. As novel approaches are developed, such as gene therapy, additional studies will be required to evaluate the efficacy, safety, and cost-effectiveness of both the new and existing techniques.

However, regardless of future advances, the success of these complex surgeries will remain dependent upon the basic principles essential to achieving a solid arthrodesis: proper patient selection, selecting an appropriate bone graft

material, optimizing the biological environment, preparation of the fusion bed, and maintaining adequate biomechanical stability during bone formation.

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Techniques for the Osteoporotic Spine That Needs Fusion

26

Paul F. Heini

26.1 Introduction

The increasing number of elderly people is a worldwide phenomenon. Degenerative changes are related to age and so is osteoporosis that is present to a certain extent nearly in every elderly patient [1, 2]. In the majority of cases, standard approaches for treating degenerative spine problems are also applicable in the elderly, as long as the degree of osteoporosis is moderate, which means a T-score of the lumbar spine above −1.5. Problems may arise when the surgeon faces deformities and/or segmental instabilities in combination with significant osteoporosis (T-score lower than −1.5). The bone mineral density correlates with the holding power of pedicle screws, as demonstrated in several in vitro and in vivo studies [3]. The individual situation must be assessed for every single screw, as high loads on the bone-implant interface are present until fusion is achieved.

Until recently, such cases appeared exceptional; however, in the near future, such problems will become routine component of spine surgery as an increasing number of elderly people will be seeking a surgical solution for their spine troubles. If a surgical stabilization is performed in the osteoporotic spine, the delicate biomechanical equilibrium might be disturbed, leading to implant loosening and increased risk for fractures of adjacent vertebrae or accelerated adjacent segmental degeneration. This should be taken into consideration when dealing with spine problems in osteoporotic patients. There exists a lack of reliable information regarding complications [4]. However, keeping in mind that the early fracture risk in deformity correction in the elderly is reported by 13 % and by 26 % for junctional kyphosis, we can expect significantly higher numbers in the severely osteoporotic patient [5].

The treatment of vertebral fractures in the osteoporotic spine with cement reinforcement is well established [6], especially in acute fractures with a progressive vertebral body collapse [7, 8]. On the other hand, the widespread use of these techniques is questioned by two randomized controlled studies comparing vertebroplasty with a sham procedure [9, 10]. This note is necessary as the solution for critical osteoporotic situations suggests the use of bone cement in order to enhance stability. A recent survey in Germany reveals that nearly 80 % of German spine surgeons use cemented screw fixation in their daily work [11].

Some surgeons advise the use of long fixation procedures with multiple anchoring points, while others use combined screw and hook constructs for increased holding power [12]. The latter type

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_26

of fixation provides optimal stability at the periphery of a construct. The hook prevents the screw pullout efficiently; in vitro measures demonstrate a significant increase of the stiffness of the screw hook construct by nearly 50 % – the same effect as cement reinforcement [13].

26.2 Unique Considerations

In degenerative problems in the elderly with osteoporosis, the following main topics are discussed and presented:

- Spinal stenosis in relation with an osteoporotic fracture or segmental instability
- Treatment option for degenerative scoliosis
- Adjacent segmental degeneration and junctional kyphosis
- Discoplasty – an alternative for anterior column support

26.3 Spinal Stenosis in the Setting of Osteoporotic Fracture or Segmental Instability

Spinal stenosis is a disorder which incidence is increasing dramatically as the population ages [14, 15]. Oftentimes, the problem remains unnoticed by the osteoporotic patients, as their demands are low. However, a mild compression fracture may turn a silent stenosis into an acute problem with sciatica or even cauda equina-like symptoms. For this situation, surgical treatment is required and consists of decompression and stabilization. The stabilization might be achieved either by cement reinforcement of the fractured vertebra or with instrumentation [16–19]. The decision is based on the general health situation of the patient, as well as the specific local spine situation (deformity, slip, severity of osteoporosis). In these patients a decompression only is usually not appropriate due to its destabilizing effect [18, 20].

The possibility of a decompression in combination with vertebroplasty, kyphoplasty, or stentoplasty might be taken into consideration as long as there is no segmental instability in the presence of competent facet joints in combination with a minor vertebral fracture. Some authors combine such a procedure with an interspinous stabilization procedure [8, 21–24]. Technically, a microsurgical decompression is performed according to the needs in order to clear the spinal canal – then a percutaneous cement augmentation if needed in combination with a kyphoplasty or stentoplasty is performed [8]. A detailed description of the surgical technique for vertebroplasty is available elsewhere [25].

In spinal stenosis with segmental instability, i.e., degenerative slip with or without a fracture, stabilization and fusion are considered.

The application of PMMA to increase the stability of spinal implants has been used for a long time [26–28]. Vertebroplasty offers the option of using the same fixation principles as those for normal bone [29]. To increase the stability of the screws, a standard open or closed vertebroplasty procedure is performed in which the pedicle screws are implanted before the cement has set. This technique allows the use of any standard stabilization system. Alternatively, perforated or fenestrated screws can be placed in a standard fashion and the cement subsequently injected through the screws. The amount of cement per screw varies between 1 and 4 cc. Leakage remains a critical issue and therefore highly viscous cement is a must – the newer cement generations (Vertecem® or Confidence®) have very long working times and provide enough time to perform a safe augmentation and controlled screw placement. The question of whether or not an instrumented vertebra requires augmentation remains obscure. A tool for the intraoperative assessment of bone quality did provide useful information in a pilot study – however, it is not yet widely available [3]. If increasing the implant size (length and/or diameter) appears insufficient to achieve good fixation, the use of cement should be considered [30]. So far, the use of cement seems to not have negative effects, except the increased surgical efforts and the risk of cement injection. Furthermore, an increased fracture risk is related to the length of fixation [4]. If the T-score of the spine is very low, the use of cement-reinforced fixation should be considered. However, the bone density assessed by a standard

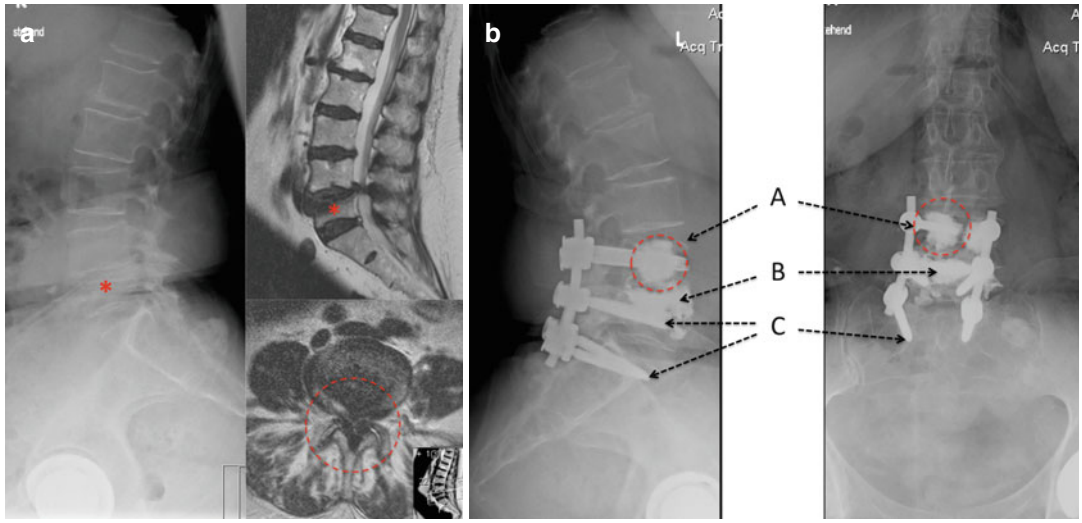


Fig. 26.1 A 84-year-old obese female in good health. Spontaneous fracture of the L5 vertebra occurred with simply sitting. The patient noted acute onset of bilateral leg pain when sitting or standing. (**a**) Standing plain radiographs revealed a mild compression fracture of the L5 (*asterisk*) that was confirmed on MR with evidence of bony edema. Spinal stenosis was present. (**b**) Treatment involved decompression and cemented fixation of the pedicle screws in the L4 vertebral body. 3 cc of cement was administered per screw (*A*). The interbody defect was filled with a discoplasty procedure (*B*). The screws in L5 and S1 demonstrated sufficient purchase and therefore were not cemented. The maximal screw dimensions were chosen in terms of length and diameter (*C*)

DEXA measure per se is not a reliable indicator for cement augmentation, and therefore, clinical experience often supports the benefit of cement usage to decrease implant loosening and improve screw insertional torque [3, 31, 32]. In multilevel fixation procedures, the risk of fracture of the terminal instrumented vertebra is significant. Therefore, even in the "osteopenic" spine, cement reinforcement of the most rostral screws should be considered. Furthermore, there is increasing consensus that protective cement reinforcement/vertebroplasty of the adjacent vertebrae should be considered [4, 33, 34] (Fig. 26.1).

26.4 Degenerative Scoliosis and Loss of Spinal Balance

Aging degenerative deformities are complex situations [35]. With them, postural problems are very common. A central or foraminal stenosis often coexists [36]. Traditional open surgery with long posterior stabilization is related with a major complication risk [37, 38].

Lateral interbody fusion through a transpsoas approach has been shown to be extremely effective in deformity correction by a less invasive technique [39, 40]. In the osteoporotic spine, however, the issues are related to cage subsidence and secondary loss of correction [40, 41]. Prophylactic cement reinforcement can help to overcome this limitation and provide sufficient support for the cages [40]. There is a need for aggressive cement filling. The vertebroplasty procedure can be performed in the same session prior to the lateral correction or as a staged procedure. The latter strategy is the one preferred by the author, especially when multiple vertebrae are to be treated. The intervention is performed under local anesthesia/sedation. In multiple-level cases, two sessions are required, as the amount of cement should not exceed 30 cc in one session due to the risk of fat embolism. The main procedure consists of the scoliosis correction using a mini-open lateral approach. The technique aims to be a stand-alone procedure as long as the rotational deformity remains moderate (Fig. 26.2). Otherwise additional posterior percutaneous

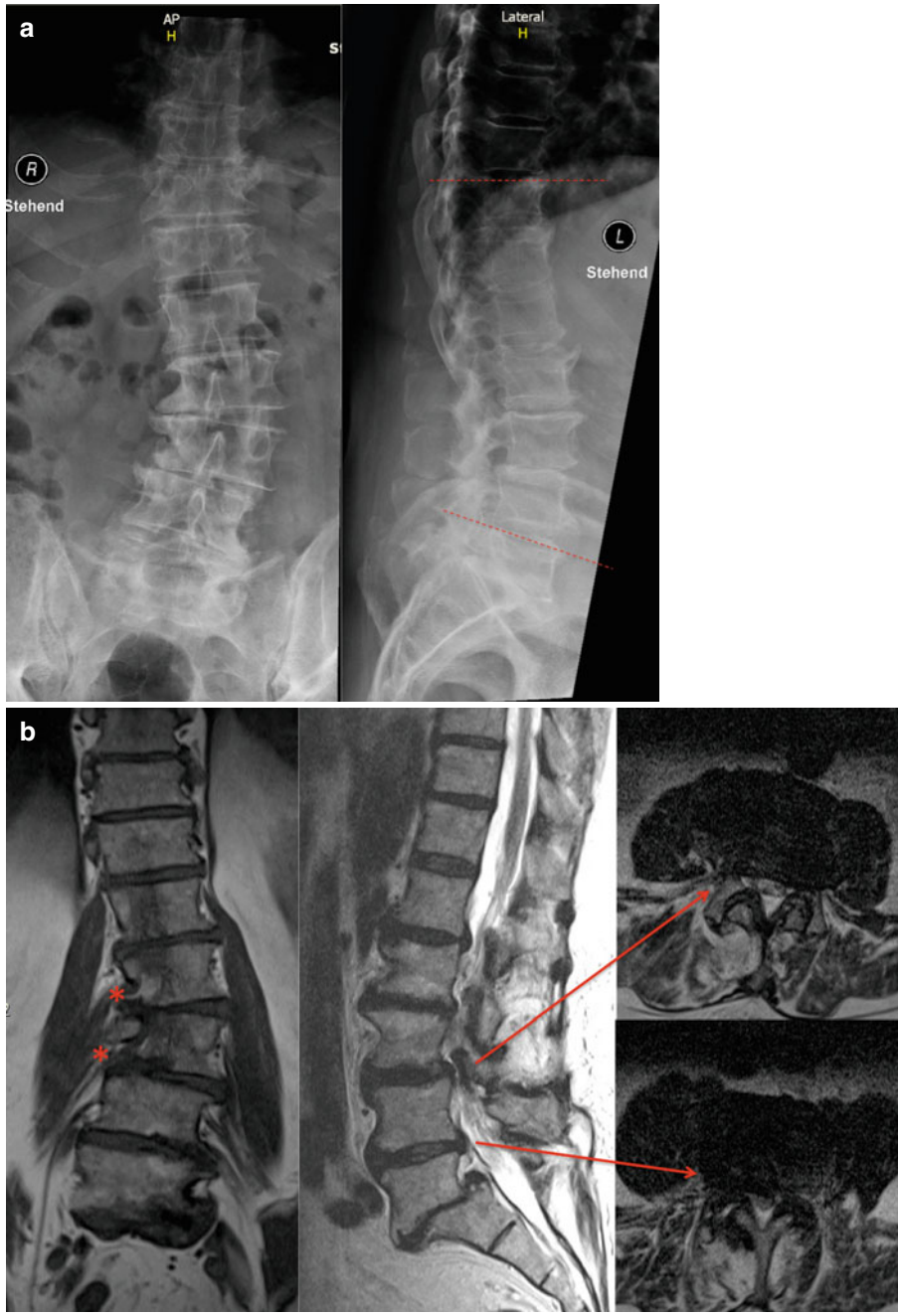
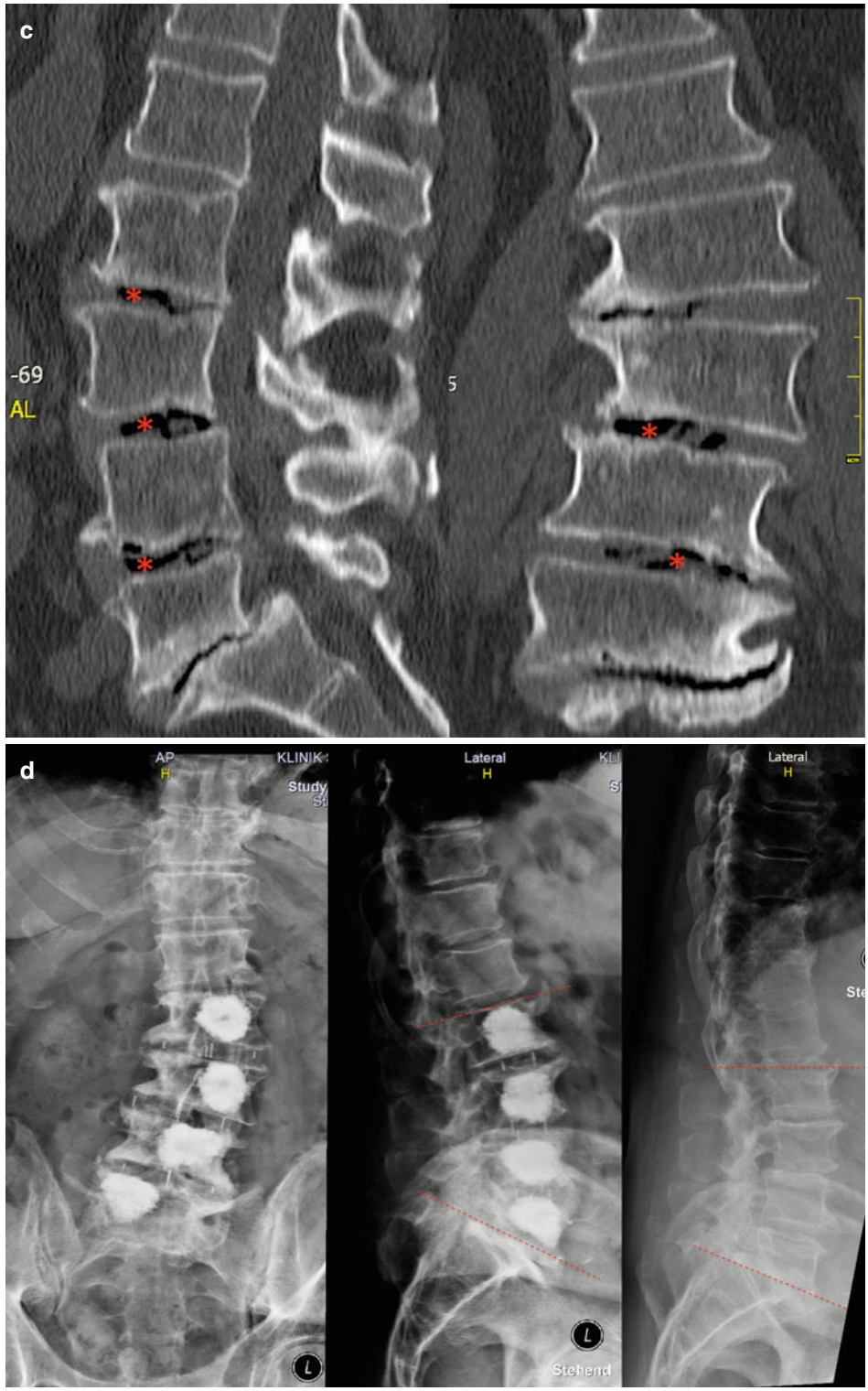


Fig. 26.2 Degenerative scoliosis and spinal stenosis: An 80-year-old patient presented with equal leg and back pain. (**a**) The standing plain radiographs demonstrated loss of lumbar lordosis and a degenerative scoliosis related to shortening of her left leg. (**b**) MRI revealed stenosis at L3–L4 and L4–L5 and a severe foraminal narrowing at L3–L4 and L2–L3 (*asterisk*). (**c**) CT demonstrated a vacuum phenomenon at L2–L3, L3–L4, and L4–L5 (*asterisk*). (**d**) Treatment consisted of a vertebroplasty procedure from L2 to L5 and then a segmental anterior correction via the lateral approach from the right side. Iliac crest bone graft was harvested and enhanced with demineralized bone matrix. X-rays at 2-year follow-up demonstrated a well-restored and well-maintained lumbar lordosis when compared to the preoperative standing films. Fusion was not yet complete at all levels. The patient has had a very satisfactory postoperative course without leg symptoms and only minor back pain, not requesting any medication. The reason for a vertebroplasty in this patient was her general health condition: the presence of obesity, diabetes, and renal disease. A DEXA demonstrated a T-score of −2.0 in the lumbar spine. CT did not reveal any relevant reactive bony sclerosis at the concavity of the deformity (**c**). These factors were taken into consideration in deciding to use cement augmentation



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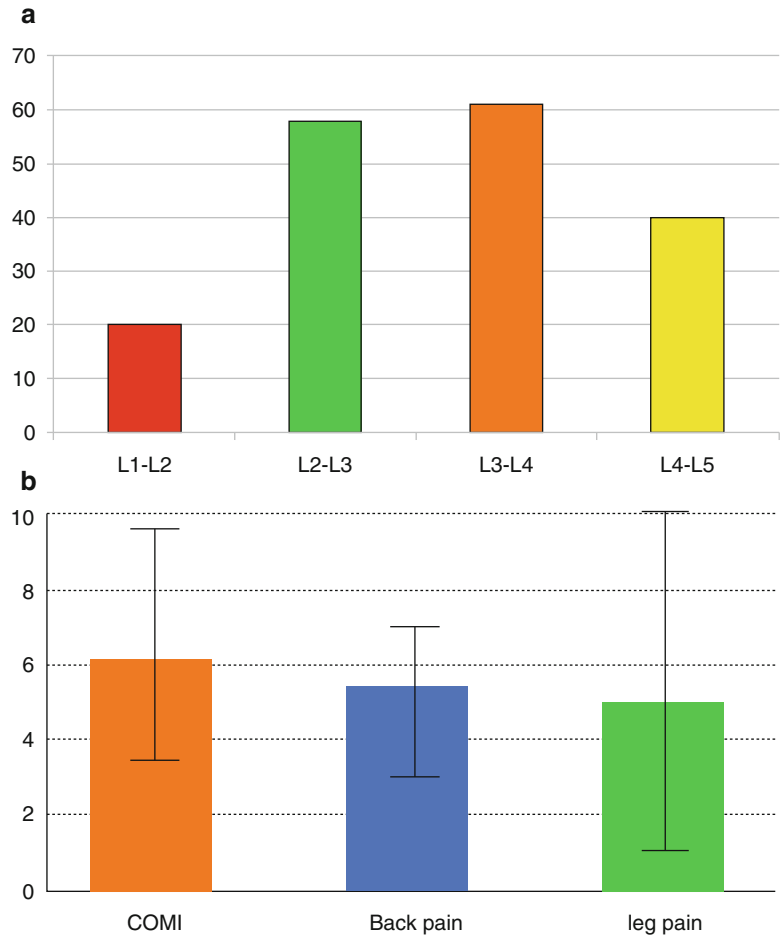

Fig. 26.3 (**a**) Distribution of levels treated for degenerative deformity correction (60 patients, 179 levels). (**b**) Clinical outcome 1 year postoperative. COMI/ individual parameters (mean, min, max). *COMI* core outcome measure index

screw fixation is performed in combination with cement-reinforced screws.

We studied 60 cases operated through a lateral approach for degenerative deformities (scoliosis/ loss of lordosis) in patients with osteoporosis treated with vertebroplasty and segmental correction. Seven patients underwent an additional posterior percutaneous stabilization within the first 3 months after the lateral intervention due to secondary loss of correction. The clinical outcomes were encouraging. However, 60 % of patients did note approach-related discomfort and side effects in the early phase postoperatively which include pain and numbness in the groin and anterior thigh and weakness of the psoas on the side of approach. The use of iliac crest bone graft is of limited value, especially in the osteoporotic patient. Osteoconductive bone substitutes and allograft material also demonstrate unreliable fusion rates with frequent secondary loss of correction. We have found that BMPII works best in these cases for stand-alone interventions, although it must be clear that evidence for its efficacy in this application has not been shown and a myriad of complications are reported in connection with its use in this setting [42]. The distribution of levels and the 1-year clinical outcome are presented in Fig. 26.3.

26.5 Junctional Kyphosis in the Osteoporotic Spine

Posterior deformity correction is associated with a significant potential for complications such as adjacent-level degeneration or vertebral fractures. There is no consensus on how the degree and extent of the instrumentation may affect the risk of junctional failure. Many factors are related to junctional failure. Sagittal balance is not the only critical parameter; sarcopenia plays an important role. Furthermore neurodegenerative disorders, such as Parkinson's disease, have a significant impact [43]. Failure usually occurs during the early postoperative period. It typically involves the adjacent segments, as demonstrated by instability when comparing the standing postoperative X-ray with a CT or an MRI in the supine position. Extension of the construct is often needed, and in the presence of a junctional fracture, the use of cemented screw fixation and protective percutaneous cement augmentation may be required [4, 5]. The use of a "discoplasty procedure" can provide anterior column support and thereby avoid an additional anterior procedure (Fig. 26.4).

26.6 Discoplasty: Anterior Column Support with PMMA

In cases of segmental instability with a collapsed disk space, the disk height restoration can occur just by positioning the patient on the operating table. The same is true for certain fractures with a kyphotic deformity. Interbody spacers (TLIF, PLIF cages) that work effectively in a healthy

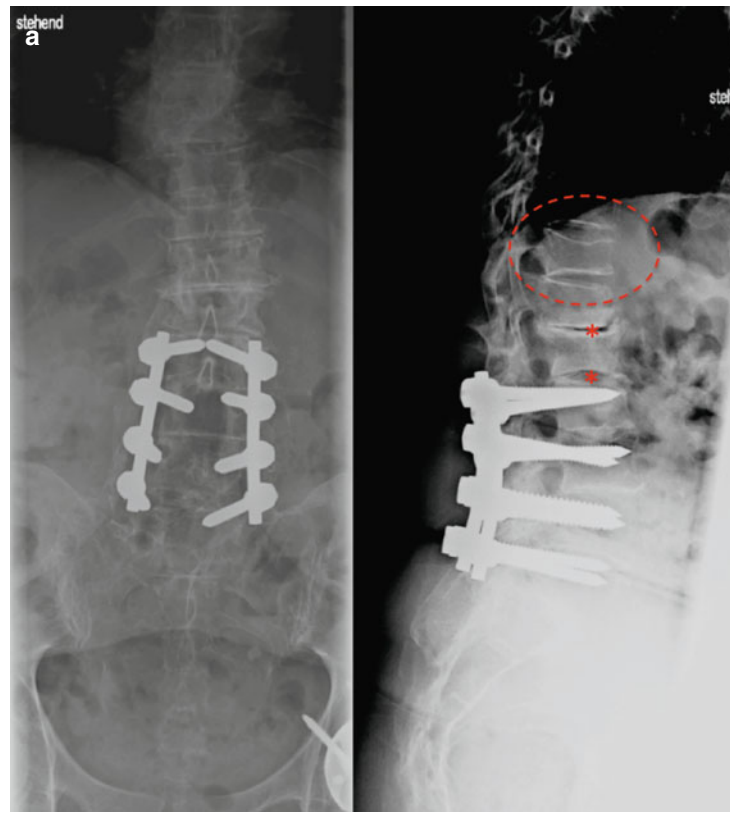

Fig. 26.4 (**a**) 78-year-old female patient presented 5 years after a successful decompression and spinal fusion from L2 to L5 with new leg symptoms due to a severe adjacent-level degeneration. The disk space was collapsed at L1–L2 and T12–L1 (*asterisk*). Furthermore there was a vertebral fracture of T11. (**b**) A decompression and extension of stabilization was performed to T10. The disk spaces at T12–L1 and L1–L2 were treated with cement injection. Early postoperatively (6 months), an adjacent-level fracture occurred that resulted in paraparesis due to cord compression at the T9–T10 level. A revision surgery was performed with decompression and extension of the stabilization to T7 with a protective vertebroplasty of the adjacent levels up to T4. The patient had a stable postoperative course as demonstrated 2 years after her last intervention (**c**)

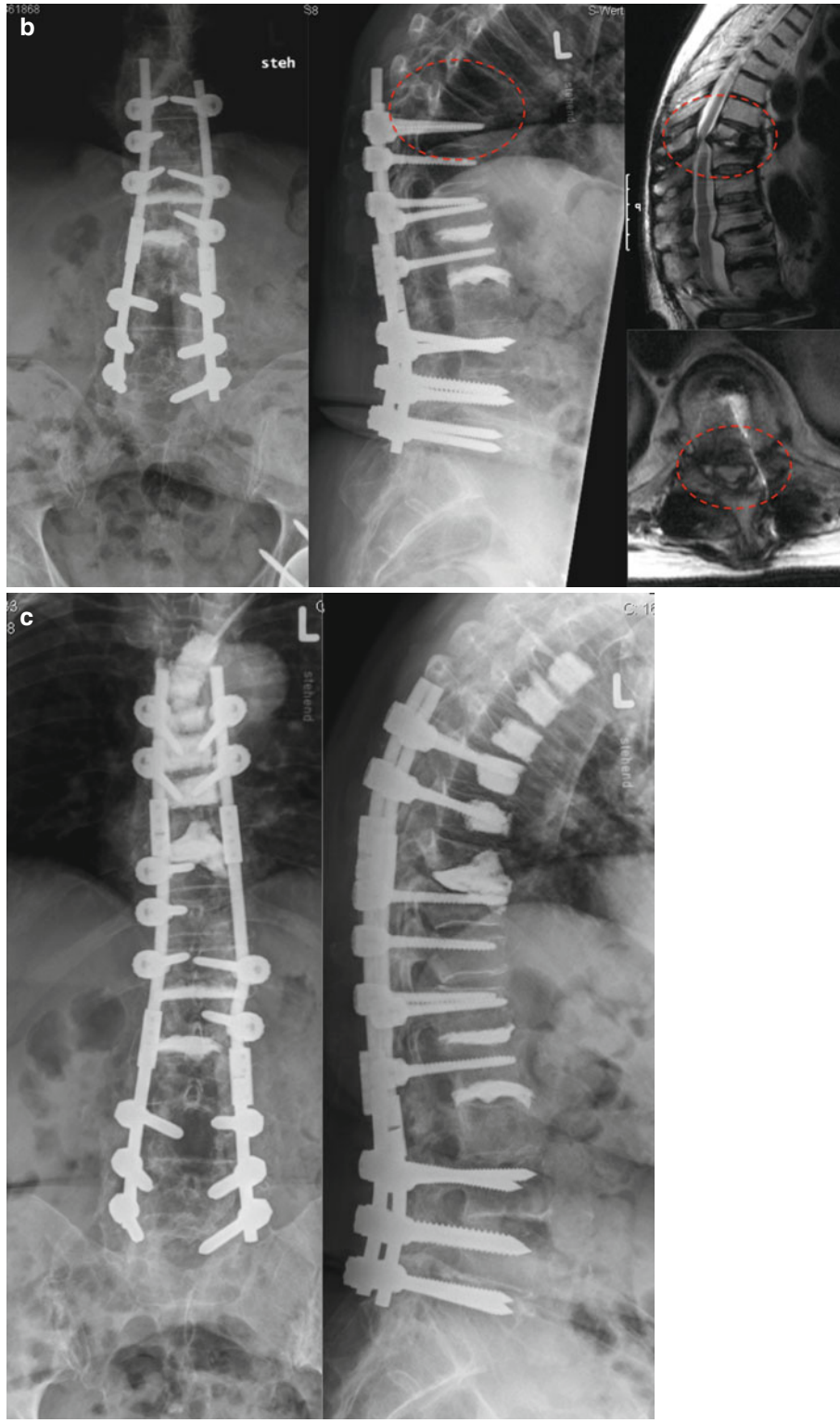

Fig. 26.4 (continued)

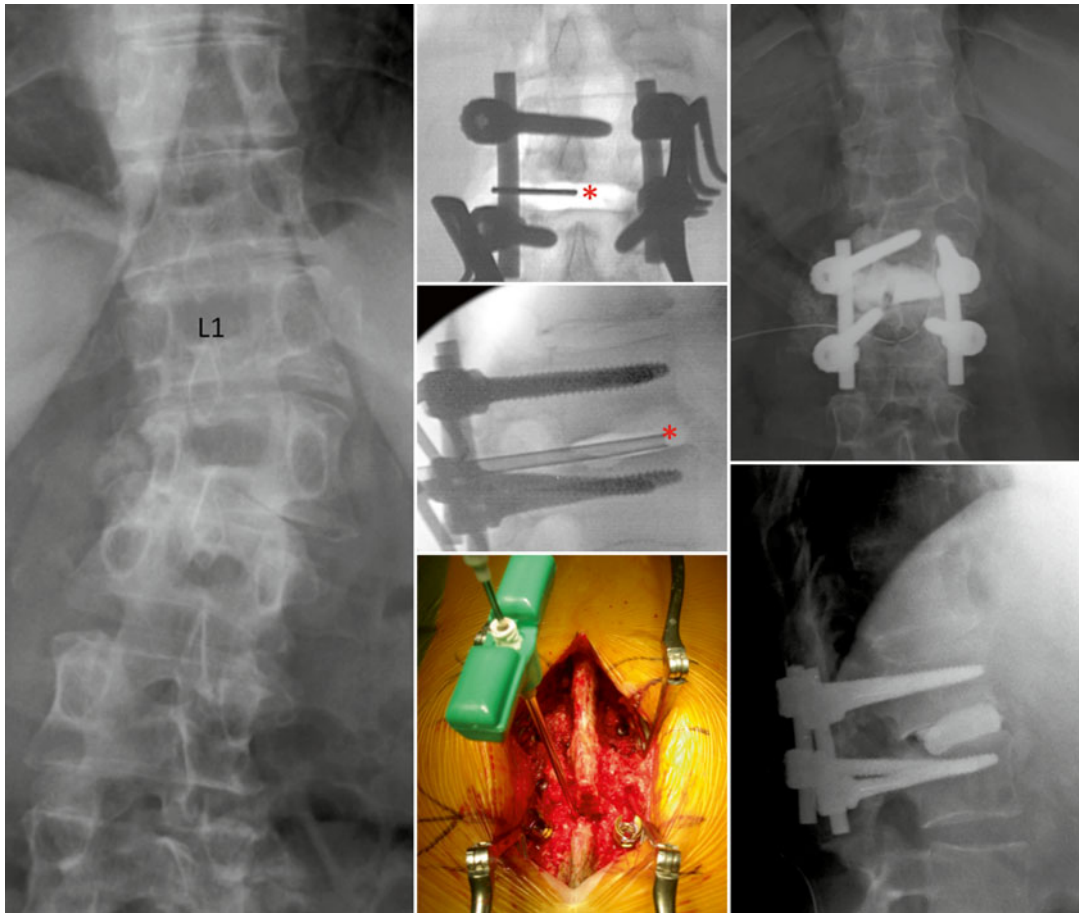

Fig. 26.5 Discoplasty for anterior column support: The segmental collapse of L1–L2 in this patient was related to foraminal root compression. After surgical correction there was an obvious void in the disk space (*asterisk*). A filling cannula was inserted through the canal beside the thecal sac into the disk space and the void was filled with PMMA. An instrumented fusion was performed in addition. The discoplasty procedure provided a custom-made spacer with optimal anterior column support

bone show a very limited supporting surface and are therefore associated with a significant risk of subsidence in the osteoporotic spine [44]. In addition, the surgical procedure must be expanded considerably for disk removal and cage placement. Therefore, the use of a transdiscal cement injection either in an open fashion through the spinal canal or percutaneously via the foramen through Kambin's triangle can provide optimal anterior column support. Discoplasty provides a custom-made spacer with a maximal supporting surface. The technique is effective in cases in which the disk space is empty and collapsed but the segment remains mobile. The annulus must be intact and there exists no need to evacuate the disk space. A filling cannula for vertebroplasty is placed into the disk space and high viscous cement is injected into the disk – the annulus provides a containment that prevents the cement from leaking. The procedure is performed under fluoroscopic control. Additional stabilization and fusion of the motion segment(s) are mandatory (Fig. 26.5).

Conclusion

The increasing number of elderly people represents a huge socioeconomic burden in general and is specifically challenging for the

medical field [45]. For the spine surgeon, the osteoporotic spine represents the most challenging problem [1, 2]. There are certainly well-established treatment modalities for many spine disorders (stenosis, deformity, instability) – but in combination with osteoporosis, common techniques may fail (i.e., a decompression may provoke a secondary vertebral fracture, a vertebral fracture can turn a silent spinal stenosis into an acute sciatica or paresis that need emergent surgery, a segmental stability may promote an adjacent vertebral fracture, and so on) [4, 5]. So far the most efficient means to overcome the mechanical limitations related with the osteoporotic spine is the use of bone cement [29, 46]. PMMA can enhance the anchoring of pedicle screws, and it can protect adjacent vertebrae from a fracture [34]. The use of PMMA is related with specific risks (cement leakage/embolism, fat embolism) that have to be weighed against the possible benefits [25]. Besides the mechanical problems related with the osteoporotic spine, one must consider the general health state of a patient and carefully balance the risks and benefits of a specific treatment individually for each patient [37].

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The Choice of TLIF for Lumbar Interbody Fusion

27

David Straus, Ricardo B.V. Fontes, and Vincent C. Traynelis

27.1 Introduction and Literature Review

The development of posterior approaches for lumbar interbody fusion within the context of degenerative disk disease (DDD) is inherently related to the concept of discogenic pain and its treatment as described by Cloward in 1953 [1]. Lumbar interbody fusion (LIF) had been occasionally utilized since the beginning of the twentieth century for the treatment of spinal tuberculosis and other infectious etiologies – Muller reported on the transperitoneal LIF for tuberculosis as early as 1906 [2]. Its utilization for degenerative conditions, however, was seen as some sort of taboo at that time – most spine surgeons, particularly those with a neurosurgical background, viewed leg pain resulting from direct neural compression and inflammation secondary to a herniated disk fragment as the only degenerative condition worth operating on, one that simple diskectomy could properly address [3]. However, when back pain ensued following a diskectomy procedure, it was still seen as an unfortunate occurrence that should be graciously endured by the patient as an acceptable trade-off for the relief of debilitating leg pain.

In order to address the issue of back pain, non-instrumented, in situ fusions such as described by Hibbs were attempted in conjunction with diskectomy, and the results were not only considered unsatisfactory, but the entire procedure was felt to be unnecessary: Dandy famously stated in 1944 that thorough debridement of the disk space was enough to induce collapse and arthrodesis following diskectomy [4, 5]. Van Wagenen and Dandy may have packed the interspace with autologous bone following diskectomy even before 1953, but Cloward is usually credited as the first to describe posterior LIF in greater detail, along with developing a pathophysiological theory to support it, carefully planning the grafts and designing a series of instruments to assist in nerve root and dural retraction [1, 4]. Cloward reported excellent results, including a perfect fusion rate, supporting this technique so staunchly as to state that it should be performed following every diskectomy [6].

Despite Cloward's praise for the technique he developed, it was slow to gain acceptance. Concerns over nerve root retraction, donor site morbidity, graft protrusion, long hospital stays, and the degree of bed rest and bracing necessary to achieve arthrodesis were important factors [7]. Fusion rate on the other hand was far from the alleged 100 % and collapse due to violation of

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_27

the vertebral body end plate still a frequent occurrence [8]. Most authors advocating non-instrumented PLIF also maintained that integrity of the posterior joints was necessary to avoid instability; therefore, some residual pain could be a result of inadequate decompression [9]. Introduction in 1988 of pedicle-based posterior spine instrumentation in conjunction with LIF enabled a more thorough decompression since reconstruction of a posterior tension band was possible; earlier mobilization after surgery and obviation of postoperative bracing were added benefits [7]. PLIF is now almost universally done with the adjunct of pedicle screw-based instrumentation; addition of intertransverse graft material has been variably employed, with conflicting reports of its efficacy [10]. However, even today, reports claiming fusion rates are similar with non-instrumented LIF are found in the literature [11].

The next important development happened in the 1990s, with the description by Harms of posterior interbody fusion through a so-called transforaminal approach, or TLIF [12, 13]. This approach to the disk is performed through the intervertebral foramen, i.e., a more lateral approach than the Cloward's PLIF, therefore necessitating no manipulation of the thecal sac or roots. Though initially described as an open procedure with unilateral diskectomy and backed up by bilateral pedicle screw instrumentation, a number of modifications have been reported in the 15 years since the original report. These variants include more invasive operations, designed to achieve better fusion rates, e.g., with bilateral access to the disk, and also less invasive variants, including unilateral pedicle screw fixation and the so-called "mini-open" (transmuscular approach with pedicle screw insertion under direct vision) and minimally invasive techniques (only the interbody component is performed through a tubular system, backed up by percutaneous screw placement).

The minimally invasive variants of TLIF have sought to reduce damage to surrounding structures; this has been demonstrated in terms of reduced blood loss during surgery, serum markers of muscle injury, in-hospital narcotic use, length of hospital stay, return to work rates, and late postoperative imaging, for example. Late outcome data, however, is essentially equivalent across all techniques when fusion does take place: these have almost universally helped patients with radiated complaints that can be successfully localized to a vertebral level, of which the perfect example is spondylolisthesis. Less satisfactory results have been obtained with back pain and revision surgery but TLIF can still be an option when nonoperative treatment fails. While there is no high-level data, long-term clinical outcomes from these various TLIF techniques have been consistently similar across a number of studies [14–18]. Blood loss [19], postoperative pain [16], hospital length of stay [19], and muscle damage [20, 21], however, have been shown to be decreased in the mini-open technique as compared to the open technique, generating a possible cost-effectiveness advantage of this procedure over the open TLIF technique [16]. The mini-open technique, however, consistently requires increased radiation exposure to both the patient and surgeon [19]. Though reports have varied, a recent meta-analysis identified nonsignificant trends for increased incidence of graft malposition, nonunion, and reoperation rates with the mini-open technique and nonsignificant trends toward increased incidence of durotomy and infection with the open technique [19]. Overall operative time was similar between the mini-open and open TLIF technique [19], though individual reports have demonstrated significant differences in both directions [20, 22–25], indicating operator familiarity plays an important role in the execution of each technique.

Adjunctive instrumentation is routinely used in current practice. Most commonly, bilateral pedicle screw fixation is utilized to provide internal fixation and posterior tension band reconstruction for LIF procedures. Even though unilateral screw fixation may be sufficient for TLIF, clinical reports have reported conflicting and potentially worse outcomes [26, 27], and there is biomechanical evidence that bilateral pedicle screw fixation most closely approximates the properties of the native lumbar spine, whereas non-instrumented and unilaterally instrumented interbody constructs show increased mobility

especially in lateral bending [26]. Two recent small randomized, controlled trials have revealed significantly less improvement in radiated complaints and more cage migration when compared to bilateral pedicle screw fixation [28, 29]. While various alternative contralateral instrumentation techniques such as facet screws have also been reported [30], there is insufficient outcomes data in the literature to make any further assessment of their role in TLIF.

There is also variation in the type of interbody spacer to use for LIF procedures. Autologous iliac crest graft has been used extensively in spine fusions and has demonstrated a favorable profile, though concerns related to donor-site morbidity [31, 32] have led to the search for additional options. Machined allograft spacers, bioabsorbable spacers, and cages of various compositions including BAK, titanium, PEEK, and ceramic spacers have been employed as interbody grafts [33]. Cage shape does not appear to alter the biomechanical properties of the interbody graft if posterior pedicle screw fixation is employed [34], and the risk of graft subsidence is most related to patient factors, particularly bone mineral density [35].

There is no consensus in the literature regarding the ideal fusion technique for the lumbar spine. Circumferential fusion has several theoretical advantages over posterolateral fusion: according to Wolff's law, a distraction-type/interbody graft has the highest fusion potential; the bone graft in LIF is placed in the load-bearing surfaces of the anterior and middle spinal columns, and the vertebral interspace has significantly better vascularity than the posterolateral space [36]. From the biomechanical standpoint, LIF has the potential to restore interspace height, lumbar lordosis, and coronal and sagittal balance of the lumbar spine, also resulting in foraminal decompression. Posterior approaches for LIF have the added advantages of allowing direct neural element decompression through the same route. However, clinical trials looking mainly at 1- and 2-level fusions have failed to demonstrate a clear advantage of P/TLIF over posterolateral fusion in terms of validated outcome measures. The frequently quoted randomized trial from the Swedish Lumbar Spine Study Group established the superiority of arthrodesis over nonoperative care in patients with chronic low back pain thought to originate from spondylosis. In a sub-analysis of the surgical arm comparing the three different techniques employed in that study (in situ fusion, instrumented posterolateral, and circumferential, of which approximately 25 % were PLIFs), it was found that there was no statistically significant difference in outcome [37]. A follow-up study from the same group comparing posterolateral fusion and PLIF for patients with isthmic spondylolisthesis also failed to demonstrate a difference in outcome [38]. A sub-analysis of the surgical group from the SPORT study has failed to reveal significant differences in the treatment of degenerative spondylolisthesis between non-instrumented in situ fusion, posterolateral fusion with pedicle instrumentation, and posterior interbody fusion in the long term. These results, however, stem from a nonrandomized, non-blinded study design with considerable selection bias, as the authors themselves pointed out [39].

It is uncertain how the utilization of rhBMP-2 will impact this comparison; its off-label use in TLIF has become very popular in the United States [40, 41]. Recent concerns related to unintended complications from rhBMP-2 have been raised and include reports of postoperative radiculitis, heterotopic ossification, and vertebral body osteolysis [42]. Furthermore, the biomechanical advantages of circumferential fusion may become more evident over longer fusions where sagittal balance is a strong consideration, high-grade spondylolisthesis, and/or revision surgery – given its transforaminal nature, the surgeon may be able to completely avoid a prior laminectomy defect to introduce the interbody graft. Given its safety and reliability proven in the 15–20 years of utilization, TLIF is the author's fusion technique of choice for the lower lumbar spine.

27.2 Surgical Indications and Technique

Despite the paucity of clear level 1 evidence to elucidate the precise indications and contraindications for LIF, these techniques have emerged as

core procedures in lumbar spinal surgery and represent commonly employed means of achieving lumbar arthrodesis in a variety of pathological conditions. LIF is often used in the management of both mobile and immobile spondylolistheses [43], degenerative lumbar deformities [44], pseudoarthroses [45], and radiculopathies from recurrent herniated nucleus pulposus [22]. LIF may also be applied to select patients with degenerative disk disease and concordant intractable axial back pain [18, 46]. The primary technical contraindication for LIF is incompetent vertebral bodies or end plates (from trauma, tumor, infection, or osteoporosis) [33]. Contraindications specific to the PLIF technique – given the necessary retraction of the thecal sac and nerve roots to achieve interbody graft placement – include epidural fibrosis, lesions at or above L3 (given the risk of retracting the conus medullaris), and conjoined nerve roots [33].

As discussed above, LIF offers a number of important biomechanical advantages over posterolateral lumbar fusion (PLF), including circumferential fusion, foraminal decompression, and improved environment for arthrodesis. It also provides an important technique for lumbar arthrodesis when alternative techniques are suboptimal. Anterior lumbar interbody fusion (ALIF) offers similar biomechanical advantages of LIF, but circumferential fusion with ALIF requires a staged or "front-back" procedure with increased procedure time and blood loss [47], and approach-related complications including retrograde ejaculation and visceral and vascular injuries detract from this approach [48]. Lateral lumbar interbody fusion (LLIF) provides advantages similar to ALIF but exchanges the risk of sympathetic, visceral, and vascular injury for the risk of lumbar plexus injury and the necessity of disrupting the iliopsoas muscle for exposure [49]. LIF offers an important surgical technique for achieving lumbar arthrodesis offering a distinct risk-benefit profile that has established itself as a mainstay in surgical treatment of degenerative lumbar spinal diseases.

Appropriate preoperative imaging should be available for review in the operating room. In many cases this will include MRI or CT myelogram, standing radiographs with flexion and extension views and noncontrast CT. Close examination should identify sites of radiographic compression and have relevant clinical correlations. Noncontrast CT may provide further data for planning and sizing of pedicle screws. Attention should be paid to identifying transitional lumbosacral vertebral levels, and in such cases extra attention must be given to intraoperative fluoroscopic localization. After induction of general anesthesia, the patient is flipped prone onto an open Jackson table with all pressure points padded. Physiologic alignment is attempted in order to achieve acceptable alignment of the fusion construct. Fluoroscopy is used to confirm alignment and level and to plan the skin incision. The patient is prepped and draped in the standard manner. In our current practice, we have abandoned the medial PLIF technique in favor of a transforaminal approach in order to minimize nerve root retraction. For the conventional open variant of TLIF, a midline incision is made through the epidermis and dermis and superficial hemostasis is obtained. Following radiological confirmation of the correct vertebral level, exposure of lamina, facets, pars interarticularis, and transverse processes is performed while avoiding removal of soft tissue on the facet joints and ligaments outside of the fusion segment, particularly at the rostral level (Fig. 27.1a).

The osseous exposure of the TLIF often requires a complete, unilateral facetectomy; while some surgeons may prefer to leave a medial bridge of the lamina and articular process, we strive to maximize our decompression of the neural elements. This is begun by performing a hemilaminotomy and connecting this to a transverse osteotomy at the level of the pars interarticularis (Fig. 27.1b). The remainder of the superior articular process of the caudal vertebrae is removed to the level of the pedicle (Fig. 27.1c). The ligamentum flavum is resected and the lateral dural edge is exposed; this may be tailored to the degree of central stenosis. This should provide exposure of the axilla of the exiting nerve root; any retraction is rarely needed to access the disk (Fig. 27.1d).

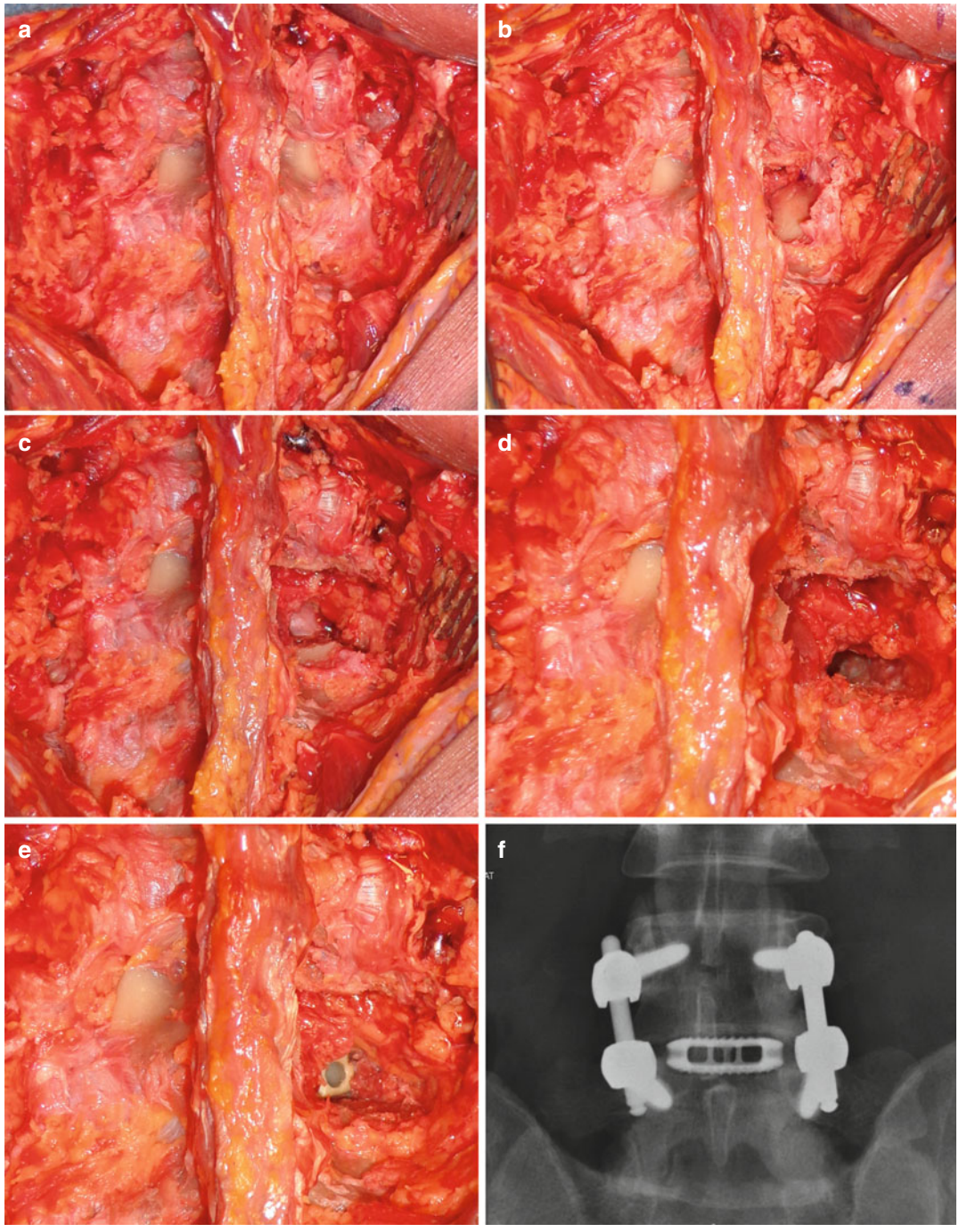

Fig. 27.1 Steps for an open right L4–L5 TLIF. (**a**) Exposure of the lamina and articular and transverse processes. (**b**) Osteotomy at the level of the right L4 pars interarticularis. (**c**) Resection of the right superior L5 articular process exposes the L4 nerve root and the L4–L5 disk. (**d**) Thorough diskectomy is performed without retraction of L4 nerve root. (**e**) Insertion of the cage is performed at a 45° angle and positioned across the midline. (**f**) Postoperative radiograph demonstrates ideal cage position and pedicle instrumentation

Bleeding from the epidural venous plexus is controlled with bipolar cautery and hemostatic agents. The annulus is incised, posterior osteophytes are removed, and a diskectomy is performed using curettes, rongeurs, and disk shavers. The trajectory of the diskectomy and the interbody graft is at a 45° angle to the disk space (as opposed to the directly ventral trajectory of the PLIF interbody graft) in order to achieve a graft placement that crosses the midline of the vertebral body (Fig. 27.1e). The end plates are prepared with a variety of instruments according to surgeon's preference and an interbody graft is placed with fluoroscopic guidance. Interbody graft placement may vary by case: more anteriorly placed grafts provide increased lordosis in cases where deformity correction is prioritized, and more posteriorly positioned grafts provide increased foraminal decompression. Biomechanically, the TLIF interbody graft should cross the midline to avoid inducing a coronal imbalance, cover more than 20 % of the end plate surface [50], and avoid the central region where the end plate is structurally weakest [51]. Uni- or bilateral pedicle screw instrumentation, posterolateral fusion, hemostasis, and wound closure are performed in the usual manner (Fig. 27.1f). Off-label utilization of rhBMP-2 is also utilized by some surgeons in the interspace (inside or outside the allograft) or the posterolateral space, particularly in patients at high risk of pseudarthrosis.

Mini-open and tubular variations of TLIF are also favored by our group. Utilizing fluoroscopy or intraoperative navigation, a paramedian incision is planned 4 cm off the midline. A series of tubular dilators are used to create a transmuscular (Wiltse-type) working channel. Ideal docking position for a TLIF is over the ipsilateral pars interarticularis with an expandable (mini-open variant) or fixed 26 mm working tube. Neural element decompression and preparation of the interspace are performed in the same manner utilizing adapted instruments with a bayoneted shaft so as not to obstruct the field of view. Expandable dilators allow for a working space of 45–50 mm, so single-level pedicle screw instrumentation can then be placed under direct vision; otherwise percutaneous instrumentation is utilized. Given the increased radiation exposure inherent to mini-open TLIF procedures, a further alternative is to replace fluoroscopy with O-arm guidance, thus decreasing radiation exposure [52, 53] and potentially improving accuracy of pedicle screw insertion [54].

27.3 Complications

Fusion rates are comparable between P/TLIF procedures, with both achieving high rates of arthrodesis, upward of 90 % in most reported studies (average-pooled fusion rate of 93.2 %) [55–60]. A recent review described the average published rates of major complications associated with LIF procedures [61], noting a 4.9 % (0–7 %) incidence of neurological injury, a 5.3 % (0–11 %) rate of radiculitis, a 10.6 % (0–35 %) rate of hardware or graft migration, a 7.3 % (2–14 %) incidence of durotomy, and a 3.7 % (0–9 %) incidence of infection. The higher reported rate of neurological complications in PLIF as compared to TLIF has in part heralded the increased utilization of TLIF over PLIF approaches for posterior lumbar interbody fusions [58].

Insertion of the intervertebral cage is the additional step that sets P/TLIF apart from other forms of posterior instrumented fusion and therefore carries the additional risks. Intervertebral graft displacement into the spinal canal was a much-feared complication before the advent of supplementary pedicle screw fixation but now is exceedingly rare; the cage must be snug against the end plates and ideally distract slightly the interspace. This distraction needs to be counterbalanced with the risk of end plate violation and fracture, particularly in osteoporotic patients and more recent self-expanding cages. Distraction in these patients can also be performed on the pedicle screws firmly anchored in cortical bone, less affected by osteoporosis. Other maneuvers such as alternatively distracting the interspace from both sides may also be employed.

The anterior annulus fibrosus should never be violated during the diskectomy and end plate preparation process: extreme care must be taken during this step, particularly with automatic dis-

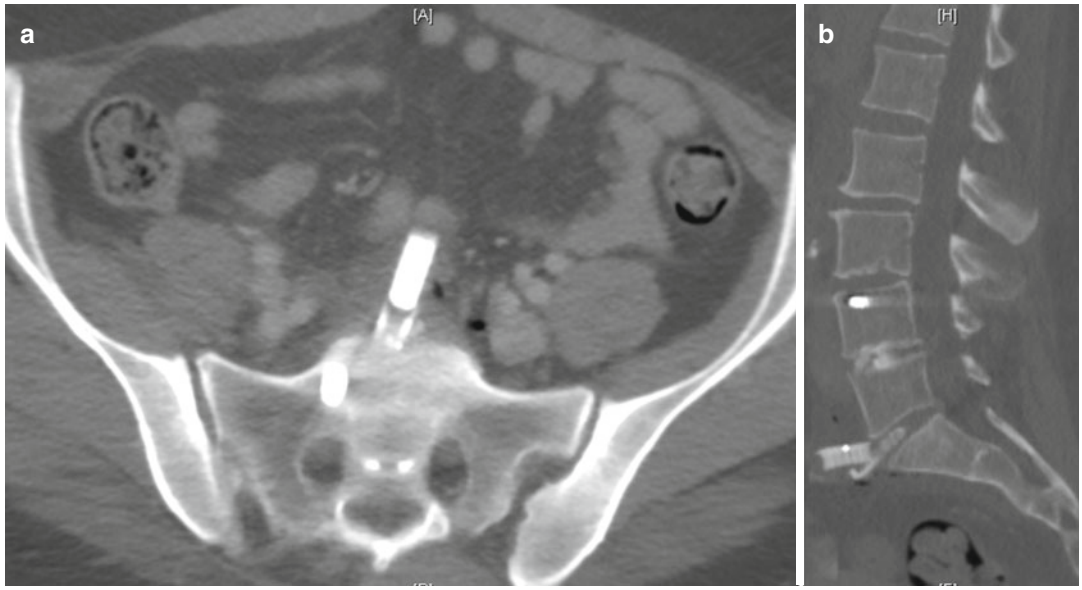

Fig. 27.2 Axial image (**a**) and sagittal reconstruction (**b**) of a CT of the abdomen demonstrating violation of the anterior annulus and intra-abdominal intervertebral implant. This occurred at the L5–S1 level and therefore below the aortic bifurcation; the patient underwent laparotomy and ALIF

kectomy devices and stackable or self-expanding cages. Expulsion of the graft into the abdomen may be catastrophic at L4–L5 or above due to large vessel injury. Immediate general or vascular surgery assistance and emergent laparotomy may be a lifesaving measure in these cases (Fig. 27.2).

As discussed above, variable fusion rates can be found in the literature for posterior LIF; there is no clear advantage of one technique over another. It is our opinion that thorough debridement of the interspace is the biggest determinant of fusion, rather than utilization of one specific posterior LIF variation. Less nerve root retraction is necessary for TLIF, but extreme care should be taken to avoid cautery around the dorsal root ganglion, which may lead to postoperative dysesthesia that may be particularly difficult to treat.

Conclusion

Posterior interbody fusion is a safe and time-tested technique that may lead to excellent stabilization of the motion segment even after a very aggressive neural element decompression. As with any other surgical techniques applied to degenerative spinal disorders, its effectiveness is limited by the ability of the clinician to adequately examine the patient, correlate his or her complaints to radiological findings, and select the appropriate surgical technique.

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Anterior Lumbar Interbody Fusion (ALIF)

28

Seth M. Zeidman and Daniel J. Hoh

Anterior lumbar interbody fusion (ALIF) is a valuable surgical technique for complete disk removal, restoration, and maintenance of intervertebral and foraminal height, improving lumbar lordosis, and immobilization of painful or unstable motion segments. ALIF compared to other posterior-based fusion techniques has the distinct advantage of preserving the posterior supporting elements of the spine including the paraspinal muscles and the posterior bony and ligamentous structures as well as avoiding any direct nerve root manipulation. An anterior approach to the lumbar spine also facilitates a more thorough disk excision and consequently allows for placement of a larger interbody fusion device. While ALIF is a popular technique for lumbar arthrodesis, it is often combined with posterior fixation (anterior/posterior fusion) to provide a more rigid biomechanical construct compared to ALIF alone.

The history and development of ALIF reflect the progression of spinal surgery, as advances in techniques, devices, and fusion adjuncts have driven evolution of ALIF to improve patient outcomes and safety. Over the decades, a variety of operative methods and materials have been developed to facilitate both access to the disk space and achieving arthrodesis. This includes a range of surgical approaches including standard open laparotomy and transperitoneal, retroperitoneal, laparoscopic, and minimally invasive exposures. Various interbody grafts and devices have also been explored to increase the likelihood of fusion including autograft, allograft, synthetics, and osteobiologic agents as well as interbody cage technology designed for restoring intervertebral height, lordosis, and fixation.

To truly understand anterior lumbar interbody fusion is to gain a fundamental understanding of the ongoing quest to improve patient outcomes through a solid bony arthrodesis, with minimized tissue destruction, optimized spinal alignment and biomechanics, and protection of neural elements.

28.1 History

The first reported case of an anterior approach to the lumbar spine was in 1933 by Capener and Burns who described their experience with the transperitoneal approach for the treatment of spondylolisthesis. In 1948, Lane and Moore demonstrated good outcomes with ALIF via a transperitoneal approach with allogeneic bone graft to treat lumbar degenerative disorders. Cloward

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_28

described ALIF in the early 1950s for the treatment of low back pain for degenerative spine conditions; however, this procedure did not gain immediate favor due to fairly high nonunion rates (30–40 %). Prior to the 1950s, most anterior lumbar approaches were extensive transperitoneal exposures, with their indications extended by the application of anterior interbody fusion methods. The Hong Kong procedure as described by Hodgson and Stock in 1956 employed ALIF as a successful modality for treating select cases of spinal tuberculosis. In 1957, Southwick and Robinson introduced the retroperitoneal approach, as an alternative exposure with potentially decreased morbidity. The transperitoneal approach involves incision of both the anterior and posterior peritonea. In contrast, the retroperitoneal approach maintains the integrity of the peritoneum by accessing the spinal column laterally behind the peritoneal sac. As a result, the retroperitoneal approach is associated with less intraoperative and postoperative bowel complications.

Since the 1990s, there has been a resurgence of anterior lumbar surgery. Increased popularity for ALIF has coincided with the advent of new interbody fusion and fixation devices such as threaded or tapered titanium cages and the development of less invasive approaches including endoscopic, laparoscopic, and mini-open techniques.

28.2 Indications

28.2.1 Degenerative Disk Disease

ALIF is most commonly indicated for the treatment of lumbar degenerative disease. The use of ALIF to treat chronic low back pain associated with degenerative disk disease is one of its most frequent indications, yet remains arguably the most controversial. The cause of chronic low back pain is often difficult to determine. Potential etiologies associated with persistent low back pain include degenerative disk disease, spondylolysis, spondylolisthesis, or iatrogenic segmental instability.

The intervertebral disk has been implicated as an etiology of chronic low back pain based on clinical, basic science, and epidemiological research. However, there remains a lack of consensus regarding the appropriate and accurate diagnosis and treatment of intervertebral disk disorders. Radiographic imaging, often with multiple diagnostic studies used in conjunction, is necessary to make an accurate diagnosis. Functional testing such as diagnostic spinal injections or provocative discography may also play a role in identifying the source of pain. Diagnostic injections, including epidural steroids and selective nerve or facet blocks, are commonly used to better identify the pain generator. However, there is little data to support or refute the use of injections as screening tools for lumbar fusion. Provocative discography, which includes disk stimulation and morphological evaluation, is often used to distinguish a painful disk from other potential sources of pain. Despite the extensive literature, controversy continues about the accuracy and therefore utility of provocative discography.

Lumbar discography should be performed by those well experienced with the procedure and in sterile conditions with a double needle technique and fluoroscopic imaging for proper needle placement. Information assessed should include the volume of contrast injected, pattern of dye distribution, and pain response with particular emphasis on locality and similarity to presenting complaints. Frequently, discography is followed by axial computed tomography to further characterize disk morphology and degree of degeneration.

Most of the current literature supports the use of discography in select situations. Indications for discography include, but are not limited to, the following:

(1) Further evaluation of abnormal disks to help assess the extent of degeneration and correlate with the clinical symptoms. Such symptoms may include recurrent pain from a previously operated disk or lateral disk herniation.
(2) Patients with persistent, severe symptoms in whom other diagnostic tests have failed to confirm a suspected disk as the source of pain.
(3) Assessment of patients who have failed to respond to surgical intervention for either painful pseudarthrosis, a symptomatic disk in a posteriorly fused segment, or a possible recurrent disk herniation.

(4) Assessment of disks prior to fusion to determine if the disks within the proposed fusion segment are symptomatic and to determine if disks adjacent to the proposed fusion are asymptomatic.
(5) Assessment of candidates for minimally invasive surgical intervention to confirm a contained disk herniation or to investigate dye distribution pattern before chemonucleolysis or percutaneous procedures.

Despite continued debate regarding the appropriate surgical indications for chronic low back pain, ALIF has become a popular treatment modality for lumbar degenerative diseases, although surgery is generally recommended only when all reasonable conservative measures (pain medications, nerve sheath injections, physical therapies, braces, etc.) have failed. ALIF is particularly well suited for degenerative disk disease. ALIF indirectly decompresses exiting nerve roots by increasing intervertebral height and opening narrowed neural foramina. Further, ALIF immobilizes the motion segment by fusing the vertebra adjacent to the disk space.

28.2.2 Spondylolisthesis

ALIF can also be effective for treating spondylolisthesis or other degenerative or iatrogenic-related instability; however, in these instances, supplemental posterior fixation to reestablish the posterior tension band and for rigid stabilization is frequently necessary. Some may argue that patients with a low-grade (grade I) spondylolysis or spondylolisthesis may be effectively treated with ALIF as an isolated procedure. Present data regarding the effectiveness of stand-alone ALIF in grade II spondylolisthesis is inconclusive. Biomechanical data related to the degree of vertebral translation concomitant with grade III or greater spondylolisthesis suggest that stand-alone ALIF in these settings may be predisposed to a high pseudarthrosis rate [1]. Therefore, in grade III or greater spondylolisthesis, instrumented posterior fusion in addition to ALIF is strongly recommended, whereas a stand-alone ALIF is only a reasonable option in grade I situations.

28.2.3 Failed Spine Surgery

Attempting posterior revision surgery in patients with failed prior posterior surgery can be hazardous. In this clinical scenario, an anterior approach may obviate many of these potential risks and increase likelihood for a successful patient outcome. An anterior approach avoids working through scar tissue and the significant risk of both neural injury and dural violation. Additionally, some patients continue to have pain after posterolateral spinal fusion despite apparently solid arthrodesis [2]. One potential etiology is pain that arises from an abnormal disk within the fused levels. Low back pain that continues or recurs after apparently solid posterolateral spinal fusion may be caused by painful disk(s) at motion segment(s) within the fusion, as a solid posterolateral spinal fusion may not protect residual disks from injury. Anterior interbody fusion can provide significant improvements in pain and function and a high degree of patient satisfaction in this clinical setting.

28.2.4 Other Indications

ALIF frequently plays an important role in the treatment of spinal deformity. Structural interbody support is an effective method for minimizing longitudinal rod and screw–bone interface strain. Moreover, anterior load-bearing structural grafts and interbody devices have been shown to increase construct stiffness, decrease the incidence of posterior implant failure, permit the use of smaller diameter longitudinal rods, and may enhance the rate of successful spinal arthrodesis [1]. Therefore, in clinical situations such as correction of deformity where the spinal implants are subjected to greater biomechanical stress, incorporating ALIF into the surgical construct facilitates correction, provides load sharing, and improves arthrodesis.

An anterior approach for debridement and fusion with autologous bone graft is also an effective surgical modality for treating pyogenic spondylodiscitis. ALIF allows for thorough removal of infected tissue; establishment of viable, normal

bony surfaces; and arthrodesis with generally autologous graft to prevent chronic instability and the development of chronic pain. Recent studies have focused on the safety and use of titanium and synthetic implants as well as osteobiologic agents in the setting of spinal infection.

28.3 Contraindications

ALIF has a broad range of applications and indications for pathologies affecting the lumbar spine, with relatively few contraindications. In general, contraindications to ALIF are limited to approach and bone quality. Patients with preexisting medical conditions or prior surgeries involving the abdomen or retroperitoneal space may have an unacceptably high risk associated with performing an anterior surgical approach. In these instances, the assistance of an experienced vascular, urologic, or general surgeon is recommended to obtain exposure. Alternatively, a strictly posterior-based approach may be entertained in order to completely avoid the attendant risk of performing an anterior surgical procedure in these patients.

Because ALIF relies on the integrity of the adjacent vertebra in compressive loading of the interbody graft, ALIF is contraindicated in patients with severely low bone mineral density. Patients with osteoporosis are at high risk for failure of the vertebral end plates with subsidence of the interbody graft or device into the vertebral body, resulting in instability, deformity, pain, and potential neurologic compromise. In patients with low bone mineral density that require ALIF, supplemental posterior pedicle screw instrumentation is recommended to off-load stress at the implant–endplate interface.

28.4 Techniques

Anterior lumbar approaches provide excellent visualization of the vertebra and the entire disk space for diskectomy, fusion bed preparation, graft placement, and, in certain cases, instrumentation. During the surgical exposure, numerous vascular, visceral, muscular, urogenital, and nervous structural elements are at risk. The anatomic proximity of these structures to the site of decompression, grafting, and instrumentation further increases the chance of injury. Other more distal structures are also at risk with overly aggressive mobilization and retraction. A detailed understanding of the relevant regional anatomy and the potential for iatrogenic injury is critical to minimize morbidity associated with these procedures.

ALIF may be utilized as an isolated procedure or in conjunction with posterior spinal fusion. The method by which ALIF is accomplished depends largely on the surgeon's preference, training, and experience. There are many factors to consider in determining whether to use anterior-only or combined anterior and posterior techniques in the pediatric and adult population. Anterior-only approaches are more likely to apply to younger, healthier patients with normal bone stock and limited pathology. Patients with large deformities, borderline bone stock, and multi-segmental pathologies are more likely to benefit from a combined approach. Minimally invasive techniques – open or laparoscopic – require greater intraoperative attention to detail and preoperative surgical planning.

While overall techniques can be complex and variable, all can be divided into four basic parts:

A. **Preoperative Planning/Templating**: Before surgery, the surgeon refers to various imaging studies to determine what size implant(s) the patient will need. The implants are used to help promote fusion of two vertebrae in the spine.
B. **Approach/Exposure**: A variety of methods can be used to access the anterior lumbar spine. These include laparoscopic, open, mini-open, and balloon-assisted endoscopic retroperitoneal gasless (BERG) techniques.

28.4.1 Laparoscopic/Transperitoneal

Both laparoscopic and transperitoneal techniques are effective ALIF approaches. Both approaches involve surgical exposure that passes through the

abdominal cavity and the peritoneal sac. While the laparoscopic approach does involve using smaller port incisions, compared to a larger single abdominal incision for a transperitoneal approach, the laparoscopic approach does not demonstrate a definitive advantage particularly at the L5–S1 level.

With the transperitoneal approach, the surgeon makes a skin incision; dissects through the subcutaneous tissue, fascia, and muscles; and incises the anterior abdominal peritoneum to enter the abdominal cavity. Retraction of the abdominal viscera is performed, and the surgeon incises the posterior peritoneum to expose the great vessels (aortic artery, vena cava vein, and common iliac arteries and veins) and anterior aspect of the spine.

In the 1960s, Harmon reported the advantage of avoiding damage to the nerve roots with an anterior approach. He also described decreased blood transfusion, reduced hospital stay, elimination of pain, and high fusion rates. Zdeblick and David [3] reported their experience with 50 patients undergoing either laparoscopic transperitoneal or open retroperitoneal approaches. They found a significantly higher incidence of complications in the laparoscopic group (4 % vs. 20 %) and a tendency for decreased exposure resulting in limited fusions. Because of the increased incidence of retrograde ejaculation, and the increased operating room time, they ultimately abandoned the transperitoneal insufflation technique and the retroperitoneal gasless video-assisted technique. They found that with either the mini-open laparotomy approach or the traditional flank open approach, there was a lower incidence of retrograde ejaculation, decreased blood loss, shorter operating time, decreased cost, as well as the ability to use standard instruments.

28.4.2 BERG Technique

Balloon-assisted endoscopic retroperitoneal gasless (BERG) techniques for anterior lumbar interbody fusion have also been described. The retroperitoneal space is accessed similarly to the technique of total extraperitoneal laparoscopic hernia repairs, via a balloon spacer and carbon dioxide insufflation. Also termed lumboscopy, this technique has the advantage of being performed minimally invasively and does not require violation of the peritoneum. A recent experience with 46 patients reported complications in 3 patients (7 %), requiring hardware removal in 1 patient [4].

Gazzeri et al. [5] analyzed their series of a simplified endoscopic approach to the anterior spine and made a review of the retroperitoneal endoscopically assisted approach to the anterior lumbar spine in the international literature. They determined that the BERG technique is a safe, effective, simplified, less technically demanding alternative approach when performing ALIF procedures, without the morbidity associated with laparoscopic or traditional approaches.

28.4.3 Mini-Open

The mini-open retroperitoneal approach possesses a number of theoretical advantages; however, the individual surgeon's preference ultimately is likely to be the dictating factor in selecting this operative approach. Surgical exposure is created by bluntly dissecting behind the abdominal cavity. In this approach, the peritoneal sac is mobilized and retracted laterally. The peritoneum is dissected away from the great vessels, and the anterior spine is exposed without entering the peritoneal cavity.

The open retroperitoneal exposure for anterior spine surgery is technically challenging yet ultimately rewarding. The distinct advantage of accessing the entire disk anteriorly as opposed to limited disk access posteriorly, as well as the emergence of lumbar total disk arthroplasty, has resulted in a rise in popularity for the mini-open approach.

With a mini-open retroperitoneal approach, the superior hypogastric plexus is mobilized, with the peritoneum sweeping the small neural plexus from left to right, thus protecting it from surgical trauma. This is a distinct advantage compared to the transperitoneal approach in which the surgical dissection occurs directly over the

superior hypogastric plexus, increasing the likelihood of damage.

C. **Diskectomy and Disk Space Preparation**: After exposure of the disk space and the adjacent vertebral end plates has been obtained, the surgeon begins the diskectomy. Complete diskectomy is performed while maintaining integrity of the bony end plates. Release of the posterior annulus is not necessary; however, in certain instances, it may be beneficial. Preserving the bony end plates is critical for preventing subsidence of the bone graft and/or interbody device into the adjacent end plates. Careful but gentle scraping with a rasp exposes bleeding subchondral bone without appreciably compromising endplate integrity. Once this step is complete, the graft or device to be implanted is sized and selected to maximize fit and fill within the interspace.
D. **Instrumentation/Devices**: After appropriate preparation of the disk space, a graft or interbody device is inserted to promote fusion of the two adjacent vertebrae. Fusion adjuncts or osteobiologic agents are often supplemented to facilitate bony arthrodesis.

28.4.4 Femoral Ring Allograft (FRA)

Femoral ring allograft (FRA) is ideal for ALIF due to its osteoconductivity and large load-bearing surface which provides some immediate stability. Also, FRA eventually is resorbed and replaced by host bone via reverse creeping substitution. In contrast to bone used for posterolateral onlay fusion, FRA in ALIF is placed under compressive forces which according to Wolff's law increases the likelihood of successful arthrodesis. However, the use of stand-alone FRA without spinal fixation demonstrates a particularly high pseudarthrosis rate, suggesting that complete immobilization of the motion segment and graft may be necessary for optimal fusion.

FRA, which is primarily a cortical allograft, undergoes the same incorporation process as cancellous autograft but at a slower rate because of its compact nature. High bone density limits angiogenesis, and incorporation can only occur following osteoclast invasion. Initially, this process leads to a mechanically weaker construct because bone resorption proceeds more rapidly than new bone formation. This process is known as "reverse creeping substitution" in contrast to what is experienced by cancellous grafts. If the graft is subjected to excessive strain, microcracks may develop, and, if revascularization is not adequate, clinically significant fractures may develop before reverse creeping substitution produces a successful fusion. The structural support can decrease by as much as 40–50 % of the initial strength at 6 months after implantation. Allograft bone also tends to cause resorption of the patient's own bone (osteolysis) at the graft/vertebral endplate interface early in the postoperative course and can actually lead to instability.

28.4.5 Threaded Cortical Bone Dowels (TCBD)

Allograft threaded cortical bone dowels (TCBD) were briefly popular in the mid-1990s as an interbody graft option. However, the incidence of technical failures and complications related to bone dowels exceeded 17 % in one series and resulted in a high rate of poor outcomes in patients when used as a stand-alone ALIF device [6]. It should be noted however that the incidence of clinical failures with the use of TCBDs was decreased when supplemented with anterior or posterior spinal fixation [7] or when combined with the osteoinductive growth factor, recombinant human bone morphogenetic protein-2 (rhBMP-2) [8].

Burkus et al. [8] randomized 131 patients with lumbar spondylosis undergoing single-level ALIF with TCBD to receive either rhBMP-2 or autologous bone graft. At 12 months, all patients treated with TCBD and rhBMP-2 demonstrated radiographic evidence of new bone formation and incorporation of the allograft into the adjacent vertebral end plates. Conversely, only 89 % of patients treated with TCBD and autograft had evidence of fusion at 1 year, with a decrease in fusion rate to 81.5 % at 24 months. Given the 100 % fusion rate with the addition of rhBMP-2, they concluded that TCBD can be used for stand-alone ALIF when combined with this particular

osteoinductive agent. Because the bone dowels are threaded, they further suggested that TCBD may function to stabilize the bone–implant interface, resisting motion and risk of expulsion.

28.4.6 Threaded Titanium Cylindrical Cages

Threaded titanium cylindrical cages are interbody fusion devices that also provide some degree of fixation without requiring harvest of large structural autograft with a broad load-bearing surface. These devices are implanted in the interspace after reaming a screw path through the subchondral bone of the vertebra adjacent to the disk space. Threaded titanium cages do not truly fixate adjacent vertebral bodies like pedicle screw–rod-based systems; however, they do provide interference fixation. Ultimately, ligamentous annular tension due to interspace distraction combined with loading forces maintains the construct until bony fusion occurs.

There is data to suggest, however, that ligamentous annular tensioning rapidly decreases within 15 min due to stress relaxation of the soft tissues. The underlying biologic property of creep intrinsic to annular tissue allows for gradual relaxation of annular tension and loss of construct stability. It also stands to reason that the magnitude of preload across the disk space and cage due to body weight and muscle activity varies with daily activities in the absence of supplemental posterior spinal fixation. Therefore, until complete bony arthrodesis occurs, stand-alone ALIF with threaded titanium cages does not completely immobilize the motion segment. Because of the suboptimal biomechanics of stand-alone ALIF with threaded cages, this construct design is generally limited to collapsed disk spaces where there is maximal annular tensioning and at L5–S1 where there is minimal motion. Stand-alone ALIF with threaded titanium cages is not recommended for multi-level fusions or at higher lumbar segments.

Another limitation of threaded titanium cages is that bone must be removed from the subchondral end plates in order to create a screw tract for the cage. Particularly in larger disk spaces, more bone must be reamed, thereby weakening the integrity of the adjacent vertebral end plates and increasing the risk of subsidence. Increased subsidence has been observed particularly at the L4–L5 level compared to L5–S1 when using threaded cages for ALIF [9]. Subsidence is also associated with increased reaming depth and with larger cage sizes [9]. Lower risk of subsidence is seen with single-level dual-standard cage constructs.

Sasso et al. [10] prospectively studied fusion rate after stand-alone ALIF at L4–L5 or L5–S1 with either FRA or titanium threaded cages. Both interbody devices were packed with autogenous iliac crest bone graft. At 12 months, 97 % of patients treated with titanium threaded cages demonstrated radiographic fusion compared to only 40 % of patients with FRA. At 24 months, 97 % of the titanium cage group continued to show evidence of fusion, while only 52 % of the FRA group was fused. While back disability index and neurologic scores did not significantly differ between groups, the titanium cage group did have a significantly higher fusion rate and had fewer secondary supplemental fixation procedures compared to the FRA group.

One frequent criticism of titanium cages is that the extent and quality of new bone growth, incorporation, and fusion is difficult to assess on plain x-ray due to the radiopaque metal composition of the cage. Polyether ether ketone (PEEK) is radiolucent, and similar cylindrical threaded cages have been designed with this material. Postoperative assessment of new bone growth after ALIF with PEEK cages is better visualized through the interbody device. PEEK cages however do not adhere to the bony end plates as well as titanium cages, resulting in decreased pull out force, and therefore are rarely used as stand-alone devices [11]. The advent of three-dimensional computed tomography reconstruction, however, has facilitated radiographic evaluation of fusion even with titanium-based interbody cages.

28.4.7 Threaded Lordotic Cages

Tapered or lordotic threaded cages were developed in order to better maintain or restore lumbar lordosis (Fig. 28.1a, b). Maintaining lordosis at

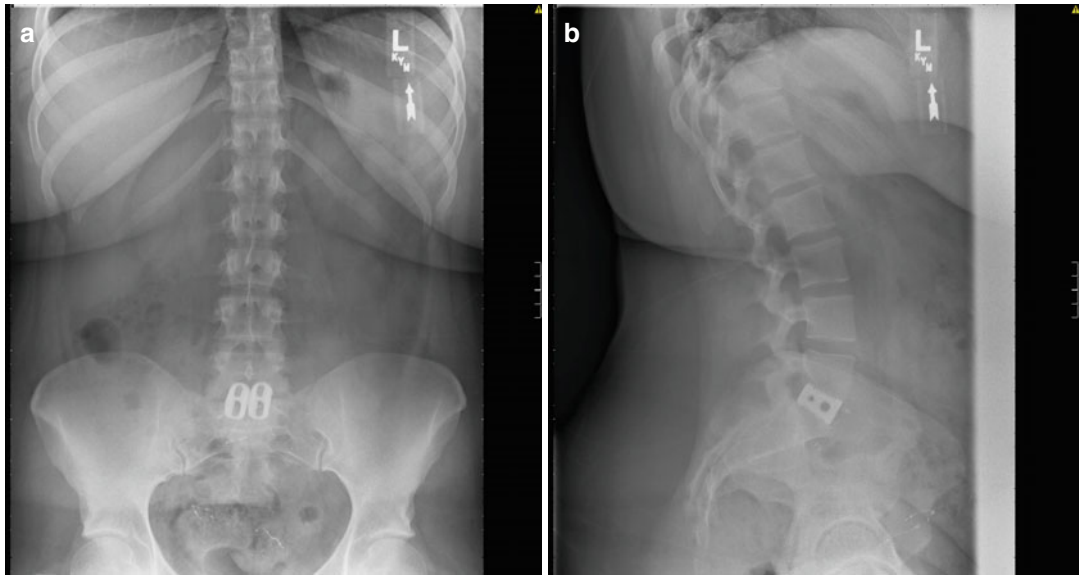

Fig. 28.1 Posteroanterior (**a**) and lateral (**b**) radiographs demonstrating L5–S1 anterior lumbar interbody fusion with titanium lordotic cage

the fused segment is critical. Loss of lordosis, even at a single level, can affect the mechanics of adjacent segments and overall spinal alignment. Further, excessive disk space distraction with a parallel cage can distract facet joints at the same level resulting in loss of segmental stiffness or hypermobility in extension.

A retrospective study of patients undergoing stand-alone ALIF for degenerative disk disease was performed to determine if different aspects of disk space preparation and cage design affect clinical outcome [12]. The investigators observed that endplate preservation during disk space preparation was associated with improved anterior and posterior disk space distraction. They also found that use of a lordotic or tapered cage led to greater restoration of segmental lordosis than a standard cylindrical cage. These benefits associated with endplate preservation and use of a lordotic cage resulted in improved clinical outcomes as early as 3 months postoperatively and were maintained over a 2-year follow-up period.

Segmental lumbar lordosis can be achieved with parallel cylindrical cages through asymmetric reaming of the vertebral end plates. By removing more of the posterior aspect of the disk space, the adjacent vertebra rotates sagittally about their respective internal axis of rotation to settle on the cylindrical cage, creating segmental lordosis. Over-reaming of the posterior aspect of the disk however inhibits interbody distraction and thereby decreases restoration of foraminal height.

28.4.8 Posterior Spinal Fixation: Pedicle Screw and Translaminar Screw Constructs

The use of stand-alone interbody devices for ALIF has been met with mixed clinical success. As a result, many supplement ALIF with posterior spinal fixation with or without posterior intertransverse fusion (360° or circumferential fusion) to increase stabilization, enhance arthrodesis, and ideally improve clinical outcomes (Fig. 28.2a, b). The use of supplementary posterior fixation has been demonstrated to improve stabilization in multiple directions and increase fusion. Holte et al. [13] found that FRA combined with posterior spinal instrumentation resulted in a 98 %

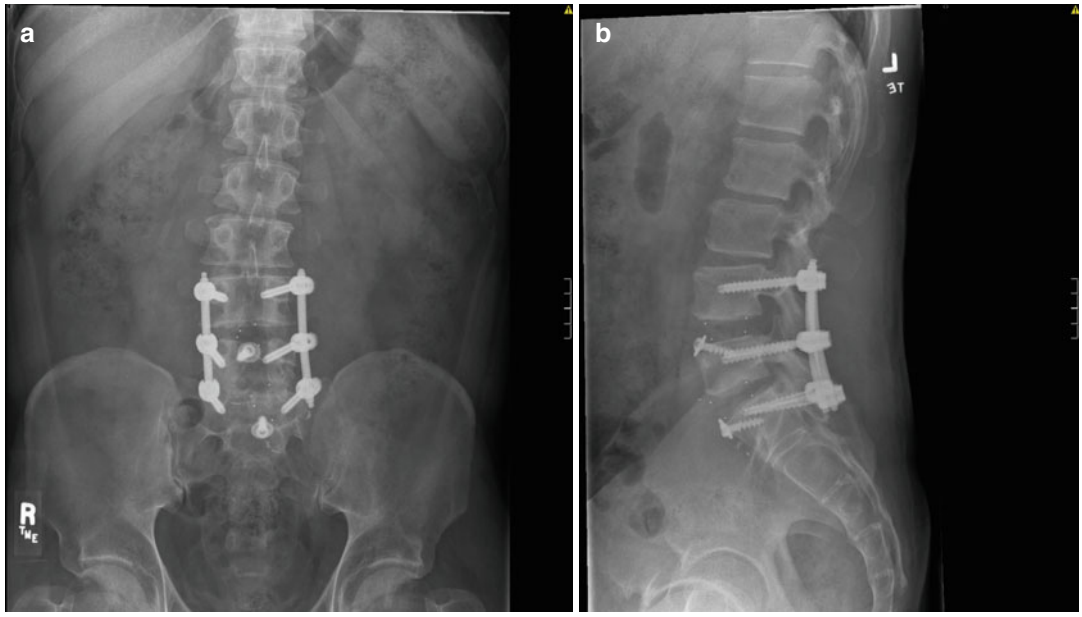

Fig. 28.2 Posteroanterior (**a**) and lateral (**b**) radiographs demonstrating L4–5, L5–S1 anterior lumbar interbody fusion with femoral ring allograft and supplemental posterior transpedicular fixation

fusion rate compared to a 75 % fusion rate with stand-alone FRA. A recent study using thin-section computed tomography revealed an 89 % fusion rate with pedicle screw–rod fixation compared to a 51 % fusion rate with stand-alone ALIF [14].

Transpedicular fixation with a pedicle screw–rod construct remains the biomechanical gold standard for internal stabilization. Pedicle screws when affixed to a connecting rod have the unique capacity for three-dimensional control with restriction of motion in all planes. Conventional open pedicle screw placement, however, adds considerably to the morbidity of the surgical procedure. Besides a separate posterior incision, extensive muscle dissection and retraction is necessary to visualize the appropriate anatomic landmarks for pedicle screw placement. This can result in increased tissue injury, blood loss, operative time, postoperative pain, recovery period, and potential for nerve root or facet injury.

Alternative less invasive options for posterior spinal fixation exist. Translaminar facet screws are placed either via a mini-open technique or percutaneously over a guide wire, thereby reducing operative morbidity. A study investigated fusion rates for patients undergoing either stand-alone ALIF or ALIF with either translaminar, unilateral pedicle, or bilateral pedicle screw constructs. Thin-section computed tomography was used to assess for radiographic evidence of fusion. Patients undergoing unilateral or bilateral pedicle screws had higher fusion rates (89 % and 88 %, respectively) compared to translaminar screw (58 %) fixation or stand-alone ALIF (51 %) [14]. Alternatively, Best and Sasso [15] found that translaminar screws were associated with decreased pain scores, fewer complications, and decreased incidence of reoperation compared to pedicle screws. Recently, percutaneous transpedicular screw fixation has been developed that allows for percutaneous placement of cannulated pedicle screws over a guide wire. Novel instrumentation has been designed to allow for percutaneous insertion of a connecting rod. The long-term benefit of percutaneous pedicle screws compared to conventional open pedicle screws in terms of stabilization, enhancing fusion, and operative morbidity, however, remains to be determined.

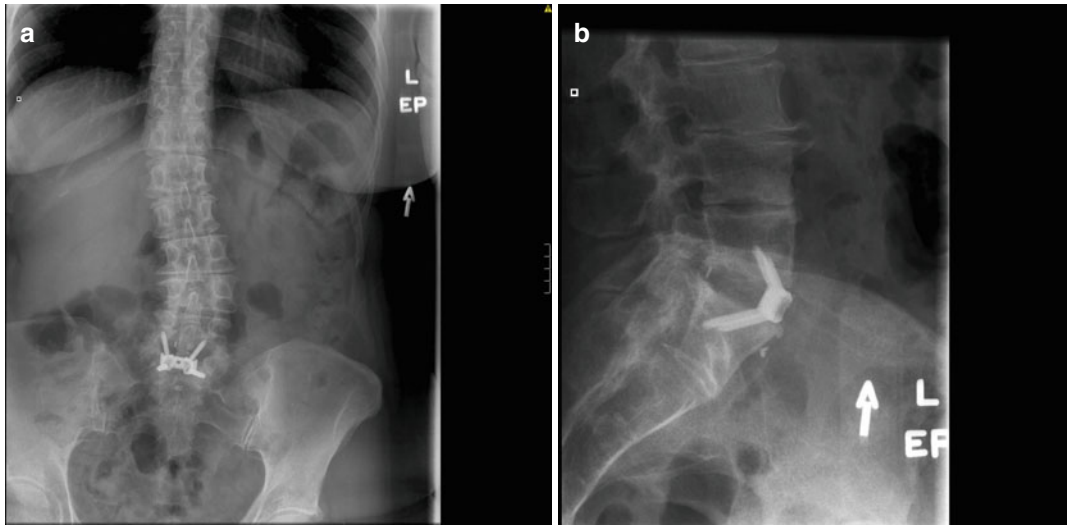

Fig. 28.3 Posteroanterior (**a**) and lateral (**b**) radiographs demonstrating L5–S1 anterior lumbar interbody fusion with a composite cage–screw device

28.4.9 Anterior Spinal Fixation: Anterior Lumbar Plate and Composite Device

In 1959, Humphries et al. first reported the use of an anterior lumbar plate to stabilize the motion segment after ALIF. Until recently, anterior lumbar plate fixation, however, did not gain popularity due to several factors. The primary concern was that obtaining access for application of the implant was limited due to surrounding vascular, gastrointestinal, and urologic structures. Implants that provided sufficient stability were often too bulky or cumbersome. Additionally, problems with device migration and screw backout plagued many of the early iterations of such instrumentation. Recently, however, lower profile anterior lumbar screws and plates have been designed which achieve better screw–bone purchase by fixating the cortical bone of the apophyseal ring. More recently composite devices which incorporate anterior screws through an interbody cage allow for an even lower profile design, effectively eliminating the offset of the anterior plate as well as providing direct fixation of the cage to the adjacent vertebral bodies. As a result, the use of anterior lumbar fixation combined with ALIF has increased in popularity, largely due to the benefit of a single anterior approach technique.

Anterior plate fixation with an interbody device improves construct stiffness and reduces range of motion compared to a stand-alone interbody construct. Glazer et al. [16] found that in human lumbar cadaveric spines, anterolateral instrumentation enhances stability of a femoral ring allograft. Similarly, Kuzhupilly et al. [17] reported significant improvement of the stability of FRA in extension when anterior crossed screws were inserted through the FRA into the adjacent vertebral bodies. Gerber et al. [18] found that a triangular anterior plate is equivalent to pedicle screw–rod fixation in limiting flexion, extension, axial rotation, and shear forces. However, pedicle screw–rod fixation remains superior to anterior plate fixation in restricting lateral bending [19]. It should be noted that in this study, specimens were tested after diskectomy and bilateral facetectomy, which may not represent the most common clinical scenario in which these devices may be employed. Recent data suggests that a composite device consisting of anterior lumbar screws that thread through an interbody cage into the adjacent vertebral bodies provides equivalent stabilization to an anterior cage with pedicle screw fixation and equivalent if not greater stabilization than ALIF with translaminar facet screws (Fig. 28.3a, b).

28.5 Graft Material

Autogenous bone remains the gold standard for graft material. Autograft combines the essential properties of osteogenicity, osteoinductivity, and osteoconductivity necessary for successful arthrodesis. In addition, autograft can be harvested to include cortical bone for structural support in load sharing. In the past, structural iliac crest bone graft was harvested for ALIF. This technique, however, is associated with a high complication rate including chronic pain, blood loss, infection, and pelvic fracture. Further, iliac crest bone graft has limited load-sharing capacity given the available size of the graft and therefore is susceptible to fracture, particularly without supplemental posterior fixation. Alternatively, autologous cancellous bone marrow can be harvested and packed into FRA or cages to combine the optimal biomechanical support of these interbody devices with the enhanced fusion potential of autologous bone.

Alternative strategies for harvesting autologous bone for ALIF have been explored. One technique involves obtaining a core of local bone from the adjacent vertebral body for autograft and replacing the void with a beta-calcium triphosphate plug [20]. This method has been evaluated both in animal and clinical studies and has been demonstrated to be effective. Harvesting a cylinder of autograft from the adjacent vertebral body is an efficient and less morbid technique than iliac crest bone graft. However, when using this technique with posterior pedicle screw stabilization, careful planning with regard to the site of bone removal and screw trajectory must be made to ensure optimal screw fixation without violating the defect.

Allograft in the form of FRA is a commonly used graft material for ALIF. FRA is particularly attractive as it provides a broad load-sharing surface, is readily available, and avoids the morbidity of harvesting autologous bone. FRA is primarily an osteoconductive graft and lacks any osteoinductive or osteogenic potential. As a result, stand-alone ALIF with FRA results in low fusion rates. Therefore, FRA for ALIF generally requires either rigid immobilization with spinal fixation and/or the addition of fusion adjuncts with osteogenicity or osteoinductivity to promote arthrodesis.

The discovery of bone morphogenetic proteins (BMP) and the subsequent ability to use recombinant human gene technology to produce synthetic BMP have revolutionized ALIF. BMPs are a group of osteoinductive proteins that form part of the TGF-β superfamily. Several different types of BMPs have been identified and have been implicated in bone and cartilage formation as well as angiogenesis. BMPs appear to operate by binding to mesenchymal stem cell receptors, initiating a complex cascade of events that leads to cell differentiation and proliferation, promoting in vivo bone formation. Among bone morphogenetic proteins, BMP-2 and BMP-7 have been the subject of considerable attention as particularly powerful osteoinductive agents.

Commercial manufacturing of recombinant human BMP-2 (rhBMP-2) as InFuse (Medtronic, Memphis, TN, USA) has been most widely studied as an osteobiologic adjunct for fusion. A Food and Drug Administration (FDA) study was performed to assess the safety and efficacy of rhBMP-2 in a tapered interbody cage for ALIF [21, 22]. The investigators found that rhBMP-2 is safe and could effectively replace autogenous bone graft for ALIF, thereby avoiding donor site complications. Not unexpectedly, recent clinical trials have been performed to demonstrate equivalency of rhBMP-2 to autologous iliac crest bone graft in both anterior and posterolateral lumbar fusions.

It should be noted, however, that BMP-2 does not only increase bone formation but appears to upregulate bone resorption as well. This is likely due to BMP-2 stimulation of both osteoblast and osteoclast differentiation from progenitor cells. This characteristic is clinically relevant as the use of rhBMP-2 with FRA in stand-alone ALIF has been demonstrated to result in increased graft fracture and nonunion compared to FRA packed with autologous iliac crest bone marrow [23]. Likely, rhBMP-2-induced osteoclast activity resulted in advanced resorption of the femoral ring allograft as well as erosion of the adjacent vertebral end plates leading to graft fracture,

subsidence, and nonunion. Therefore, posterior pedicle screw fixation is generally recommended when using rhBMP-2 combined with FRA to maintain stability during the upregulated osteoclast phase until new bone formation occurs.

28.6 Complications

Complications associated with ALIF can be divided into those related to the surgical exposure and those that occur with diskectomy, graft insertion, and hardware placement. Most intraoperative complications of concern during ALIF are associated with the surgical approach, because with appropriate exposure, potential problems with diskectomy, graft insertion and hardware placement are generally minimized. In fact, one of the main advantages of the ALIF approach is that effective anterior exposure facilitates disk removal, endplate preparation, insertion of a biomechanically optimal graft or device, and placement of anterior fixation if necessary, while protecting the neural elements and surrounding dura.

The list of critical structures at risk in the abdomen and retroperitoneum during surgical exposure for ALIF is lengthy. These include the psoas muscle, small intestine, colon, rectum, bladder, kidneys, ureters, diaphragm and crura, medial arcuate ligament, esophageal hiatus, thoracic duct, lumbosacral plexus, greater splanchnic nerves, phrenic nerves, sympathetic chain, superior and inferior hypogastric plexus, aorta, vena cava, segmental and radicular arteries, common iliac vessels, iliolumbar veins, and medial sacral artery.

28.6.1 Vascular Injury

The major risk of ALIF with perhaps the most critical consequence is injury to a great vessel. Depending on the vertebral level, ALIF is associated with risk of injury to the iliac arteries and veins. Vascular injury with anterior exposure is a potentially life-threatening complication as rapid excessive blood loss can occur with a large tear or avulsion of a vessel. Rate of vascular injury after anterior lumbar exposure is reported to be 1–15 %. Venous injury is particularly difficult as these vessels are not easily repaired, even by an experienced vascular surgeon. The incidence of venous injury in primary anterior surgery for lumbar disorders has been reported from 0 to 25 %, depending on case series, approach, and degree of venous injury recorded.

In a review of 345 anterior lumbar procedures performed on 338 patients, the incidence of a major vascular complication was 2.9 % [24]. There were nine injuries involving the common iliac vein and one aortic injury. Current or previous osteomyelitis or discogenic infection, previous anterior spinal surgery, spondylolisthesis, osteophyte formation, transitional lumbosacral vertebra, and anterior migration of the interbody device are associated with increased risk of vascular complication as these lead to scarring and adherence of vessels. Proper identification with gentle blunt dissection of these vessels from the peritoneum and the anterior spine minimizes the risk of vascular injury. Liberal use of topical hemostatic agents can help control minor bleeding from small vessel injuries while preserving vascular patency. Radicular vessels that are sacrificed require proper suture or clip ligation as these vessels tend to retract when cut and may lead to bleeding that is difficult to control otherwise. In some cases where the vessels cannot be safely mobilized or when bleeding is difficult to manage, the spinal procedure may need to be aborted and a posterior approach taken once the patient is medically stable.

A vascular structure that is uniquely troublesome during ALIF and deserves special mention is the iliolumbar vein. The iliolumbar vein is commonly, but inconsistently, seen as a vessel branching directly off the vena cava or the left iliac vein. When originating from the vena cava, it is technically termed the L5 vein, whereas it is designated the iliolumbar vein when it arises from the left iliac. After its origin, the iliolumbar vein courses directly lateral to join with the highly variable ascending lumbar vein complex. This ascending venous system, which drains blood from the extraspinal venous plexi, is

located on the lateral aspect of the vertebral body at the level of the neural foramen. The iliolumbar vein is frequently tethered and is at risk for being avulsed during dissection of the neurovascular and soft tissues structures of the anterior lumbar spine. Complete iliolumbar vein disruption can result in copious bleeding that cannot be controlled with direct pressure or topical hemostatic agents. Furthermore, the use of excessive cautery in this region carries an unacceptable risk of hypogastric plexus injury. Therefore, special attention is necessary when identifying the iliolumbar vein during exposure and prior to vena cava or iliac vein mobilization. When the iliolumbar vein is identified, it is recommended to suture ligate and divide it, thereby effectively eliminating risk of avulsion or laceration.

28.6.2 Retrograde Ejaculation

In 1965, the first description of retrograde ejaculation as a consequence of anterior lumbar surgery was reported. Since then, the true incidence of retrograde ejaculation has been debated with the reported incidence ranging from 0.42 to 22 %. Many have argued that postoperative retrograde ejaculation is frequently under reported contributing to a lack of consensus as to its actual incidence. Retrograde ejaculation occurs in males as a potential complication unique to anterior lumbar exposure to the L5–S1 disk space. Retrograde ejaculation is believed to be due to damage to the superior hypogastric plexus of the sympathetic system located ventral to the L5 and S1 vertebral bodies. This plexus is formed by contributions from the paramedian lumbar sympathetic chains with bilateral damage causing ejaculatory disturbances. Small nerves directly over the interspace control a valve mechanism that causes semen to be expelled with sympathetic activity during sexual intercourse. Dissection over the disk space may injure the nerves, thereby disabling coordinated innervation of the valve. As a result, ejaculate travels into the bladder rather than out the urethra. While many patients describe that the sensation of ejaculation is unchanged, in order to reproduce, special harvesting techniques must be utilized or preoperative banking of sperm is necessary. While the incidence of retrograde ejaculation is still unclear, complete or partial resolution appears to occur in approximately one-third of patients over 1–2 years.

Several factors may increase the risk for postoperative retrograde ejaculation. Surgeon inexperience, use of monopolar cautery, and laparoscopic or transperitoneal approach have been associated with increased risk [25, 26]. In a study of 215 laparoscopic ALIF performed with a threaded titanium cylindrical cage, a 5.1 % incidence of retrograde ejaculation was observed [27]. In a similar study of laparoscopic ALIF with threaded bone dowels or titanium cages, 15.9 % of male patients developed retrograde ejaculation [28]. Regarding transperitoneal versus retroperitoneal approach, in a survey of 20 surgeons with 15–20 years experience and a total of 4,500 anterior lumbar fusions, researchers found that incidence of retrograde ejaculation was not related to approach [29]. The authors suggested that careful surgical technique, proper visualization of the nerves prior to mobilization off the disk space, and avoiding electrocautery in the area are more relevant towards decreasing the risk of retrograde ejaculation. Additional recommendations include that incision of the posterior peritoneal plane along the right side of the aorta and right common iliac artery is helpful as the left-sided sympathetic nerves are commonly dominant. Subsequent mobilization of this flap with the plexus from right to left has been associated with decreased incidence of inadvertent injury to the hypogastric plexus. Injection of saline solution into the dorsal peritoneal tissue to gently develop the plane is also a useful technique for elevating the peritoneum from the nerves.

28.6.3 Ilioinguinal/Iliohypogastric Injury

Injury to the ilioinguinal and the lateral branch of the iliohypogastric nerves can occur as they course over the iliac crest, although this complication has rarely been reported after exposure for

ALIF. Patients with ilioinguinal or iliohypogastric injury present with numbness or paresthesias affecting the medial upper thigh. Of reported cases of ilioinguinal or iliohypogastric injury after ALIF, most had complete resolution of symptoms within 6 months.

28.6.4 Sympathetic Plexus Injury

The lumbar sympathetic chain courses along the lateral aspect of the vertebral body and is at risk for injury with anterior lumbar exposure. Characteristically, patients with sympathetic chain injury complain of a cold foot on the side contralateral to the approach. This paradoxical effect is due to loss of sympathetic tone with increased vasodilation in the foot ipsilateral to the approach, providing the sensation that the contralateral foot is cold. Regardless, patients who report decreased temperature in either limb after anterior lumbar surgery necessitate evaluation of distal pulses for the possibility of arterial compromise. Ultimately, sympathetic nerve injury can be an unavoidable surgery-related complication after anterior-based approaches. Fortunately, for most patients there are no significant long-term sequelae, although a minority may suffer from prolonged dysesthesias.

28.6.5 Lymphocele

Postsurgical lymphoceles can occur at sites of surgical disruption of lymphatic circulation. While postsurgical lymphocele is a common complication of thoracic, pelvic, or groin surgery, they rarely occur after abdominal exposures for spine surgery, despite an extensive lymphatic network surrounding the abdominal aorta. Particular concern for lymphatic disruption, however, may be at the L5–S1 level where there may be greater risk of lymphatic violation around the iliac arteries and veins. The uncommon experience of lymphocele after abdominal approaches may be secondary to reabsorption of extravasated lymphatic fluid by the large surface area of the peritoneal cavity during transperitoneal exposure. By contrast, during a retroperitoneal approach where the peritoneal sac is maintained, lymphatic fluid may become sequestered in the retroperitoneal space. When postsurgical lymphocele is suspected with a retroperitoneal fluid collection, the differential diagnosis includes abscess, ureteral injury, pancreatic injury with pseudocyst formation, and CSF leak with pseudomeningocele [30]. Of note, in the rare instances of reported postsurgical lymphocele, they frequently were undetected at the time of the primary surgical procedure.

28.6.6 Revision Anterior Lumbar Surgery

With the increase in popularity of anterior lumbar surgery, there has consequently been a rise in anterior revision procedures. While complications associated with revision anterior surgery have been described, the incidence of complications for revision procedures is unclear. After prior surgery, scar tissue and adhesions to vascular and visceral structures pose risk for inadvertent injury during repeat surgery. The risks associated with anterior revision surgery and interbody device removal are suspected to be three to five times higher than for the initial surgery [31, 32]. Particularly, complication rates are higher for revision surgery at a previously operated level, compared to revision surgery at an adjacent or higher level.

28.6.7 Adjacent Segment Degeneration

A primary complication of any spinal fusion procedure is pseudarthrosis. Fusion rates for ALIF are generally high with many reporting 90–95 % arthrodesis, with better success for single-level procedures and nonsmokers. High fusion rates after ALIF are not surprising given that ALIF facilitates effective endplate preparation, allows for placement of a large interbody graft, and loads the graft in compression which further increases bone healing. Nonunion is more likely

to occur in smokers, patients with failed prior surgery, multi-level fusions, and patients who have been previously treated with radiation. It is also important to note that radiographic evidence of fusion is not necessarily required for successful clinical outcome, as a stable, fibrous nonunion may also sufficiently provide enough stiffness to alleviate symptoms.

A potentially more relevant concern after ALIF is the development of adjacent segment degeneration at levels above or below a successful fusion. Biomechanical studies have demonstrated that intradiscal pressures are abnormally elevated at levels adjacent to a simulated fusion in cadaveric specimens. Animal studies have shown that increased facet loading and facet motion occurs at levels adjacent to a motion segment that has been rigidly fixated. Increased pressure or asymmetric and localized stresses within the disk can affect changes in the proteoglycans and ultimately result in increased risk of disk degeneration and prolapse.

Interestingly, adjacent segment changes may be more likely to occur after an anterior lumbar fusion compared to a posterior fusion. Cadaveric spines fixated with screws and wires in an experimental model of anterior lumbar fusion demonstrated increased motion at the superior adjacent segment. Using methyl methacrylate to simulate anterior and posterior fusion, Esses et al. showed that anterior fusion resulted in greater increase in motion at adjacent levels than posterior fusion and was similar to the effect seen with a simulated circumferential fusion.

One issue that remains to be elucidated is the effect of parallel versus lordotic cages on the development of adjacent segment degeneration. Fixation of a lumbar motion segment in increasing degrees of kyphosis is known to increase posterior column loading and laminar strain at the superior adjacent level. Kyphotic malalignment of a fused segment causes compensatory hyperlordosis at the rostral segment which in turn leads to contractures of the posterior ligamentous complex at that level. Alternatively, placement of a tapered or lordotic cage may similarly result in compensatory mechanisms at the adjacent levels. In an animal model of ALIF with paired tapered cages, a significant increase in intervertebral motion and intradiscal pressure was observed at the adjacent segments with flexion loading suggesting an attempt to compensate for the lordosis created at the fused segment [33].

Conclusion

Anterior lumbar interbody fusion is an important staple in the armamentarium of spine surgeons. The benefits of an anterior lumbar approach include broad exposure of the disk space allowing for thorough diskectomy, effective endplate preparation, appropriate sizing and placement of an optimal interbody graft, and anterior fixation if necessary. ALIF also has the advantage of protecting the neural elements and surrounding dura and, as a result, is a particularly attractive option in patients with prior posterior surgery. With the placement of broad interbody grafts or devices under compressive loads, ALIF imparts high fusion rates and provides an extremely rigid construct when supplemented with posterior spinal fixation. Therefore, ALIF is a potentially useful complement to fusion constructs that are under large biomechanical stresses such as in deformity surgery or complex reconstructive procedures. While there are potentially significant risks associated with an anterior approach, a variety of techniques are available and may be adopted by appropriately trained spine surgeons or performed with the assistance of experienced vascular, urologic, or general surgeons. Ultimately, decision to perform ALIF as opposed to other spinal fusion techniques is dictated by the patient's underlying pathology, anatomy, and associated medical comorbidities paired with the surgeon's preference, education, experience, and overall expertise.

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Interbody Fusion Through the Transpsoas Approach

29

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29.1 Introduction

Spinal fusion has been used extensively in the management of various lumbar spine pathologies such as tumors, spinal instability, deformity, and stenosis. There has been a tremendous advancement in minimally invasive spine surgery (MISS) techniques that can help avoid the morbidity of traditional open anterior or posterior surgery while achieving the same clinical and functional outcome. The advantages of minimally invasive surgery including less tissue trauma during the surgical approach, less postoperative pain, shorter hospital stays, and faster return to activities of daily living have been very appealing for both patients and surgeons alike [1]. The transpsoas approach for lateral lumbar interbody fusion (XLIF (extreme lateral interbody fusion): NuVasive, Inc., San Diego, CA ARIA: Stryker, Inc., Kalamazoo, MI, COUGAR: Depuy Spine, Inc., Raynham, MA Ravine: K2M, Inc., Leesburg, VA DLIF (direct lateral interbody fusion): Medtronic, Inc., Minneapolis, MN Transcontinental: Globus Medical Inc., Audubon, PA) was developed as an alternative to the traditional anterior approach [2]. This minimally invasive technique can be used to gain access to the lumbar spine via a lateral approach that passes through the retroperitoneal fat and psoas major muscle (Fig. 29.1). It provides a less invasive access to the anterior and lateral aspect of the lumbar spine while minimizing potential complications such as postoperative ileus, bowel and vascular injury, and retrograde ejaculation associated with the traditional anterior approach. Moreover, this approach can be accomplished without the need of access surgeons. In addition, the preservation of the anterior longitudinal ligament and posterior tension band offers additional stability compared to traditional anterior or posterior approaches.

The minimally invasive transpsoas approach to the lumbar spine was first described by Pimenta et al. [3] and Bergey et al. [4] using the endoscope in 2001 and 2004, respectively, and possibly evolved from the initial endoscopic minimally invasive laparoscopic procedures described by McAfee and Fedder in the 1990s [5, 6]. It was subsequently described by Ozgur et al. [2] using the microscope and expandable tubular retractors in 2006 for lumbar interbody fusion. Over the recent years, the transpsoas approach has gained tremendous popularity, and its application has been broadened from diskectomy and interbody fusion to treatment of vertebral fractures, tumors, and spinal deformities [7].

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_29

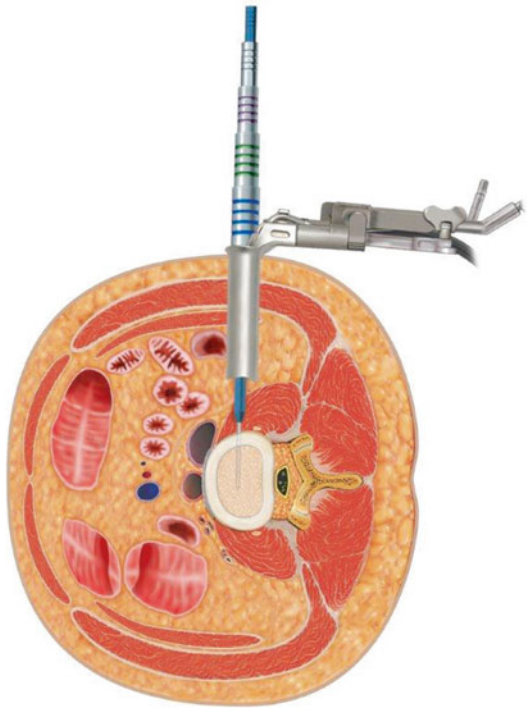

Fig. 29.1 Illustration demonstrating the trajectory of transpsoas approach (Image reproduced with permission from Medtronic, Inc: Medtronic Sofamor Danek; 2004. This spinal system incorporates technology developed by Gary K. Michelson, MD)

29.2 Indications

The transpsoas approach provides a relatively easy and safe surgical corridor to the anterior and lateral aspect of the vertebral column and disk space without the need for retraction of the peritoneum or mobilization of the great vessels. The lateral corridor provided allows the spine surgeon to place a relatively large graft more anteriorly, thereby facilitating the restoration of disk height and lumbar lordosis while proving good axial support. Indirect foraminal decompression and unbuckling of posterior longitudinal ligament can be achieved through restoration of disk height. Additional stabilization can be provided using lateral plate or percutaneous posterior instrumentation (Fig. 29.2). A recent biomechanical study by Fogel et al. [8] found that the laterally inserted cage alone can provide significant reduced range of motion in flexion-extension; additional stabilization with lateral plate, posterior spinous process plate, or bilateral pedicle screws can provide additional stability in lateral bending and axial rotation, but the exact type of fixation used did not make a statistically significant difference in stability. The original indication for lateral interbody fusion delineated by Ozgur et al. was for patients with low back pain associated with degenerative disk disease but without severe central canal stenosis. Subsequently, the transpsoas approach was increasingly performed for degenerative disk disease or adjacent segment disease where interbody fusion is desired, most commonly from L1 to L5 [9–12]. With the increased familiarity with the transpsoas approach and advancement in spinal instrumentation technology such as expandable cages, the application of the lateral approach has been broadened to include treatment of vertebral fractures, tumors, and spinal deformities [7]. Transpsoas approach has also been used for lumbar disk replacement with favorable results [13]. Table 29.1 summarizes the indications suitable for the transpsoas approach. Relative contraindications to this technique may include vascular abnormalities precluding access, significant spondylolisthesis, previous retroperitoneal surgery, and severely collapsed disk spaces.

29.3 Anatomy

The anatomical structures relevant to the transpsoas approach include the external and internal oblique muscles, transversus abdominis muscle, transversalis fascia, retroperitoneal fat, quadratus lumborum, psoas muscle, and the lumbar plexus [12]. A thorough understanding of local anatomy is essential for optimal surgical outcome and complication avoidance. The external oblique, internal oblique, and transversalis muscles are three layers of muscle that form the lateral abdominal wall. The transversalis fascia is immediately deep to the transversus abdominis muscle, covering the retroperitoneal fat. The retroperitoneal fat has a characteristic yellow appearance that serves as a helpful indicator of the presence of retroperitoneal space. In the retroperitoneal

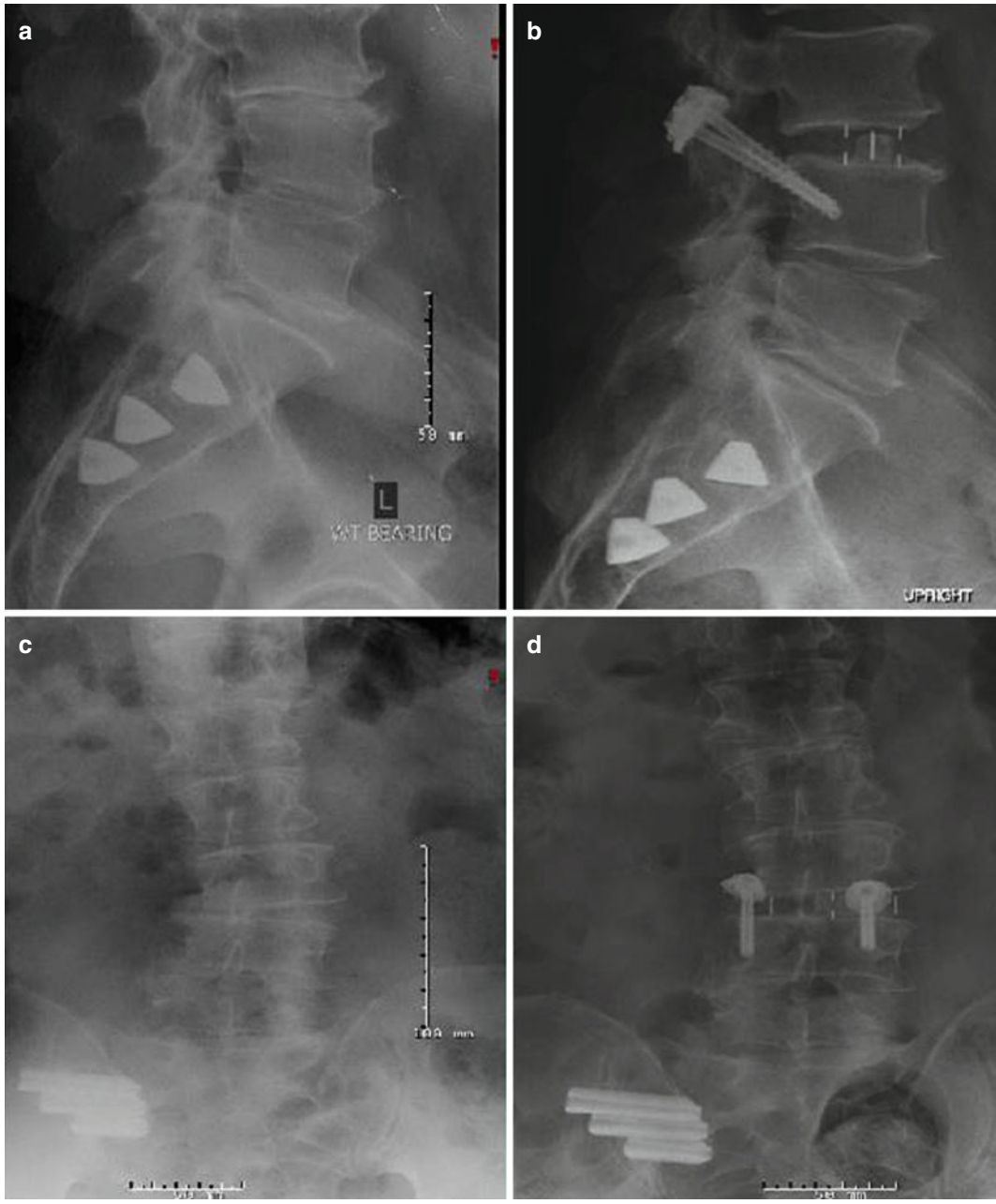

Fig. 29.2 (**a**, **c**) Preoperative radiograph of a patient with L3–L4 degenerative disk disease with asymmetric disk collapse and resultant far lateral foraminal stenosis; (**b**, **d**) postoperative X-rays of the same patient after L3–L4 transpsoas lumbar interbody fusion and posterior transfacet screws demonstrating restoration of disk height and indirect foraminal decompression

space, the quadratus lumborum muscle originates from the last rib and the transverse processes of the upper lumbar vertebrae and inserts to the internal lip of the iliac crest. The psoas muscle is situated anterior to the quadratus lumborum; it originates from the transverse processes and lateral aspect of the lumbar vertebrae and joins the iliacus muscle inferiorly and insert into the lesser

trochanter of the femur. The transverse process and quadratus lumborum muscle are good anatomical landmarks for the posterior boarder of the psoas muscle.

The lumbar plexus is formed by the lumbar nerve roots with minor contribution from the T12 root (Fig. 29.3a). It travels between superficial and deep parts of the psoas major muscle. Major branches of the lumbar plexus include the iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous, obturator, and femoral nerves in addition to the lumbosacral trunk. The superior part of the plexus is usually located in the posterior one-fourth of the L1 to L2 vertebral body and travels progressively more anteriorly as the lumbar plexus descends. With the exception of the genitofemoral nerve, majority of the lumbar plexus branches are located in the posterior half of the L1 to L4 vertebral body, which makes the anterior half of the L2 to L4 vertebrae the optimal surgical corridor for the transpsoas approach [11]. Uribe et al. [12] and Moro et al. [11] in a cadaveric study nicely demonstrated the lumbar plexus anatomy in relation to the transpsoas approach and divided the area between the anterior and posterior edges of the vertebral body into four zones, Zone I (anterior quarter), Zone II (middle anterior quarter), Zone III (middle posterior quarter), and Zone IV (posterior quarter), as shown in Fig. 29.3b. The safe zone to prevent direct nerve injury from L1–L2 to L3–L4 was located at the middle posterior quarter of the VB (midpoint of Zone III), and the safe anatomical

Table 29.1 Indications for the transpsoas approach

Transpsoas approach for lumbar interbody fusion
Degenerative disk disease
Low-grade spondylolisthesis (grade I or II)
Adjacent segment disease
Foraminal stenosis from collapsed disk without need for posterior decompression
Degenerative scoliosis
Transpsoas approach for total disk replacement
Degenerative disk disease
Transpsoas approach for corpectomies
Burst fracture
Tumor
Deformity

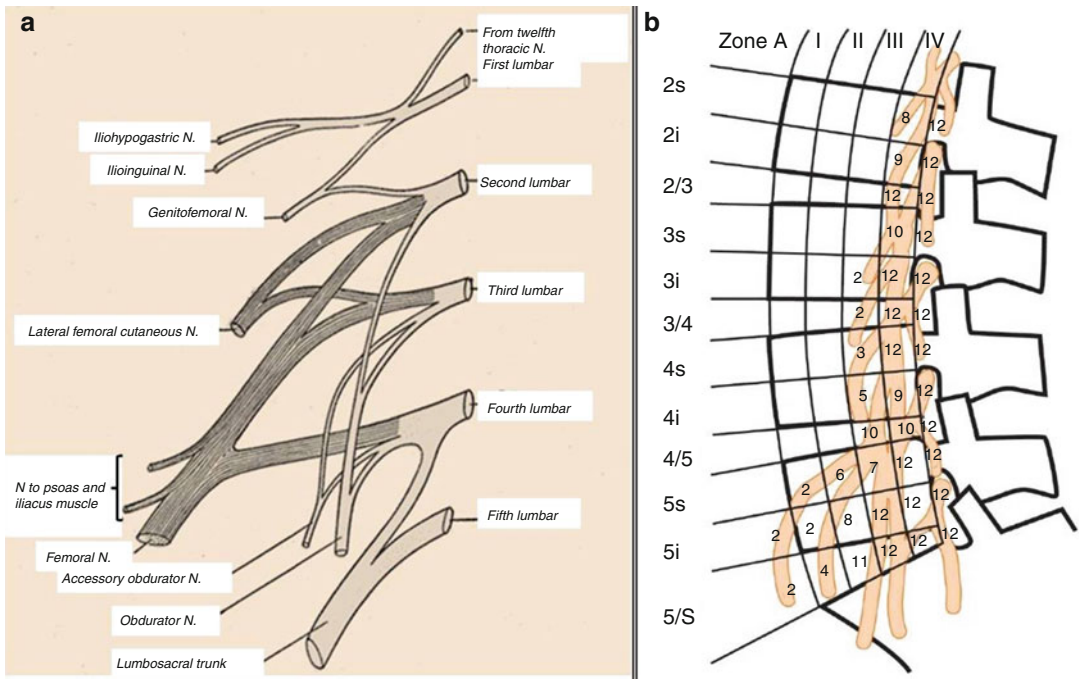

Fig. 29.3 (**a**) Illustration demonstrating lumbar plexus anatomy; and (**b**) "safe zones" for transpsoas approach (Image reproduced with permission from Medtronic, Inc: Medtronic Sofamor Danek; 2004)

zone at the L4–L5 disk space was at the midpoint of the VB (Zone II–Zone III demarcation). The genitofemoral nerve is formed by the L1 and L2 nerve roots and assumes a more anterior course (Zone II at the L2–L3 space and in Zone I at the lower lumbar levels L3–L4 and L4–L5) than the rest of the lumbar plexus, which predisposes itself for injury during transpsoas approach especially at L3 and below which may result in pain and paresthesias in the medial thigh and scrotal area. Apart from within the psoas muscle, there is potential risk of injury to the ilioinguinal, iliohypogastric, and lateral femoral cutaneous nerves in the retroperitoneal space where these nerves run along the posterior abdominal wall and then course obliquely, inferiorly, and anteriorly across the surgical corridor within the abdominal muscles to reach the iliac crest and the abdominal wall and it should be kept in mind [14]. Transpsoas approach to the L4–L5 disk space may be associated with higher risk of injury to the lumbar plexus and can often be limited by a high-riding iliac crest. Flexing the operating table or resection of the iliac crest can help to obtain lateral access in the setting of high-riding iliac crest. Transpsoas approach to the L1–L2 disk space may be limited by a low-lying 12th rib, which may require rib resection or intercostal approach. Though attempted in cadaveric studies with additional surgical maneuvers, L5–S1 is typically not amenable to transpsoas approach without significant neurological complications due to the traversing lumbar plexus at this level [15].

29.4 Operative Technique

29.4.1 Preoperative Planning

Thorough review of preoperative imaging studies and careful surgical planning are imperative to any surgical procedure, but they are especially important in the transpsoas approach. The anatomy of the psoas muscle, spinal curve, adjacent vessels (aorta, vena cava, iliac vessels, etc.), as well as the location of the iliac crest and the 12th rib should be carefully studied to ensure the intended level can be safely reached from the lateral approach. Any prior abdominal or retroperitoneal surgery should be noted since scarring may complicate the dissection from that particular side. Though it is the surgeon's preference, it may be advantageous to approach the spine from concavity of the curve if multiple levels need to be treated as they can be reached through a single skin incision. When a single level is treated, or when there is a significant rotatory scoliosis, approaching from the convexity side may provide shorter working distance to the disk space and a more open disk space. In general, the anterior half of the disk space should be targeted (Fig. 29.4a); in the setting of low-grade spondylolisthesis, the inferior vertebral body should be used as reference. Patients with high-grade spondylolisthesis and severe deformity have dramatically higher risk for complications and alternative approaches should be considered.

29.4.2 Neuromonitoring Setup

Real-time EMG monitoring of the lumbar plexus and nerve roots is paramount to ensure safe passage of the tubular retractors during psoas dissection [16]. Nerve stimulation probe should also be set up to facilitate safe muscle dissection and tubular retractor placement. Clear communication with the anesthesia team is also important to avoid using any long-acting paralytics during induction and/or other agents that can interfere with EMG monitoring during the procedure. The dilators for this approached are designed in such a way that they can be integrated with EMG-stimulating capabilities unidirectionally, with an isolated stimulating surface on the dilator. Using triggered electromyography (tEMG), as the dilator is rotated within the psoas muscle, stimulating areas are localized circumferentially which are very helpful in predicting the position of motor nerves. In general, tEMG thresholds for response below 5 mA indicate direct contact, between 5 and 10 mA indicate close proximity, and 11 mA or more indicate farther proximity from intrapsoas nerves [16].

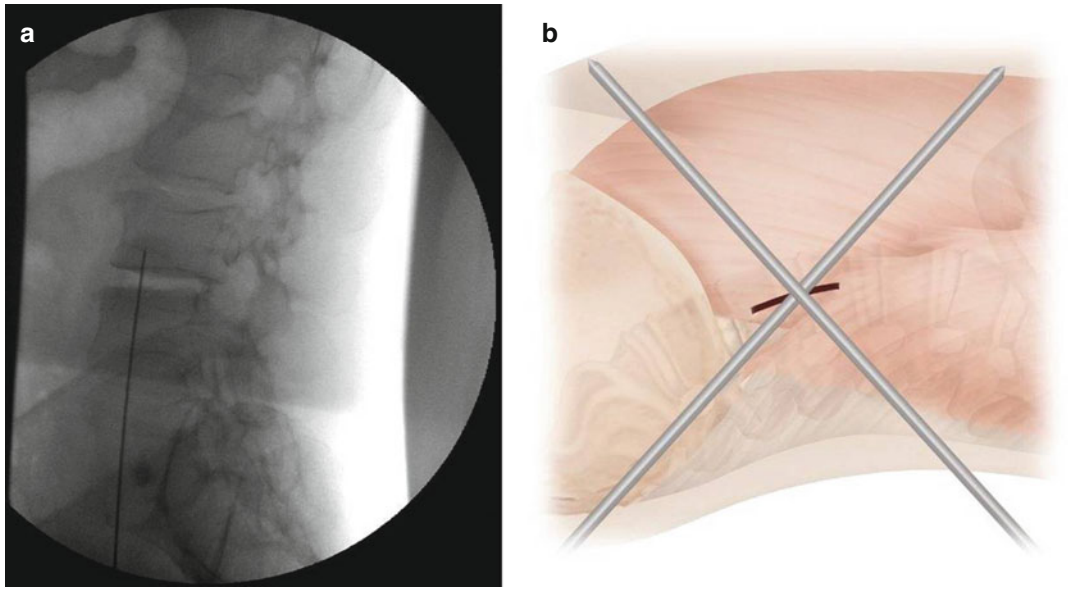

Fig. 29.4 (**a**) Intraoperative radiograph demonstrating using K-wire to target the anterior half of the disk space; (**b**) illustration demonstrating using K-wires to mark the skin incision (Image reproduced with permission from Medtronic, Inc: Medtronic Sofamor Danek; 2004)

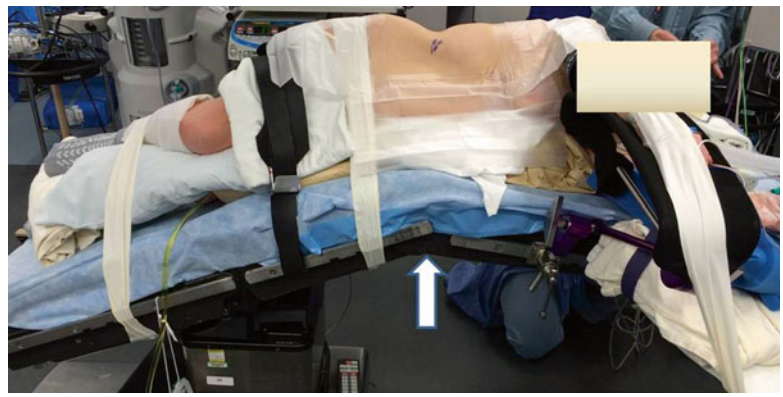

Fig. 29.5 Intraoperative photo demonstrating patient positioning. Notice the iliac crest is positioned over the break of the operating table (*arrow*)

29.4.3 Patient Positioning

The patient is placed on a radiolucent, articulating table in true lateral decubitus position with the sagittal plane of the patient being 90° to the floor. The patient's iliac crest should be at the break of the articulating table (Fig. 29.5). The bottom leg is kept straight with a slight bend at the knee; the top leg is flexed to relax the ipsilateral psoas muscle to facilitate dilation. All pressure points should be well padded. The patient is then secured to the operating table with a 3 in. tape with or without a bean bag. The table is then flexed to increase the angle between the iliac crest and rib cage to facilitate access to the disk space, which can be particularly important when the intended level is the L4–L5 disk space and the iliac crest is in the way. All EMG leads should be checked to ensure proper connection.

29.4.4 Fluoroscopic Localization

The C-arm is brought into the field and an AP radiograph is first taken to ensure the patient is in a true lateral position. Two K-wires can then be

used as radiomarkers to localize the intended disk space with one K-wire in the middle of the intended disk space and the other one bisecting the anterior and posterior halves of the vertebral body (Fig. 29.4b). A 1.5 in. horizontal skin incision is then marked. When multiple levels are treated, a single vertical or oblique incision may be used with the incision centered at the middle of the intervening vertebrae.

29.4.5 Surgical Technique

The patient is prepped and draped in the standard fashion. The previously marked skin incision is opened and dissection is carried through the subcutaneous fat layer to expose the external oblique fascia. Subsequently, a scissor should be used to make a fascial incision along the orientation of the muscle fibers. A Kelly clamp is then used for blunt dissection through the muscle layers of the lateral abdominal wall (external oblique, internal oblique, and transversalis abdominis muscles). The transversalis facia is located just deep to the transversalis abdominis muscle and a blunt opening is made to access the retroperitoneal space. The characteristic yellow color of the retroperitoneal fat confirms entry into the retroperitoneal cavity. A blunt dissection is then performed to palpate and visually expose the psoas muscle just deep to the retroperitoneal fat and the quadratus lumborum muscle. The transverse process marks the posterior boarder of the psoas muscle. Finger palpation is also used to ensure the peritoneal contents are displaced anterior to avoid peritoneal injury during docking of the tubular retractors.

A neural stimulation probe with 8 mA stimulation is carefully guided down and inserted into the psoas muscle, with it centered at the anterior half of the intended disk space (Fig. 29.6a). Lateral X-rays are used to confirm its proper location. If any neural structure is identified during insertion, the probe should be repositioned slightly anterior to avoid the traversing nerve. After the probe is properly placed, AP and lateral X-rays are obtained to confirm probe location. A K-wire is then placed through the probe cannula into the intended disk space. AP and lateral X-rays are again taken to confirm proper location of the guidewire. The initial dilator is then inserted over the K-wire. Special attention should be paid to any EMG changes during dilation at this time. EMG changes may indicate nerve compression and may require reposition of the dilators. After the final tubular dilator is placed, retractor blades with proper depth are inserted and secured. The retractor is then expanded if necessary to allow adequate access to the disk place. Stability shims or pins are then inserted to secure retractors in place. AP and lateral radiographs are again used to confirm proper retractor placement. As the most common neurological postoperative complications are transient motor weakness/palsy and sensory dysesthesia, which can sometimes be permanent, a supra-psoas shallow-docking method has been described which might be a safer alternative and may help minimize morbidities by eliminating or reducing direct psoas injury [17]. The annulus is then incised and a complete diskectomy is carried in the usual fashion similar to the anterior and posterior approaches. Once the diskectomy is completed, a Cobb is inserted into the disk space and a mallet is used to release the contralateral annulus and/or osteophyte on the contralateral side using fluoroscopic guidance (Fig. 29.6b). Gentle tapping should be used with a sudden loss of resistance a confirmation for adequate release. The end plates are then carefully prepared and freed of any residue cartilage or disk material.

The disk space is then distracted with progressively larger trial spacers to obtain the desired disk height and to achieve indirect foraminal decompression. Once desired height is determined and confirmed by radiographs, the interbody spacer is then placed under fluoroscopic guidance. Care should be taken to insert an adequate size implant so as to cover the apophyseal ring on both the sides to reduce the chances of subsidence. An optional lateral plating system may be used at this time if posterior instrumentation is not planned. The retractor system is then removed with attention to hemostasis. The retraction time of the psoas muscle should be recorded and minimized to minimize nerve compression

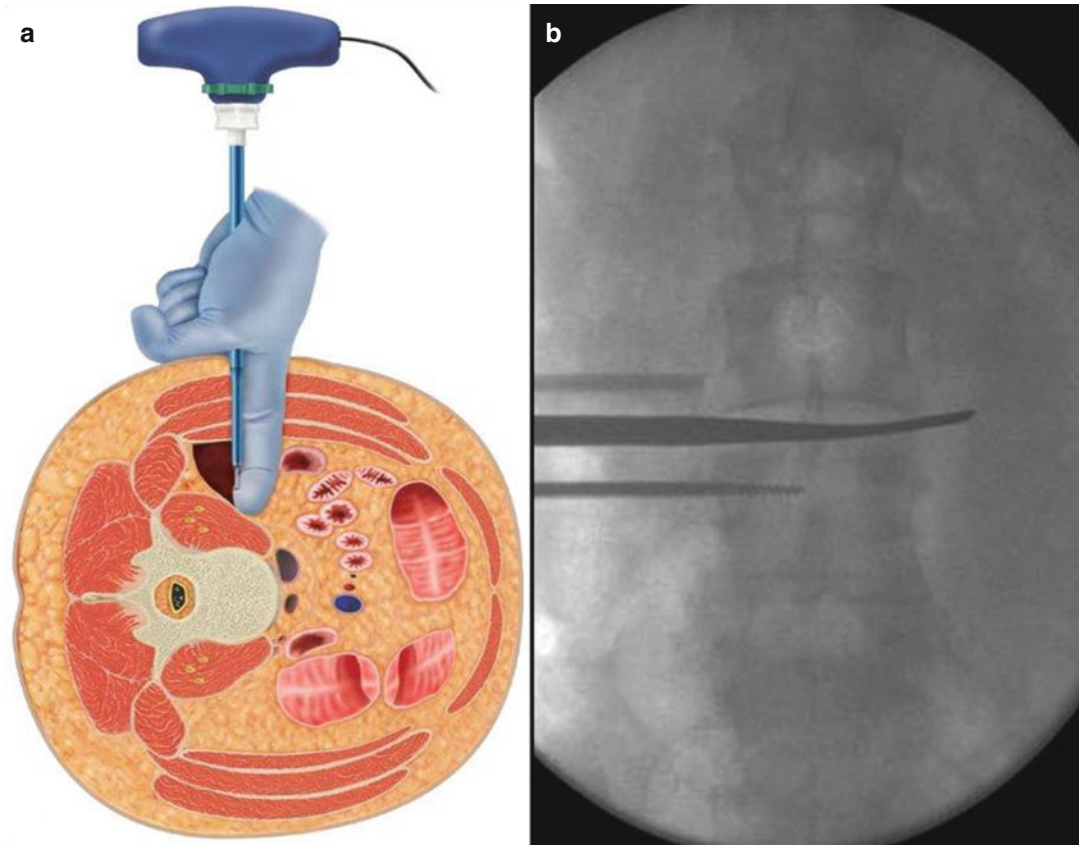

Fig. 29.6 (**a**) Illustration demonstrating using finger to guide the stimulation probe through the psoas muscle. (**b**) Intraoperative X-rays demonstrating releasing of the contralateral annulus using a Cobb (Image reproduced with permission from Medtronic, Inc: Medtronic Sofamor Danek; 2004)

and stretch. The external oblique fascia layer is closed with interrupted sutures carefully so as not to include the nerves traversing the muscle in the stitch and the skin closed in a standard fashion.

29.5 Potential Complications

Despite the numerous advantages the transpsoas approach offers, it has its own sets of complications. Postoperative sensory disturbances including transient thigh pain and paresthesias have been reported in up to 63 % of patients, though majority of these symptoms do resolve within 1 year [18, 19]. Postoperative motor deficit such as iliopsoas weakness has been reported ranging from 0.7 to 33.6 %, which also improves over 2–3 weeks and is likely due to dissection through the psoas muscle and placement of the tubular retractors [20]. Many surgeons would not even consider transient iliopsoas weakness as a complication as it is more or less an expected outcome following a transpsoas approach. Other more serious and permanent complications such as lumbar plexus or nerve root injuries are reported to occur in up 3.4 % of patients [20]. Postoperative abdominal paresis (pseudohernia) has also been reported to occur in 4.2 % of patients [21]. Understanding the potential risk of injury to the ilioinguinal, iliohypogastric, and lateral femoral cutaneous nerves not in the retroperitoneal space where they travel obliquely, inferiorly, and anteriorly to reach the iliac crest and the abdominal wall may help avoid this complication. Devastating but rare complications such as bowel, kidney, ureter, or vascular injuries

can also occur, and timely intraoperative consultations with general surgery or vascular surgery colleagues are essential to minimizing morbidity and optimize patient outcome [22]. Understanding the regional anatomy and careful review of all preoperative radiology is key to avoiding these complications. A detailed and thorough discussion regarding these potential complications with the patient should be done preoperatively.

Conclusion

In summary, the transpsoas approach offers many advantages and provides a minimally invasive surgical corridor to the anterior and lateral thoracolumbar spine. However, like with any surgical approach, proper patient selection and sound surgical indication in addition to meticulous surgical technique are keys for good surgical outcomes. The spine surgeons should understand the limitations and potential complications with the transpsoas approach and have a frank preoperative discussion with patients. The transpsoas approach is a valuable and important tool for spine surgeons, in addition to the anterior and posterior approaches. It can provide excellent outcome in appropriately selected patients with the right indications.

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Oblique Lumbar Interbody Fusion 30

Clément Silvestre and Pierre Roussouly

30.1 Introduction

With the increasing number of spinal fusion performed [1–3], spine surgeons need to be acquainted with a variety of fusion procedures. Lumbar interbody fusion has become a popular technique for treating spinal conditions such as spondylolisthesis, degenerative disk disease, recurrent disk herniation, pseudarthrosis, and spinal deformity. Thus, treatment strategies have evolved from posterior fusion alone or anterior fusion alone to 360° fusion. The latter two require an interbody fusion, either during the posterior approach (posterior lumbar interbody fusion or transforaminal lumbar interbody fusion) or during a second-stage procedure such as anterior lumbar interbody fusion (ALIF), oblique lumbar interbody fusion (OLIF), or direct lumbar interbody fusion (DLIF or XLIF®). These different approaches to reach the interbody space have been described, as have their advantages and disadvantages. Anterior lumbar interbody fusion provides direct access to the disk with potential improvement of fusion rate but also carries the risk of injury to the iliac vessels, peritoneal content, and ureteral and autonomic nervous system [4]. The traditional anterior retroperitoneal approach can also result in pain, muscular atony, or herniation of the abdominal wall [5]. In an attempt to decrease the complications related to traditional exposures, various minimally invasive techniques have been developed to minimize the incidence of pain and abdominal wall atony or herniation after anterior lumbar interbody fusions [5–7]. Laparoscopic procedures have been proposed but are not widely used due to the steep learning curve, technical complexity, and limited visualization of the spine associated with the technique, as well as the absence of clear benefit over open procedures in terms of complication rate and outcome [8–11]. Conversely, mini-open techniques have gained wider acceptance among surgeons performing anterior lumbar interbody fusion because they allow direct access and visualization of intervertebral disks in order to achieve more complete diskectomy and theoretically a better fusion, while potentially decreasing morbidity [5–7, 11].

Mayer [12] described a minimally invasive anterior approach to the lumbar spine through a retroperitoneal access for L2–3 to L4–5 disks and

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_30

a transperitoneal access for L5–S1 disk, performed after prior posterior instrumentation and fusion. He presented his technique on 25 patients and observed solid anterior fusion for all patients with minimal blood loss and no evidence of technique-related complication. The technique involves a muscle-splitting approach through a 4-cm oblique skin incision parallel to the fibers of the external oblique abdominal muscle that is extended to 6 cm if exposure of two disks is required. Kaiser et al. [11] reported their experience for single- or two-level anterior interbody fusion using the technique described by Mayer [12] on 51 patients, showing 3.9 % and 17.6 % of intraoperative and immediate postoperative complication rates, respectively. They also suggested that the mini-open technique is associated with decreased incidence of retrograde ejaculation. Saraph et al. [13] compared the technique of Mayer [12] to the traditional anterior retroperitoneal approach for anterior interbody fusion. After a mean follow-up of 5.5 years, fusion rate and complication rate were similar between the two groups, but intraoperative blood loss, operation time, and postoperative back pain were decreased with the mini-open technique. Interestingly, there were three patients with postoperative weakness of abdominal muscles in the group undergoing traditional approach ($n=33$), as opposed to none in the mini-open group ($n=23$). Other mini-open anterior approaches to the lumbar spine have also been proposed [10, 14], but these techniques involve opening the rectus sheath and mobilizing the rectus abdominis muscle with theoretically increased potential for abdominal wall morbidity. However, these techniques are useful when a more direct anterior approach is required.

Recently, the authors have used a minimally invasive retroperitoneal anterior approach referred to by the authors as the oblique lumbar interbody fusion (OLIF) [15]. This approach is similar to that of Mayer [12] for anterior lumbar interbody fusion. The authors progressively slide from the Mayer approach, which was during the 1990s and beginning of the 2000 more aggressive than now with many comorbidities such as wall pain or atony. Those were due to a long and posterior incision carrying the risk to injure the troncular nerves for wall muscles. Initially, the results of the study concerning the comorbidities of minimal invasive OLIF were published [15], on a series of 179 patients and the potential complications associated with the technique. Now, our expertise has evolved and increased until more than 733 cases.

30.2 Materials and Methods

30.2.1 Minimally Invasive Oblique Lumbar Interbody Fusion

The patient is positioned in lateral decubitus and a radiograph is made in order to identify the intervertebral levels to approach. A 4-cm skin incision, centered on the spinal segment to expose, is made in the lateral abdominal region parallel to the fibers of the external oblique muscle (Fig. 30.1a). The incision is made perpendicular to the line joining the anterior superior iliac spine to the umbilicus at one third of the distance from the anterior superior iliac spine, similar to the McBurney incision. We can also define this point as a soft point of the muscular wall; indeed, as for the neck and C6, you can reach and touch the spine, sometimes feel the psoas, with a deep palpation. And this is possible even on fatty patient. The approach is usually carried on from the left side but can also be performed from the right side such as for right lumbar scoliosis. External oblique, internal oblique, and transverse abdominal muscles are then dissected along the direction of their fibers in this muscle-splitting approach (Fig. 30.1b). The retroperitoneal space is accessed by blunt dissection and the peritoneal content is mobilized anteriorly. The psoas muscle is identified. We must emphasize at this time of the procedure that the psoas must be reclined posteriorly while the sympathetic chain and the ureter are mobilized anteriorly. The safer way to manage this stage is to be in the sheath of the psoas. It is important to minimize as much as possible the retraction of the psoas in order to decrease the incidence of postoperative pain – in particular cruralgia – secondary to injury of the lumbar plexus or psoas fibers. Four Steinman

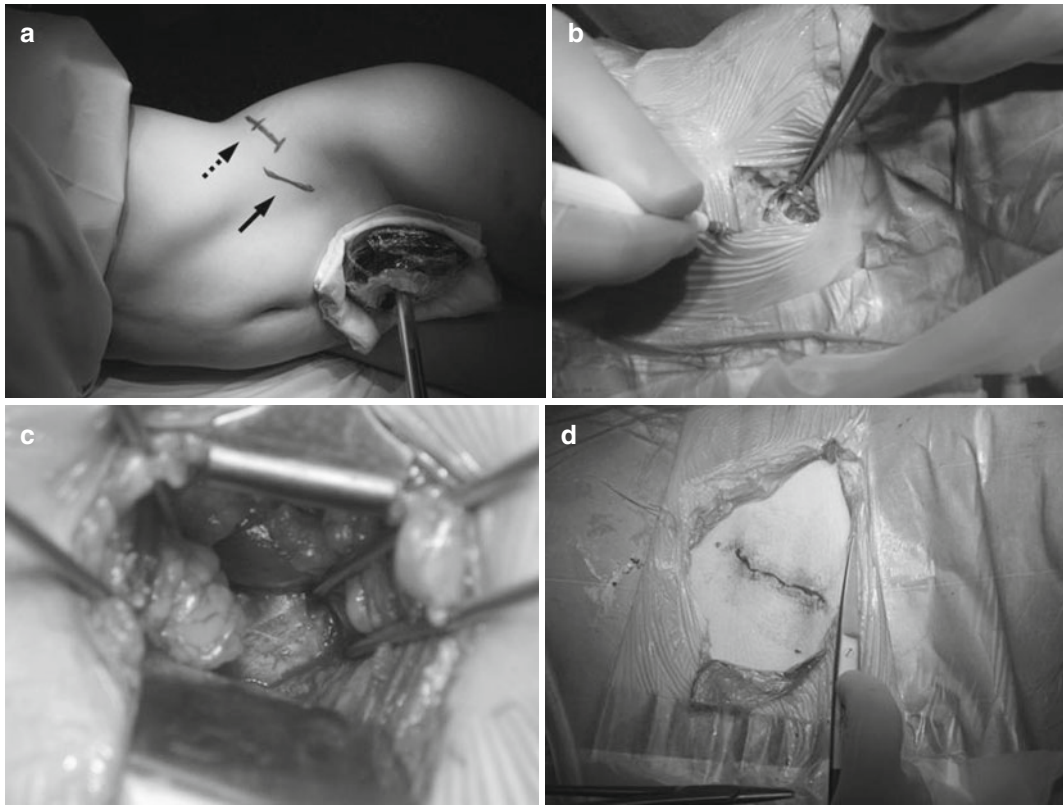

Fig. 30.1 (**a**) A 4-cm skin incision (*solid arrow*) is made in the lateral abdominal region along the fibers of the external oblique muscle. The level of the L4–L5 disk (*dotted arrow*) was located using the C-arm. (**b**) External oblique, internal oblique, and transverse abdominal muscles are dissected along the direction of their fibers. (**c**) The intervertebral disk is exposed using handheld retractors and Steinman pins. (**d**) Skin closure

pins are used to expose the intervertebral disk without having to ligate segmental vessels (Fig. 30.1c). A window of only about 1 cm made in the annulus fibrosis is required anterolaterally to perform the diskectomy and insert the cage. A radiograph is done to confirm the proper level before proceeding to interbody fusion. It provides you indication about your anteroposterior positioning in the disk and may be helpful during the diskectomy and insertion of the implant. Segmental vessels usually do not need to be ligated unless the vertebral body needs to be exposed. At L4–L5, the disk space can be obstructed by the iliolumbar vein, in which case it needs to be ligated.

Up to three disks can be approached using the same 4-cm incision through a "sliding window" technique without the need to extend the incision, by taking advantage of the mobility of the abdominal wall. The described minimally invasive technique is well suited for exposure of L2–L3 to L4–L5 disks, but rarely, L1–L2 and L5–S1 disks can also be exposed. Exposure of L1–L2 disk is limited by the chest cage and can be performed only in the presence of relatively horizontal and mobile floating ribs. As for L5–S1 disk, its access is limited by the iliac wing and by the need to mobilize iliac vessels.

After diskectomy (Fig. 30.2a), vertebral endplates are prepared in order to expose the subchondral bone. The cage is filled with bone graft and/or substitute (Fig. 30.2b) and inserted in a press-fit fashion into the exposed disk spaces that remained open after the posterior procedure (Fig. 30.2c). If required, autogenous iliac graft can also be harvested from the same incision.

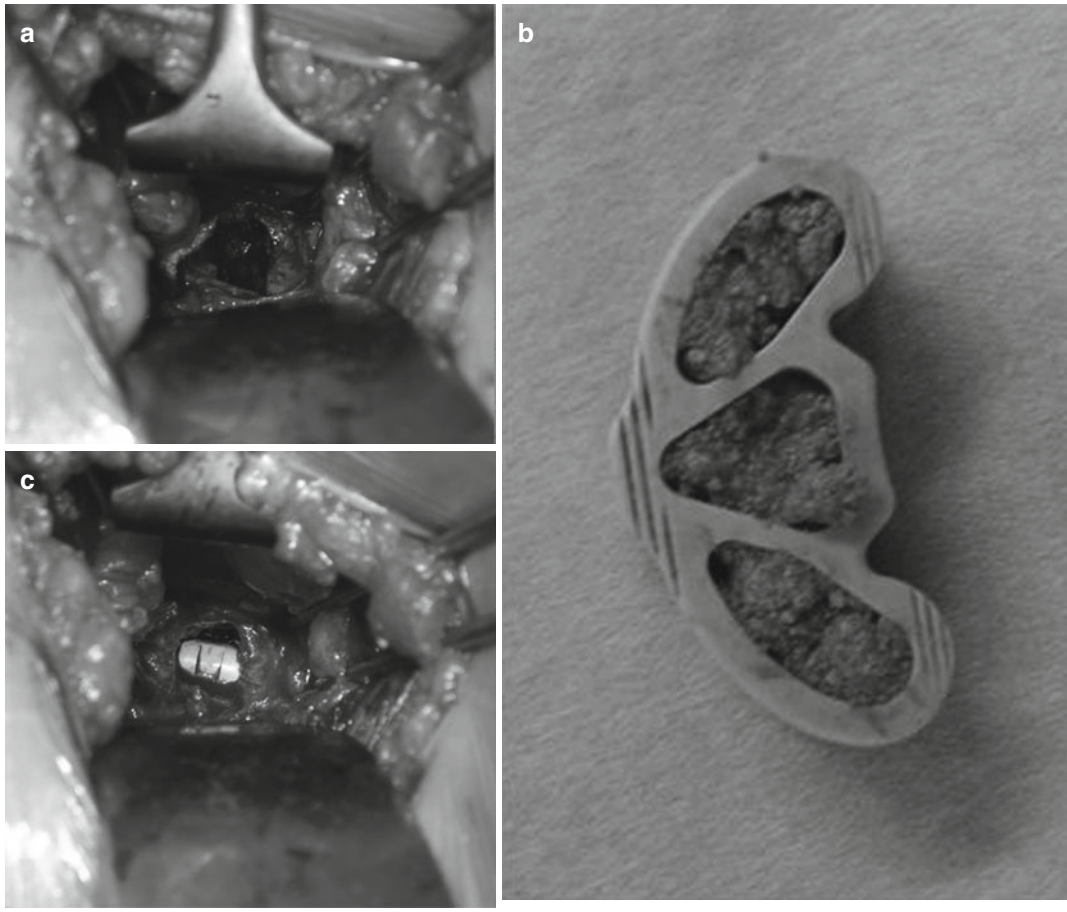

Fig. 30.2 (**a**) Exposure of disk space. (**b**) Filling of banana-shaped PEEK cage using bone substitute. (**c**) Cage inserted into exposed disk space after endplate preparation

Abdominal muscle planes are closed sequentially and the skin is closed using subcutaneous and subcuticular sutures (Fig. 30.1d). Although the procedures were performed without magnifying loupes or surgical microscope, it can be used for improved vision. In addition, a headlight or better a small light inserted in the wound by the retractors can be useful especially in deepest or overweight patients.

30.3 Results

Here are described main results about the first 179 patients of our series [15].

The main results and main complications are still the same, even if we reach the top of the learning curve.

Patients were aged 54.1 ± 10.6 years (range: 14.9–77.4). There were 148 females and 31 males aged 54.5 ± 11.0 years (range: 14.9–77.4) and 52.2 ± 8.7 years (range: 27.2–67.7), respectively. There were 118 primary cases and 61 revision cases. There were few occurrences of revision after previous anterior approach. Diagnosis at time of surgery is shown in Table 30.1. Weight and BMI were, respectively, 67.1 ± 14.5 kg (range: 35–116) and 24.8 ± 4.1 kg/m^2 (range: 15.6–38.6).

Four patients with scoliosis and one patient with L4–L5 degenerative spondylolisthesis had a right-sided approach.

Details of the levels approached with the respective operative blood loss, operative time, and length of hospital stay are provided in Table 30.2. The procedure was performed at

L1–L2 in 4, L2–L3 in 54, L3–L4 in 120, L4–L5 in 134, and L5–S1 in 6 patients.

The procedure was done at a single level for 31 %, two levels for 60 %, and three levels for 9 % of patients. Figure 30.3 shows radiographs of a patient with three-level OLIF at L2–L5, while Fig. 30.4 shows two different patients with L1–L3 and L4–S1 OLIF, demonstrating the potential use of the described technique for approaching L1–L2 and L5–S1 levels, respectively.

In three patients of this series, and very few of all the patients treated, the procedure was aborted for one level mainly due to the too narrow disk space and sometimes due to an iliolumbar vein too important in regard to the disk L4–L5 whose mobilization would be too risky. Sometimes, approaching L2–L3 level was not possible due to a prominent rib cage, and only L3–L5 OLIF was performed.

Operative blood loss was 99.5 ± 254.0 ml for all patients, averaging 56.8 ± 131.3 ml per level. It was lowest for single-level approaches (53.9 ± 78.3 ml) and highest for two-level approaches (124.1 ± 319.1). In 98 % of cases, operative blood loss was 400 ml or less.

As for operative time, it was 53.8 ± 18.7 min for all patients with an average of 32.5 ± 13.2 min per level. It was lowest for single-level surgery (42.4 ± 16.8 min), increasing to 57.4 ± 14.8 min for two-level and 70.3 ± 26.4 min for three-level approaches. The length of hospital stay was 7.1 ± 3.5 days for all patients. It was similar for patients undergoing single-level (6.5 ± 2.3 days), two-level (7.5 ± 4.0 days), and three-level (6.7 ± 3.4 days) procedures. However, some patients had to stay longer at the hospital while waiting for transfer in a rehabilitation center. Now, this length of hospital stay has decreased to 4–5 days. Maybe the length of stay could be less, but due to our health system policy, patient must stay four nights in the hospital.

The main complications are exposed in Table 30.3. The most common complication was incisional pain (2.2 %), followed by lower extremity symptoms from sympathetic chain

Table 30.1 Diagnosis at time of surgery

Diagnosis	Number of patients
Primary surgery	
Spinal deformity	65
Spondylolisthesis	32
Degenerative disk disease/facet arthrosis	19
Post-traumatic kyphosis	2
Revision surgery	
Pseudarthrosis	18
Adjacent segment disease	18
Spinal deformity or imbalance	13
Spinal stenosis/post-laminectomy syndrome	10
Spondylolisthesis	2

Table 30.2 Levels approached with respective operative blood loss, operative time, and length of hospital stay

Approach	Number of patients	Operative blood loss (ml)	Operative time (min)	Length of hospital stay (days)
Single-level	55	53.9 ± 78.3	42.4 ± 16.8	6.5 ± 2.3
L1–L2	1	150	50	4
L2–L3	5	60.0 ± 82.2	44.0 ± 17.1	8.2 ± 1.9
L3–L4	7	41.4 ± 35.2	37.9 ± 16.0	6.1 ± 2.6
L4–L5	43	53.0 ± 83.5	42.7 ± 17.4	6.4 ± 2.3
Two-level	108	124.1 ± 319.1	57.4 ± 14.8	7.5 ± 4.0
L1–L3	2	200.0 ± 212.1	67.5 ± 10.6	12.5 ± 2.1
L2–L4	29	104.5 ± 104.5	58.3 ± 14.9	7.9 ± 4.0
L2–L3, L4–L5	2	500.0 ± 707.1	72.5 ± 17.7	4.0 ± 1.4
L3–L5	68	123.6 ± 378.6	55.7 ± 15.0	7.2 ± 4.0
L4–S1	6	75.0 ± 61.2	63.2 ± 10.1	8.0 ± 3.5
Three-level	16	93.8 ± 106.3	70.3 ± 26.4	6.7 ± 3.4
L1–L4	1	200	75	16
L2–L5	15	86.7 ± 106.0	70.0 ± 27.3	6.1 ± 2.3

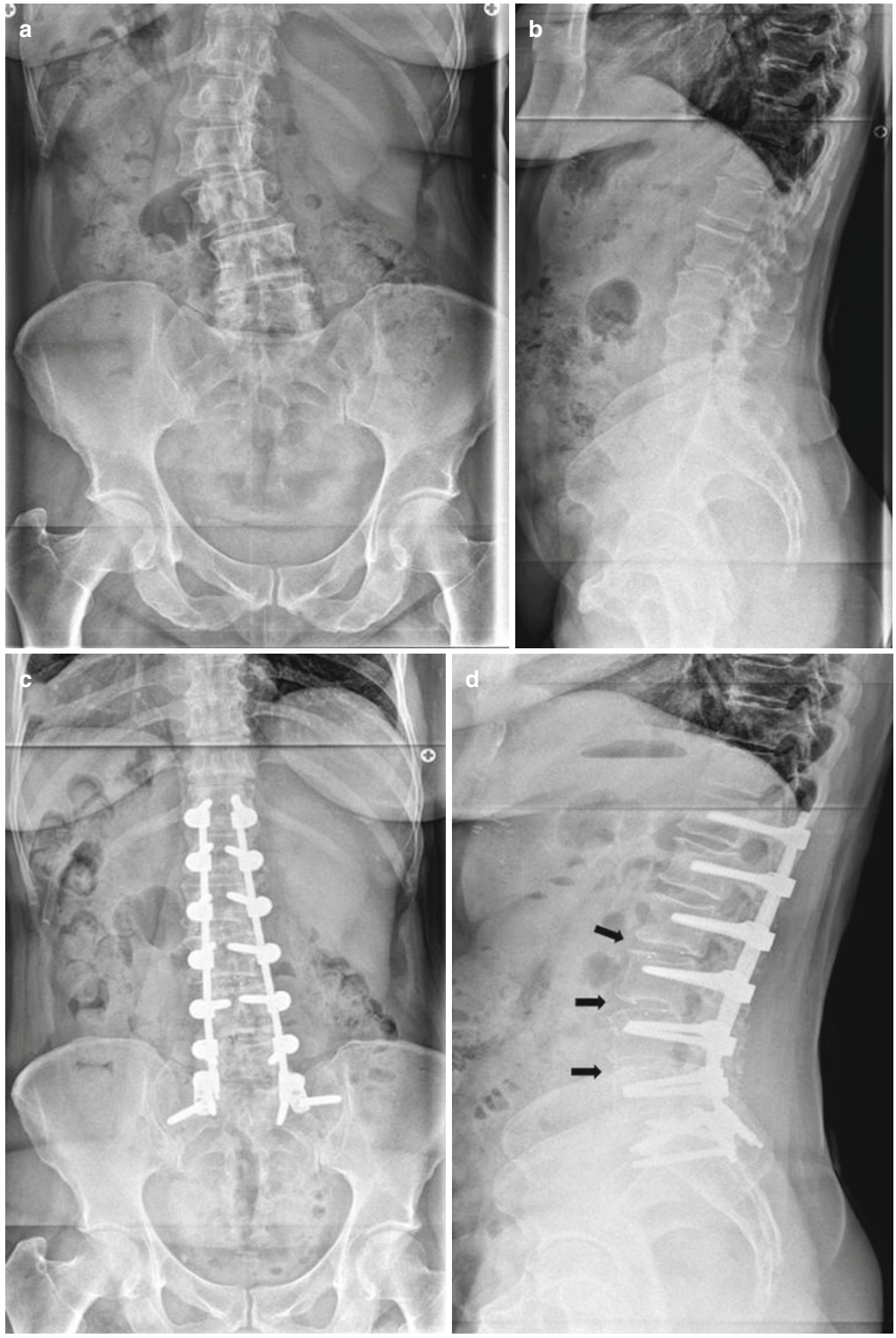

Fig. 30.3 Preoperative (**a**, **b**) and postoperative (**c**, **d**) radiographs of a 45-year-old female with degenerative scoliosis undergoing three-level OLIF, showing the presence of radiopaque markers of the interbody cages from L2 to L5 (*full arrows*)

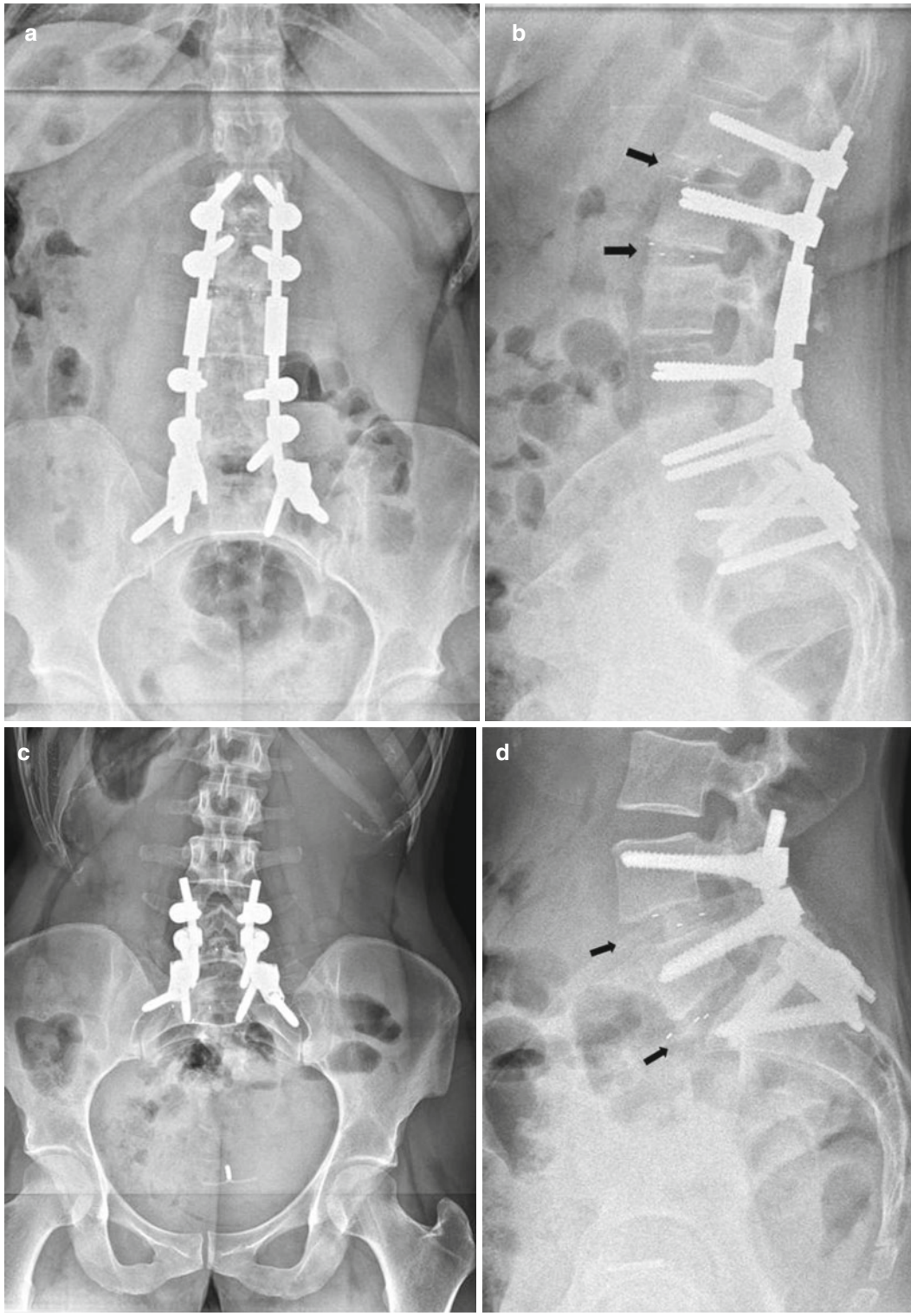

Fig. 30.4 Postoperative radiographs of two different patients undergoing OLIF at L1–L3 (**a**, **b**) and L4–S1 (**c**, **d**)

Table 30.3 Complications

Complication	Number of patients
Incisional pain	4
Lower extremity symptoms related to sympathetic chain injury	3
Neurological deficit	2
Iliac vein laceration and bilateral femoral deep venous thrombosis	1
Iliac vein laceration	1
Iliolumbar vein laceration	1
Pseudomembranous colitis	1
Ileus	1
Peritoneal laceration	1
Cerebrovascular accident	1
Postoperative peripheral ischemia in lower extremities	1
Ipsilateral transient psoas paresis	1
Ipsilateral transient groin numbness	1
Symptomatic pseudarthrosis requiring revision ALIF	1

injury (1.7 %). There was no occurrence of abdominal muscle weakness, nor herniation, nor retrograde ejaculation.

In the original series, there were two patients with neurological deficit after left-sided L3–L5 OLIF. There was one more patient if we consider the whole series (733 patients). The first patient had left L4 paresthesia and L3–L4 motor weakness (grade 4 strength) presumably due to nerve stretching from restoration of disk height. For this case, surgery was uneventful and postoperative imaging did not show any misplacement of the interbody cages. The neurological deficit remained stable, but she was diagnosed with pancreatic adenocarcinoma and died 4 months after the OLIF procedure. A second patient had right L4–L5 paresthesia and weakness (grade 0 strength), as well as grade 3 strength in right S1 postoperatively. Preoperatively, she already had weakness of her right lower extremity as a sequelae of poliomyelitis at a young age. CT scan showed prominent cage of 36 mm length at L3–L4 and L4–L5 compressing the dural sac contralaterally on the right side. She then underwent revision through the same incision with placement of shorter cages of 30 mm length at L3–L4 and L4–L5 but did not recover from her neurological injury. Since this incident, we made a new implant with a new shape, and we also changed the inserter in order to have a better central positioning of the implant instead of a too latero-oblique traject.

For the last patient who had a neurological injury, during the procedure, the approach performed was too posterior and the surgeon reclined the psoas anteriorly instead of posteriorly. Consequently, during the diskectomy, the L4 nerve root was injured. The patient suffered for a partial deficit that recovered after few months of rehabilitation.

One patient presented with ipsilateral weakness (grade 4 strength) of hip flexion after L3–L5 OLIF but recovered full strength after 15 days. Due to the transient nature of the weakness, it was attributed to local pain from the surgical approach (manipulation of abdominal and/or psoas muscles). Another patient undergoing L3–L5 OLIF had hypoesthesia at the upper medial aspect of the left thigh after surgery, which returned to normal as noted at the 9-month follow-up visit. It was presumed to be caused by stretching of the ilioinguinal nerve located between internal oblique and transverse abdominal muscles at L4–L5 level near the anterior part of the iliac crest.

Two patients sustained intraoperative iliac vein laceration that was repaired primarily with nonabsorbable sutures. One of these patients lost 100 cc intraoperatively and presented bilateral edema in lower extremities postoperatively due to deep femoral venous thrombosis requiring anticoagulation treatment. Another patient had an iliolumbar vein laceration leading to 1,000 ml blood loss that ceased after ligation. One patient decompensated from preexisting peripheral arterial disease and presented rest pain in both lower extremities postoperatively due to peripheral ischemia. He improved with nonsurgical treatment consisting of fluid repletion and aspirin. One patient sustained a left-sided cerebrovascular accident secondary to a patent foramen ovale associated with an aneurysm of the interatrial septum. He was treated with thrombolysis and

had no residual deficit from his cerebrovascular accident.

30.4 Discussion

We present the largest cohort to date in the literature pertaining to this approach. As opposed to other studies referring to this approach [11–13], the current study shows that the original technique can be modified in order to address three levels through a "sliding window" using the same 4-cm incision. It also shows that L1–L2 disk can be approached in selected cases for which floating ribs are relatively horizontal and mobile. As for L5–S1 disk, OLIF through a retroperitoneal approach was performed successfully in six patients, but it had to be aborted in one patient. In addition, one patient required revision of L5–S1 interbody fusion due to symptomatic pseudarthrosis after L4–S1 OLIF. Due to the technical complexity of approaching L5–S1 using the retroperitoneal OLIF technique secondary to the need to mobilize iliac vessels and to the presence of the iliac wing, the authors suggest that another approach such as the transperitoneal approach described by Mayer [12] be strongly considered when anterior fusion of L5–S1 is required.

Surprisingly, operative time (53.8 ± 18.7 min) was markedly decreased in the current series when compared to previous reports [11–13]. The authors hypothesize that three factors could have contributed to that finding. First, no microscope was used, thereby decreasing the number of manipulations during surgery, especially when radiographs are needed. Second, all surgeries were performed through the same retroperitoneal approach while previous reports used a transperitoneal approach for L5–S1 disk. Lastly, fusion was performed using bone substitute only, without harvesting autogenous iliac crest bone graft, which can increase operative time. Although autogenous iliac crest bone graft can be harvested from the same incision, it was not performed in the current study in order to avoid donor site morbidity and because the authors believe that using bone substitute was sufficient to achieve adequate rate of fusion clinically, in the context that all patients had also been stabilized posteriorly using segmental instrumentation.

Overall, minimally invasive OLIF carries about the same risks (rate and type of complications) as in traditional anterior approaches [4]. In this series, the most common complications were incisional pain (2.2 % of patients) and lower extremity symptoms due to sympathetic chain injury (1.7 % of patients). Vascular injury (iliac or iliolumbar vein) occurred in three patients (1.7 %) and could be repaired successfully despite the small incision. There are many potential advantages related to the OLIF technique. First, because it is a muscle-splitting approach, the incidence of abdominal wall pain is decreased and it becomes easier to develop a "sliding window" to access multiple levels through a small incision. Second, the incision for the OLIF technique is more anterior to the traditional anterior approach and therefore spares the proximal nervous trunks innervating the abdominal muscles. Accordingly, there was no occurrence of abdominal wall atony or herniation in the current series. In addition, the OLIF technique requires only minimal posterior retraction of the psoas to insert the banana-shaped cage, thereby reducing the incidence of postoperative crural- or psoas-related pain. Finally, the OLIF technique could decrease the length of hospital stay although it remains to be verified. In the present study, the mean length of hospital stay was only 7.1 ± 3.5 days, but it has to be mentioned that some patients had to stay longer at the hospital while waiting for transfer in a rehabilitation center.

Based on the results, age, weight, BMI, and the number of levels approached were not associated with the occurrence of complications. Although the procedure has been performed on patients with weight and BMI of up to 116 kg and 38.6 kg/m^2, it could be use safely in these cases. Moreover, the positioning of the patient on the table makes the approach easier due to the fact that bowels and the abdominal fat go anteriorly.

A banana-shaped cage was used in association with the OLIF procedure in an attempt to facilitate the insertion of the cage and to minimize the rate of neurological injury. With such cage, less posterior reclination of the psoas is needed to insert a cage, and the concavity of the cage decreases the risk of injury to the dural sac centrally. However, as shown in one case with a neurological deficit, the risk of injuring contralateral traversing nerve roots is still present and therefore underlines the need to adequately assess the position of the cage either visually or radiographically. In order to decrease the incidence of this complication, the authors recommend using cages of 30 mm length or shorter in the lumbosacral spine. In the first 179 results, the authors used a banana-shaped cage normally designed for a TLIF approach so the ancillary was not adapted for an OLIF approach. Now, with a new design of the cage and a review of the inserter, the cage is better positioned at the center of the disk space and the trajectory in the disk is strictly laterolateral and less oblique. Thus, the risk of contralateral lesion of the root has decreased, and using long cages as 36 mm or more is no more damageable.

All the techniques used to achieve an anterior fusion with a posterior fusion and instrumentation have some benefits and inconvenient. The surgeons have to choose the most appropriate technique, adapted to their skills and to the better strategy for the patient. Thus, Table 30.4 shows the advantage and inconvenient for all the techniques in order to choose the better strategy.

30.5 Evolution

We have seen that OLIF procedure is a safe and mini-invasive procedure. With the consequences of the development of the technique and evolution of this application, the surgeons' skills improve too. Actually, with the same OLIF approach, we can perform a partial corporectomy as we tend to after posterior transpedicular osteotomy, in order to provide more stability of the spine and avoid

Table 30.4 Main advantage and inconvenient of each technique

	OLIF	Direct LIF	TLIF
Operative time	Decreases the posterior procedure	Decreases the posterior procedure	Increases the posterior procedure
	Requires a second and mini-invasive stage	Requires a second stage	One stage circumferential fusion
Disk access	2 or 3 levels	1 or 2 levels	1 or 2 levels. Three levels are rare
Nerve roots injury	Almost zero	Needs neuromonitoring due to a high risk of damage	Radicular pain postoperatively is very common
Disk shape	Can be done in all shape of disk. Even in disks closed posteriorly	Can be done in all shape of disk. Even in disks closed posteriorly	Easier in disk posteriorly opened
Height disk	Can be done in all height of disk. Even in very height disk (>14 mm)	Can be done in all height of disk	Difficult when more than a 10- or 12-mm cage is required
L5–S1 access	Possible in selected cases	Impossible	Possible, but more difficult
L2–L3 access	Possible	Impossible	Possible, but more difficult
L1–L2 access	Possible in selected cases	Impossible	Possible in selected cases

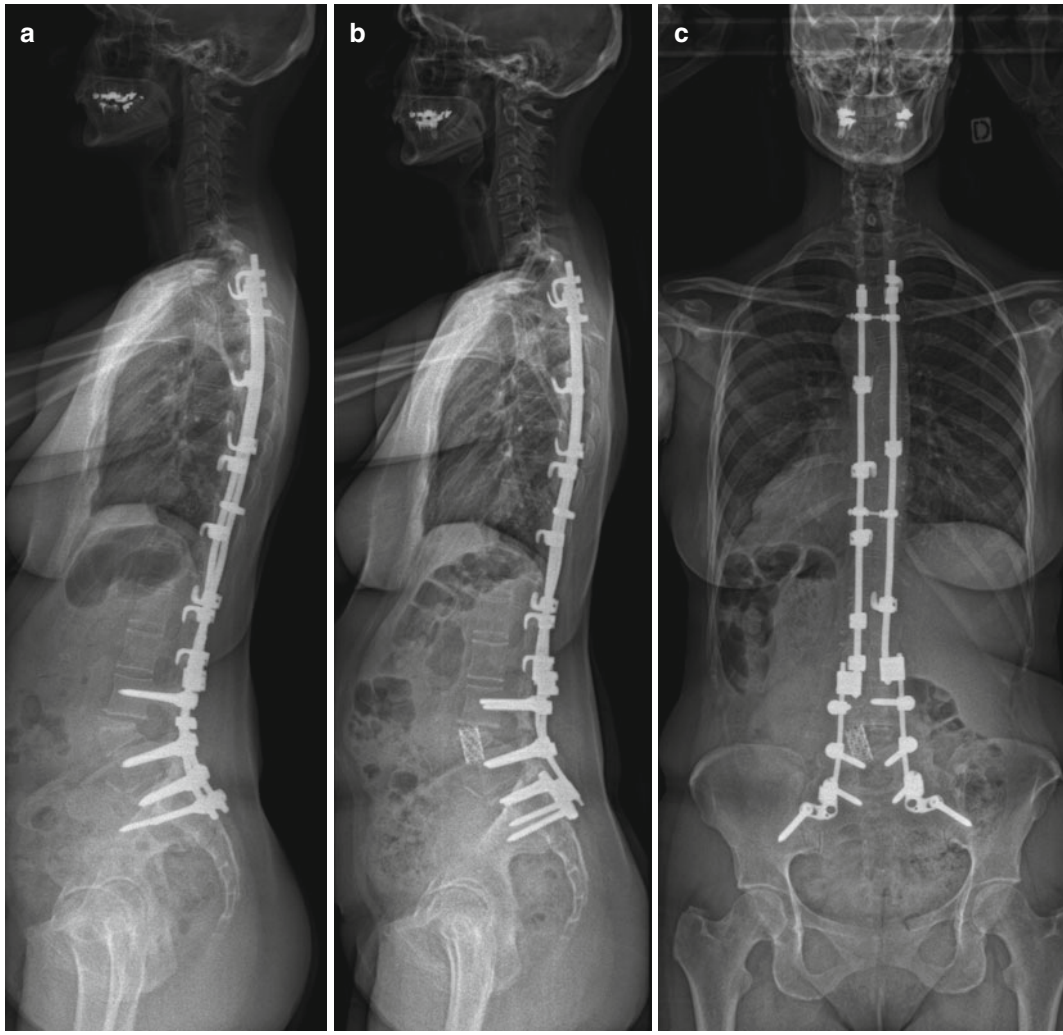

Fig. 30.5 Preoperative radiographs of one patient after lumbar PSO. (**a**) Postoperative radiographs of the patient after partial corporectomy on L4 by OLIF approach (**b**, **c**)

rod breakage and pseudarthrosis. The procedure is strictly the same; the skin incision is not so long and could be stretched by the retractors. The four Steinman pins are inserted in the vertebra above and below the osteotomized vertebra. Next, diskectomies of the two disks above and below are done. Managing the vertebra's pedicular vessels could be required, because most of the time, a lot of fibrosis recover this vessels. Thus, their identification, dissection, and ligature may be sometimes difficult. Then, the vertebra is osteotomized with bone scissor. Calibration of the corporectomy cage is done and finally, the cage is inserted (Fig. 30.5).

Of course, this OLIF approach can be done for a stand-alone anterior fusion with a stabilized cage provided on the market or with an anterior instrumentation (Fig. 30.6).

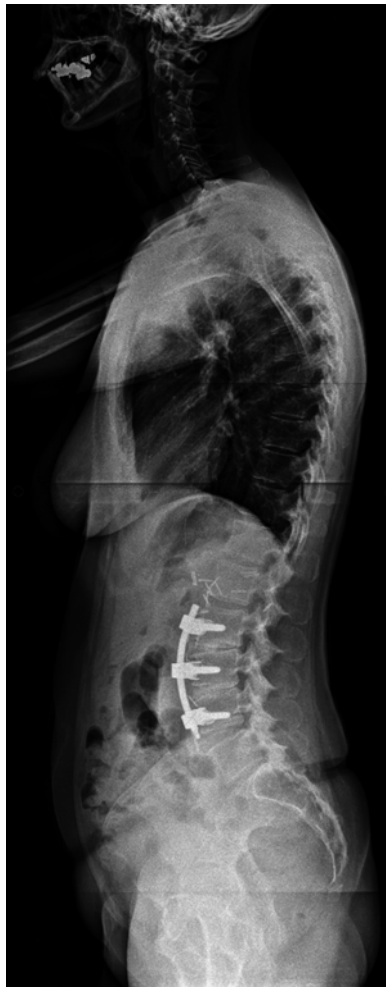

Fig. 30.6 Postoperative radiograph of one patient after anterior fusion alone by OLIF approach

Conclusion

The technique was used effectively and safely for up to three levels from L2 to L5 using a "sliding window" approach. The described technique is associated with a risk of complications that is similar to that reported for traditional anterior approaches, with the advantage of decreasing the risk of abdominal wall weakness or herniation. For selected cases, it can also be performed at L1–L2 and L5–S1, although another approach might be preferred at L5–S1 due to the risks associated with mobilization of the iliac vessels and to the presence of the iliac wing. Because of the new design of implants and development of this technique, the risk of contralateral compression of dural sac and nerve roots during insertion of interbody devices becomes quite rare and the procedure is now quite safe. Thus, OLIF can be applied to other procedures besides diskectomy and interbody fusion.

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31 Instrumented PLIF in Lumbar Degenerative Spine: Principles, Indications, Technical Aspects, Results, Complications and Pitfalls

Olivier Launay, Gilles Perrin, and Cédric Barrey

31.1 Introduction

Historically, lumbar fusion has been described as a treatment of symptomatic spondylolisthesis, degenerative scoliosis and spinal stenosis associated with instability [1–3]. Lumbar fusion is also performed after posterior decompressive procedure when evidence of preoperative lumbar spinal deformity or instability that could worsen after laminectomy alone exists [4].

Burns [5] reported the first case of lumbar interbody fusion in 1933. From an anterior approach (anterior lumbar interbody fusion, i.e. ALIF), he used an autogenous tibial peg to treat an adolescent with spondylolisthesis. The posterior lumbar interbody fusion (PLIF) procedure was first described in 1944 by Briggs and Milligan [6], who used laminectomy bone chips in the disk space as interbody graft. In 1946, Jaslow [7] modified the technique by positioning an excised portion of the spinous process within the intervertebral space. It was not until 1953 when Cloward [1] described his technique, which used impacted blocks of iliac crest autograft that the popularity of PLIF technique increased. The PLIF procedure was found to have substantially increased fusion rates, often in excess of 85 %. Despite controversy about the efficacy of lumbar interbody fusion, because of the introduction of pedicle screw fixation [8], some clinicians have continued to use this procedure as Lin [9], Branch [10] and Takeda [11]. Then, advances in bone physiology, biomechanics, and fusion techniques with synthetic interbody implants have renewed interest in posterior interbody fusion. The BAK cage, which is a perforated stainless steel cylinder and filled with local autologous bone graft, was developed by Bagby and Kulisch [12, 13]. The concept was to use two parallel implants interposed between the vertebral bodies, with distraction, that restored the disk space, and the compression of the implants against the subchondral bone produces immediate stability [14]. More recently, interbody cages have become popular and are now composed of a wide range of materials, such as titanium mesh, carbon fibre and polyether ether ketone (PEEK) [15]. Finally, the addition of pedicle screws increases the stability of the construct and has been reported to significantly increase the fusion rate of this procedure compared with stand-alone grafts [16, 17].

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_31

31.2 Rationale

Damage and degeneration of the lumbar disk can be the result of ageing, activity and trauma. Therefore, the degradation of the disk matrix leads to loss of disk height with or without bulging of the intervertebral disk and distension of the ligaments that create segmental instability. Thus, constraints on facet joints are increased and that may cause deformation, hypertrophy or subluxation of the facet joints like in spondylolisthesis. Moreover, mechanical stress causes hypertrophy and fibrosis of the ligamentum flavum. All these processes, including decreased disk height, facet joint and ligamentum flavum hypertrophy and vertebral endplate osteophytosis, may result in central canal stenosis, and/or lateral recess stenosis and/or foraminal stenosis [18]. Moreover, spinal stenosis may be emphasised by congenital abnormalities, or disorder of postnatal development [19].

Nerve root and cauda equina compression may arise from the combination of prolapsed disk, vertebral bone lesions anteriorly, but also from degenerated facet joint and hypertrophied ligamentum flavum posteriorly. Most often, degenerative spondylolisthesis occurs at the fourth lumbar vertebrae in middle-age women. As a result of a slipping forward of the vertebrae, cauda equina and spinal nerve roots may be tightened between the edge behind the top of lower vertebrae and frontal edge of the lower part of upper lamina, also linked to the subluxation of the facet joints.

Imaging studies are indispensable for diagnostic evaluation and treatment planning in symptomatic patients. There are many morphometric methods for the description of the spinal canal. Such terms as absolute and relative spinal stenosis are defined by purely radiological criteria and lack any clinical correlation. Lumbar MRI is the standard procedure for the demonstration of stenosis and cauda equina compression. As reported in the literature, its sensitivity is 87–96 % and its specificity is 68–75 % [20]. Lumbar CT may be useful for the assessment of bone condition and potential osteoporosis with a view towards the planning of surgery. On the other hand, lumbar myelography with post-myelographic CT should now only be performed in exceptional cases. The main indications for this invasive study are the presence of metal implants in the lumbar spine that would make MRI uninterpretable because of artefacts [21]. In our practice, we perform routinely full spine radiograph in order to analyse sagittal balance and lumbar dynamic radiographs to explore segmental instability. Electrophysiological studies are mainly useful in that they can reveal potential differential diagnoses.

One of the major objectives of spinal fusion is to relieve pain arising from spinal structures by removing potentially pain-generating disk tissue and stabilising one or more motion segments. Various methods of posterior lumbar fusion (PLF) have long been used for this purpose. Interbody fusion procedures became more widely used for their stabilising effect on the spine segment and as the role of the lumbar disk as a pain generator became better appreciated. The primary concept behind lumbar interbody fusion is that by removing all or most of the disk and stabilising the operated segment with bone graft, the primary pain generator is removed. Stabilising the segment should then eliminate mechanical stimulation that may provoke symptoms and may avoid future problems associated with collapse of an unsupported space. In a biomechanical study, interbody fusion was found to be stiffer than posterior lumbar fusion [22]. In addition, the surface area between the host bone and the graft is much greater with interbody fusion than with intertransverse process fusion.

The two primary purposes of interbody fusion are to relieve pain and stabilise the symptomatic spine segment. In cases of disk-related pain, the symptom-related tissue is removed. However, the removal of this tissue may cause the disk space to collapse with a concomitant narrowing of the foramen and related changes of the facet joints, causing nerve root compression. By filling the disk space with bone graft, the disk space height is re-established. This may also increase the height of the foramen. The bone graft grows into the bone of the adjacent vertebra, fusing them into a single unit. This stabilising effect is

particularly important in cases of pseudarthrosis, spondylolisthesis, spinal instability and postlaminectomy syndrome.

Evidence supports interbody fusion over posterior fusion alone in the treatment of lumbar disk-related pain. Weatherley [23] reported using discography to identify symptomatic disks at the level of a solid posterior fusion. More recently, successful outcome was reported for such patients with persistent symptoms despite a solid posterior fusion when symptomatic disks within the previously fused segment were treated with ALIF [24]. Results of a biomechanical study found that following simulated posterior fusion with pedicle screw fixation, the intradiscal pressure during spinal flexion was as great as that measured in the intact, nonoperated segment [25]. These studies provide biomechanical and clinical support for the need to use an interbody fusion technique to adequately address pain arising from the disk. ALIF and PLIF have been found to be effective in the treatment of disk-related pain [26–31], particularly that associated with a chemically sensitised disk identified by discography [32]. Fusion not involving an interbody technique has yielded poor results for disk-related pain [32–34]. The potential benefits of using cages in interbody fusion procedures are that they may increase the chances of achieving a successful fusion and they provide some immediate stability to the operated segment whilst the bone graft incorporates [35].

Several cages are designed to be implanted into the disk space using either the anterior or posterior approach. Based on the review of the literature, there is no general preference for the approach to be used. The decision regarding the type of approach should be made based on several factors, such as the sagittal balance, pathology present, spinal anatomy, patient's history of prior surgery (either approach may be more difficult if there is significant scarring from prior surgeries), vascular anatomy (and conditions that may make an anterior procedure more difficult, such as calcification of vessels) and the surgeon's individual training and experience.

The main challenge in the surgical treatment of lumbar degenerative spinal stenosis is to achieve adequate decompression of the neural structures without inducing iatrogenic instability, keeping or restoring a good lordosis and correcting or preventing spinal deformity. Sometimes nerve root decompression could be achieved only by restoration of the height of the intervertebral space and by a large opening of the lateral recesses and the foramen. Large bone resection may be indeed required. Decompression surgery for spinal stenosis due to degenerative changes producing claudication is successful in most patients. According to the literature the rate of further spinal instability is from 5 to 10 % and the risk of postoperative additional forward slip in degenerative spondylolisthesis is assessed between 10 and 18 % of the patients treated without fusion [36, 37]. Even if further horizontal dislocation did not lead to worse clinical results, it is logical for the surgical treatment not only to aim the most efficient decompression of the neurological structures by using adequate bone resection and restoration of the intervertebral height by the distractive interbody fusion, but also the second aim for surgery is to prevent postoperative destabilisation by using the same intervertebral fusion.

31.3 Indications

The principal indication for lumbar interbody fusion surgery is the stabilisation and fusion of adult spinal instability and/or deformity. Therefore, lumbar fusion has been described as a treatment of symptomatic spondylolisthesis, degenerative scoliosis and spinal stenosis associated with instability [1, 2, 9, 38]. For those with lumbar stenosis but without spondylolisthesis (deformity), the surgical management has traditionally involved posterior decompressive procedures, including laminectomy or laminotomy, and judicious use of partial medial facetectomies and foraminotomies, with or without diskectomy [39, 40]. In patients with evidence of spinal instability, however, in situ posterior lumbar fusion is recommended as a treatment option in addition to decompression in the setting of

lumbar stenosis [39]. Due to early surgical failures (the mean rate of poor outcome is 20 % in large series of laminectomies [36, 37]) and late deteriorations due to iatrogenic instability (5–18 %), restenosis (7 %) or disk herniation at adjacent spinal levels (10 %), careful selection of patients for fusion must be carried out by assessing radiological parameters that are associated with the greatest risk of postoperative destabilisation.

Secondary indications include recurrent lumbar disk herniation, where extensive bony removal is necessary for exposure of the disk fragments, lateral or massive disk herniations, failed previous lumbar fusions by other techniques and discogenic low back pain [38]. Because the cause of spinal pain is not completely understood and remains controversial, surgical efforts to treat such conditions also remain controversial [41]. The description of spinal pain is often referred to as "lumbar segmental instability" [42, 43] caused by degenerative disk disease [34] or facet joint syndrome [42, 44] when no signs of increased motion or spondylolisthesis exist [45].

As a consequence, the main parameters for indication of fusion after surgical decompression are (Fig. 31.1) as follows:

- Sagittal orientation of the facet joints
- Total facetectomy
- Lumbar stenosis associated with lumbar previous idiopathic scoliotic deformity
- Degenerative scoliosis
- Intracanal synovial cysts alone or associated with listhesis
- Flat back with loss of lordosis
- Degenerative spondylolisthesis
- Recurrent lumbar disk herniation
- Secondary displacement after failed previous decompressive surgery

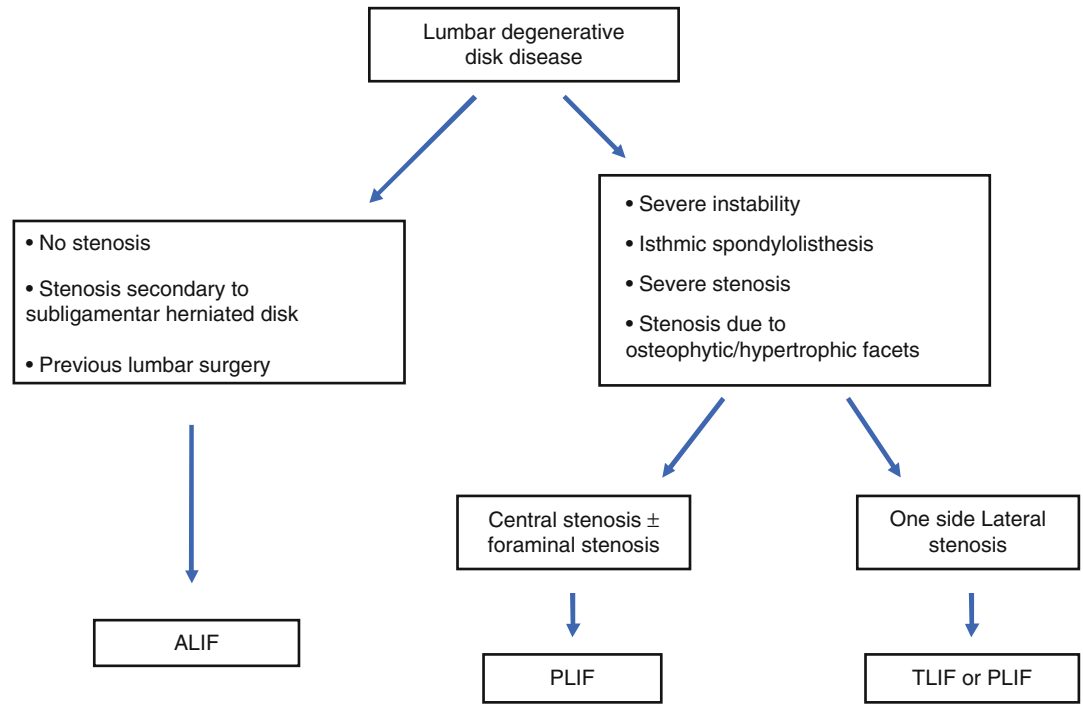

Fig. 31.1 Surgical indications of fusion in lumbar stenosis

31.4 Technical Aspects (Fig. 31.2)

To perform PLIF, patients are positioned in the prone on chest and iliac crests rolls in order to lower intra-abdominal pressure and improve venous drainage. Arms are placed on arm boards with abduction limited to 80° as to prevent brachial plexus injury.

A dorsal midline incision is made and subcutaneous tissues are dissected with monopolar until the deep fascia. This fascia is incised adjacent to the spinous processes bilaterally preserving supra-spinous ligament. Then the para-spinous muscles are released from the laminae in a subperiosteal fashion, and the dissection is taken out to the facets bilaterally until the transverse processes are visualised. Lateral radiographs should be obtained to confirm the operative levels prior to arthrodesis. Then, soft tissues should be removed on and around the lamina, pars, facet joint and dorsal transverse pro-

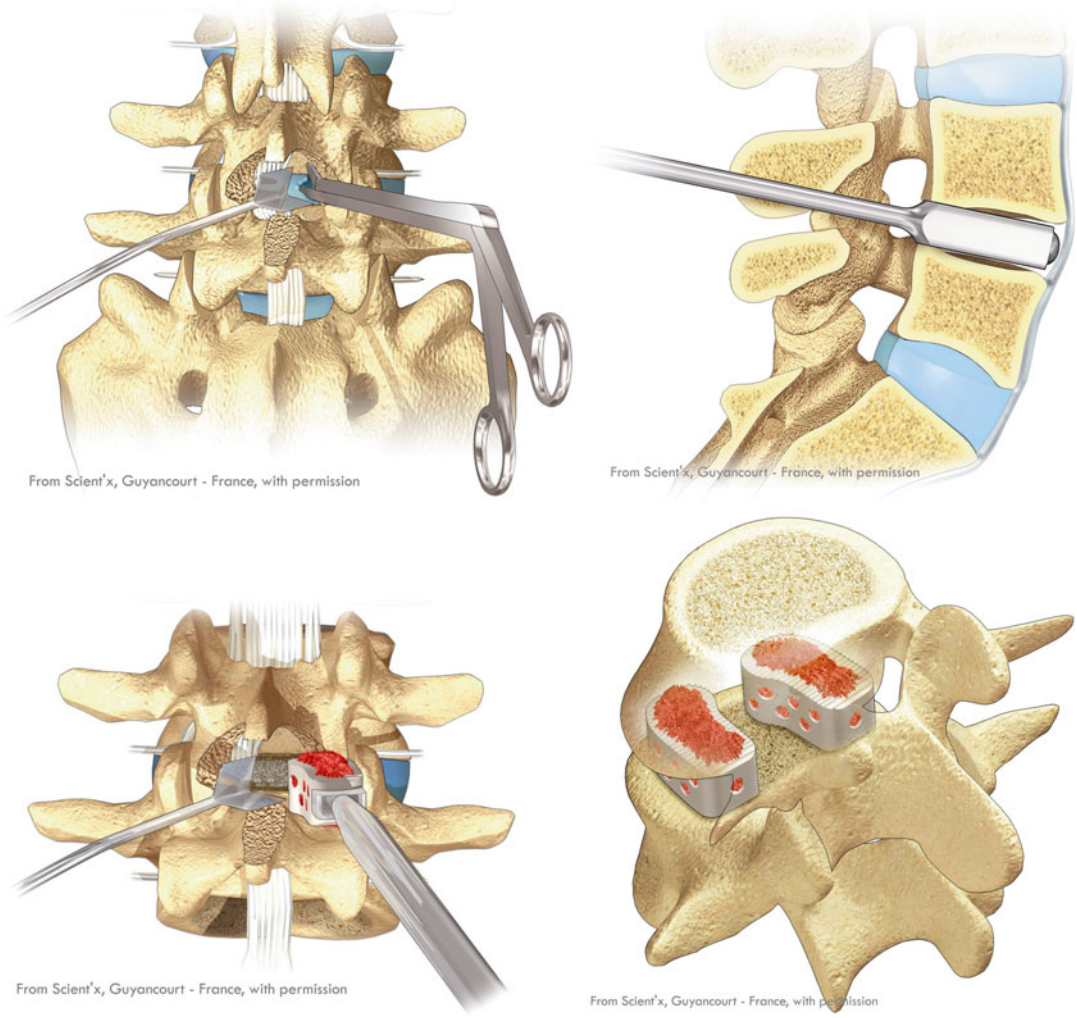

Fig. 31.2 Ten main surgical steps for PLIF procedure: (1) Complete exposure of the posterior arches of the two adjacent vertebras, (2) bilateral facetectomy (inferior facets of upper vertebra and superior facets of lower vertebra), (3) insertion of pedicle screws, (4) laminotomy with control of the adjacent nerve roots (i.e. the two upper and the two lower roots), (5) complete diskectomy via bilateral approach, (6) intervertebral distraction through the disk space, (7) cleaning of the end plates using curettes and/or dedicated rasps, (8) insertion of lordotic peek cages filled with autologous bone graft, (9) contouring of the rod, (10) rod placement with compression performed along the rod between the screw heads

cesses including the facet capsule and intrafacet synovium. After all, the fixation with pedicle screws is realised prior to the decompression, therefore limiting the risk of neural and dura mater injury during screws insertion and reducing the timing with the canal opened (associated with potential epidural bleeding). In addition slight and gentle distraction between the screw head using appropriate distractor could facilitate the insertion of the interbody implants. For this procedure, a facetectomy is done, keeping the bone that will be morselised for future graft, and then pedicle screws are inserted with lateral radiograph control bilaterally for all interbody fusions. Laminotomy and foraminotomy can be performed as needed for neural decompression of the thecal sac and nerve roots.

In most cases, complete laminectomy is not necessary and only partial laminotomy of the upper vertebra is sufficient to perform the decompression and to permit the insertion of the interbody cages. Epidural veins must be coagulated to avoid bleeding and cut to move apart neural elements without tether and discover disk space. Care should be taken to protect neural structures with nerve root retractor. Another cause of epidural bleeding is the emissary vein of the vertebral body, which can be plugged by haemostatic gauze. Complete diskectomy and endplate preparation are performed, also removing the cartilaginous end plates using rasps. Then, spacers are inserted in order to progressively distract the disk space and determine the adequate gauge implant size (Fig. 31.3). Morselised autogenous bone, obtained from the laminectomy, is packed anteriorly before the implants are placed. According to our experience, the dimensions of the cages have to be high

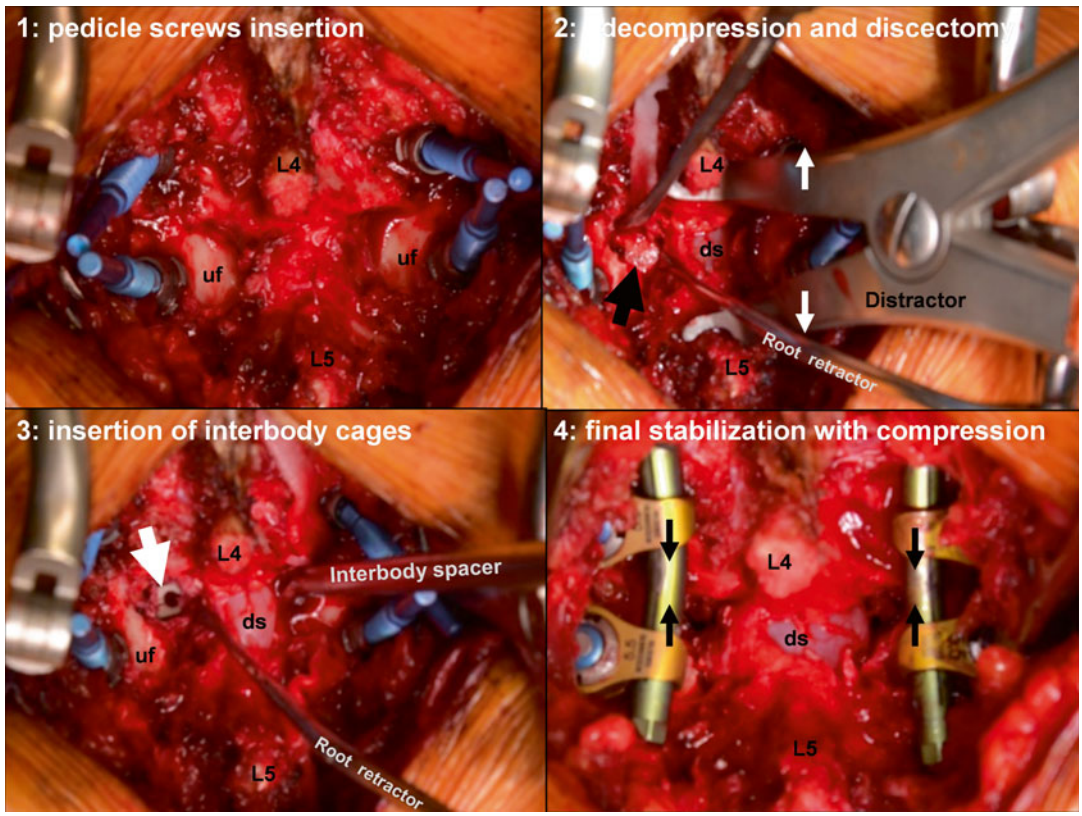

Fig. 31.3 Main surgical steps of PLIF procedure with perioperative views. Control of the four adjacent nerve roots, i.e. right and left L4 and L5 roots for L4–L5 level, is crucial to avoid any damage to neurologic structures. Intervertebral distraction on one side can be helpful to complete the decompression on the other side. *uf* upper facet, *ds* dural sac

enough (at least 10 mm) and large (25 mm) to obtain a good primary stabilisation and thus a good fusion. Also, wedge-shaped cages (8° lordotic at minimum) are superior to rectangular cages in restoring segmental lordosis and sagittal alignment and avoiding flat back deformity [46]. The cages, filled with autogenous bone (perfectly cleaned with removal of all soft tissues), are inserted into the disk space with the medial aspect on the pedicles bilaterally. Then pedicle screws and rods are compressed to restore segmental lordosis and promote fusion by graft compression. After haemostasis is ensured, the wound is irrigated and closed in layers. A subfascial drain may be left.

31.5 Advantages/Limitations

Unlike posterolateral intertransverse fusion, PLIF is a biomechanically optimal fusion because the graft and/or the interbody implant maintains the disk height (i.e. the lateral foraminal opening), protects the nerve roots, restores weight bearing to anterior structures and controls both horizontal and vertical instabilities. The cagelike implants (titanium or polyether ether ketone (PEEK) cages) meet the mechanical requirements for PLIF by serving both a mechanical function and a biologic bone growth function. The cages stretch the intervertebral space to its normal anatomic height and prevent the postoperative collapse of the graft. The implant is packed with cancellous bone graft obtained from the laminectomy [47]. PLIF and anterior lumbar interbody fusion (ALIF) with cages, without a complementary posterior fixation for 360° stabilisation, are associated with pseudo-arthrosis, secondary displacement and subsequent complications. The role of the pedicle screw-based posterior fixation is first to carry out temporary control of AP, lateral or rotational translation before the achievement of the definitive bone fusion, second to enhance osteogenesis and third to allow early mobilisation without the need of a postoperative corset to avoid external contention (except in case of osteoporosis), loss of lordosis and further destabilisation at the adjacent level to the arthrodesis.

PLIF is neither useful nor safer when reoperations are performed and in which the spinal canal was already opened. There exists an increased risk of dural breach and neural injury due to fibrosis and nerve root distortion. ALIF or TLIF may be a good alternative for these patients, thus avoiding the dissection in the region of the epidural fibrosis. Another drawback of this technique is the blood loss that can be excessive, particularly in older patients. Also, in patients with a high pelvic incidence, ALIF may be a better alternative. ALIF facilitates a good fusion and restores an optimal sagittal balance. This parameter is crucial to respect, because the L4–S1 segment represents two-third of the total lumbar lordosis. As a consequence, arthrodesis should be performed with these parameters in mind.

31.6 Complications (Table 31.1)

Posterior lumbar interbody fusion provides circumferential release of the dural sac and/or nerve roots as well as a biomechanically stable construct with anterior and middle-column load sharing combined with pedicle screw devices. However, PLIF has some risks for surgical complications [48]. Along with risks related to the surgical approach, the use of implants increases

Table 31.1 Complications due to PLIF procedures

Perioperative complications	Late complications
Dural laceration, cerebrospinal fluid (CSF) leakage: 4–17 %	Subsidence rare
	Pseudarthrosis: 2–15 %
Neurological complications:	Cage migration: rare
Transient (radicular pain, weakness) 3–17 %	Adjacent segment disease (no specific to PLIF): 3–11 %
Permanent (radicular pain, weakness) 0–7.5 %	
Deep wound infection: 0.5–5 %	
Hematoma: 1.2 %	
Pedicle screw misplacement: 4 %	
Injury to major abdominal vessels	
Pulmonary embolism: 0.4 %	

the risk for additional complications [49]. Complications are divided here into perioperative complications that occurred during and within 1 month of surgery and late complications after 1 month of surgery.

31.6.1 Perioperative Complications

The incidence of perioperative complications following single-level PLIF has been reported to be 18–37.5 % [48, 50], and the incidence after two-level PLIF has been reported as 46 % [51]. Moreover, Deyo et al. found that patients who underwent lumbar surgery with fusion had a complication rate twice as high as those who underwent surgery without fusion [49]. Amongst several kinds of fusion techniques, PLIF is considered one of the most technically demanding procedures and a definite learning curve exists. One of the most dangerous manipulations in PLIF is excessive retraction of the dural sac with the cauda equine and nerve roots whilst removing disk material and inserting cages and bones. Nerves are often taut and immobile because of severe adhesion due to canal stenosis. Surgeons may unknowingly retract the dural sac beyond a critical pressure and/or period whilst concentrating on the disk space. Neurological deficits have been reported in only 2 % of patients after posterolateral lumbar fusion, in which access to the disk is not required [52]. Hosono et al. found that the surgery duration was the only significant risk factor for neurological complications and therefore suggested that the dural sac or roots should have been retracted for unusually long periods in patients presented with neurological deficits [49]. Also, the rate of neurological complications in procedures with total facetectomy is much lower than procedures with partial preservation of facet joints. It may reduce the intensity and period of retraction of the dural sac and nerve roots and the risks of neurological complications by taking advantages of the large working space provided by total excision of bilateral facet joints.

As a consequence, perioperative complications of PLIF procedures are as follows:

- Dural laceration, cerebrospinal fluid (CSF) leakage: 4–17 % [53, 54]
- Neurological complications
  Transient (radicular pain, weakness) 3–17 % [54, 55]
  Permanent (radicular pain, weakness) 0–7.5 % [54, 55]
- Deep wound infection: 0.5–5 % [49, 53]
- Hematoma: 1.2 %
- Pedicle screw misplacement: 4 %
- Injury to major abdominal vessels [56]
- Pulmonary embolism: 0.4 %

31.6.2 Late Complications

The intracorporeal penetration on the cages or subsidence, and thus the loss of the restored intervertebral height, is perhaps the most significant late complication. It mainly occurs in osteoporotic patients, but remains rare – one patient in the authors' series [55].

Pseudarthrosis is an uncommon complication of PLIF – less than 2 % [54, 55].

Cage retropulsion after PLIF is another complication that has been described. The risk factors are insufficient cage size, multilevel fusion, inadequate seating of the cage anteriorly and surgery at segment L5/S1. Fundamental techniques in performing PLIF must be mastered as follows:

- The degenerated disk materials must be removed and the end plates cleaned from cartilaginous layers thoroughly.
- The cage must be inserted without damaging the bony end plates.
- Undersized cages should not be selected.
- Adequate compressive force must be applied to the disk space by the pedicle screws.
- Use of lordotic cages [57].

A prospective randomised study reported that fusion accelerates degenerative changes at the

adjacent segment of the fused spine, compared with naturally occurring changes [58]. Spinal fusion alters the biomechanics of spinal motion and increases intradiscal pressure or the load on facet joints of the adjacent motion segment of the fused spine [59]. Within 5 years of lumbar fusion surgery, the clinical incidence of symptomatic adjacent segment disease (ASD) is reportedly 5.2–18.5 % [59] and the incidence of additional surgery for symptomatic ASD is reportedly 3–11 % [60, 61]. Moreover, the deterioration rate for repeat PLIF (44 %) [62] is higher than that for initial PLIF (5.2–18.5 %) [59]. Biomechanical studies have demonstrated greater intradiscal pressure at the adjacent segment in double-level fusion than in single-level fusion [59]. This is one reason why repeat PLIF leads to higher incidence of ASD than the initial PLIF. Deyo et al. [63] reported in their study of 31,543 patients with surgery for lumbar stenosis that prior spinal surgery was the strongest risk factor for repeat surgery and that the hazard ratio for this was 1.58. These results suggest that patients undergoing repeat PLIF for ASD would incur more risk factors for additional surgery than those undergoing single- or double-level PLIF at the initial surgery. Furthermore, age was reported to be a major risk factor for ASD [59, 60].

31.7 A Comparison of PLIF and TLIF

Interbody fusion techniques have been developed to preserve the load-bearing capacity of the spine, restore local lordosis and facilitate compressive loading onto interbody graft – all of which enhance the potential for fusion acquisition [64]. Lumbar interbody fusion with supplemental posterior pedicle screw fixation (“circumferential” fusion), based on biomechanical evaluation, stabilises all three columns of the spine and has been used routinely for the operative treatment of painful spinal disorders. PLIF, TLIF and ALIF approaches are the most frequently performed options and, when accompanied by posterior pedicle screw fixation, result in circumferential fusion. Each of the former procedures has advantages and drawbacks.

Posterolateral graft and fixation is easily added to the PLIF, further enhancing spinal stability and the induction of fusion.

Unfortunately, the PLIF is usually limited to use at levels below L3, because of the risk of damage to the conus medullaris and to the cauda equina that may result from bilateral root retraction here. The suggested modification of PLIF presented by Harms and Jeszenszky [65], the TLIF, is equivalent to the PLIF and is simpler and safe, and some believe superior in result. The technical advantages of the TLIF include avoidance of thecal sac and/or nerve root retraction injury, safe performance below L3 and a decrease in epidural bleeding and scarring [65–67]. Harms and Jeszenszky, in their presentation of the original TLIF procedure, as well as many other authors of biomechanical reports, have recommended additional posterior pedicle screw fixation to enhance stability.

The PLIF and TLIF are familiar to most spine surgeons and both require only a single approach. These two procedures have therefore recently become the most popularly used techniques to treat spinal disorders. They are associated with a few differences with regard to the actual surgical technique, however. The TLIF requires a complete unilateral facetectomy and spares the contralateral lamina, facets, and pars interarticularis. The PLIF procedure requires a bilateral laminotomy as well as partial, and at times complete, facetectomy to place an adequate interbody spacer device. The TLIF implants are usually semilunar and only one is implanted, whereas those used for PLIF are cubic or cylindrical in shape and are placed in pairs resulting in a greater surface of bone graft and better distribution of loads. With the PLIF procedure, a portion of the posterior longitudinal ligament (PLL) is cut to position the interbody space devices, whereas the TLIF procedure preserves most of the PLL [68].

On the other hand, the diskectomy and clearing of end plates performed during PLIF procedure

via bilateral approach are probably more complete and have better quality compared to TLIF.

From a biomechanical consideration perspective, Sim et al. showed that the PLIF provides a higher immediate stability than the TLIF, especially for the lateral bending motion. The implant position in the disk space, however, is not an important factor for the immediate stability of a single-level TLIF. If the TLIF implant is placed further anteriorly, although there were no statistically significant differences in this study, there is a tendency for this position to be more stable [68].

Another difference between PLIF and TLIF is that performing a TLIF at the L5–S1 segment is quite difficult due to the pelvic position that prevents the good positioning of the cage in the disk space.

31.8 Tips and Tricks

- During exposure, a goal should be to avoid dural tear and nerve roots injury that can result from the manipulation of instruments and also to reduce the amount of bleeding coming from the canal (epidural veins).
- During the procedure when the nerve roots are retracted to prepare the disk space, there is most often significant bleeding that arises from the emissary vein of the vertebral body. This may be difficult to stop. The most effective strategy is to clog the vein with haemostatic gaze and thus to perform an embolisation of the vein.
- When preparing the disk space, the vertebral bodies must be maximally distracted in order to put the higher cage (10–12 mm of height in most cases). The distractor used should be 1 or 2 mm higher compared to the implant to facilitate the insertion of the cage on the contralateral side. It also facilitates the decompression of the nerve roots in the foramen and confers maximum stability to the spine – thus avoiding the retropulsion of the cage.
- Morselised and perfectly cleaned bone is compressed into the cage, but the area of fusion is quite reduced. To enhance the chance of fusion, we also put morselised bone into the anterior disk space before inserting the cages.
- The five key points to restore lumbar lordosis during PLIF procedure are as follows:
  1. Patient positioning
  2. Use of lordotic cages
  3. Optimal size for the cages
  4. Optimal AP placement of the cages (placed at the anterior part of the disk space)
  5. Posterior inter-pedicular compression after cage insertion

31.9 Clinical Cases

Clinical cases are illustrated in Figs. 31.4, 31.5, 31.6 and 31.7.

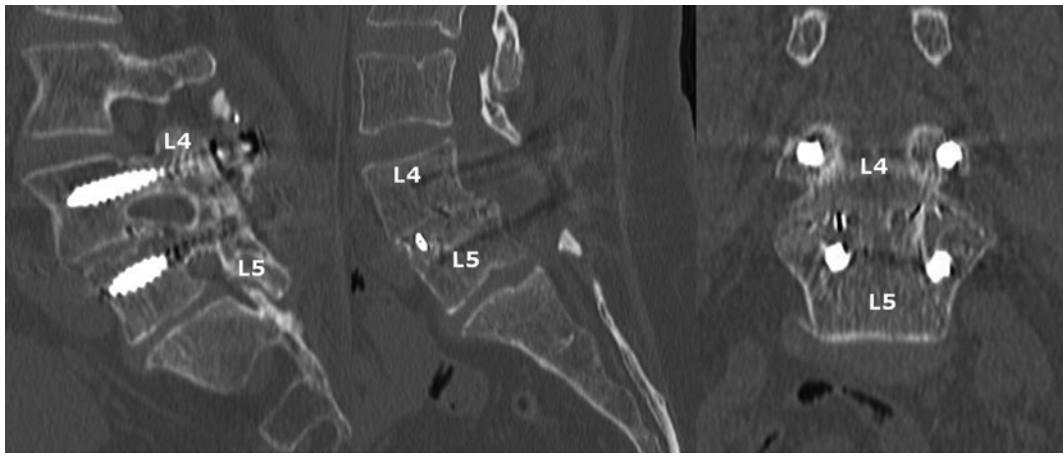

Fig. 31.4 CT scan in sagittal and coronal views that demonstrate a solid fusion with remodelling of the bone graft between L4 and L5 after a PLIF procedure

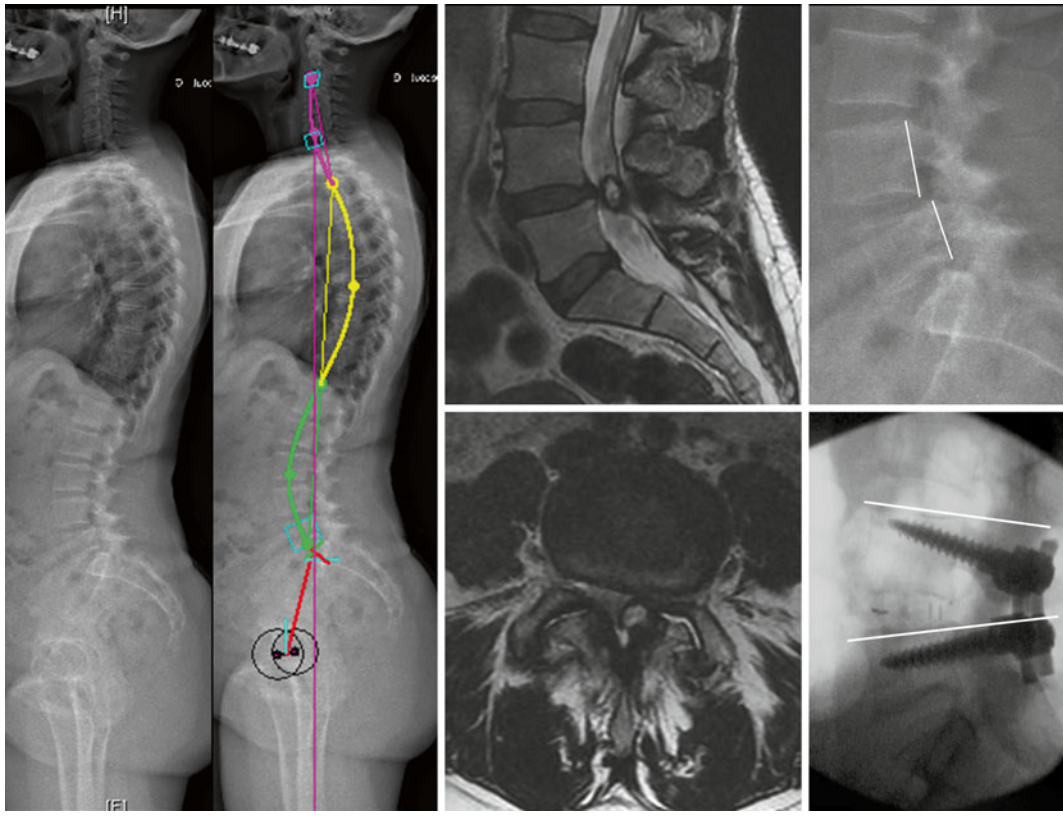

Fig. 31.5 A 54-year-old woman operated with an L4–L5 PLIF procedure because of a degenerative L4–L5 spondylolisthesis with an intra-canalicular synovial cyst

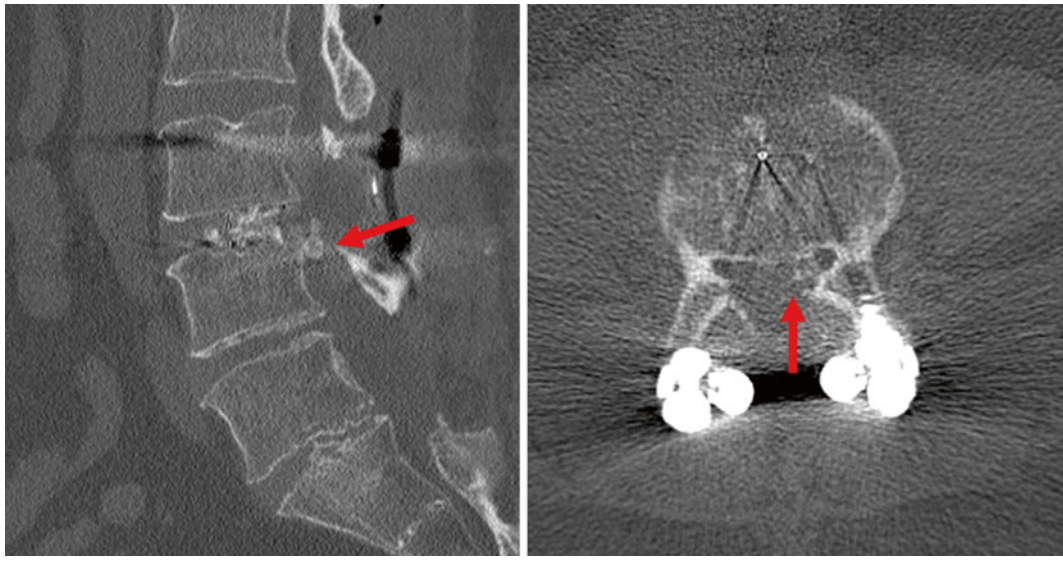

Fig. 31.6 A 56-year-old man who underwent an operation for lumbar stenosis via an L3–L4 PLIF procedure that suffered postoperatively from left cruralgia. An emergency CT scan was performed, which demonstrated morselised bone graft located in the left recess (*red arrows*). The patient underwent immediate reoperation to decompress the nerve root and remove the bone graft that had migrated into the canal

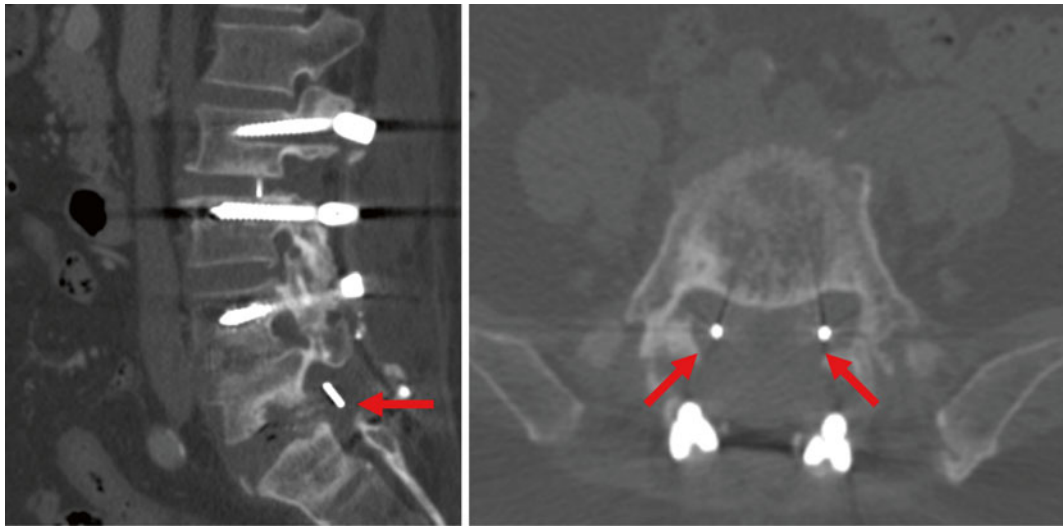

Fig. 31.7 CT scan with sagittal and axial views that demonstrate bilateral cage retropulsion into the recess (*red arrows*). The patient suffered from bilateral sciatica, which necessitated reoperation for cage repositioning

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Part VI

Minimally Invasive Techniques

32 Degenerative Disk Disease: Stages of Degeneration, Low Back Pain, and Insights on Intradiskal Therapies

Jean-Louis Husson, Jean Lombard, and Florian Cueff

32.1 Stages of Degeneration and Low Back Pain (and Why We Need a New Classification System)

32.1.1 Spinal Degeneration Cascade

Although the spinal degeneration cascade proposed by Kirkaldy-Willis and Farfan [1] is still very relevant, it is incomplete. It does not capture the early lesions in some of the stabilizing disk and ligament structures from a purely histological point of view, despite being the subject of a significant body of research (cell culture, genomics, etc.), nor does it capture lesions that do not cause excessive joint motion.

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32.1.2 Acquired Degenerative Intervertebral Dysfunction (ADIVD)

To eliminate confusion surrounding the use of the term "instability," which only corresponds to stage II of the Kirkaldy-Willis cascade, we would like to propose a new term: *acquired degenerative intervertebral dysfunction (ADIVD)* [2]. This condition refers to a benign mechanical disorder of segmental vertebral function due to degeneration and is hence acquired. It takes into account all of the lesions in the stabilizing structures, with movement disorders characterized as being qualitative and/or quantitative in nature, whether to a greater or lesser extent.

32.1.3 New Four-Stage Classification for Progressive Spinal Degeneration

This new term allows us to represent every stage of the progressive loss of stability in the degenerative lumbar spine due to ADIVD (Fig. 32.1) [2]. This four-stage classification encompasses the same I, II, and III stages proposed by Kirkaldy-Willis and Farfan [1], but adds stage 0, where minimal dysfunction is present.

Stage 0: Minimal Dysfunction
This is the initial phase of elastic deformation due to the disk losing its viscoelastic properties. Lesions are only visible on histologic

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_32

examination and only rarely manifest themselves as acute lumbar immobilization.

Stage I: Minor Dysfunction

This is the intermediate phase of elastic deformation with pure loss of stability, marked by lower back pain and brief episodes of posterior facet joint locking, which can occur at one or multiple levels and cause referred pain. This corresponds to Maigne's notion of painful minor intervertebral dysfunction (PMID).

Stage II: Major Dysfunction

This corresponds to Kirkaldy-Willis' stage of instability. This is the advanced stage of elastic deformation, with a dynamic, progressive loss of stability. Radiological and clinical signs of dynamic stenosis appear, leading to lumbar and sciatic symptoms due to changes in the spinal canal volume without anatomical modifications. Any disk protrusion, posterior facet osteoarthritis, or retrolisthesis can then alter the volume of the nerve root canal during the stage of static-dynamic stenosis and trigger neurogenic claudication symptoms. Next, the disks undergo plastic deformation because of water loss. This results in permanent lateral stenosis, made worse by the consequences of the loss of stability (osteophytes, abnormal movements).

In terms of functional signs, the only aspect that all authors agree on is the presence of mundane mechanical low back pain in combination with pseudoradicular pain, or Maigne's referred pain; true radicular pain is rare.

There is no correlation between various clinical examination techniques and objective measurements. A comparative study of patients with suspected instability and patients in a control group was performed using a twist CT scan [3]. The findings disproved Graf's hypothesis [4] that posterior facet separation

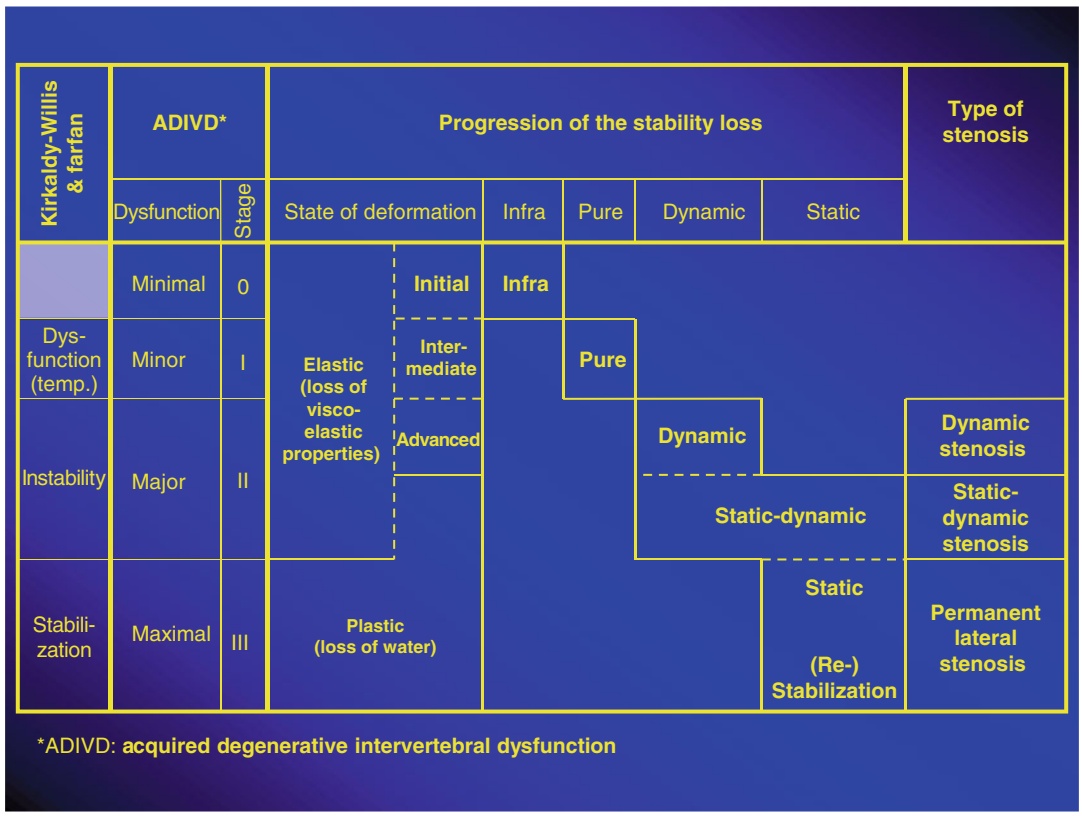

Fig. 32.1 Diagram capturing the progressive loss of stability due to acquired degenerative intervertebral dysfunction (*ADIVD*)

was a pathognomonic sign of instability, since separation was also observed in patients who were asymptomatic. Pain in the posterior joint structures during trunk rotation or when striking the heel to the ground is only one of the many clinical signs of instability. The duration of pain relief after peri- or intra-articular lidocaine or corticosteroid injection is shorter in cases of facet pain due to instability than in cases of pain due to facet joint arthritis.

Stage III: Maximal Dysfunction

This corresponds to the final degenerative phase, characterized by structures that become wedged together and restabilize the spine, or the appearance of Junghanns degenerative spondylolisthesis or rotational dislocation, which causes degenerative lumbar scoliosis in adults.

The clinical symptoms including pain can either stem from the bone, adjacent spinous processes rubbing together (Baastrup's disease), the posterior facet joints, or even be referred.

32.1.4 Need for Additional Examinations

The lack of specific symptoms, their multifactorial nature, and the lack of relationship between movement quantification and pain intensity make it challenging to understand the clinical picture of ADIVD. It also explains why the physician must turn to various types of additional tests [2]. Standard A/P and lateral and three fourth X-rays form the basis of the evaluation, along with dynamic views, which were first proposed by Nachemson in 1944. These were followed by many studies attempting to define segmental vertebral motion, quantify it, define standards, and as a consequence, get closer to the pathology using quantitative and hopefully reproducible data. Although these were all high-quality studies, there was no general agreement. However, White and Panjabi [5] were credited for showing that the vertebral unit had 6° of freedom. The twist CT scan is the only dynamic test with some evaluation potential, not necessarily by using true measurements, but by subjectively evaluating posterior facet joint separation in extreme positions of active rotation [3]. Magnetic resonance imaging (MRI) can reveal early signs of nucleus pulposus dehydration, which shows up as reduced T2 hypersignal. Modic underlines the lack of correlation between three levels of spinal cord signal intensity and degenerative disk disease and between clinical symptoms and anatomical disruptions [6, 7]. Pfirmann [8] subsequently proposed a treatment algorithm based on MRI classification of lumbar intervertebral disk degeneration.

32.2 Overview of Intradiskal Therapies

Conservative treatment encompasses several well-known nonsurgical and rehabilitation methods. Among the various intradiskal therapies currently being used to treat herniated lumbar disks and diskogenic lower back pain, we discuss the two we are most familiar with: radiofrequency (RF) ablation and nucleus pulposus implant.

32.2.1 Radiofrequency Intradiskal Techniques for Treating Herniated Lumbar Disks and Diskogenic Lower Back Pain

32.2.1.1 Introduction

Percutaneous intradiskal RF techniques are an integral part of the fairly complex treatment of low back pain or radicular diskogenic lumbar pain. These techniques came to the forefront when the chymopapain enzyme used for chemonucleolysis was discontinued. They were developed in parallel with nucleolysis techniques, which use chemical agents instead.

All RF techniques are performed through a minimally invasive transforaminal approach, the same approach used for a diskogram in Kambin's triangle [9, 10] under the outgoing nerve root. A thin catheter is used to deliver a variable dose of thermal energy to a specific part of the lumbar disk; this catheter is connected to a preprogrammed external RF generator that can deter-

mine the disk impedance, among other variables. The catheter is removed at the end of the procedure. This procedure, which is carried out in an ambulatory care setting under local anesthesia or with neurosedative agents, must be performed in the appropriate aseptic environment with fluoroscopy. Prophylactic antibiotics during the procedure are recommended.

The exact mechanism of action is not well understood. It is based on the principles of decompressing the disk and/or destroying the disk's peripheral neoinnervation and neovascularization, along with altering the disk's collagen.

The clinical outcomes for these procedures are a function of patient selection and the technical requirements of the procedure, which are very specific. These techniques are aimed at relatively young patients who have failed a full course of conservative treatment and physical therapy, prior to discussing surgical disk stabilization. Even if only temporarily effective, these radiofrequency techniques can be used as patient selection criteria for disk arthroplasty or interbody fusion, as the success of intradiskal treatment confirms that the pain originates in the disk. If not effective, another surgical procedure can be performed without any additional problems.

32.2.1.2 History and Classification

In the mid-1970s, chemical nucleolysis was only performed with chymopapain. Since chymopapain was first introduced in 1963, its efficacy (70–80 % good and very good results) has been demonstrated in several randomized studies and compared with surgical treatment [11–13]. When the manufacture and sale of chymopapain were discontinued in 2001 for financial reasons, other percutaneous intradiskal therapies such as RF developed rapidly.

There are two main types of RF therapies:

- Those that target the nucleus pulposus, such as disk decompression (e.g., Nucleoplasty® by ArthroCare)
- Those that target the annulus fibrosis, such as annuloplasty with intradiskal electrothermal therapy (IDET) (e.g., SPINECATH and ACUTHERM from NeuroTherm)

Among these techniques, some are best suited to nerve root compression (Nucleoplasty, ACUTHERM) and others to isolated disk disease (SPINECATH).

32.2.1.3 Advantages

Generally, the risks associated with this procedure are considerably reduced because intradiskal RF ablation is performed through a percutaneous approach and the procedure is short (less than 20 min).

- Local anesthesia or neurosedative agents are sufficient for these minimally painful procedures. This allows for continued oral communication with the patient about pain and neurological signs.
- The spinal canal is not breached and there are no epidural scars. The posterior musculature is not touched.
- The risk of sepsis is negligible.
- Only a very small part of the disk structure is removed.

32.2.1.4 Common Mechanisms of Action

Percutaneous techniques are indicated in early degenerative disk disease, at a stage where the disk is still hydrated.

Diskogenic pain is provoked by excessive pressure on the disk, along with inflammation and hyperinnervation of annulus fibers within the fissures. Contained disk herniation within the annulus is only one of the degenerative stages.

Several mechanisms of actions have been proposed to explain the effectiveness of these procedures:

- Denaturation of type I collagen (greater stiffness and dehydration)
- Nuclear cavitation leading to reduction in nucleus volume and reintegration of annular fragments (disk nucleoplasty)
- Destruction of annular fissures and destruction of peripheral inflammatory neovascularization and newly formed pain receptors (annuloplasty)
- Disintegration of the herniated mass (annuloplasty)

32.2.1.5 Patient Selection and Results

RF ablation techniques are aimed at patients with diskogenic lower back pain, with or without small contained disk herniation, with or without compressive or referred radiculalgia. As with every treatment, the outcomes are a function of patient selection. The outcomes are also affected by the procedure quality, catheter placement, navigation within the disk, and the surgeon's practices.

The minimum imaging assessment consists of weight-bearing and dynamic X-rays, MRI without contrast, and CT scan.

The indications are:

- Diskogenic lower back pain and lumbar radicular pain due to contained disk herniation that has not responded to at least 6 months of well-conducted conservative treatment and physical therapy. Individual background variables such as the presence of secondary gains or social and professional conflicts must also be evaluated. Components of the diskogenic lower back pain diagnosis may include the outcome of the corset test and a negative result after facet joint block. Other diagnostic tools include the diskography results associated with provoked pain and evidence of posterior fissure. This evaluation is recommended before performing RF ablation to evaluate disk pressure (if the goal is to reduce it) or to eliminate the presence of non-contained disk herniation.
- Involvement of one or two levels. The procedure is harder to perform at L5–S1 in men because the disk is embedded into the iliac crests.
- MRI: type 0 Modic changes.
- Disk height >70 % on weight-bearing X-rays.

The contraindications are suspicion of facet-related low back pain, extruded disk, spondylolisthesis or retrolisthesis, symptomatic lumbar stenosis, disk asymmetry, scoliosis, type I Modic changes (inflammatory changes in vertebral end plates), collapsed disk, and epidural leakage on diskogram (non-contained hernia).

32.2.1.6 Intradiskal RF Ablation Techniques

There are two types of techniques, aimed either at isolated disk degeneration or contained disk herniation.

Treatment of Isolated Disk Degeneration

- The SPINECATH IDET [14] is an annuloplasty procedure where a bipolar RF catheter is inserted into the posterior or lateral section of the annulus (until the fissure is reached). Fluoroscopy is used to verify the catheter position (Fig. 32.2) and then thermal energy (40–60 °C) delivered over a 5-cm area for 16 in. Optimal placement of the catheter can be challenging, as the entire posterior annulus must be covered without breaching it (Fig. 32.3). Moderate resurgence of the diskogenic pain during the procedure is a sign of efficacy.

  Several nonrandomized studies have reported moderate improvements with 50 % pain reduction after 1 year [15–18]. Two randomized studies found good results versus placebo in terms of reduction in the Oswestry Disability Index (ODI) [19, 20].
- Percutaneous intradiskal RF thermocoagulation (PIRFT) techniques are used to perform nucleoplasty with monopolar radiofrequency; ALAR, RADIONIC, and DISKIT have been gradually abandoned because of disappointing results and lack of reliable basic research [21, 22].

Treatment of Contained Disk Herniation

- Laser diskectomy was first introduced in 1986 [23]. This is not actually an RF technique, but one where the nucleus is vaporized using a laser diode. This procedure is aimed at treating lumbar radicular pain due to contained disk herniation. The needle or catheter is introduced in the center of the disk and then moved to the posterolateral side toward the suspected hernia. Intermittent bursts of energy are given up to a total dose of 1,200–1,600 J to

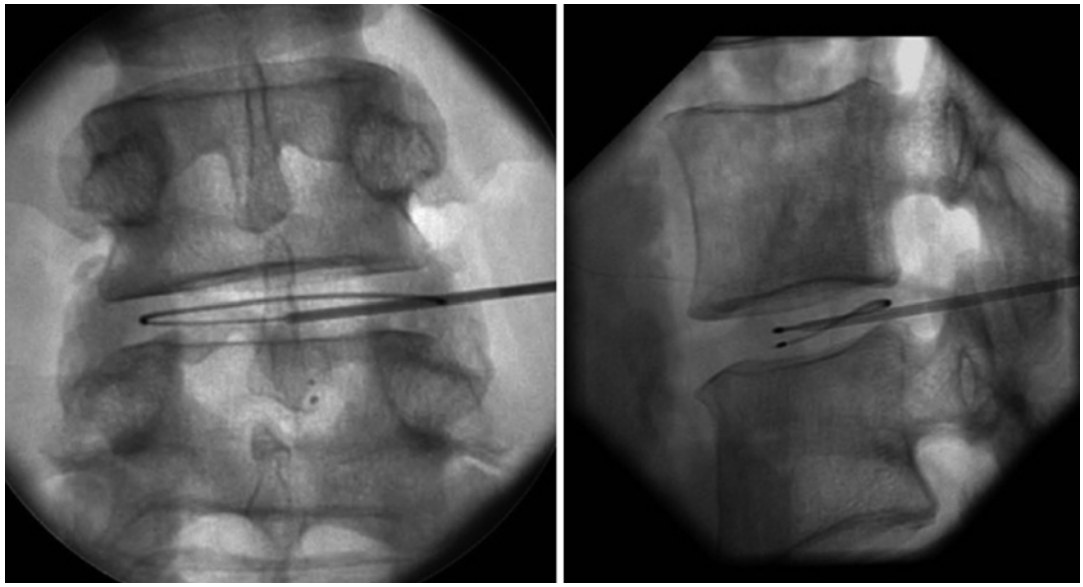

Fig. 32.2 Unrolled configuration of the SPINECATH IDET (NeuroTherm) on A/P (*left*) and lateral (*right*) fluoroscopy views

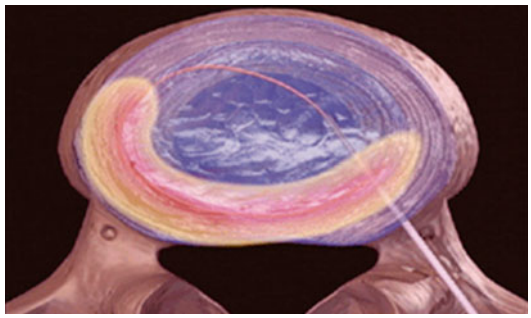

Fig. 32.3 Drawing of the optimal position of the SPINECATH catheter

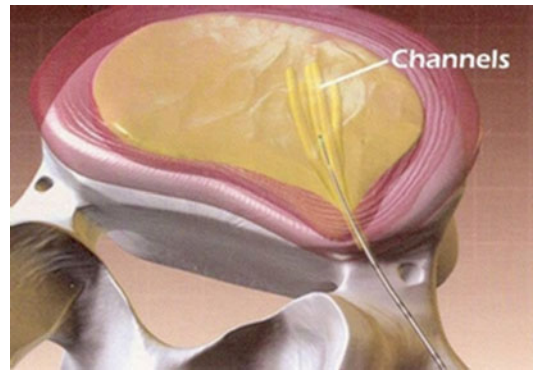

Fig. 32.4 Drawing of catheter positioning used during disk decompression (Nucleoplasty® by ArthroCare)

vaporize part of the nucleus [23]. This technique is demanding and requires optimal placement of the powerful catheter. Secondary end plate inflammatory lesions have been described by Cvitanic in 30 % of cases [24], as well as a few cases of thermal discitis with flare-up of the low back pain.

Several studies have reported good results and pain reduction in about 70 % of cases [25–27]. This pain reduction occurs 6–8 weeks after the procedure. The best indication seems to be contained herniation or failed disk decompression using radiofrequency energy (nucleoplasty) for the same indications. However, the efficacy of this technique has yet to be truly demonstrated [28].

- DISK nucleoplasty™ is a newer technique introduced by ArthroCare. This technique consists of RF catheter coblation (cold ablation) to induce nucleus cavitation (Fig. 32.4) and reduce intradiskal pressure. Less heat (40–70 °C) is produced than with a laser, thus the risk of end plate damage is lower. The indications are midline- or lateral-contained

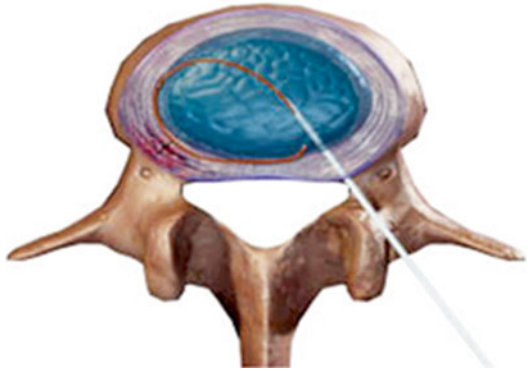

Fig. 32.5 Drawing of ACUTHERM™ decompression catheter (NeuroTherm) being used to treat a lateral disk herniation

herniation in minimally degenerated disks. In an animal model, this treatment was shown to alter cytokines such as IL-1 and IL-8 [29]. Cohort studies have shown significant decrease in VAS pain and with good results in 70–80 % of cases [30–32].

- The ACUTHERM IDET is an annuloplasty technique derived from the SPINECATH system (same RF generator) that uses a catheter to provide targeted disk decompression. A catheter heats the area of the disk-nerve root impingement, which alters the collagen and reduces the hernia by desiccation. This technique can be used with foraminal hernias (Fig. 32.5).

Other Percutaneous Techniques

These other techniques revolve around chemonucleolysis (injection of a chemical agent) and percutaneous diskectomy (mechanical action), for example:

- Nucleolysis with Hexatrione®, which has been abandoned because of the risk of disk calcification
- Ozone chemonucleolysis
- Absolute alcohol nucleolysis
- Discogel® nucleolysis

Discogel® (jellified ethanol, manufactured by Gelscom in France) is an implantable device that is a promising treatment for contained disk herniation. It aims at improving water diffusion from the periphery to the center of the disk. The gel's viscosity keeps the alcohol from leaking outside the disk. Results of a pilot study were encouraging [33]. A study funded by the PHRC in France is currently under way. We will soon be publishing the results of 35 patients that were treated with Discogel®.

32.2.1.7 Conclusion

Percutaneous intradiskal RF techniques are easy to perform in the hands of a trained surgeon. They are minimally invasive for disk and perivertebral structures and have a low complication rate, but require specific instrumentation and consumable products (RF generator and catheter).

Their main role resides in treating diskogenic lower back pain at an early, nonsurgical stage of the disease progression and as an alternative to traditional diskectomy surgery for treating disk herniation. However, the uptake of these techniques has been limited because of persistent questions about their efficacy, despite numerous publications.

32.2.2 Nucleus Pulposus Implant: Preliminary Results of a Memory-Coiling Spiral Implant

32.2.2.1 Introduction

The aftereffects of disk nucleus ablation have been evaluated clinically and biomechanically. During an in vitro study, Brinckmann [34] found progressive loss of disk height and increased radial disk bulging proportional to the mass of the excised nucleus tissue. This loss of disk height can lead to overload of the posterior facet joints and biological changes in the joint cartilage [35, 36]. These changes can cause painful spondylarthrosis and eventually require surgical treatment. After nucleus removal, kinematic studies have shown increased range of motion and clear displacement of the center of rotation in flexion/extension and lateral bending [37–39].

32.2.2.2 Design Specifications for a Memory-Coiling Spiral Nucleus Pulposus Implant

Our primary goal was to come up with an original method to replace only the nucleus pulposus through a minimally invasive procedure that would be an extension of the surgical diskectomy procedure used to treat disk herniation and to maintain the physiology of the mobile spinal segment and adjacent disks [40–44]. For this "memory-coiling spiral" implant, the memory effect is achieved through a specific manufacturing process where the base polycarbonate urethane elastomer (Sulene™ PCU, previously produced by Centerpulse, now Zimmer) is modified at the molecular level. When implanted in its unrolled state into the empty intradiskal cavity, the implant spontaneously regains its pre-formed spiral shape and completely fills the cavity without mechanical fixation (Fig. 32.6).

By restoring or maintaining maximum disk height, normal lumbar lordosis is preserved and the congruence between the facet joints is preserved as best as possible. Together, these limit the occurrence of secondary facet-related pain. This design provides a certain degree of pain-free interbody stability, preserves the mobility of the intervertebral segment, and avoids the need for another surgical procedure.

To meet these objectives, the intervertebral disk implant needs to have the following properties: non-compressible, elastic, and able to withstand continuous cyclic loading in various directions and no mechanical axis or fixed center of rotation so as to not introduce abnormal loads that could lead to painful joint dysfunction or localized overloading of the adjacent vertebral end plates. The centers of rotation of this new implant do not need to be positioned precisely during surgery as do other implants [45]. The implant's center continuously changes during movements within an area that is specific to each level and each movement.

The implant must fill the intradiskal void created by percutaneous diskectomy as completely as possible. This will restore internal disk preloads and, as a consequence, the biomechanical conditions required for healing of the type II collagen fibers in the outer annulus (which have a half-life of about 7 months, provided they are not in an advanced stage of degenerative disk disease). In this scenario, the outer annulus has some functional recovery capacity and is able to maintain its "new" nucleus without causing disk prolapse or predisposing it to expulsion into the medullary canal.

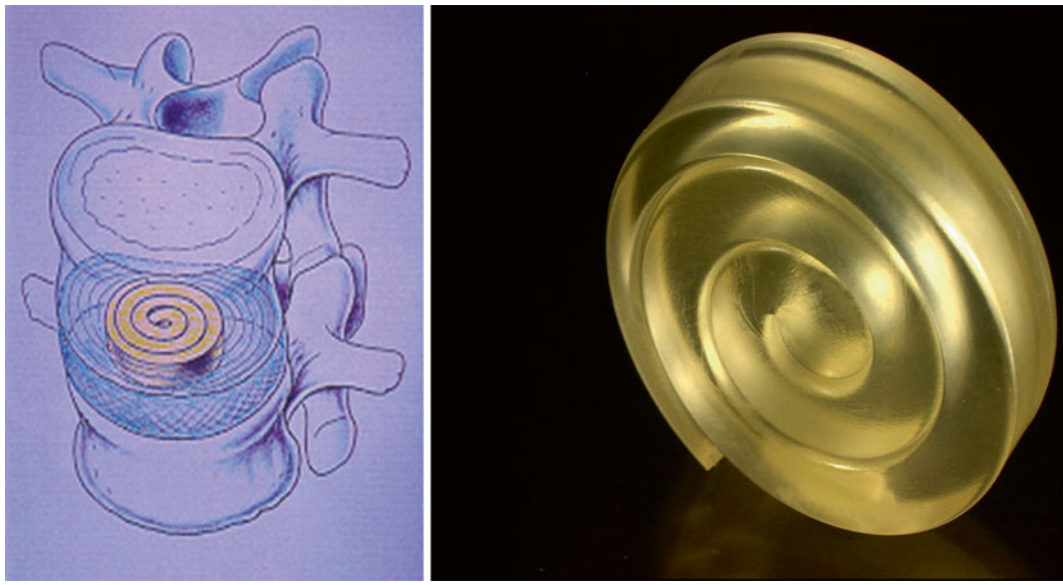

Fig. 32.6 Drawing of the nucleus pulposus memory-coiling spiral implant (*left*) and photo of the actual product (*right*)

This implant truly differs from other nucleus replacement implants because it preserves the adjacent vertebral end plates [45] and avoids or delays continued degeneration of the outer annulus by keeping it in a functional state.

This implant must be biocompatible, reliable, and not undergo any material degradation over time. In addition, it must be easy to remove through the same surgical approach.

32.2.2.3 Materials and Methods

Properties of the Implant Material

Some of the implant's most important properties—non-compressible, highly compressive, tensile and shear strength, and excellent fatigue and tear resistance after being cut—are made possible by the raw material used. The spiral implant is made of polycarbonate urethane elastomer that has excellent biocompatibility (ISO 10993, FDA Tripartite Guidance) and biological stability. Although it has been used in other implantable medical devices, it had never been implanted inside an intervertebral disk. Biocompatibility testing was performed by placing the implant in the cervical disks of two sheep who where then sacrificed 3 and 6 months later. Histology studies showed excellent biocompatibility of this material inside a disk [40, 41].

Implant Geometry

The implant has a spiral shape. A specific manufacturing process is used where the base polycarbonate urethane elastomer is modified at the molecular level to give it memory-shape properties (Fig. 32.6). Because of the device's properties, it can be inserted through a small opening in the annulus fibrosis. This opening is the same one used to treat the disk herniation. There seems to be no theoretical or practical reasons why a helix-shaped disk implant cannot be used, as suggested by Edeland [46, 47].

This "new" nucleus restores internal preloads and seems to have the ability to directly self-anchor. It is protected because the outer annulus has regained its basic functionality due to the disk height being restored and the fibers being correctly reoriented and reloaded. Together, this ensures that the surgical opening made for the diskectomy and implantation closes itself without the need for surgical glue.

Based on disk height measurements obtained at L3–L4, L4–L5, and L5–S1 from a large number of patients, the ideal implant thickness was determined to be 6 and 8 mm. These are the two sizes currently available.

Mechanical Properties

The implant must be able to withstand several million compressive cycles without tearing or wearing down. Dynamic and static compression tests confirmed that this objective was met, as there were no implant failures. Fatigue testing was performed under physiological conditions (37 °C Ringer solution) with 1200 N compressive loads placed in multiple directions (axial compression, ±5° off-axis compression) for up to 50 million cycles.

In situ biomechanical studies with three human cadaver specimens were performed to evaluate the effect of the proposed implant on spinal kinematics from full flexion to full extension of L4 relative to L5. Three conditions were tested in sequence: intact disk, after nucleotomy (disk removed), and then after spiral implant insertion [38, 39]. While nucleotomy reduces disk height and increases facet joint compression, the spiral implant restores the lost height and resets the facet joints in their proper position. Although the sample size was too small to perform statistical testing ($n=3$), the curves measured from full flexion to full extension led us to conclude that the spiral implant does not change the overall kinematics of the segment (Fig. 32.7).

To determine the implant's effect on deformation of the adjacent vertebral end plates, seven functional spinal units were instrumented with strain gauges [48]. Up to 500 N was applied in axial compression, off-center flexion, extension, lateral bending (left and right), anterior-posterior shear, and medial-lateral shear. Three conditions were tested in sequence: intact disk, after nucleotomy (disk removed), and then after spiral implant insertion. There were no differences in the deformation of the central part of the end plate relative to the intact condition (except for

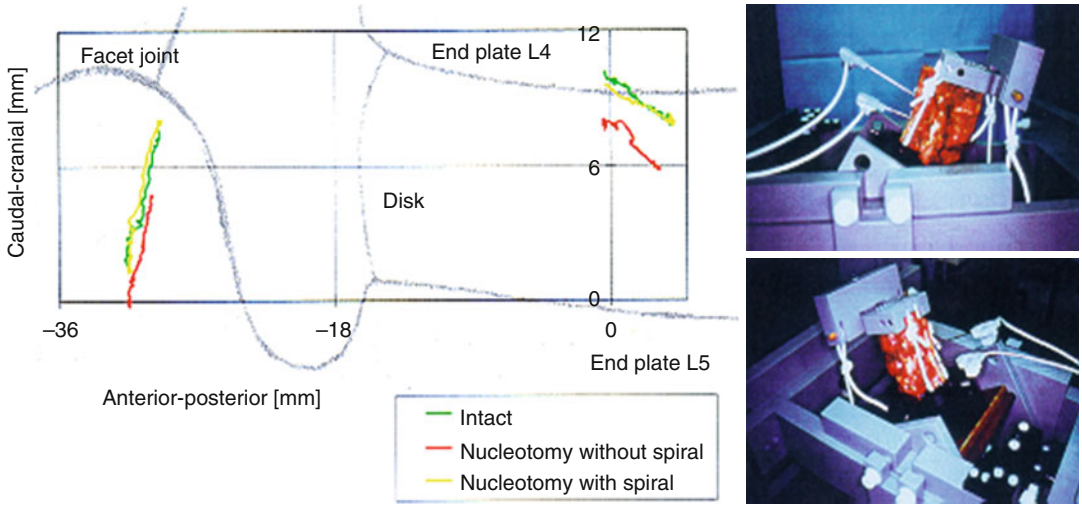

Fig. 32.7 Kinematic *curves* measured in situ in the sagittal plane (full flexion to full extension) of L4 relative to L5. Measurements taken with an intact disk, after nucleotomy (disk removed), and then after spiral implant insertion in cadaver specimen No. 2 (*left*); FasTrak simulator (*right*) [38]

posterior shear). The spiral implant increased the deformation of the central part of the end plate relative to the nucleotomy condition, thereby reducing the loads on the facet joints. There was no implant migration, no matter the direction of load application.

Patient Selection

For the pilot clinical study and then the multicenter European study, very narrow inclusion and exclusion criteria were applied during patient selection [49].

Inclusion criteria: age 18–65 years, suffering from single-level radiculalgia or lumbar radicular pain with more leg pain than lower back pain due either to lateral disk herniation or single-segment acquired intervertebral disorder [2] secondary to stage II degenerative disk disease (instability in the Kirkaldy-Willis classification), and has not responded to well-conducted conservative treatment. These two etiological presentations had to be localized to a single level between L2 and S1. MRI was used to confirm the annulus was not significantly altered and still had some functional recovery capacity, and the posterior disk height in the involved level was at least 5 mm.

Exclusion criteria: previous spine surgery; multilevel spinal disorder (disk herniation, acquired degenerative intervertebral dysfunction); medial disk herniation; factors that could increase the risk of faulty positioning at the involved level (highly biconvex-shaped disk, lesion in adjacent vertebral end plates due to intracancellous hernia); significant central, lateral, or foraminal spinal stenosis; symptomatic degenerated facet joints; degenerative spondylolisthesis beyond grade I; isthmic spondylolisthesis; severe osteoporosis, active infection; bone tumor or congenital bone abnormality; associated severe disease; and more than 40 % overweight.

Study variables: According to the study protocol, the patients received clinical and imaging examinations before the procedure, immediately postoperative, then at 3, 6 months, and 1, 2, and 5 years after the surgery. The clinical outcomes were visual analog scale (VAS) for low back pain and radiculalgia according to Huskisson, type and amount of analgesics used, neurological evaluation (sensory, motor, reflexes), angulation while looking for Lasègue's sign (positive straight leg raise test), activity level according to the Oswestry Disability Index (ODI), and patient satisfaction.

The imaging assessment combined static A/P and lateral X-rays with an MRI exam. The latter was intended to evaluate the position of the radiolucent implant, the disk height, and the vitality

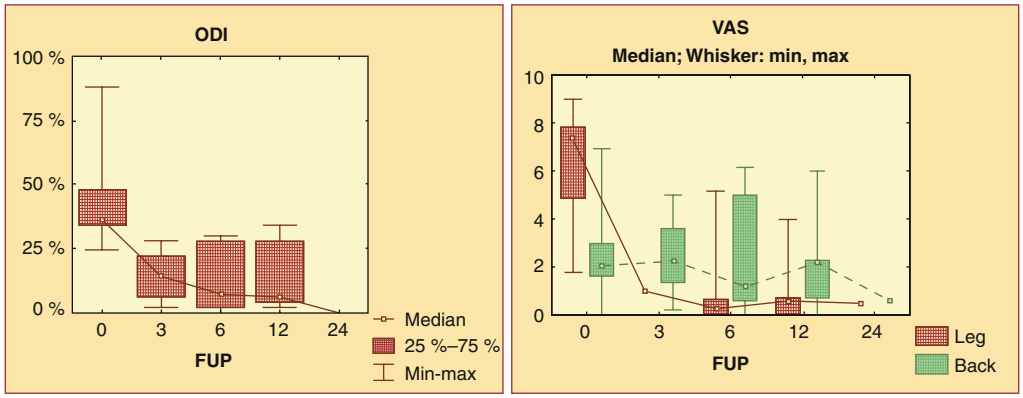

Fig. 32.8 Pain (VAS) and functional outcome (Oswestry Disability Index) for the entire patient series with a memory-coiling spiral implant, where FUP is the time after implantation in months

and function of the outer annulus. Segmental motion was evaluated using dynamic A/P and lateral X-rays performed 2 and 5 years after implantation. The function of the facet joints was evaluated 2 years postoperative using a dynamic twist CT-scan test [3].

32.2.2.4 Results

The clinical and radiological results of the first nine cases included in the prospective, pilot, non-comparative, multicenter European study initiated in September 2001 will be reviewed here [49]. There were eight men and one woman. The average age at the time of surgery was 37.4 years (range 23–51). The follow-up ranged between 6 and 64 months. The surgical indication in all patients was disk herniation with radicular symptoms, with six also having low back pain. L5–S1 was involved in six cases and L4–L5 in three cases. In six cases, the surgical approach was on the right side and in three cases, on the left. The average diameter of the spiral implant was 21 mm (range 17–24).

Clinical results for the entire series are provided in Fig. 32.8. The VAS for radiculalgia and low back pain was clearly lower in all patients after the surgery. There were no intraoperative complications. No neurological deficits were observed during the follow-up examinations. Function based on the ODI was improved in all patients. Three intradiskal implant modifications were visible on MRI. Although there were no clinical symptoms, all three implants were explanted as a preventative measure.

The clinical, X-ray, and MRI assessments were used to evaluate these outcomes and look for direct and indirect signs of changes in implant positioning and its potential effects. The patient with the longest follow-up (24-year-old female) underwent implantation on May 27, 1997. She was a licensed nursing assistant who had ongoing L5 right radiculalgia with motor deficit in the foot associated with ongoing low back pain due to lateral L4–L5 disk herniation on the right side (Fig. 32.9a). Since conservative treatment was not effective, she underwent surgical diskectomy and then spiral implant insertion. She was evaluated 3, 6, 12, 24, 48, and 64 months after the procedure. After 64 months, the clinical assessment found no radicular pain or low back pain, no functional limitations with a finger-to-floor distance of 0 mm, normal extension (Fig. 32.9b), and no social, professional, or recreational limitations. The patient was very satisfied with the implantation procedure because she was able to bring two pregnancies to term and was able to return to work in the same job.

MRI was used to evaluate any changes in position, shape, coiling, translation, rotation, or displacement within the implant's cut plane. No changes were observed in six of the nine cases (Fig. 32.10a), including patient 1 with 64 months of follow-up (Fig. 32.10b). In the remaining three

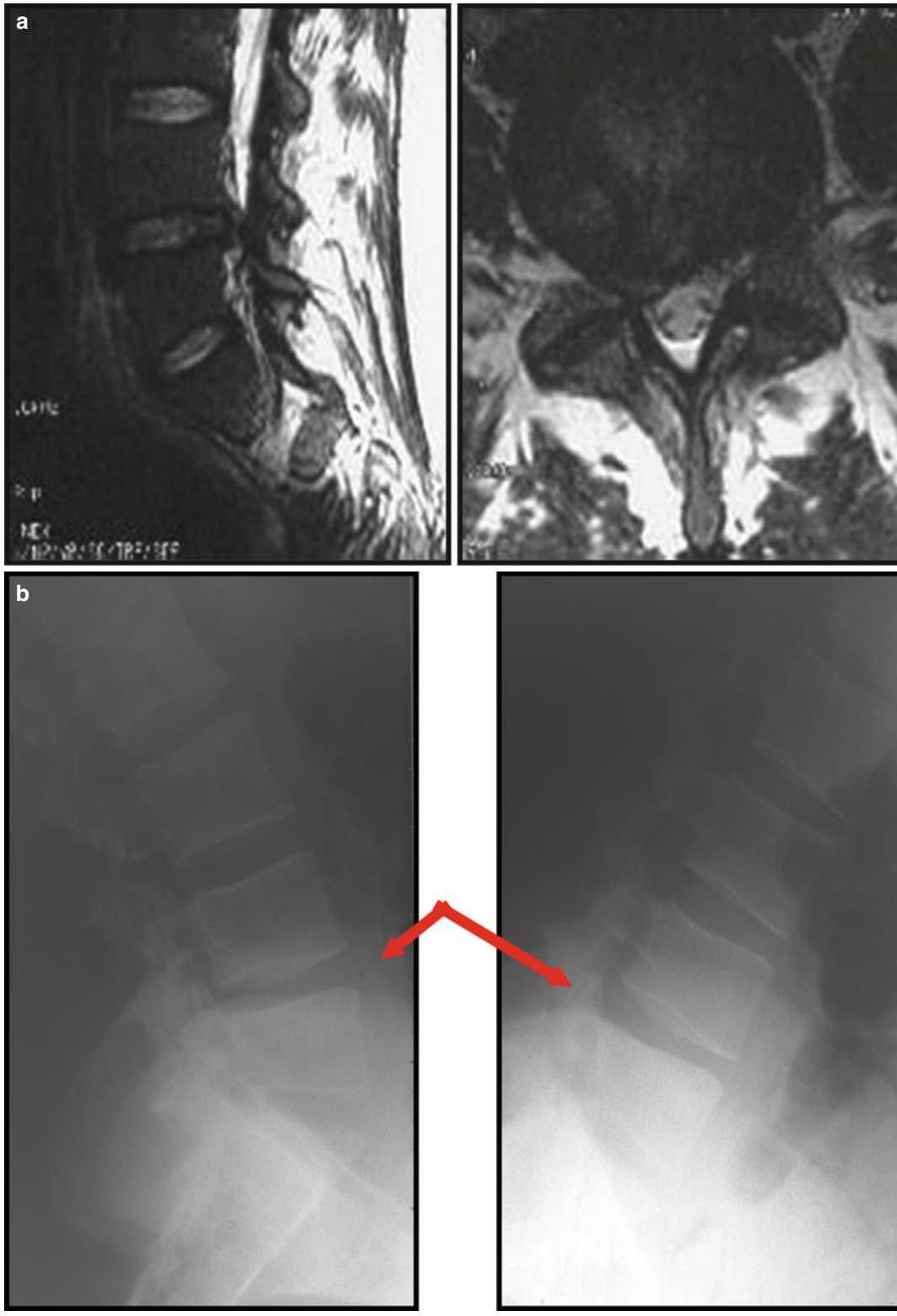

Fig. 32.9 (**a**) Preoperative MRI for patient no. 1; *left* lateral disk herniation at L4–L5. (**b**) Dynamic flexion-extension X-rays at 64 months postoperative for patient no. 1; normal spinal mobility and preserved disk height. *arrows* operating level

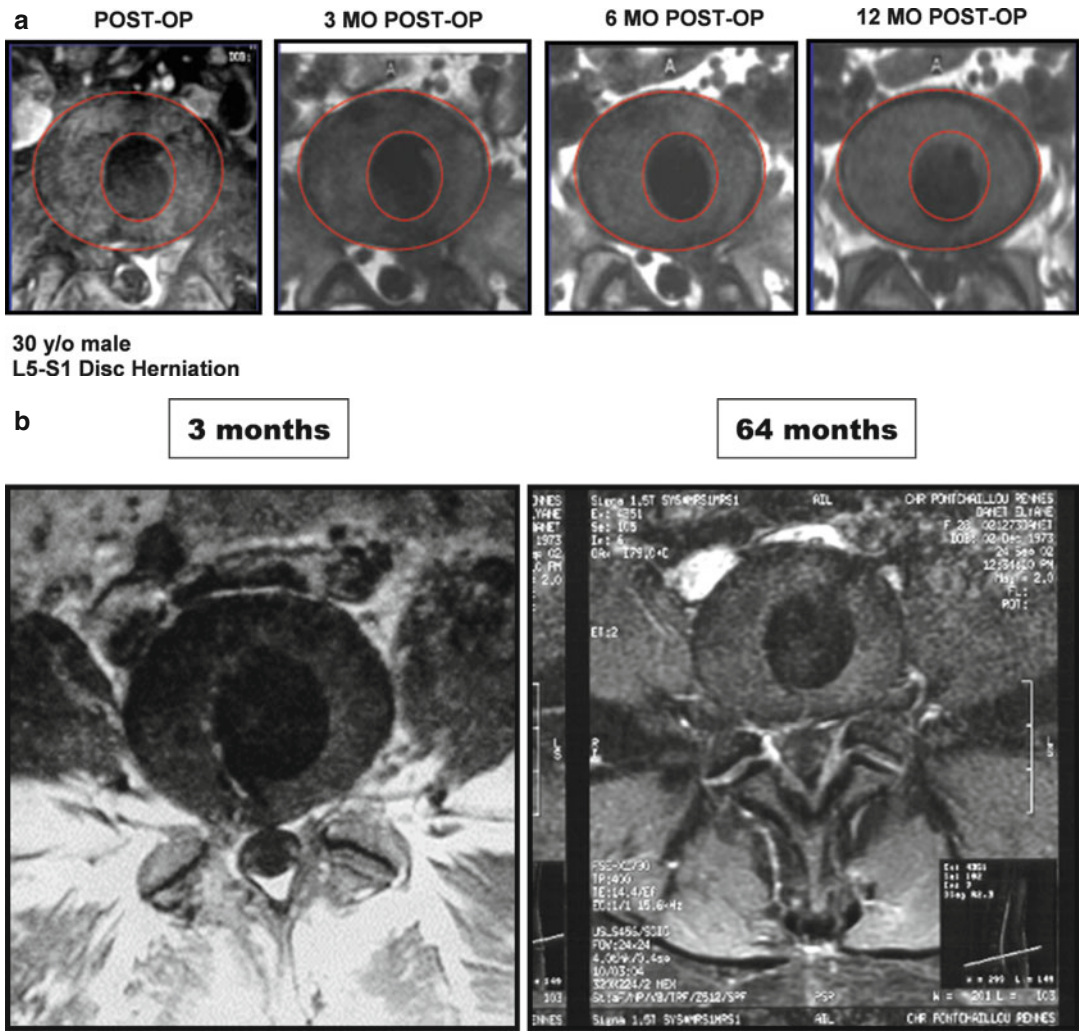

Fig. 32.10 (**a**) Results at 12 months postoperative for patient no. 4; no change in the position, shape, coiling, translation, rotation, or cut plane of the implant. (**b**) MRI at 64 months postoperative for patient no. 1; no changes in the implant

cases, the clinical assessment was satisfactory at 12 months postoperative, but the MRI revealed two cases of intradiskal shape change (uncoiling), posterior translation, rotation of the central part, and displacement within the cut plane, and one case of general posterior intradiskal movement without uncoiling. Based on the MRI findings, the implants were removed in all three patients as a preventative measure.

The MRI also revealed direct signs of efficacy of the nucleus pulposus implant. We found continued vitality and function of the outer annulus after 64 months (Fig. 32.10b) and maintained disk height in all patients both on X-rays (Fig. 32.9b) and MRI (Fig. 32.10b).

The linear mobility in flexion/extension was found to be normal in dynamic X-rays 1, 2, and 5 years postsurgery in the first three patients, and proper lumbar lordosis had been restored and/or maintained (Fig. 32.10b). Rotational mobility was evaluated in the first two patients at 2 and 5 years postsurgery using the twist CT scan [3]. This test revealed that the facet joint function had been fully preserved (Fig. 32.11).

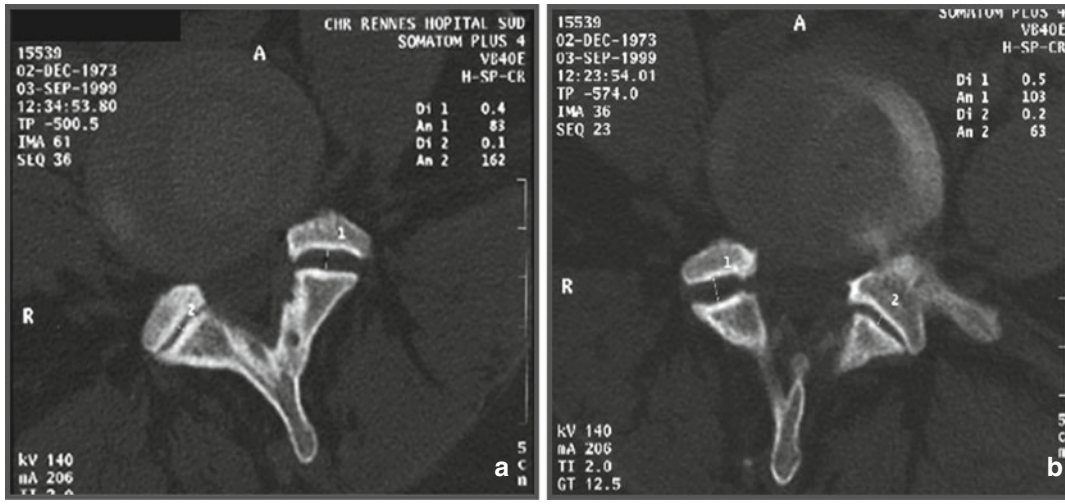

Fig. 32.11 Twist CT scan at 24 months postoperative for patient no. 1; facet joints appear to function normally

32.2.2.5 Conclusion

The memory-coiling lumbar nucleus pulposus spiral implant restores spine biomechanics by reestablishing normal spine kinematics and by restoring and/or maintaining intervertebral disk height and proper facet joint positioning through better load distribution. Biomechanical testing has demonstrated that the spinal implant stays in place and that it distributes loads with proper support from the anterior spine.

Patients who have received this implant up to now have achieved significant pain reduction and were very satisfied with the procedure. Under these conditions, the memory-coiling spiral implant seems to be sound, tangible, and effective, but it can only be used if the outer annulus is intact. Since this excludes post-diskectomy indications, the implant design will be further developed to integrate new ideas. Its effectiveness and easy application—due to a standardized approach—its shape memory properties, and the potential for minimally invasive insertion are all steps forward within the realm of non-fusion techniques, especially relative to other nucleus implants such as the prosthetic disk nucleus (PDN) device [45].

32.3 Proposed Conservative and Surgical Treatment Indications for Various Stages of Lumbar Spine Degeneration

Treatment indications for cases of acquired degenerative intervertebral dysfunction (ADIVD) are first and foremost a function of the four stages of the new classification for loss of stability in the degenerative lumbar spine described earlier. They also take into consideration several other criteria: presence of spinal stenosis (dynamic or static), presence of translational deformity, presence of posterior facet osteoarthritis, disk condition, recovery potential of the annulus fibrosis evaluated on MRI using the Modic stages [6, 7] and the Pfirrmann algorithm [8], and posterior disk height (more or less than 5 mm) (Fig. 32.12).

Stage 0: Minimal Dysfunction

The goal is to prevent the changes observed in the basic structural components from getting worse by using good spine health habits, such as daily exercise to maintain the capacity of the stabilizing muscles.

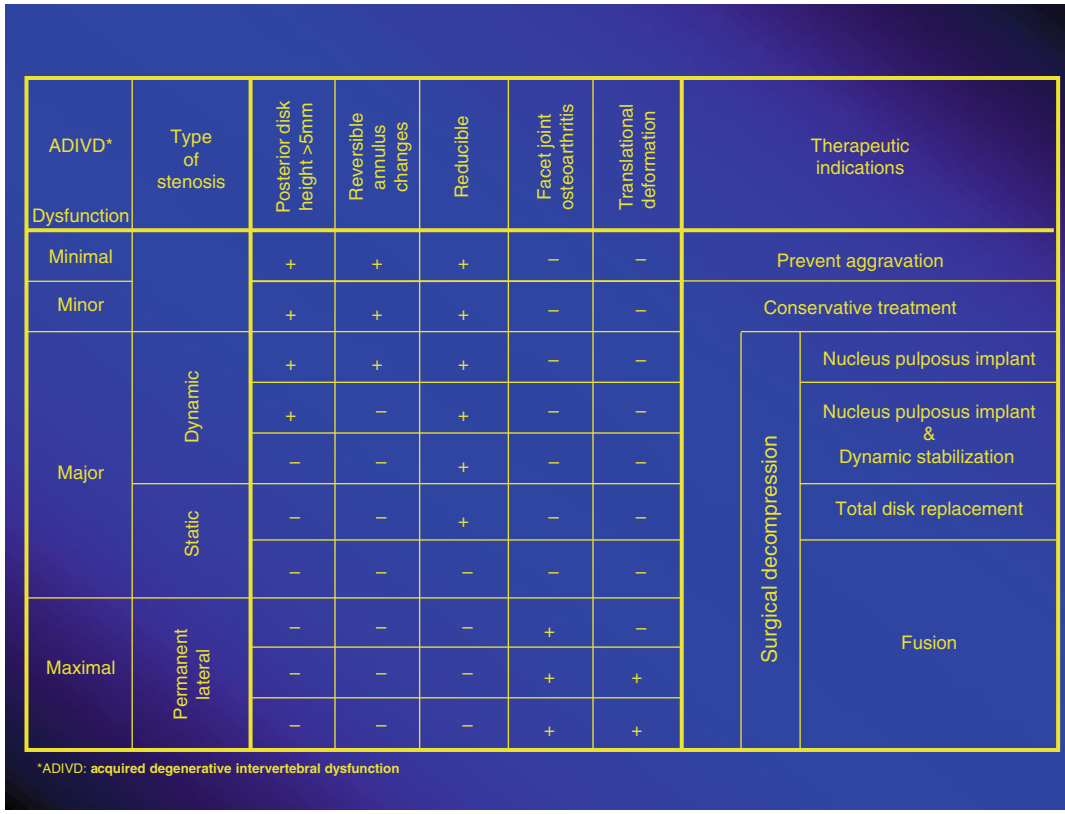

Fig. 32.12 Indications for conservative and surgical treatment of acquired degenerative intervertebral dysfunction (*ADIVD*)

Stage I: Minor Dysfunction

After 48–72 h of conservative treatment with analgesics, muscle relaxants, and NSAIDs to reduce the acute phase, manipulations can be performed within the limits of pain, along with relaxation massage and gentle physical therapy. Intra-articular injections may be needed in cases of strong periarticular or interspinous ligament reactions. Rehabilitation that combines lumbar and pelvic stabilization, by reinforcing the dynamic control over the lumbar, abdominal, and pelvic muscles, with relaxation of the anterior or posterior lower pelvic girdle muscles through specific postural stretching, is often indicated, along with overall rebalancing of the spine-pelvis-femur complex.

Stage II: Major Dysfunction

The first step is to apply *conservative treatment*, which consists of standard medical treatment (analgesics, muscle relaxants, and NSAIDs), immobilization of the thorax and pelvis using braces with lumbar-abdominal muscle reinforcement, and rebalancing of the spine-pelvis-femur complex.

Surgical treatment is only indicated after well-conducted conservative treatment has failed and would be performed in two progressive conditions:

- In cases of *dynamic stenosis*, when there is no translational deformity or posterior facet arthritis, reduction is possible, and the posterior disk height is more than 5 mm, a nucleus pulposus implant can be proposed

if the annulus fibrosis is minimally altered on MRI according to the Modic stages [6, 7] and the Pfirrmann algorithm [8], and the fibrous annulus has changes that can be reversed [2, 49].

- If the spinal canal volume is altered but no anatomical changes are present, posterior or posterolateral dynamic stabilization can be proposed if the loss of stability is reducible and there is no posterior facet joint osteoarthritis.
- In cases of *static stenosis* where the anatomical volume of the nerve root canal is altered, either due to disk protrusion or retrolisthesis during extension, or due to posterior facet joint osteoarthritis, rehabilitation can be proposed in combination with gentle vertebral traction in a pool; if this fails, total disk replacement can be proposed as long as the deformity has not translated and there is no posterior osteoarthritis; otherwise, only fusion is indicated, especially if two separate levels are affected, in combination with either a disk-specific procedure or nerve root decompression. Any surgical procedure at this stage that modifies the statics and dynamics of the spine-pelvis-femur complex must be followed by overall rebalancing treatment.

Stage III: Maximal Dysfunction

Conservative treatment should be used initially while making sure not to interfere with spontaneous restabilization by needlessly trying to increase vertebral mobility. Instead, the goal should be to correct static and dynamic imbalances by stimulating spinal antigravity muscles and readjusting muscles mainly in the anterior and posterior lower pelvis area. Use of external bracing is indicated for more at-risk patients. Surgical treatment is only indicated after well-conducted conservative treatment has failed. The goal will be to decompress the nerve root, possibly in combination with fusion or fusion alternatives.

Conclusion

The clinician, who must attempt to quantify purely subjective functional signs such as pain, while relying on a challenging physical examination, can only deliver a subjective interpretation because of the lack of paraclinical, morphological, static, dynamic, electrophysiological, histological, and pathognomonic criteria on which a decision can be made.

These uncertainties, along with the risk of being misled due to semantics, led us to propose the term "acquired degenerative intervertebral dysfunction (ADIVD)" to more accurately take into account the pathological, biomechanical, and clinical reality of progressive lumbar spine degeneration and to help frame the indications. We hope this will make it easier to choose the appropriate treatment among the many available.

Acknowledgments The authors wish to thank Joanne Archambault and Réto Braunschweiler for the help provided during the preparation of this book chapter.

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Lumbar Spine Injections: An Evidence-Based Review

33

Byron J. Schneider, Neal Varghis, and David J. Kennedy

33.1 Introduction

Lumbar spine injections are frequently used for both diagnostic and therapeutic purposes in patients suffering from painful disorders of the spine. There are a wide variety of potential pain generators in the lumbar spine including the intervertebral disk, zygapophyseal joint, and nerve roots among others. Similar to surgery, injection therapy is by definition target specific. Given this variety of pain generators and the invasive and focal nature of an injection, it is crucial to accurately review the efficacy literature on these techniques. It is imperative to not combine nonspecific diagnoses such as low back pain when evaluating the efficacy of a procedure. It is equally imperative to consider that not all techniques are the same. For instance, the literature has repeatedly demonstrated that nonimage-guided (aka "blind") injections have a very low accuracy, thus negating the ability to be target specific. Nonimage-guided injections, such as muscle trigger point injections, have not only been shown to have poor accuracy, but they also have been found to be no more effective than sham treatments. These procedures will therefore not be discussed in this chapter. There are also other injections that have no credible published efficacy data, and these too will not be covered. This chapter will thus focus on the commonly preformed image-guided injections. In doing so it will focus on the literature behind the most common injections. Each section will cover the basic principles, evidence-based outcomes, and technical considerations. The chapter will cover procedures targeting the lumbar intervertebral disks, the zygapophyseal joint, and the epidural space.

33.2 Lumbar Zygapophyseal Joints

Joel E. Goldthwait first suggested that lumbar zygapophyseal (aka Z-joints or facet joints) could cause low back pain back in 1911 [1]. Later, the discovery of facet joint nociceptors gave credence to this [2]. Much more recently, Kaplan then demonstrated that lumbar z-joint pain could be provoked by capsular distention [3]. Lumbar z-joint pain is the most common source of low back pain, and depending on how the diagnosis is

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_33

made, it is the predominate source of low back pain up to 45 % of the time [4–6]. The most common cause of lumbar z-joint pain is osteoarthritis; however, other causes such as trauma, infection, synovial impingement, inflammatory arthritides, villonodular synovitis, and pseudogout are also painful processes that can affect the lumbar z-joints [7–11]. Risk factors for lumbar z-joint degeneration include age, genetics, joint tropism, disk degeneration, and abnormal spine alignment [12, 13]. Cadaveric studies have found that nearly 60 % of people demonstrate signs of z-joint osteoarthritis by the age of 30 and nearly everyone has signs of z-joint osteoarthritis by the age of 60 [14], with the most common level affected being L4/L5 [14, 15].

33.2.1 Diagnosis

It is important to note that the degree of osteoarthritic degeneration is not directly correlated with degree of pain, and unfortunately, there are no specific physical exam maneuvers or radiographic findings that can always correctly identify those suffering from z-joint pain [12]. There are however clinical findings that are more suggestive of low back pain arising from the z-joints. These include age over 65, pain relieved by lying down, and the absence of pain being aggravated by coughing and absence of pain being aggravated by flexion [16]. Another study suggested that paraspinal tenderness correlates with z-joint arthropathy [17]. While the presence of these has been suggested to increase the likelihood of low back pain being due to z-joints, they are not specific. One study found that there was no diagnostic value in any clinical exam maneuvers for identifying z-joint-mediated low back pain [5, 16, 18–20]. In a review of the literature in 2008, Bogduk concluded that "the failure of multiple studies to identify any clinical features that are indicative of lumbar z-joint pain leaves diagnostic blocks as the only means of diagnosing this entity" [21].

Intra-articular z-joint injections were first described in 1976 by Mooney and Robertson [22]. Intra-articular anesthetic blocks involve injection of anesthetic into the z-joint to evaluate if the patient's pain is alleviated by anesthetizing the z-joint itself. However, in the initial study by Kaplan that demonstrated lumbar z-joint pain could be provoked by capsular distention, he also demonstrated that anesthetizing the medial branches prior to repeating the provocative capsular distention negated the painful response in eight of nine subjects [3]. This led to the concept of medial branch blocks, which can be defined as a "diagnostic procedure designed to test if a patient's pain is mediated by one or more of the medial branches of the lumbar dorsal rami" [23]. In other words, pain relief from lumbar medial branch blocks implies that the anesthetized nerve mediates the patient's pain. Using a triple placebo-controlled block as the gold standard, Lord et al. found that intra-articular injections had less sensitivity and specificity than diagnostic medical branch blocks [24]. Utilizing appropriate image-guided technique, lumbar medial branch blocks have also been proven to be target specific [25]. Therefore medial branch blocks are the preferred method for diagnosing z-joint pain and have superiority over intra-articular blocks because they are easier to perform, safer to perform, more easily subjected to controls, have better sensitivity and specificity, and have proven therapeutic utility in that they predict response to radiofrequency neurotomy [23].

33.2.2 Relevant Anatomy

The lumbar z-joint is a diarthrodial synovial joint that contains a joint space within a fibrous capsule. Anteriorly the capsule blends with the ligamentum flavum [20]. They are crescent shaped with the concave side facing the spinous process, resulting in the posterior aspect of the joint with a more sagittal orientation compared to the more coronal orientation of the anterior aspect. This is important to note as during an intra-articular injection, the posterior aspect of the joint is targeted. Moving caudally the general orientation of the z-joints becomes more coronal. The more coronal orientation allows the lower lumbar spine

to better resist shear forces [13]. There are two recesses which are located at the superior and inferior aspects of the posterior z-joint; the inferior recess is larger of the two, while the superior recess is closer to the spinal nerves, and thus the inferior recess is the target of intra-articular injections [26].

The innervation to the z-joints has been well described. Dorsal rami arise from the spinal nerve in the intervertebral foramen and branch into the medial, intermediate, and lateral branches. An exception to this is the L5 dorsal ramus, which does not have an intermediate branch. Z-joints are innervated by the medial branches of the dorsal rami, once again with the exception of the L5 dorsal ramus, which innervates the respective z-joint prior to branching into a medial and lateral branch. The medial branch of the dorsal rami courses inferiorly between the superior articular process (SAP) and transverse process, hooking medially around the SAP and passing under the mamillo-accessory ligament. As such, any given lumbar medial branch actually runs along the vertebral body below that of the spinal nerve from which it arises. For example, the L4 medial branch courses along the L5 vertebral body. The resulting nomenclature is that each z-joint is innervated by branches from the level above the level of the z-joint itself. For example, the L4–L5 z-joint is innervated by medial branches of the L3 and L4 dorsal rami.

33.2.3 Contraindications

Absolute contraindications include systemic or localized infection, bleeding diathesis, and possible pregnancy. Relative contraindications include hypersensitivity or allergies to the medications to be used.

33.2.4 Intra-articular Joint Injection

The procedure is performed with the patient in the prone position. Correct identification of the target level is identified using fluoroscopy with an AP view. The fluoroscope is then positioned to the minimal obliquity that is required to identify the posterior joint space of the target z-joint. Local anesthetic is injected superficially. A spinal needle is then inserted parallel to the trajectory view toward the posterior inferior joint space. The needle is advanced until the joint capsule is penetrated (Fig. 33.1). Once the joint capsule is penetrated, confirmation of correct placement is performed with use of AP and lateral views. At this point, a small amount of nonionic contrast is administered under live fluoroscopy (Fig. 33.2). Care should be taken to notice any vascular uptake. If flow into the joint is confirmed in the absence of vascular uptake, the injectate is administered. The injectate is most often a combination of an anesthetic and steroid; however, the small volume of the joint only facilitates a 1–1.5 cc injectate. Full technical description of the procedure is available in the second edition of the International Spine Intervention Society (ISIS) guidelines [23].

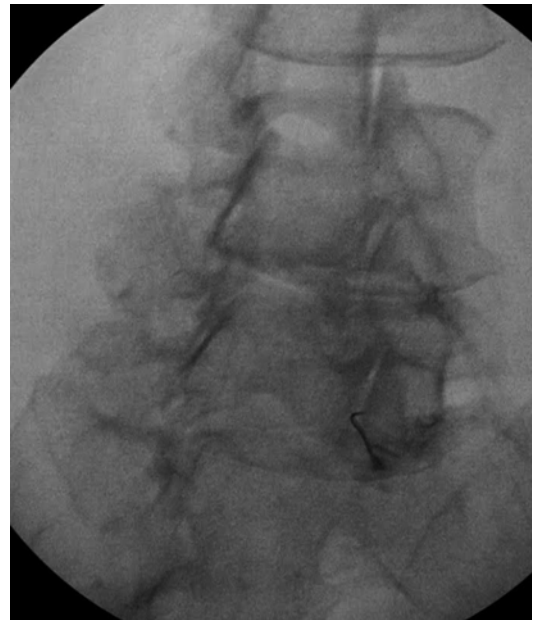

Fig. 33.1 Needle enter right L5/S1 zygapophyseal joint

33.2.5 Medial Branch Blocks

Fluoroscopic imaging, starting with an AP view and transitioning to more oblique views as

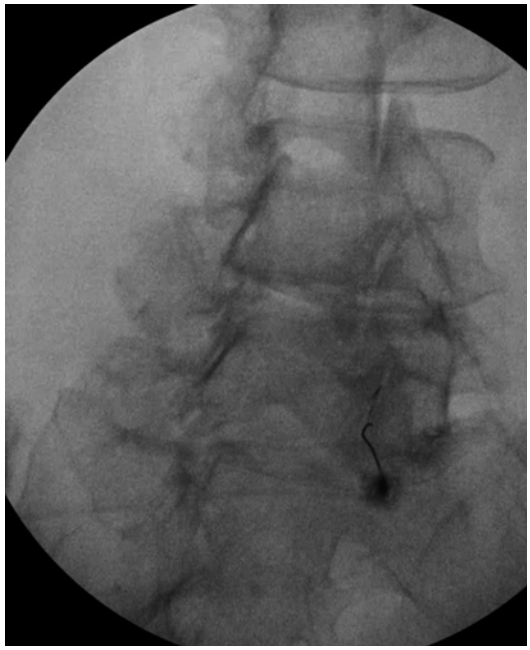

Fig. 33.2 L5/S1 zygapophyseal joint injection with intra-articular contrast

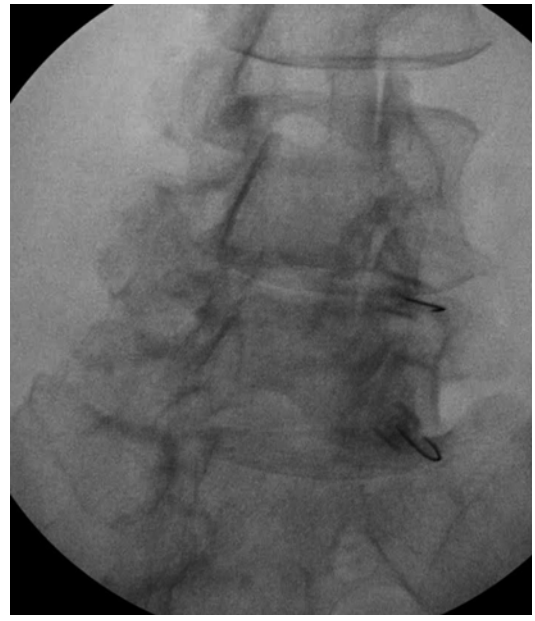

Fig. 33.3 Oblique view with needles over L4 medial branch and L5 dorsal ramus to anesthetize the L5/S1 facet joint

needed, is used to visualize the target (Fig. 33.3). The target is the space between the superior border of the transverse process and the mamillo-accessory notch at the junction of the superior articular process and the transverse process. The superficial skin can be anesthetized with a small amount of local anesthetic, followed by the use of a spinal needle, which is then introduced and directed toward the target until a bony stop is reached. Care must be taken to avoid needle placement that is too far posterior along the bulk of the superior articular process (SAP) itself or placement too far lateral along the transverse process itself. AP and lateral views must be used to confirm correct positioning (Fig. 33.4). A small amount of contrast is injected while visualizing under live fluoroscopy to assure proper placement and the absence of venous flow (Fig. 33.5). If vascular flow is encountered, the needle should be repositioned and contrast reinjected to assure that the flow has abated. Next a small amount of concentrated anesthetic (0.3–0.5 mL) is injected. Larger volumes should be avoided so as to minimize unintended spread of anesthetic. Targeting of the L5–S1 facet joint is slightly different as the

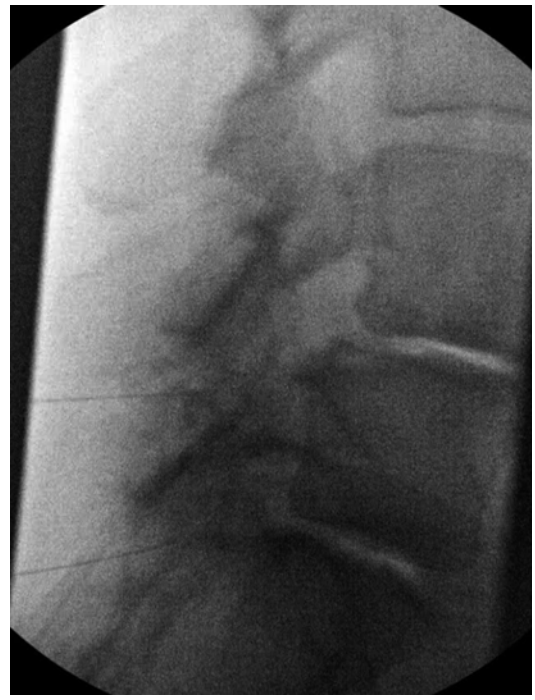

Fig. 33.4 Depth view for diagnostic medial branch blocks

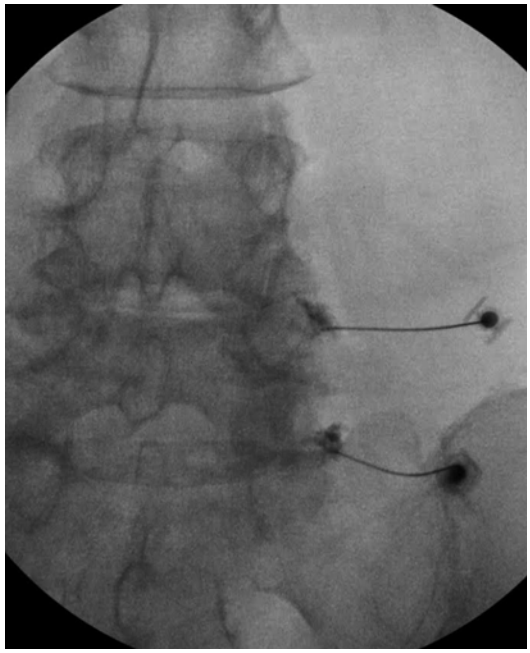

Fig. 33.5 AP view for diagnostic medial branch block with contrast placed to assure no aberrant vascular flow

L5 dorsal ramus crosses the sacra ala as opposed to the transverse process. The target for this injection is 5 mm below the superior junction between the sacral ala and the S1 SAP. When MBBs are performed according to the guidelines, no significant complications have been reported [23]. Technical complications such as thecal puncture only occur if the procedural guidelines are not followed and the needle is grossly misplaced. Full technical description of the procedure is available from ISIS [23].

The purpose of an MBB is to precisely deliver local anesthetic to anesthetize a medial branch and subsequently evaluate the patient's response. Therefore, careful documentation of the patient's pre- and post-procedure pain level is required. In general the patient must be experiencing his or her typical pain prior to the procedure. After the injection pain level should be recorded in a pain diary in a systematic fashion, at intervals of at least 30–60 min for the remainder of the day. Pain levels should also be recorded at less frequent time intervals over the course of the next few days. The utility in the test truly lies in the information obtained from a properly conducted block and not in the execution of the block itself [23]. Without an accurately maintained pain diary, a perfectly performed MBB loses all potential benefit. Maintaining an accurate pain diary in real time limits the potential for recall bias. The 2004 ISIS guidelines recommend a formal post-MBB assessment by an assessor other than the performing physician; however, this is not practical in most practices. Ideally relief based on a numeric or visual analog scale, patients should also track pain medication requirements and ability or inability to perform tasks that are typically pain limited.

33.2.6 Intra-articular Z-Joint Injections

In terms of diagnostic utility, intra-articular z-joint injections have fallen out of favor. Birkenmaier found that using pericapsular injection of anesthetic to predict response to denervation procedures had poorer outcomes than when MBBs were used [27]. Three randomized controlled trials that evaluated the use of intra-articular injections of local anesthetic as a prognostic tool have been published, two of which were equivocal [28, 29] and one that was definitively negative [30]. In addition to improved diagnostic utility, medial branch blocks are also used in place of intra-articular anesthetic blocks because they are easier to perform, safer to perform, more easily subjected to controls, and have proven therapeutic utility in that they predict response to radiofrequency neurotomy [23].

There is limited data on the therapeutic utility of intra-articular z-joint injections as well. In uncontrolled studies the success rate for lumbar intra-articular steroid injections has varied widely, with reported success rates between 18 and 63 % [31, 32]. Only two RCTs evaluating the efficacy of lumbar z-joint intra-articular steroid injections have been published. In one of the studies, 8 mL of injectate was used and compared intra-articular anesthetic, extra-articular anesthetic, or intra-articular saline and found no difference at 3 months between the groups [33]. However, since the z-joint can only hold 1–2 mL,

the validity of this study is in question. The other study evaluated patients who had immediate pain relief from intra-articular anesthetic injection and randomized them to receive either intra-articular corticosteroid or intra-articular saline [34]. There was no difference between the groups at 1 and 3 months; however, at 6 months the intra-articular steroid group was statistically more likely to have improved. The authors attributed this to concurrent therapies received by certain patients in the study, even though the results at 6 months remained statistically significant even after assuming that all patients with concurrent treatment did not improve.

In 1996, Dolan reported that positive findings on single-photon emission computed tomography (SPECT) scans may correlate with greater levels of pain relief for up to 3 months following intra-articular z-joint steroid injections [35]. Similarly, Ahmad and Ackerman published a study of patients with low back pain and isolated z-joint inflammation seen on SPECT imaging and compared outcomes at 12 weeks between those that received intra-articular steroid plus anesthetic and those that received medial branch perineural steroid and anesthetic. The number of patients with greater than 50 % pain relief at 12 weeks was 61 % in the intra-articular group, which was statistically significantly greater than in the perineural group (26 %) [36]. A study by Pneumaticos also found that the patients with SPECT positive imaging had significantly better outcomes at 1 month and 3 months with intra-articular injections compared to patients that did not have facet joint abnormalities on SPECT [37]. However there was no difference between the groups at 6 months. Another recent study that compared the effect of intra-articular z-joint steroid injection with intramuscular steroid injection for presumed z-joint-mediated low back pain found slight increase in outcomes with respect to physical function and reduction in NSAID use in the intra-articular group [38]. However the effect size of these results was small, there was no control arm to the study, and all subjects in the intra-articular group received bilateral injections at L3–L4, L4–L5, and L5–S1 as opposed to selecting the joints thought to be most likely involved. Others have reported that intra-articular steroids are no better than sham injections [21]. Given the mixed literature, it is likely that there is a subset of the population that does significantly respond to intra-articular steroids, that being those with joint inflammation seen on SPECT.

As opposed to steroids, hyaluronic acid is another injectate that has been studied for the treatment of z-joint-mediated low back pain. Hyaluronic acid has been used in other joints with osteoarthritis to theoretically improve the viscoelastic properties of the defective synovial fluid and thus decrease pain [39]. Fuchs et al. compared the efficacy of intra-articular hyaluronic acid versus intra-articular steroid with 6-month follow-up and found that both groups demonstrated significant improvement in pain scores and function over the 6-month period [40]. There were no significant differences between the two groups in any of the outcome measures except for faster onset of symptom relief within the steroid group. Unfortunately the study did not include a control arm, which given the limited data on the efficacy of intra-articular steroids limits the utility of such a non-inferiority design study. However, at the very least there is theoretical benefit of hyaluronic acid over steroids given the reduced side effect profile of hyaluronic acid compared to steroids.

Given the presence of a better diagnostic test and limited evidence on the therapeutic utility of therapeutic intra-articular facet injections, defined indications for facet joint injections have not been published.

33.2.7 Medial Branch Blocks

Medial branch blocks have a well-established diagnostic utility and are thus possibly indicated in a patient that has chronic or subacute low back pain thought to be mediated by structures innervated by the medial branches, in most cases the z-joints, and confirmation of this will alter management. Not all patients with low back pain require MBBs. Examples of patients not needing an MBB would be those with low-level pain that does not result in functional limitations, when the

pain is thought to be due to other structures, when pain is still in the acute stages, or when the first step in treatment is conservative therapy regardless MBBs are not indicated [23]. It is also important to have ruled out more serious possible causes of low back pain such as infection and tumors, at least through history and examination if not through other diagnostic tests, prior to proceeding with MBBs as a diagnostic test.

To fully address the use of MBBs requires a more in-depth discussion about the false positives of MBBs, false negatives of MBBs, what constitutes a positive finding with a single MBB, the number of medial branch blocks required, and ultimately establishing cutoffs for what constitutes a true positive result from MBBs.

While a full discussion of radiofrequency ablation (RFA) is covered elsewhere in this textbook, the practical use of what level of response to MBB constitutes a positive MBB is directly tied to the ability of MBB to predict response to the efficacy of radiofrequency neurotomy. As the criteria for what constitutes a positive MBB become more stringent, the likelihood of successful RFA also increases. In general, when nearly complete relief of symptoms is required from MBB in order to proceed with RFA, outcome data on the efficacy of RFA is very strong [41, 42], whereas relaxed criteria for percent relief of symptoms from MBB have led to less profound outcomes in the subsequent RFA that were performed [28, 30, 43]. When looking at pain relief as a general topic however, studies have found that as little as 30 % pain relief is clinically meaningful in chronic pain conditions [44]. Other studies indicate that 50 % in pain reduction improves a patient's quality of life [45]. Elsewhere in the pain literature, 50 % pain relief is the most commonly used dichotomous outcome measure [46]. So while the academic benefit of using more stringent criteria for what constitutes a positive MBB and how this then lends itself to having more robust positive findings when investigating RFA, at least some consideration must also be made to the proponents of less stringent criteria for what constitutes a positive MBB even if this results in less robust pain relief in the less ideal patients for RFA in light of the fact of what other literatures suggest that is clinically meaningful to the patient. Regardless of these theoretical differences, on the most basic level, pain relief from lumbar medial branch blocks implies that the patient's pain is mediated by the anesthetized nerve, and if there is no pain relief, the target nerve is deemed not to be contributing to the patient's pain. Nonetheless, additional safeguards must be in place to minimize the chance of false positives. Consideration must also be made about possibilities of false negatives.

33.2.7.1 False Positives

Depending on how a positive response is defined, rates of false-positive results from single MBBs in the lumbar spine have been reported to be between 17 and 41 % [5, 47, 48]. Many argued that such high false-positive rate when only single MBB is used has rendered them invalid [48–50]. To mitigate false-positive responses, both dual and triple blocks have been proposed. Dual anesthetic blocks include performing the procedure twice with two different anesthetic of differing duration and evaluating if the patient's pain relief is concordant with the duration of each anesthetic. In order to prevent false positives due to the patients' potential bias toward desiring a positive response, the patient should not be instructed as to the expected duration of relief if pain relief may be achieved. A triple block includes a dual block in addition to performing the procedure with saline as a placebo. Triple blocks are not commonly performed for a variety of reasons, including but not limited to cost, efficiency, and the ethics of performing invasive procedures with placebo medications. ISIS recommends dual comparative blocks as a viable alternative to placebo-controlled blocks [23]. True positive finding with comparative local anesthetic blocks is when a patient reports duration of pain relief that corresponds to the expected duration of action of the anesthetic used, in essence that the patient experiences pain relief with both blocks but longer relief when the longer-acting anesthetic is used [51].

A study that looked at cervical facet pain found that while the specificity of dual comparative MBBs was 88 % specific, it was only 54 %

sensitive [52]. Accordingly, a 12 % false-positive rate is much lower than when single blocks are used and is well within acceptable levels when compared to other diagnostic tests. However, the low sensitivity also suggests that false negatives must also be considered when performing MBBs. And while the risk of a false-positive test is that a patient may undergo an un-needed radiofrequency neurotomy, false negatives are potentially worse than false positives as they withhold potentially beneficial treatment from a patient.

33.2.7.2 False Negatives

False negatives will theoretically increase as more stringent criteria are applied for what constitutes a positive MBB. There are many reasons a false-negative response may occur, including but not limited to concurrent pain generators, inaccurate technique, excessive or inadequate use of superficial local anesthetic, and vascular uptake of injectate [53]. Procedural-related pain may preclude the patient from properly identifying that their typical pain has been alleviated. Fortunately, there is evidence that a single-needle approach to block multiple medial branches reduces procedural-related pain compared to conventional multiple needle site entry techniques [54]. There may also only be partial pain relief in the instance that there are multiple pain generators. Pain can concurrently be originating from the contralateral side, additional segmental levels, or an alternate painful structure. The patient may have difficulty in recognizing relief of their z-joint-mediated pain if these other possible pain generators continue to cause pain, resulting in a false-negative response. Some argue that it is unreasonable to expect complete pain relief from MBB as z-joint degeneration and pain rarely occurs in isolation of other potential sources of LBP. Radiologic studies demonstrate that significant z-joint degeneration never occurs in the absent of disk degeneration [55]. Even more, loss of disk height can accelerate or precipitate z-joint degeneration [56]. Conversely other studies have suggested that multiple pain generators simultaneously contributing to pain occur in less than 5 % of low back pain patients [57]. Regardless, the argument can be made that if only partial pain relief is achieved by a MBB, simultaneous anesthetization of the other painful structure should still enable total pain relief and confirmation of pain generators [21]. Unfortunately, the literature and techniques with respect to anesthetic injections for diagnosis of other sources of low back pain are not established enough to put this theoretical argument into practice.

If the procedure is performed without the patient in their usual state of pain, eliciting enough pain relief to be significantly noticeable and thus be considered a positive test may be difficult or even impossible. Vascular uptake of the anesthetic during MBB can also contribute to false negatives, which has been documented in 3.5 % of lumbar MBBs [58]. The risk of vascular uptake can be mitigated by use of real-time contrast injection [23]. It has also been hypothesized that there are potentially anomalous innervations of the facet joint other than the medial branch blocks. In the original Kaplan study that found that anesthetizing the medial branches blocked painful responses from facet joint capsular distention in eight of the nine patients, the other patient has been postulated to have anomalous innervations [3]. If the target nerve is missed and not bathed in anesthetic, a false negative may also occur. One study that compared cervical (not lumbar) low-volume MBBs (0.25 cc vs 0.5 cc) found that the target nerve was missed 7 % of the time in both cases, but that unintentional aberrant spread occurred twice as often (38 % compared to 16 %) in the high-volume group [59]. Alternatively, another study that performed CT scans after lumbar MBB to evaluate location of contrast found that the target nerve was bathed in injectate in all 120 injections [25]. Regardless all MBBs should be done with low volumes (0.25–0.3 cc) with live fluoroscopy to assure the lack of venous uptake.

33.2.8 Facet Cyst Injections

Facet joints can develop cysts that can be readily seen on MRI imaging and if in the anterior aspect of the joint may result in radicular pain. If symptomatic, symptoms are often that of radic-

ular pain or stenosis, likely because of proximity of the cyst to the spinal nerve. Rupture of the cysts can be attempted. One study achieved 72 % success defined by avoidance of surgery and improvement in symptoms. In the same study there was a 37.5 % recurrence rate, but 45 % of recurrences responded to repeat cyst rupture [60]. Another study found that 46 % of the time surgery could be avoided [61]. Technique of cyst rupture involves anesthetizing the spinal nerve using a transforaminal approach, followed by high-volume facet intra-articular injection with anesthetic and contrast.

33.3 Epidural Steroid Injections

By definition epidural steroid injections target the spinal nerves. They are thus indicated for radicular pain. The most common causes of radicular pain are intervertebral disk herniations and spinal stenosis. It has been shown that the degree of nerve root compression does not correlate to the level of pain [62–64]. It has also been shown that pure mechanical compression of the spinal nerves produces paresthesia and motor weakness but not pain [65]. As such, it reasons that radicular pain must be caused by additional factors in addition to, if not exclusive of, root compression. Multiple studies have shown that inflammation is an essential component to the painful symptoms experienced in patients with radiculopathy [13, 66–68]. Inflammatory mediators such as phospholipase A2, prostaglandin E2, leukotrienes, nitric oxide, immunoglobulins, and cytokines such as interleukin-6 and tumor necrosis factor alpha are all involved in the inflammatory component of radiculopathy [69–71]. Various biochemical inflammatory markers must be present in order for the dorsal root ganglion to generate painful discharges [72]. Moreover, many of these inflammatory mediators such as phospholipase 2 have been found within the nucleus pulposus itself and are found in high concentrations along with inflammatory cells such as macrophages at sites of disk herniation [68, 73, 74]. Histopathological findings consistent with inflammation have also been found in nerve root specimens taken from decompression surgery [68, 75]. Corticosteroids inhibit phospholipase 2 and leukocyte aggregation at sites of inflammation; prevent degranulation of granulocytes, mast cells, and macrophages and transmission of nociceptive C-fibers; and stabilize ectopic discharge of neuronal membranes [70, 76, 77]. As such local administration of corticosteroid can theoretically result in symptom relief [78].

33.3.1 Contraindications

Contraindications include bleeding diathesis, local infection at the injection site, systemic infection, cardiovascular instability, uncontrolled diabetes, uncontrolled glaucoma, cauda equina syndrome, pregnancy, and allergy to local anesthetic or steroid medication.

33.3.1.1 Types of Epidural Steroid Injections

Caudal and Interlaminar Epidural Steroid Injection

Caudal epidural steroid injections (CESI) involves administration of steroid into the epidural space through the sacral hiatus. In 1957 Cyriax reported the first use of caudal epidural steroid injection for pain relief [79]. The first interlaminar epidural injection was described by Pages in 1921 [80]. Interlaminar injections involve delivery of medication into the posterior epidural space between the dura anteriorly and ligamentum flavum posteriorly. Both of these techniques have limited literature on their efficacy and have thus somewhat fallen out of favor when compared to transforaminal epidural steroid injection. In light of this a full description of their techniques is not warranted in this chapter.

Transforaminal Epidural Steroid Injection

The first reported TFESI was described in 1952 by Robecchi and Capra [81]. TFESI delivers steroid to the epidural space in close proximity to the affected nerve root. Compared to other approaches, it is more targeted in bathing the affected spinal nerve root close to its dorsal root

ganglion and theoretically maximizes the therapeutic effect. Derby first postulated that a transforaminal approach theoretically is superior because it can provide a high concentration of injectate directly to the posterior annulus and the ventral epidural space [82].

General Technique

The patient is positioned prone and sterilely draped. The skin is anesthetized with local anesthetic. Using the AP view the transforaminal space that is the target is identified by first squaring off the inferior end plate of the target level. Then using an oblique approach the spinal needle is advanced under the pedicle, making sure not to pass medial to the 6 o'clock position of the pedicle when viewed from a true anterior-posterior (AP) view (Figs. 33.6 and 33.7). The needle should be deep to the lamina on the lateral view and in the safe triangle on the AP view. The safe triangle is composed of the base of the corresponding pedicle, lateral border of the vertebral body, and lateral border of the exiting nerve root. Needle placement must be confirmed by both AP and lateral views. The AP view is used to confirm that the needle has not been placed too medially which increases risk of dural puncture (Fig. 33.7). The lateral view is used to confirm depth (Fig. 33.8). Contrast medium is then injected using live fluoroscopy and evaluated for transforaminal epidurogram spread and assuring that no intravascular or intrathecal spread has occurred (Fig. 33.9). After confirming appropriate contrast, spread small-volume injectate, usually consisting of 1–2 cc of anesthetic followed by 1–2 cc of steroid [23, 78].

Complications and Side Effects

Overall incidence of complications for TFESIs ranges between 5.5 and 9.6 % [83, 84]. Rates are higher for multilevel injections versus single-level injections [83]. The most common side effects include injection site pain, vasovagal reaction (3.5 %), increased radicular pain, lightheadedness, increased pain caused by direct trauma to the spinal nerve, nausea, non-positional headache, vomiting, facial flushing, and elevated blood pressure [78, 84–86]. Anesthetic

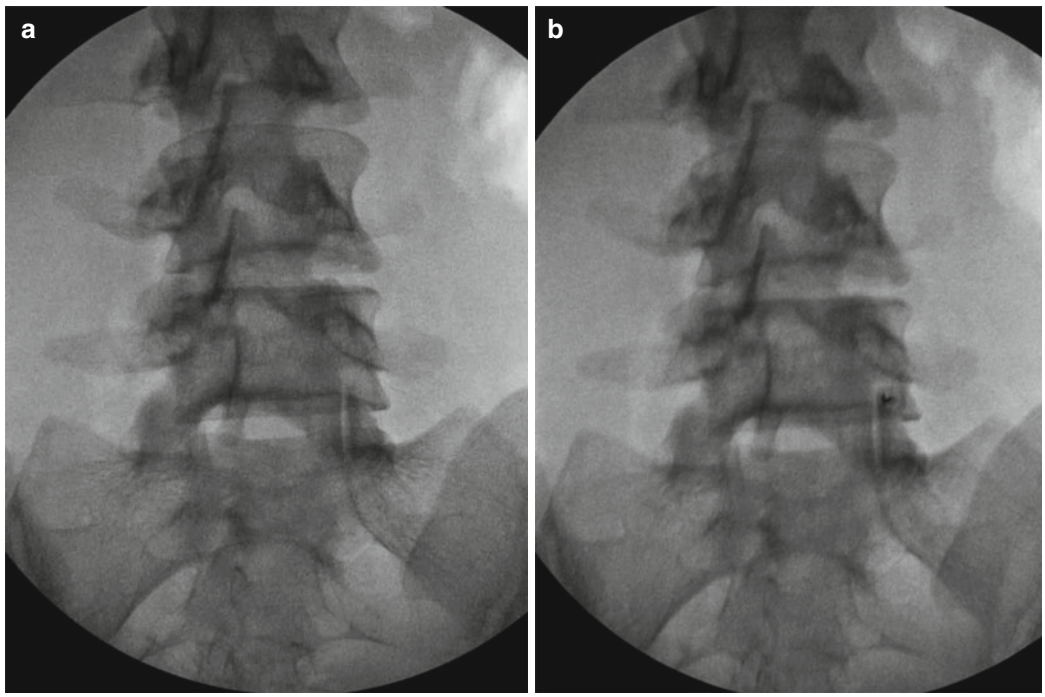

Fig. 33.6 (**a**) Transforaminal oblique view (without needle). (**b**) Transforaminal oblique view (with needle)

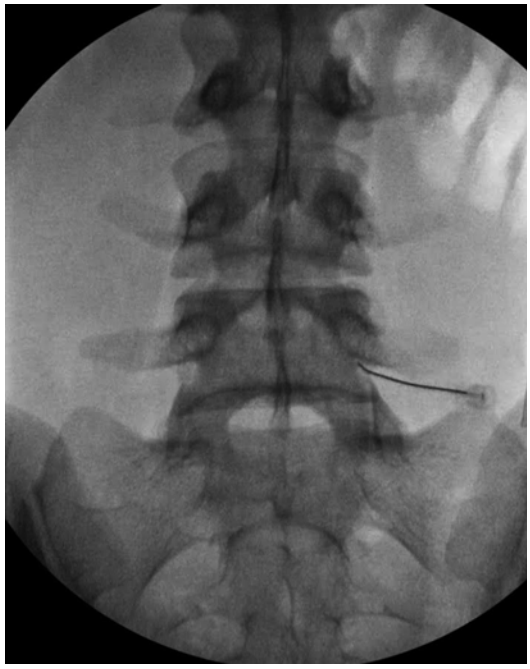

Fig. 33.7 TF AP view

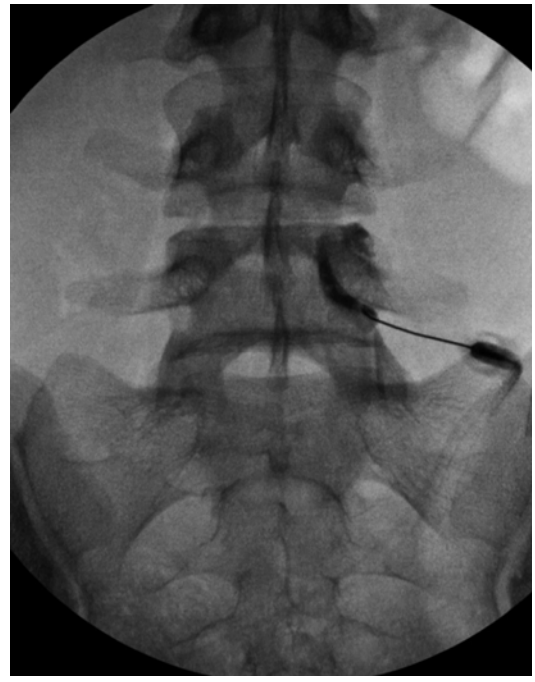

Fig. 33.9 TF AP post-contrast injection

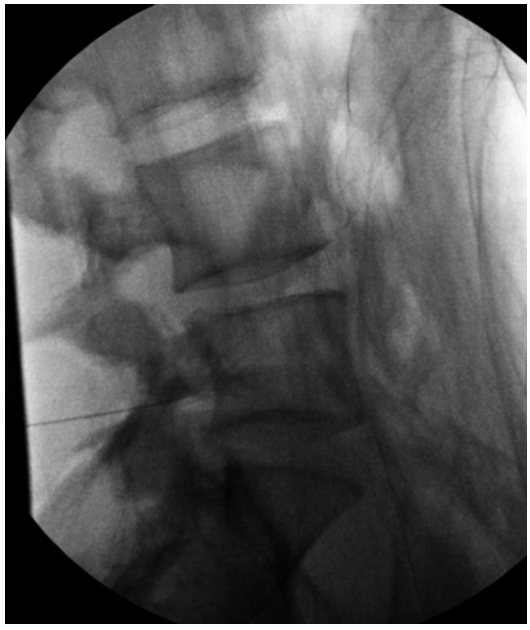

Fig. 33.8 TF lateral view

medications, contrast, and steroids can all cause allergic reaction. Steroids can also cause myopathy, fluid retention, hypertension, mood abnormalities, menstrual irregularities, hyperglycemia, and iatrogenic Cushing syndrome [87–90].

Bleeding is another possible complication. Patients with coagulopathy or on anticoagulation medications are at increased risk of bleeding complications [91–93]. Very rarely does bleeding result in epidural hematoma and compression of the spinal cord and spinal nerves, reported to occur 1 in 150,000 injections [94, 95]. Surgical evacuation is warranted in the rare event it does occur.

Infection is another known risk of all spine injections. Infection risk includes epidural abscess, diskitis, osteomyelitis, and meningitis [96–100]. Given proximity to the pelvic and abdominal cavity, gram-negative infections are more likely. If the needle is advanced too far ventral or lateral, there is also a risk of abdominal cavity puncture leading to infection [101]. Serious infection is extremely rare, occurring only 0.001–0.1 % of the time. If present, serious infections require surgical intervention 70 % of the time and often do not fully recover [102]. Fifty-three percent of the time, an infection presents as worsening pain, most often around 7 days postinjection [102].

Dural puncture is another potential complication of TFESI [103]. Dural puncture can result in positional headache. If not identified, as evidenced by flashback of CSF or by recognition of poor positioning on fluoroscopy, intrathecal administration of anesthetic can cause cauda equina, arachnoiditis, or meningitis [101]. Intradiscal injection can occur during TFESI [104–106]. The primary concern with intradiscal injection is diskitis, and prophylactic antibiotics are usually given if this complication is encountered.

Rate of intravascular injection has been reported as high as 11.2 % for all lumbar TFESIs and as high as 21.3 % for S1 TFESIs [107] (Fig. 33.10). The risk of intravascular injection is double in patients over 50 years old [108]. Most of these injections are venous in nature. The real concern is intra-arterial injection into the spinal radiculomedullary arteries. The artery of Adamkiewicz, which supplies the anterior third of the spinal cord, is often implicated in intra-arterial injections due to its location in the neural foramen. There is variability in the anatomy of the artery of Adamkiewicz as it is located on the left 63 % of the time and is between the T9 and L2 level only 85 % of the time [109–111]. Intra-arterial injection with a particulate corticosteroid during TFESI has been reported to cause spinal infarction and subsequent paraplegia [109–111].

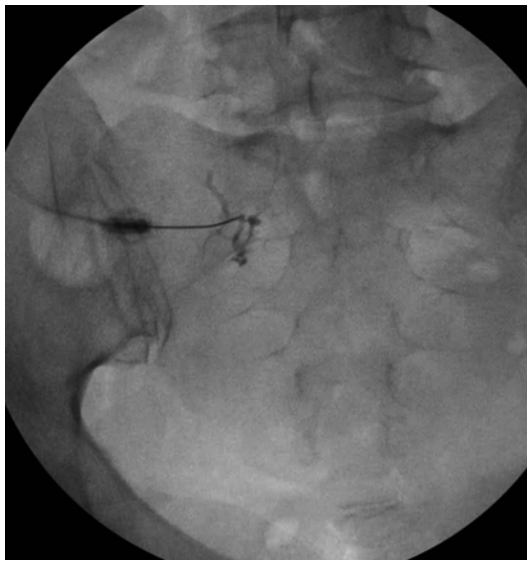

Fig. 33.10 Venous flow on S1 TF ESI

Smuck reported that intermittent fluoroscopy only identifies 57 % of vascular injections as opposed to continuous fluoroscopy [112]. Even more concerning is that confirmation of epidural spread does not rule out concomitant vascular uptake [107, 112]. Digital subtraction angiography can also be used in adjunct with continuous fluoroscopy to further enhance the ability to detect intravascular flow [101, 113].

An anesthetic test dose can also be used to reduce the risk of intra-arterial injection. And anesthetic challenge dose involves administration of anesthetic such as lidocaine after needle position has been confirmed with contrast injection and evaluating for patient response. Reported symptoms such as tinnitus, metallic taste in mouth, headache, dizziness, and sensorimotor changes in either all four or bilateral lower extremities are suggested of intra-arterial infiltration. If positive the procedure should be terminated. Despite these safeguards, irreversible paraplegia has been reported even when continuous fluoroscopy, digital subtraction angiography, and anesthetic test dose have all been implemented [114]. In addition to potentially catastrophic events, intravascular uptake may also reduce the efficacy of TFESIs [108, 115]. Additionally the use of a non-particulate, preservative-free corticosteroid such as dexamethasone could also reduce the risks of inadvertent intra-arterial injection.

33.3.2 Dosing and Number of Injections

No standard dose of steroid exists for TFESI though in a recent comprehensive review of the literature MacVicar reported in most studies that investigated TFESI used either low (40 mg)-dose methylprednisolone or high (80 mg)-dose methylprednisolone, equivalent dosing of triamcinolone or betamethasone, and that less extensive use of dexamethasone has been found in the literature [116].

There is no current literature that specifically investigates the ideal number of injections to

achieve maximal benefit. However, MacVicar pooled the number of injection data from all studies that reported categorical data on patients that achieved at least 50 % pain relief (totaling 9 studies with a total of 727 injection included) and revealed that 94 ± 2 % of patients with successful outcomes from TFESI did so with only 1 injection [116]. Of the 15 patients that had relief in a study by Ghahreman, only 5 required a second injection, and none required more than 2 [117]

33.3.3 Evidence-Based ESI for Radicular Pain Due To Disk Herniation

33.3.3.1 CESI Efficacy

The data on CESI for disk herniation is quite limited. Even more problematic is that the majority of available studies utilize blind CESI. Blind interlaminar and blind caudal approaches demonstrate a 30–40 % rate of missing the epidural space [2, 118]. Current standard of care dictates that fluoroscopy be used for such injections. This further minimized the usefulness of available literature. Also worth considering is that spread of injectate via CESI is at best up to L3–L4 and more likely only up to the L4–L5 level and that L4–L5 is the most cephalic level of pain generation that has been reported to be amenable to treatment with caudal injection [119–121].

The first evidence that CESI may be beneficial for radicular pain was published in 1971 [122]. In 1987 Matthews published results of a series of three blind CESI in patients and showed benefit in pain reduction at 3 months but not 1, 6, or 12 months [123]. It was not until Bush and Hiller published a randomized placebo-controlled study in 1991 that more significant evidence became available. They reported significant gains in mobility and quality of life at 4 weeks in the group that received CESI compared to placebo [124]. Unfortunately, the study did not differentiate between radicular pain due to stenosis and disk herniation and was limited by a very small sample size ($n = 23$). Moreover, the procedures were performed without fluoroscopy. At 1 year differences between the groups were no longer present, as the anesthetic-only control group demonstrated similar gains by that time [124].

Dincer et al. studied the efficacy of blind CESI compared to 1 month of NSAID therapy for radicular pain due to disk herniation in 64 patients and found that the CESI group had statistically greater improvement in VAS at 2 weeks, 4 weeks, and 12 weeks and in Oswestry scores at 2 and 4 weeks [125].

Another study was designed to evaluate if targeted placement of steroid using endoscopically placed steroid around the affected nerve root had greater effect compared to less targeted steroid placement via fluoroscopically guided CESI. It evaluated patients with radicular pain but excluded those with "chronic stenosis" as defined by symptoms of 18 months or longer. Both groups showed significant improvement in pain at 6 weeks, 3 months, and 6 months but no difference between the two groups [126]. While there was no control group, the results of the CESI group can be evaluated as a cohort independent of the endoscopic group, and the study can be used as evidence that CESI can produce favorable improvements in pain for up to 6 months in patients with radicular pain of less than 18 months.

There are no studies that directly evaluate the efficacy of fluoroscopically guided CESI for radicular pain due to disk herniation. At best, reviewing the available literature including the blind CESI and group subset analysis of other studies shows that there is evidence, while minimal, that fluoroscopically guided CESI may provide short-term pain relief for acute and subacute radicular pain.

33.3.3.2 Interlaminar Epidural Steroid Injection (ILESI) Efficacy

There is limited literature that supports the use of ILESI. In perhaps the best designed study aimed at evaluating ILESI, Carette published in the NEJM a randomized double-blind trial in 158 patients with radicular pain due to herniated nucleus pulposus that compared blind ILESI of methylprednisolone to interlaminar injections with normal saline and found that there was significant improvement in leg pain in the steroid group at 3 weeks and 6 weeks, but by 3 months

there was no difference between the groups. All other parameters evaluated including ODI did not reveal any differences between the two groups at 3, 6, or 12 weeks. Only group mean data was evaluated; no categorical data was included in the study [127]. In 2003 Valat et al. published a randomized double-blind control trial comparing blind interlaminar saline to blind interlaminar steroid for radicular pain due to "presumed" disk herniation with 85 patients total. Primary outcome was whether or not patient deemed their symptoms "resolved" or "markedly improved" at day 20, whereas "worse" and "slight improvement" were deemed as failure. Use of NSAIDs or surgery was also considered failure. At day 20 there was no significant difference between the groups with an intention to treat analysis; however, once patients that were lost to follow-up or excluded (11 of the 85 subjects) there was a strong trend ($p=0.054$) toward treatment "success" in the steroid group compared to the saline group. By day 35 the groups were found to have equal outcome [128]. In 2009 Parr reviewed the best available literature for interlaminar epidural injections for low back pain, including the two studies mentioned above, and concluded that the evidence is "limited for blind interlaminar epidurals in managing all types of pain except for short-term relief of pain secondary to disk herniation and radiculitis" [129]. Perhaps more importantly though, Parr noted that the evidence identified does not represent contemporary interventional pain management practices given that none of the studies identified utilized fluoroscopy. Strictly speaking, the evidence may not be extrapolated to fluoroscopically directed lumbar interlaminar epidural injections. Currently there continues to be a paucity of literature that is investigating, much less in support of, fluoroscopically guided interlaminar steroid injection. This is most likely in large part due to the major shift in clinical practice toward transforaminal epidural steroid injections.

33.3.3.3 TFESI Efficacy

Certainly the literature for caudal and interlaminar epidural steroid injections is limited and in many instances has not found these interventions to be more effective than sham treatments [127, 128, 130]. However, careful review of the available literature that specifically investigates transforaminal injections for radicular pain reveals significant and positive findings, most dramatically for herniated disk pathology. Unfortunately, some systematic reviews consider all types of epidural steroid injections as equivalent and have thus inappropriately dismissed the reported effectiveness of a TFESI [131]. Promising research evaluating the use and efficacy of TFESIs has been more abundant over the last 20 years. Some of the earlier studies demonstrated a significant surgical sparing effect of TFESI for herniated disks causing radicular pain. In 1997 Weiner and Fraser reported that 27/30 patients with severe lumbar radiculopathy had immediate pain relief after TFESI, and 22 of the 28 (79 %) patients available for longer-term follow-up had considerable and sustained relief [132]. In a randomized controlled double-blind study by Riew in 2000 that evaluated the surgical sparing effect of transforaminal anesthetic compared to transforaminal anesthetic plus steroid in 55 patients with lumbar radicular pain due to either canal stenosis or disk herniation that were scheduled for surgery, the group that received anesthetic plus steroid deferred surgical intervention 71 % of the time compared to only 33 % of the patients that received anesthetic alone [133]. This effect was maintained for 5 years [133]. The publication reported stratifying the data based on patients with stenosis and those with lumbar disk herniation but did not present the raw data nor did they comment on the efficacy of TFESI in preventing surgery based on pathology (stenosis vs disk herniation). However, they did report that in the group that avoided surgery, which was predominantly composed of patients that received both steroid and anesthetic, that the patients with stenosis had "significant relief of low back pain" ($p<0.008$) and those with disk herniation trended toward "significant relief of low back pain" ($p<0.07$) [133]. The surgical sparing effect of TFESI was also demonstrated by Wang in 2002 [134]. In a retrospective review of 69 patients with symptomatic herniated lumbar disks whom had failed conservative management with anti-inflammatories and physical

therapy who were now requesting diskectomy, only 16 (23 %) eventually went on to having surgery after receiving between 1 and 6 TFESI with a mean follow-up of 1.5 years [134]. All three studies combined provide strong evidence that for patients with radicular pain due to herniated nucleus pulposus, TFESI is an effective means of preventing surgical intervention in a significant amount of patients.

Beyond a surgical sparing effect, the literature has also supported the use of TFESI as a means of providing symptomatic relief. 50 % pain relief has been established as what patients considered a "much improved" for pain in general as well as the minimal clinically important change for radicular pain [44, 135]. Subsequently, much of the literature on ESI has appropriately used this to define what is categorically considered to be a "positive response." Another important consideration to make when evaluating studies with ordinal data such as VAS is that if mean data is used for statistical analysis of outcomes, the outcomes must be in a normal distribution. Otherwise the data should have the mode and interquartile range evaluated, not the mean. The lumping of responders and nonresponders can result in group mean scores that are worthless. Rarely are pain scores distributed in a normal bell-shaped distribution. This emphasizes that the need or importance of using categorical outcome, predefining what success is and who achieves success, is a vital step in evaluating these types of studies.

There are multiple studies that evaluated patient cohorts of various sizes that demonstrated significant pain relief in varying percentages of patients ranging from 38 to 75 % [136–140]. In 1998, Lutz reported a prospective case series of 69 patients in which "52 of 69 (75 %) patients had a successful long-term outcome, reporting at least a >50 % reduction between pre-injection and post-injection pain scores, as well as an ability to return to or near their previous levels of functioning after only 1.8 injections per patient" with a mean follow-up of 80 weeks [136]. More recently, a large retrospective study of 2,024 patients undergoing single lumbar TFESI for radicular pain either due to disk herniation or foraminal stenosis reported that 45.6 % had at least 50 % pain relief at 2 months. For patients with less than 3 months of pain, the success rate increased to 68.3 % at 2 months [137]. Unfortunately, data specifically on disk herniations or lumbar stenosis was not presented separately. In a study by Cyteval, when looking only at the subgroup of patients with radiculopathy solely due to disk herniation who had failed conservative therapy, 65 of 172 patients (38 %) had at least 50 % pain relief at 2 weeks, and 88 % of these had continued relief through 1 year [138]. Yet another study, by Narozny, found that 12 of 20 (60 %) patients with radicular pain due to disk herniation had at least 60 % pain relief at 6 months after TFESI [139]. Jeong reported on two different transforaminal approaches for lumbar radicular pain due to either central canal stenosis or disk herniation. Overall, at 4 weeks 99 of 122 (89 %) in the preganglionic approach group had good or excellent results (defined by at least 50 % reduction in pain) compared to 90 out of 127 (70 %) in the ganglionic group [140]. The difference between the two groups was no longer significant at 6 months. Overall analysis of the entire group as a single cohort of patients with radicular pain due to disk herniation that received TFESI is valuable in this case though. Overall there was still good or excellent response in 142 of the 222 subjects (64 %) for 6 months [140]. In the subset of patients with radicular pain due to disk herniation, 118 of 191 patients (62 %) had at least 50 % pain relief at 6-month follow-up [140].

As mentioned, dangerous pitfalls arise in randomized controlled trials when comparing mean pain scores from studies with non-normally distributed data as opposed to reporting predefined categorical data. A randomized controlled trial that evaluated the efficacy of transforaminal steroid versus transforaminal saline, first published in 2001, did not find benefit for TFESI at 3 or 6 months when analyzing mean group data [92]. However with subgroup analysis of the same data evaluating radicular pain due to contained herniations, the steroid group was found to have short-term benefit for radicular pain and disability [141]. At 1 year, TFESI was found to prevent progression to surgery within the same subgroup of disk herniations and when compared to the control group

found a saving of $12,666 per responder on average [141]. Additional well-designed studies that consider predefined categorical outcomes have repeatedly demonstrated convincing data in support of the use of TFESI for disk herniation causing radicular pain. In 2002 Vad published a randomized (patient selected) controlled trial that compared the efficacy of TFESIs to trigger point injections for lumbosacral radiculopathy secondary to herniated nucleus pulposus [142]. Successful outcome was categorized as predefined improvement in all three categories of patient satisfaction, Roland Morris score, and VAS pain reduction. "After an average follow-up period of 1.4 years, the group receiving transforaminal epidural steroid injections had a success rate of 84 %, as compared with 48 % for the group receiving trigger point injections"[142]. The best designed study to date that investigated the efficacy of TFESI was by Ghahreman et al. in 2010. The study was a prospective, randomized study with five arms that compared TFESI to TF local anesthetic, to TF saline, to intramuscular steroid, and to intramuscular saline and used categorical outcomes to evaluate success. They found that a significantly greater proportion of patients in the TFESI group (54 %) achieved at least 50 % pain relief at 1 month compared to the other four arms (ranging between 7 and 21 %) [117]. Pain relief was "corroborated by significant improvements in function and disability and reduction in the use of other health care" in the TFESI group. Long-term relief at 1 year was also greater in the TFESI group (25 %) than the other four groups; however, the results did not reach statistical significance. The authors of the study argued that 25 % success rate at 1 year is "patently cost-effective" considering that the cost of the alternative (surgery) is much greater than the cost of a single injection. The study also found that using transforaminal saline as a control/placebo compared to TFESI, the number needed to treat to obtain at least 50 % pain relief at 4 weeks is only three [117]! Lastly, the design of the study also makes evident that both the medication (steroid) and route of delivery (transforaminal) combine to form a compound intervention that is unique and different from systemic steroids and from transforaminal administration of other compounds [117].

In 2013 MacVicar et al. published a thorough and comprehensive review of the literature with accompanying systematic analysis of all published data regarding TFESI [116]. After plotting the success rates of outcome studies, pragmatic studies, and explanatory studies, MacVicar et al. summarized it best in saying that with regard to TFESI for radicular pain due to disk herniation, the literature is "abundant" and of "higher quality" and reveals that "about 60 % of patients seem to achieve at least 50 % relief of pain at between 1 and 2 months but that only 40 % maintain this outcome for 12 months" [116]. Specifically, their conclusions included that TFESIs are effective (more so in patients with contained disk herniations, low-grade compression, and acute symptom duration) [140, 143–145], are statistically more than placebo effects [117, 133], reduce the burden of disease by improving function [117, 142, 146] and reducing need for surgery [117, 133, 134], and ultimately are cost-effective [141].

33.3.4 Predictors of Response to TFESI

In the prospective case series published by Lutz, in patients who had pain for less than 36 weeks, the success rate was nearly 80 % versus only 65 % in patients with symptoms that present longer for longer durations [136]. Similarly, in the study by Jeong, univariant analysis revealed that pain of less than 6 months had better therapeutic effect than those with greater than 6 months of symptom duration regardless of symptoms being due to stenosis or disk herniation [140]. In a large retrospective study of 2,024 patients undergoing single lumbar TFESI for radicular pain either due to disk herniation or foraminal stenosis, the proportion of responders was significantly higher when there was less than 3 months of pain that was present (odds ratio 2.42) [137]. In the study by Cyteval on TFESI for lumbar radicular pain due to either foraminal stenosis or disk herniation, patients that had at least 75 % pain relief had a mean duration of symptoms of 3 months compared to the group that had less than 25 % pain relief who had a mean duration of symptoms of

8 months at 2-week follow-up [138]. The review article by MacVicar also pooled data from three studies that provided data on duration of radicular symptoms, in addition to other inclusion criteria, and its effect on success rates of TFESI. They concluded that while there is a statistical difference that exists of patients with pain present less than 6 month being more likely to have a positive response, the clinical effect is negligible, concluding that 70 % of patients with acute pain can expect to benefit, but up to 60 % of patients with chronic pain can still benefit as well [116]. Also of note though is that the 95 % confidence intervals between the two groups in the combined data overlapped [116].

In a review of 71 patients with lumbar radicular pain due to disk herniation treated with TFESI, clinical and radiological features were assessed for predictors of positive response, defined by at least 50 % reduction in pain 1 month postinjection [147]. The only feature that was found to be significant was grade of nerve root compression. Low-grade nerve root compression responded favorably 75 % of the time as compared to only a 26 % response rate with high-grade compression. For paracentral disk herniation, high-grade compression that is associated with poor response was defined as obliteration of periradicular CSF or fat or morphologically distorted nerve root. For foraminal/far lateral herniation, high-grade compression was defined as perineural fat obliteration in all four directions or morphologic distortion of the nerve root. Duration of symptoms, presence of neurologic symptoms, abnormal neurologic findings on exam, level of herniation, location of herniation, and morphology of disk herniation were all evaluated and not found to be a predictive response to TFESI [147]. Alternatively, in the original Ghahreman study, there was no association between the need to progress to surgery and the size of the disk herniation [117].

33.3.5 Comparative Studies

It is clear that the evidence in support of TFESI for relief of radicular pain is robust and definitive compared to the level of evidence available in support of CESI and ILESI. This has driven clinical practice largely toward predominately using this approach. Additionally, there is evidence that has attempted to directly compare the efficacy of TFESI, CESI, and ILESI.

In a retrospective review of 40 patients with radicular pain due to herniated lumbar disk, Schaufele found that 14 of 20 (70 %) of patients that received TFESI had improvement of at least 2 on a 0–10 pain score compared to only 9 of 20 (45 %) in those that received fluoroscopically guided ILESI. Follow-up was limited to 19 days only [148]. A prospective randomized trial by Thomas that compared fluoroscopically guided TFESI to blind ILESI for radicular pain secondary to lumbar disk herniation in 31 patients found that mean VAS pain score was statistically significantly lower ($p<0.04$) in the TFESI group (VAS improvement 56.8 mm) than in the ILESI group (VAS improvement 40.3 mm) at 6 months [119]. The study is limited by small sample size, ILESI being performed blind, and lack of categorical data. Nonetheless, this is valuable evidence in support of the superiority of TFESI over ILESI given with a prospective and randomized design. A similar prospective randomized trial with 64 patients that compared fluoroscopically guided TFESI to fluoroscopically guided ILESI in patients with radicular pain due to lumbar disk herniation was published by Rados in 2011. Comparing the mean pain scores and mean Oswestry scores between the two groups found that while both groups improved at 6 months, there was no statistical difference between the groups [149]. At 6 months, when comparing the percentage of patients that improved by at least two points on VAS (TFESI 84 % vs ILESI 75 %), by at least 50 % on VAS (63 % TFESI vs ILESI 53 %) or ten-point improvement on Oswestry (TFESI 66 % vs ILESI 50 %), there was again no statistically significant difference, but there was a noticeable trend toward more favorable outcomes with TFESI [149]. Collectively, the three studies support the use of TFESI over ILESI for radicular pain.

Lee reported a retrospective nonrandomized study of 233 patients who had failed conservative therapy that compared the efficacy of TFESI

versus CESI versus ILESI for radicular pain caused by either disk herniation or spinal stenosis [150]. When evaluating patients with at least 50 % pain relief at 2 months, Lee found that both TFESI and ILESI were superior to CESI for patients with either disk herniation or spinal stenosis [150]. Further evaluation of the subgroup data only in patients with radicular pain caused by disk herniation, 25 out of 38 (65.8 %) had at least 50 % pain relief at 2 months when treated with TFESI compared to only 3 out of 14 (21.4 %) in those treated with CESI and 16 out of 31 in those treated with ILESI (51.6 %) [150]. Overall, the study provides relatively strong evidence that CESI is inferior to ILESI and TFESI, and while not statistically significant, also weakly corroborates other available evidence that TFESI is likely superior to ILESI.

Ackerman evaluated 90 patients with L5/S1 disk herniations with S1 radicular pain who were randomly assigned to CESI, ILESI, and TFESI and followed for 24 weeks [145]. The number of injections in that time period ranged between 1 and 3. At 12-week follow-up, there was a trend toward TFESI being more likely to provide partial or complete relief than CESI or ILESI, but the results were not statistically significant. At 24 weeks both CESI and TFESI were statistically more likely to provide "complete relief" compared to ILESI, but there was no difference between CESI and TFESI [145].

Of the available studies, three suggest that TFESI is superior to ILESI, and two demonstrate more robust and statistically significant evidence of this. In the two studies that also included CESI, TFESI was found superior to CESI in one and equivalent in the other. Looking at the direct comparative data as whole, it becomes readily evident that TFESI provides the best outcomes of the three approaches. Ackerman also evaluated contrast spread pattern and found a statistically significant relationship between "complete pain relief" and ventral spread of contrast. A transforaminal approach was the approach most likely to achieve ventral spread [145]. This provides at least some theoretical support that explains why TFESI is more efficacious.

33.4 Lumbar Intervertebral Disks

Intervertebral disk pathology can play a role in low back pain [151]. Disks are innervated with nociceptive pain receptors by branches of the sinuvertebral nerves, gray rami communicantes, and lumbar ventral rami [152–155]. The greatest concentration of nociceptors is found within the posterior annulus fibrosus. In general the outer third of the annulus fibrosus has the greatest innervations, with there being only some innervations of the middle third and little to no innervation of the inner third [152–155]. Discography is defined by the injection of contrast into the nucleus pulposus to evaluate disk morphology and was first described in the 1940s [156–158]. This led to the development of provocative discography, which is the injection of contrast medium into the nucleus pulposus of a disk in an attempt to recreate a patient's pain and thus diagnose the ultimate source of the pain. In provocative discography, fluoroscopic imaging is used to confirm placement of contrast as opposed for morphologic evaluation of the disk. If further anatomic confirmation of positive provocative test is desired, pursual of subsequent MRI or CT scans of the injected disk can then be pursued. In large part this evolution from using discography for morphologic evaluation to provocative discography to assess for patient response to the procedure itself occurred because of a need to identify which one of the multiple morphologically abnormal disks was the primary pain generator, as often many of the morphologically abnormal disks were not painful with provocation [159].

33.4.1 General Principles for Provocative Discography

The general principle of provocative discography is that pressurizing a disk, which is the patient's pain generator, will reproduce that pain as opposed to stressing an asymptomatic disk, which should either be pain-free or generate unfamiliar pain. Delineation between reproducing the patient's pain, termed concordant pain,

and generating other pain, termed discordant pain, is important. Because the test is provocative, there is an inherent increased risk of false positives as provocative maneuvers. This necessitates internal controls for provocative discography, which have historically been a provocation of intervertebral disks adjacent to the target level. Thus according to both the International Association for the Study of Pain and International Spine Interventional Society, the diagnosis of discogenic pain requires that provocation of the target disk reproduces the patient's concordant pain and that provocation of adjacent disk does not reproduce concordant pain [23].

33.4.1.1 Procedural Considerations

Indications

The main purpose of this injection is to accurately diagnose the pain generator for potential treatment purposes. There are currently no studies available that demonstrate a better response to a given therapy in subjects with discography-proven disks as opposed to those selected by clinicians. Until appropriate medications or interventional treatments have been found, the ultimate role for provocative discography may be in surgical planning. This is especially true if the surgeon is trying to avoid fusion, or if surgery is already being planned as discography has been used in assessing if additional levels should be fused [160–163].

Contraindications

Absolute contraindications: patient unwilling or unable, inability to assess patient response during procedure, untreated localized infection, and pregnancy

Relative contraindications: allergy to materials involved, bleeding diathesis or anticoagulation therapy, systemic infection, and anatomical derangements that may make the procedure unsafe

Antibiotic Prophylaxis

Antibiotic prophylaxis such as cefazolin 1 g, clindamycin 900 mg, or ciprofloxacin 400 mg IV should be used. Reported rates of infectious diskitis are from 0.05 to 1.3 % per disk injection without the use of prophylactic antibiotics [23]. Meta-analysis reviewing the risk of diskitis with discography reveals a 0.24 % risk without antibiotic use and no reported cases when antibiotics are used [164]

Immediate Procedural Complications

Short-term complications include allergic reactions, vasovagal reactions, increased pain, bleeding, superficial infection, and penetration of the ventral ramus. More significant of a concern is infectious diskitis.

Long-Term Complications

A 10-year matched cohort evaluated asymptomatic patients that underwent three-level provocative discography and MRI evaluation and were compared with matched cohort that underwent MRI evaluation but no discography [165]. MRI evaluation looked at degenerative changes, Modic changes, and herniations again 7–10 years later. All graded MRI parameters demonstrated that disks that had been exposed to discography had significantly higher progression toward disk pathology [165]. Even more, new herniations were found to be significantly associated with the ipsilateral side of disk injection [165]. Using raw data to calculate 95 % confidence intervals, as opposed to the published chi-squared analysis, rendered the association with Modic changes and degenerative changes less statistically significant [166].

Technique

An AP view of the lumbar spine is used to properly identify the target disk. Often an adjacent disk, which is not to be the primary pain generator, is selected first. From the AP view, the fluoroscope is transitioned to an oblique view in order to visualize the ipsilateral superior articular process of the inferior portion of the target segment, with one-third of the disk being posterior to this point. Using a two-needle technique to decrease the likelihood of infection, the needle is then advanced over the inferior articular process and into the center of the intervertebral disk, while being careful to avoid the ventral ramus. In

general, the needle is introduced from the side opposite to that of the predominant side of pain in order to avoid false positives via iatrogenic procedural pain. It is essential to confirm accurate placement with both anterior-posterior (AP) and lateral views (Fig. 33.11). Once proper position inside the center of the disk is confirmed, the stylette is removed, and a pressure transducer manometer in line with a closed system containing antibiotics and contract medium is connected. Contrast medium is then slowly injected under live fluoroscopy (Figs. 33.12 and 33.13). Once contrast media is visible, this corresponds to the opening pressure that is then recorded. Opening pressure should be noted, as low opening pressure can be suggestive of annular tears, and increased opening pressure can be suggestive of incorrect needle placement. The pressure-controlled intradiscal injection continues until one of the four situations in encountered: the patient's low back pain is reproduced, contrast escapes the disk, pressures exceed 100 psi, or >4 mL of contrast is injected. If pain is reproduced, the pressure at which this occurred should be recorded. During the procedure sham provocation should be performed as well, in which the patient is told that pressurization is occurring when it is in fact not to in order to see if pain is reproduced without provocation. Full procedural guidelines are available through the ISIS guidelines [23].

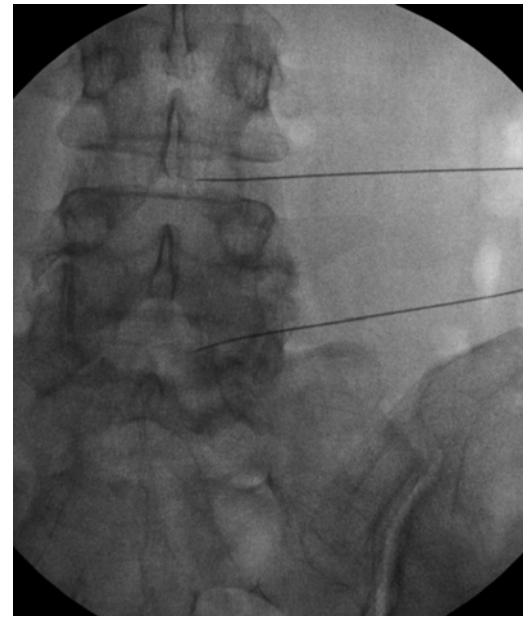

Fig. 33.11 Intradiscal AP pre-contrast

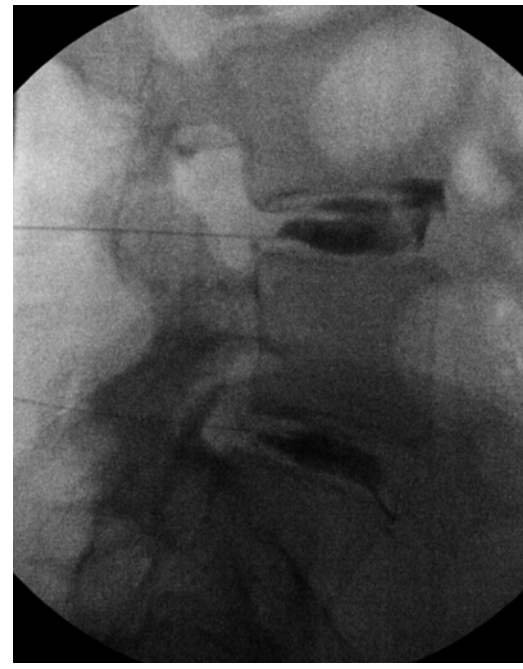

Fig. 33.12 Intradiscal lateral post-contrast

Interpretation of Results

The volume of fluid injected is proportional to the pressure applied. It reasons to suggest that any disk can be painful if enough pressure is applied, which would lead to false positives. Therefore it is important to define the pressures used during provocative discography. It is suggested that thresholds for pressure that cause concordant pain be considered when it is experienced with pressure less than 50 psi or less than 15 psi above opening pressure [23]. Pain intensity must also be considered, and if only minor pain is elicited, then the increased likelihood of false positives must be considered. This has led some authors to suggest that only a pain intensity of 7/10 should be considered positive [23]. Obviously, the more strict the criteria that are used to consider a response as positive, the lower the false-positive rate becomes.

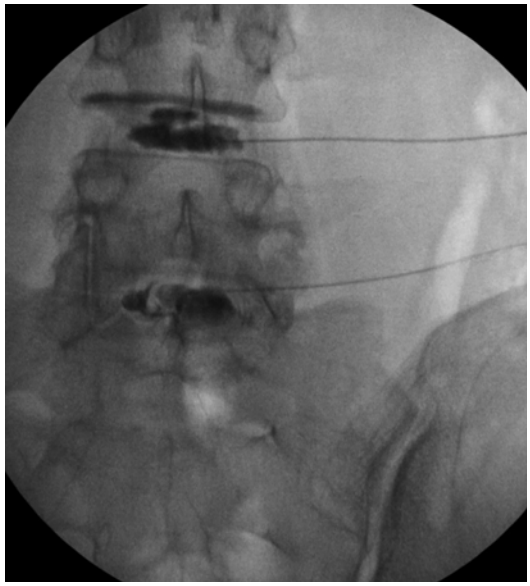

Fig. 33.13 Intradiscal AP post-contrast

False Positives

Holt published a study of asymptomatic volunteer prisoners that underwent provocative discography and found a 37 % false-positive rate; however, this study has since been refuted [167, 168], and false positives have been reported to be as low as 1 % with correct technique [169]. One systematic review with meta-analysis reported that the false-positive rate did not exceed 10 % and was possibly as low as 6 % [170]. There has been much research and debate about the false-positive rate of provocative discography. Because of the provocative nature of this technique, there is an inherent theoretical risk of higher rate of false positives. It has also been theorized that asymptomatic individuals cannot have false positives identified as concordant pain because they do not have baseline pain [171].

Carragee reported false-positive rates of 10 % (95 % CI 0–29 %) in asymptomatic patients, 40 % (95 % CI 10–70 %) in chronic pain patients, and 75 % (95 % CI 33–100 %) in somatization patients [172]. Another study looking at only asymptomatic patients found that no one experienced pain at any level with pressures of 20 psi or less suggesting that in asymptomatic patients using a threshold of 20 psi virtually eliminates false-positive response [166, 173]. Proponents of discography often point to the asymptomatic groups in such studies as proof that the false-positive rate of provocative discography is acceptably low. However, asymptomatic patients should not be undergoing provocative discography in the first place. In light of this, the false-positive rate for provocative discography must include the rate found in those with chronic pain. Bogduk et al. applied the manometric criteria from the aforementioned study by Derby and applied the aforementioned study by Carragee and determined that the prevalence of false positives decreases from 40 to 30 % in those with chronic pain and from 75 to 33 % in those with somatization disorders [27, 166, 172]. A larger study of 50 patients later reported no difference in false positives among patients with somatization disorder [174].

At best one can conclude that the false-positive rate for provocative discography including in asymptomatic individuals does not exceed 10 % and that in patients with chronic pain, false-positive rates are likely higher, making interpretation of positive responses even more difficult to interpret in this population.

Therapeutic Validity

The validity of provocative discography as a diagnostic test still remains unproven/controversial. A study by Carragee attempted to compare discography to a constructed "gold standard" of clinical outcomes [175]. Patients without any medical comorbidities with positive single-level low-pressure discography underwent 360° single-level fusion including diskectomy. The presumption was that removal of the primary pain generator should completely alleviate the patients' pain. Results were compared to strictly matched cohort undergoing the same procedure for single-level unstable spondylolisthesis. The hypothesis was that definitive surgical ablation of both of these lesions should be highly and equally effective in relieving pain and restoring function. Predetermined requirements for high-level success by measure of pain score, ODI, medication use, and return to usual work revealed that only 27 % patients in the positive discography group

had highly effective clinical outcome compared to 72 % in the spondylolisthesis group [175]. Similar results were found when evaluating for less stringent minimal acceptable outcome measures. Positive predictive value when compared to a theoretical gold standard of clinical outcome was only 42–43 %. In other words, in patients found to have discogenic pain with positive provocative discography, less than half had resolution of pain after surgical fusion.

This appears to be in contrast with data reported by Colhoun in 1988 that reported that 89 % of patients with positive provocative discography responded well to fusion compared to 52 % of patients responding well to fusion with negative provocative discography [176]. Full interpretation of the study is limited to lack of available information on details of what qualified as "positive" discography and if fusion was limited to only the level found positive on discography. Regardless, a 52 % success rate even with negative discography suggests that etiologies of pain other than discogenic pain were also addressed in this study, and nothing can be said about the specificity of discography from this study or its utility in determining who should get surgery. One would argue that, in light of the aforementioned Carragee study, performing discography in order to be able to offer patients at least a 40 % chance at having pain relieved by surgery would then also have to accept the statement that, in consideration of the Colhoun study, even with negative discography a 52 % chance at success would also prompt surgical intervention. Only if the Carragee study is completely disregarded and Calhoun's study be taken at face value can the argument that provocative discography has validated be a therapeutic utility to predict success with surgical fusion.

33.4.1.2 CT or MRI Discography After Provocative Discography

It has been theorized that there is value in post-disk stimulation CT or MRI scan in that it may reveal annular tears that would not otherwise be seen. This may provide additional evidence of what would have otherwise been missed as nucleus pulposus extravasation causing chemical radiculitis [177]. The Dallas discogram scale describes the degree of annular tear as grade I tear of the inner third, grade II tear of the middle third, grade III tear of the outer third, and grade IV tear being circumferential spread of contrast of at least 30°. There is evidence that greater pain is associated with greater degree of annular disruption; grade 0 and grade 1 disruptions were rarely painful compared to 75 % of grade III or IV disruptions being associated with concordant pain [178, 179].

33.4.1.3 Analgesic Discography

Analgesic discography is an appealing theoretical alternative to provocative discography to evaluate the etiology of a patient's pain. Instead of pressurizing the disk and looking for concordant pain, an analgesic discography relies on relief of pain after the injection of a local anesthetic. Therefore it has the significant advantage of not requiring a normal healthy disk to be injected as a control. It also would eliminate the element of manometry currently required for provocative discography. Derby et al. compared the proportions of patients that reported relief of pain following local anesthetic injection into disks that were found to be concordantly painful with provocative testing using four different protocols [180]. One group underwent pressure-controlled discography with a mixture of anesthetic and contrast and found that 7 % of patients had greater than 50 % pain relief and 3 % had greater than 80 % pain relief [181]. The second group underwent injection with anesthetic alone while being evaluated for concordant pain during injection of the anesthetic. This group had 40 % of patients that reported 50 % pain relief and 20 % reported at least 80 % pain relief [180]. The third group underwent injection of intradiscal anesthetic only into disks that were positive with provocative discography using contrast. This group demonstrated that 46.2 % of patients reported at least 50 % pain relief and 30 % reported at least 80 % pain relief [180]. Lastly, the fourth group had a catheter left in after provocative discography, and anesthetic was injected 45 min post-procedure and showed that 80 % of patients had at least 50 % pain relief and 25 % had at least 80 % relief [182].

Notably all four groups demonstrated similar rates of positive tests with provocative discography (28–41 %) [180]. However, when looking at pain relief in disks found to be painful on provocative discography, the rates differed significantly between groups. With using 50 % pain relief as a cutoff, only two groups had similar rates (40 and 46 %) with the two other groups lying on either side of this (7 and 80 %) [180]. Using an 80 % pain relief demonstrated similarity between three of the groups (20 %, 35 %, 30 %) with the other showing a lower percent response (3 %) [180]. Theoretically when compared to provocative discography, there may be discordant rates of positive tests that can be attributable to either false positives during provocative testing or false negatives during analgesic testing. If considering 80 % pain relief as a positive result, which occurred in 20–30 % of the disks found to be painful with provocative discography, one can postulate that provocative discography has false-positive rates of 70–80 % or that anesthetic discography has false negatives of 70–80 %. Without a clear reference standard, the discrepancy between the two cannot be fully defined.

Clearly analgesic discography still lacks a standardized protocol to perform the procedure, standardized testing parameters during the procedure, and a standardized way to interpret the test result before it can be a viable diagnostic tool for discogenic pain. Whether it is potentially a test that can be used in lieu of provocative discography or one that can be used in conjunction with to formulate a compound criteria including positive response to both provocative discography and analgesic discography is another question that will need to be answered in the future.

33.4.1.4 Potential Intradiscal Therapeutic Agents

Aside from the diagnostic value of either provocative or analgesic discography, the ultimate goal of medicine is to not only diagnose but also offer safe and effective therapeutic agent. There have been several treatments postulated for discogenic low back pain, including intradiscal corticosteroids, methylene blue, and fibrin sealant. Methylene blue has been postulated as a possible effective intradiscal therapy given its theoretical neurotropic effects and theoretical action as a direct inhibitor of NO synthase. Peng et al. reported significant improvements in pain, satisfaction, and disability score in a randomized placebo-controlled trial with the intradiscal injection of methylene blue versus placebo [183]. However attempts to replicate these findings by Kim et al. in a 1-year prospective study have failed, and to this point the Peng study stands alone in demonstrating utility in intradiscal methylene blue treatment [184]. Perhaps the greatest area of potential for therapeutic intervention lays in nucleus pulposus replacement, annulus fibrosus replacement, and/or sealants/adhesives. Both synthetic polymeric materials and natural biopolymers have been studied as injectable nucleus pulposus tissue replacement [185–191]. Many of these have been able to match the compression and shear moduli of native nucleus pulposus tissue [191]. However progress is still needed before these are viable therapeutic options. Also, an injectable nucleus pulposus replacement would still have the theoretical problems of leaving a puncture site through the annulus fibrosus, and as previously discussed there is evidence that this alone predisposes disks to herniation and degeneration. Schek et al. have published a possible fibrin-genipin hydrogel adhesive with a tunable mechanical property that may be able to act as a plug mechanism without causing mechanical stress on the surrounding tissue [192]. There have also been attempts to produce biomaterials for annulus fibrosus replacement; however, no materials have been found thus far that are able to match the mechanical properties of the annulus fibrosus [193–196]. More promising perhaps are potential scaffolds that would support the growth of annulus fibrosus cells. Many attempts are underway to identify materials for nucleus pulposus and annulus fibrosus repair; however, currently significant progress remains to be made before these are viable therapeutic options for patients.

In light of there being no conclusive evidence that there is any effective therapeutic intervention for discography-proven discogenic pain, coupled

with the long-term detrimental sequelae of discography, its utility is questionable at best, and use of the test should be extremely limited. In patients with chronic low back pain that are potentially undergoing fusion, there may remain a small role in discography in aiding surgical planning if the patient is willing to consider that positive discography leading to fusion of an additional level may increase chances at successful surgical outcome by up to 50 %. Otherwise, until new techniques that mitigate the proven long-term risks of discography are developed in addition to the development of successful outcomes for discography-proven discogenic pain, the clinical utility of discography is marginal.

Conclusions

The judicious use of appropriately performed injections can aid significantly in the ability to diagnose and treat patients with spine pathologies. Injections by definition are target specific and, to be useful from a diagnostic standpoint, must be done with imaging guidance. To be appropriately therapeutic they must also be judiciously used in appropriately selected patients while following appropriate technical guidelines. When done appropriately these image-guided injections have a large body of literature demonstrating their efficacy for certain disease conditions.

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34 Endoscopic Procedures for the Lumbar Spine: A Comprehensive View

Sebastian Ruetten, Martin Komp, Semih Oezdemir, and Patrick Hahn

34.1 Terminology and Definitions

Full-endoscopic lumbar surgery describes the surgical technique associated with lumbar spinal canal decompression, carried out under continuous visual control and irrigation using an approach associated with minimal trauma. It is not an endoscopic-assisted procedure through a tubular retractor. Rather, it is a uniportal technique using endoscopes with intraendoscopic working channels. Apart from reduced surgical trauma, it yields the benefits of arthroscopic procedures, such as improvement in visualization and light conditions. Two differing approaches are applied – the full-endoscopic interlaminar and the full-endoscopic transforaminal/extraforaminal approaches.

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34.2 Surgical Principle

Over the past 90 years, many different operations on the lumbar spine have been described [1–4]. In the meantime, these operations have been modified [5–12]. The focus was frequently on reducing invasiveness and improving visualization during the course of surgical intervention. The microscopically assisted technique, introduced nearly 40 years ago, remains the standard for spinal decompression operations [6, 9, 13].

Gaining access to the spinal canal using an interlaminar approach by means of complete or partial laminectomy was described at the beginning of the twentieth century [1–4]. Alternative methods for carrying out operations relating to pathology of the intervertebral disks were developed 30 years later [11]. The posterolateral approach for taking biopsies from vertebrae was described at the end of the 1940s [14]. Percutaneous operations have been applied since the beginning of the 1970s [10, 12, 15–17]. The microsurgical procedure using the microscope was also developed in the 1970s and has achieved the status of gold standard for interlaminar decompression in the spinal canal [6, 9, 13]. Endoscopes have been used since the beginning of the 1980s. Initially, they were used in order to inspect the intervertebral space after open decompressions were considered completed [8]. This developed into the endoscopic transforaminal technique with posterolateral access [18–22]. This technique was

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_34

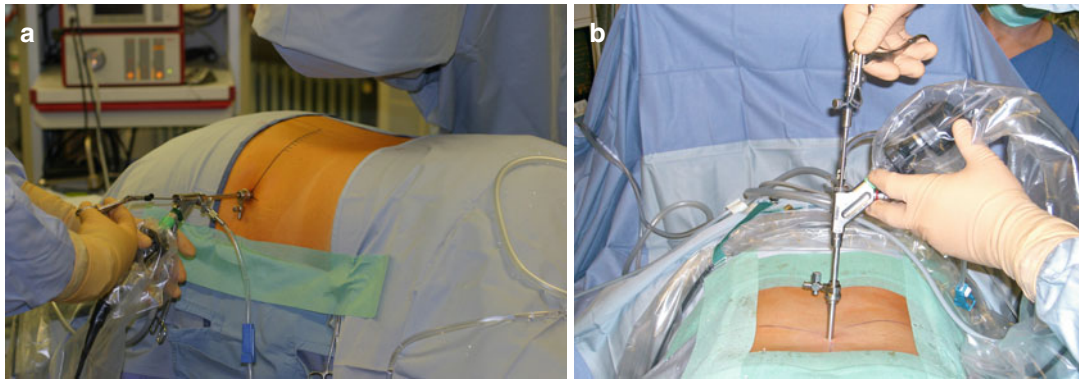

Fig. 34.1 (**a**) The lateral transforaminal approach for endoscopic surgery. (**b**) The interlaminar approach for endoscopic surgery

the most common procedure used for endoscopic operations carried out on patients with diseases of lumbar disks. Manuscripts regarding endoscopically assisted procedures have been published since the early 1990s [7, 23–26]. This relates to visualization of the open operation site using an endoscope on a monitor.

The endoscopic posterolateral transforaminal approach allows the intervertebral space to be accessed within the intervertebral foramen between the exiting and traversing spinal nerves. Direct removal of intraforaminal and extraforaminal sequestrated disk extravasations is possible through this approach [19, 27]. The removal of displaced disk material within the spinal canal under a retrograde resection, i.e., intradiskally through the annulus defect, was described and termed as the "in-out technique" [18, 28, 29]. However, there are frequently technical constraints due to specific anatomical and pathological circumstances that do not allow this technique. Direct access to extradiskal ventral epidural space with continuous visualization is hence necessary for adequate decompression. This is prevented if the posterolateral approach is being used, particularly in the caudal segments when a small intervertebral foramen deflects the endoscope from the epidural space into the disk [28, 30, 31].

As a result of these problems, the full-endoscopic lateral trans-/extraforaminal approach was developed. It provides access to the spinal canal, with a continuous view of vital anatomy (Fig. 34.1a). Working with irrigation fluid provides excellent visualization. No measurement is carried out in centimeters to define an entry point in the skin, but an individual anatomical determination is performed under radiographic control [32–34]. Despite the lateral approach and the possibility of bone resection, there are clearly defined indications – and hence also constraints. These relate to mobility and obstruction of the approach by the pelvis or organ systems [32–34].

The constraints associated with the transforaminal approach motivated development of the full-endoscopic interlaminar approach which also permits surgery on pathologies that are outside the indication spectrum of the transforaminal procedure [33–36] (Fig. 34.1b).

Today, the combination of the new surgical approaches and advanced technical developments permits the first full-endoscopic procedure under visualization, which is equivalent to conventional operations. The transforaminal procedure is subject to more constraints compared with the interlaminar procedure, but at the same time provides optimal preservation of tissue. The anatomical and pathological conditions mean that the percentage ratio of transforaminal to interlaminar procedures is about 30–70.

34.3 Patient Selection

34.3.1 General Indication

The indication for surgery must be determined according to today's standards on the basis of radicular symptoms, neurogenic claudication,

and existing neurological deficits [37, 38]. Isolated back pain cannot usually be improved by decompressing operations. Existing secondary pathologies, such as instabilities, may have to be treated at the same time using other procedures. The following anatomical indications are currently unequivocal:

- Sequestered or non-sequestered lumbar disk herniations inside the spinal canal
- Sequestered or non-sequestered lumbar disk herniations intra- or extraforaminal
- Sequestered or non-sequestered recurrent disk herniations independent of localization
- Lateral spinal canal stenosis (recess stenosis) (bony, ligamentous, diskal)
- Central spinal stenosis (bony, ligamentous, diskal)
- Spinal stenosis due to cysts of the zygapophyseal joint
- In special cases, positioning of implants in the intervertebral space
- In special cases, intervertebral debridement and draining in spondylodiskitis or epidural abscess

34.3.2 Indications for Trans-/Extraforaminal Approach

- All intraforaminal and extraforaminal disk herniations or cysts of the zygapophyseal joints are indications for the transforaminal approach.

In disk herniations within the spinal canal, the following inclusion criteria need to be taken into account due to the limited mobility:

- Location of the sequestered disk reaching cranially and caudally to maximally at the start of the pedicle above and below the level in question (Fig. 34.2a)
- In lateral X-ray pelvic overlay of the level in question to maximally at the middle of the pedicle above (Fig. 34.2b)

In the case of lateral spinal canal stenosis, only foraminal stenosis caused by intraforaminal/extraforaminal cysts of the zygapophyseal joints is regarded as an indication for the transforaminal/extraforaminal approach.

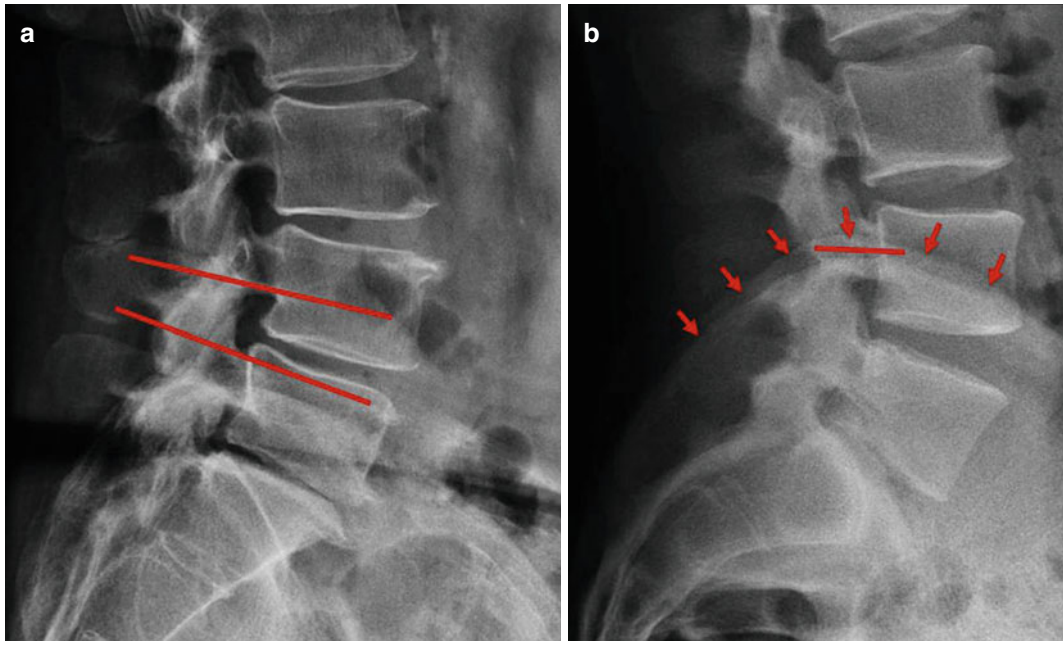

Fig. 34.2 (**a**) Maximal sequestration for the transforaminal approach (*lines*, start of the pedicle above and below the level in question). (**b**) Maximal overlaying of the pelvic for the transforaminal approach (*arrows*, iliac crest; *line*, middle of the pedicle above the level in question)

34.3.3 Indications for Interlaminar Approach

- All disk herniations or cysts of the zygapophyseal joint located within the spinal canal which cannot be operated technically in the transforaminal approach because of the criteria cited are taken as indications for the interlaminar approach.
- The interlaminar technique can be used as an alternative for surgery in all spinal disk herniations in the spinal canal comprised within the inclusion criteria for transforaminal approach.
- Recess stenosis due to bony/ligamentous/diskal pathologies.
- Recess stenosis due to cysts of the zygapophyseal joints.
- Central spinal stenosis due to bony/ligamentous/diskal pathologies.
- Central spinal canal stenosis based on cysts of the zygapophyseal joints.

34.3.4 Contraindications

- All criteria which generally apply as contraindications to decompressing operations, taking into consideration the specific technical possibilities and the inclusion criteria of each surgical procedure are considered contraindications.
- Isolated back pain caused by associated pathologies, e.g., instabilities, deformities.
- Cauda equina syndrome: a conventional procedure should be considered here, particularly for legal reasons.

34.4 Advantages and Disadvantages

34.4.1 Advantages

Conventional open surgical procedures are indispensable today and will remain so in the future. The possible complications and consequential damage entailed by such procedures are familiar. New techniques must guarantee sufficient possibilities of attaining the surgical goal which are equal to those of established procedures [39].

Full-endoscopic operation, such as a truly minimally invasive procedure, offer advantages. These correspond largely to the advantages of microscope-assisted surgery, cited in each case, over the conventional open procedure. Full-endoscopic operations may thus be classified as the next step for technical advances in surgical techniques.

- Facilitation for the surgeon, due to excellent visualization, good illumination, and expanded field of vision with 25° endoscopes
- Cost-effective procedure due to short operating time, rapid rehabilitation, high rate of return to earlier activity levels, and low postoperative costs of care
- Reduced trauma and the resultant consequences for the surrounding tissue, the stabilizing structures of the spinal canal, and the epidural space
- Facilitated revision operations
- Reduced complication rate, such as dural injury, bleeding, infections, etc.
- Monitor image as training basis for assistants
- High level of patient acceptance

34.4.2 Disadvantages

The following are cited as specific disadvantages:

- Inclusion criteria for the different approaches must be complied with:
- Limited mobility in the transforaminal approach
- Limited possibility to expand the operation in the event of unforeseen hindrances
- Full-endoscopic suturing of dura technically not possible
- Challenging learning curve
- Lumbar transforaminal risk of injury to the emerging nerves as a result of the approach

34.5 Preoperative Planning

The preoperative preparation is the same as the preparation for conventional, microsurgical operations.

34.5.1 Examinations

As with all microsurgical techniques, the intraoperative procedure must be planned preoperatively based on imaging and clinical findings. The goal is to perform the resection of spinal canal structures as sparingly as possible depending on the pathology and provide adequate neurological decompression. Conventional X-rays of the lumbar spine and MR imaging are obligatory. In applying the lateral transforaminal approach, the access pathway may not be shifted by abdominal structures. Particular attention must be paid to this in the levels cranial to L4–L5. If the findings are not entirely clear, a single abdominal CT scan should be made through the disk level for evaluation and preoperative planning.

34.5.2 Patients' Informed Consent

Patients must be informed about their disease, its possible long-term course, and consequences and, despite the minimal invasiveness and attendant advantages of the surgical procedure, all known side effects, complications, and therapeutic possibilities must be explained, as for conventional procedures. With reference to the full-endoscopic procedure, it is important to highlight that even with minimally invasive interventions, scarring may not be completely avoided. It is also important to emphasize that a switch to an open procedure may be required during the operation or subsequently in an additional procedure should unforeseen complications arise.

34.5.3 Preparation

The preoperative preparation of the patients is the same as in microsurgical techniques. A single-shot antibiotic is applied for infection prophylaxis.

34.5.4 Anesthesia

Full-endoscopic operations can usually be performed under local or general anesthesia. General anesthesia has advantages because it is more convenient for both the patient and the surgeon, permits positioning as required, and also facilitates complex work within the spinal canal. In cases of local anesthesia in the interlaminar approach, anesthesia for the route of access and also of the neural structures is necessary. Due to inflammatory processes, epidural anesthesia alone is frequently not sufficient, and therefore, intrathecal administration of local anesthetic must be carried out. In addition, systemic sedation is necessary for immobilization. Positioning entails costly control of vital parameters and correction of anesthesiological problems can be difficult.

In transforaminal approach, there is a risk of damaging the exiting nerve route passing the foramen. Theoretically, the risk can be reduced with the possibility of communicating with the patient. Thus, the operation under local anesthesia is also prevalent.

34.5.5 Positioning

The operation is performed with the patient in prone position on a radiolucent table, under two-plane radiological control. The patient lies on a hip and thoracic rolls to relieve the abdominal and thoracic organs. The operating table is lordotically or kyphotically adjustable intraoperatively at lumbar level depending on the anatomy and pathology.

34.5.6 Equipment

A radiolucent, electrically adjustable operation table and a C-arc are necessary. In addition to the surgical instruments and endoscopes, general

equipments for endoscopic operations under fluid flow are needed, such as monitor, camera unit, light source, documentation system, fluid pump, shaver system, or radiofrequency generator. Equipment available for arthroscopy or endoscopy can be used. Depending on indication, the rod-lens endoscope has an outer diameter of 6.9 or 9.9 mm. The endoscope contains an intraendoscopic, eccentric working channel with diameter of 4.1 or 6.5 mm. The angle of vision is 25°. The working sheaths used have a beveled opening which enables creation of visual and working fields in an area without clear anatomically preformed cavity (Fig. 34.3a, b).

34.6 Surgical Technique

34.6.1 Lateral Transforaminal Approach

First, the skin incision is localized. The goal is to reach the spinal canal as tangentially as possible. At levels L4–L5 and L3–L4, in lateral X-ray path, the posterior line of the descending facet usually serves as the boundary which should not be crossed toward the ventral direction (Fig. 34.4a). To avoid injury to abdominal organs, a single abdominal CT scan through the individual disk should be made for evaluation and preoperative planning, especially at the cranial levels when findings are not unequivocal. Depending on the scan, an individual, less lateral approach should be selected.

An atraumatic spinal needle is inserted through the skin incision parallel running to the disk space in the target area. A practicable end point is the contact of the dorsal annulus in the medial pedicle line. After a target wire is inserted and the cannula removed, the cannulated dilator is inserted. It is absolutely essential to ensure that the dilator is located for all work steps at the level of the intervertebral disks and not displaced cranially as this can lead to damage of the emerging spinal nerves. The target wire is removed and the operation sheath with beveled opening is pushed through the dilator. When an appropriate position is attained, the site of the sheath opening is located at the medial pedicle line and the opening itself in the lateral ray path is positioned half in the ventral epidural space and in the dorsal annulus (Fig. 34.4b, c). From this point on, decompression is performed under visualization and continuous irrigation with isotonic saline without any special additives. The entire system is left open as standard so that the irrigation fluid can flow out. Further entry into the epidural space which may be required is made under visual control.

Annulus fragments are resected for dissection medially, until the disk herniation is localized and exposed. A rongeur is used to remove the disk herniation entirely or in parts. After complete resection, an unobstructed view is provided of the decompressed area. Depending on previous dissection, the dorsal longitudinal ligament can still be seen, which can be opened as necessary. The intervertebral space can then be cleared until the free intradiskal fragments are resected (Fig. 34.5a–c). The operation is implemented in the same way even if previous operations have been carried out in the operating area. After the operation has been completed, the instrument set is removed and the stab incision is closed. Drainage is not necessary.

34.6.2 Extraforaminal Approach

The extraforaminal approach can be used for intraforaminal/extraforaminal pathologies or for anatomical/pathological conditions which preclude a harmless, direct passage of the foramen due to the restricted diameter or the position of the emerging spinal nerves.

The spinal cannula is pushed forward to the caudal pedicle under X-ray control. This is a safe zone in which the emerging spinal nerve is not damaged. Dilator and operating sheath are then inserted (Fig. 34.6a). From this point on, the operation is carried out under visualization and continuous irrigation with isotonic saline. The entire system is left open as standard so that the irrigation fluid can drain away.

Pedicle, ascending facet, and disk are dissected and the foramen is exposed. The operating sheath is used as an instrument to hold the

Fig. 34.3 (**a**) Various endoscopes with intraendoscopic working channel. (**b**) Different instruments for the endoscopic surgery

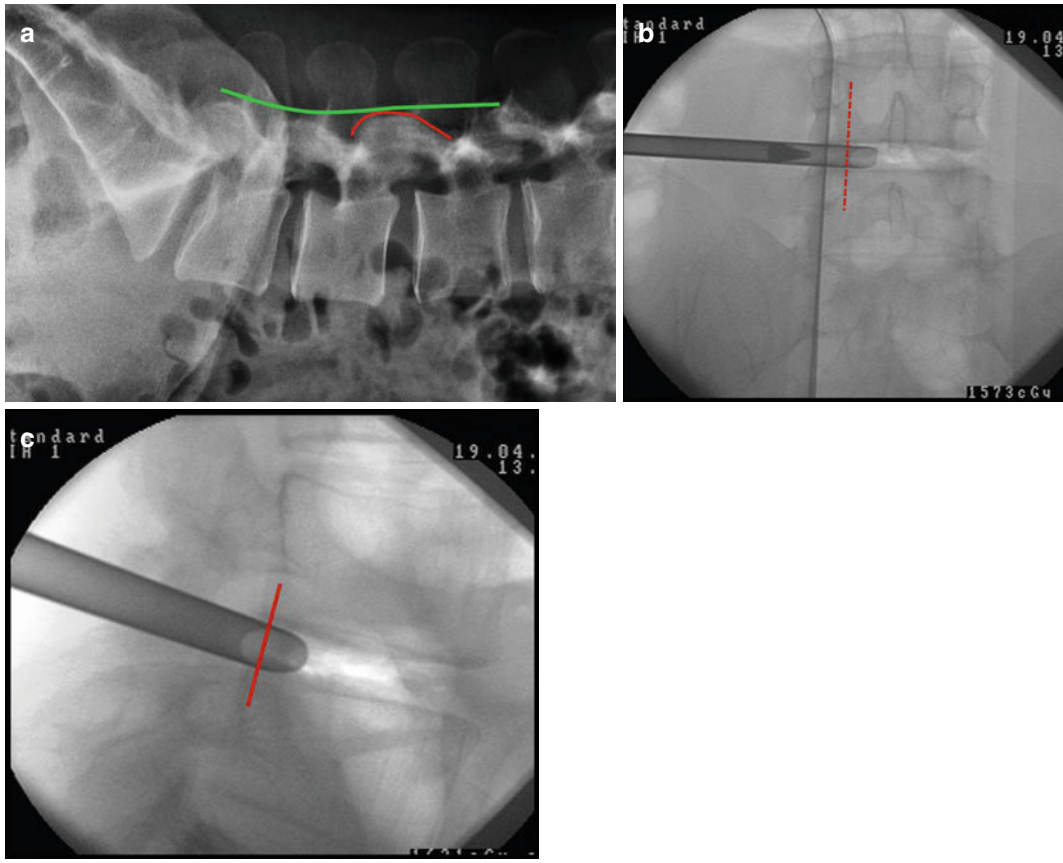

Fig. 34.4 (**a**) The posterior line (*green line*) of the descending facet (*red line*) should not be crossed toward the ventral direction for marking the skin incision. (**b**) Site of the sheath opening is located at the medial pedicle line (*red line*). (**c**) Opening of the sheath is positioned half in the ventral epidural space and in the dorsal annulus (*red line*, posterior wall of vertebral bodies)

emerging spinal nerves cranially and ventrally. The extraforaminal port should also be selected maximally lateral so that it passes under the nerve cranially without significant manipulation.

The operation then continues from this position, such as direct decompression in the foramen, entry into the spinal canal through the foramen, or prior bone resection.

In the case of intraforaminal/extraforaminal disk herniation, the approach is determined by the location of the herniation, which is generally sequestrated rostrally. The exiting spinal nerve is moved further rostrally with the operating sheath and identified. The herniation is localized, dissected, and resected. In order to gain access further cranially under the spinal nerve, it can be lifted with the movable shaft of the rongeur. In the same way, additional parts sequestrated cranially in the spinal canal can be resected. The intervertebral space can then be cleared (Fig. 34.6b, c).

In the case of intraforaminal/extraforaminal cysts of the zygapophyseal joints, dissection and precise identification of spinal nerve and cysts are important. The cysts are then opened, the material inside is removed, and the cyst walls are resected as far as possible.

Bone resection can be carried out in order to generally enlarge the foramen if it is constricted and to create a passage, but most frequently in order to achieve more mobility dorsally or caudally (Fig. 34.6d). Depending on the pathology, bone is resected in the ventral area of the ascending facet or in the cranial area of the caudal pedicle.

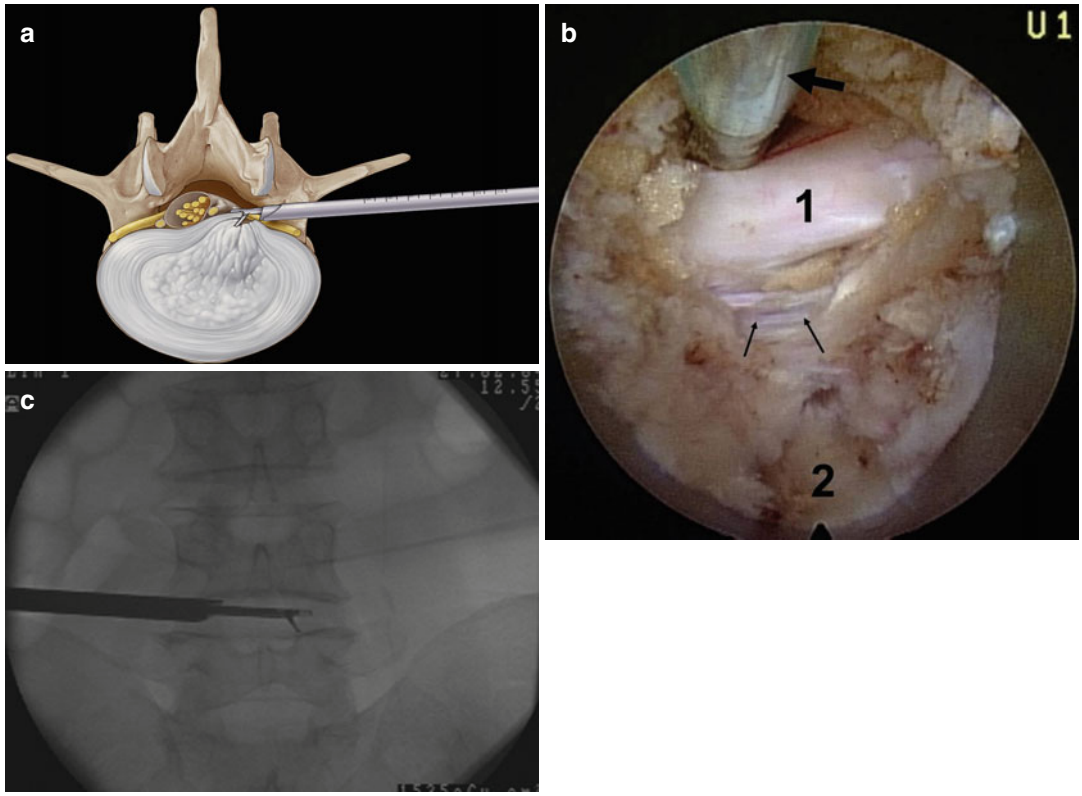

Fig. 34.5 (**a**) Transforaminal operation inside the spinal canal. (**b**) Intraoperative view after decompression (*1*, traversing spinal nerve; *thin arrows*, posterior longitudinal ligament; *2*, intradiskal; *bold arrow*, radiofrequency electrode). (**c**) Intraoperative radiographic view

The extraforaminal approach at L5–S1 or in the last level presents a special situation, since the pelvis and the transverse process exert a particular influence on the approach. The caudal pedicle (S1) is the target for the spinal cannula. On account of the pelvis, the spinal cannula generally has a steep to a virtually posterior pathway after reaching the end position. After inserting the dilator, operating sheath, and endoscope, subsequent dissection is equivalent to the process for the standard extraforaminal approach but differs in implementation as the passage selected becomes steeper. This can result in the emerging spinal nerve being dissected and exposed directly from a dorsal position after the bony structures have been exposed, similar to the interlaminar technique. The operating sheath must also be used in a similar way. The precise performance of decompression depends on the findings of each case. Drainage is not necessary.

34.6.3 Interlaminar Approach

The skin incision is made as medially as possible through the interlaminar window. The craniocaudal localization depends on the findings of the pathology.

The dilator is inserted bluntly on the lateral edge of the ligamentum flavum or on the descending facet of the zygapophyseal joint under radiographic posterior-anterior control. From this point onward, the operation is performed under radiographic lateral control. The operation sheath with beveled opening is inserted via the dilator in the direction of the ligament. The subsequent procedure is then performed under visualization and continuous irrigation with isotonic saline solution. The entire system is left open as standard so that the irrigation fluid can drain away.

In order to reach the spinal canal, the ligamentum flavum is incised laterally to approx.

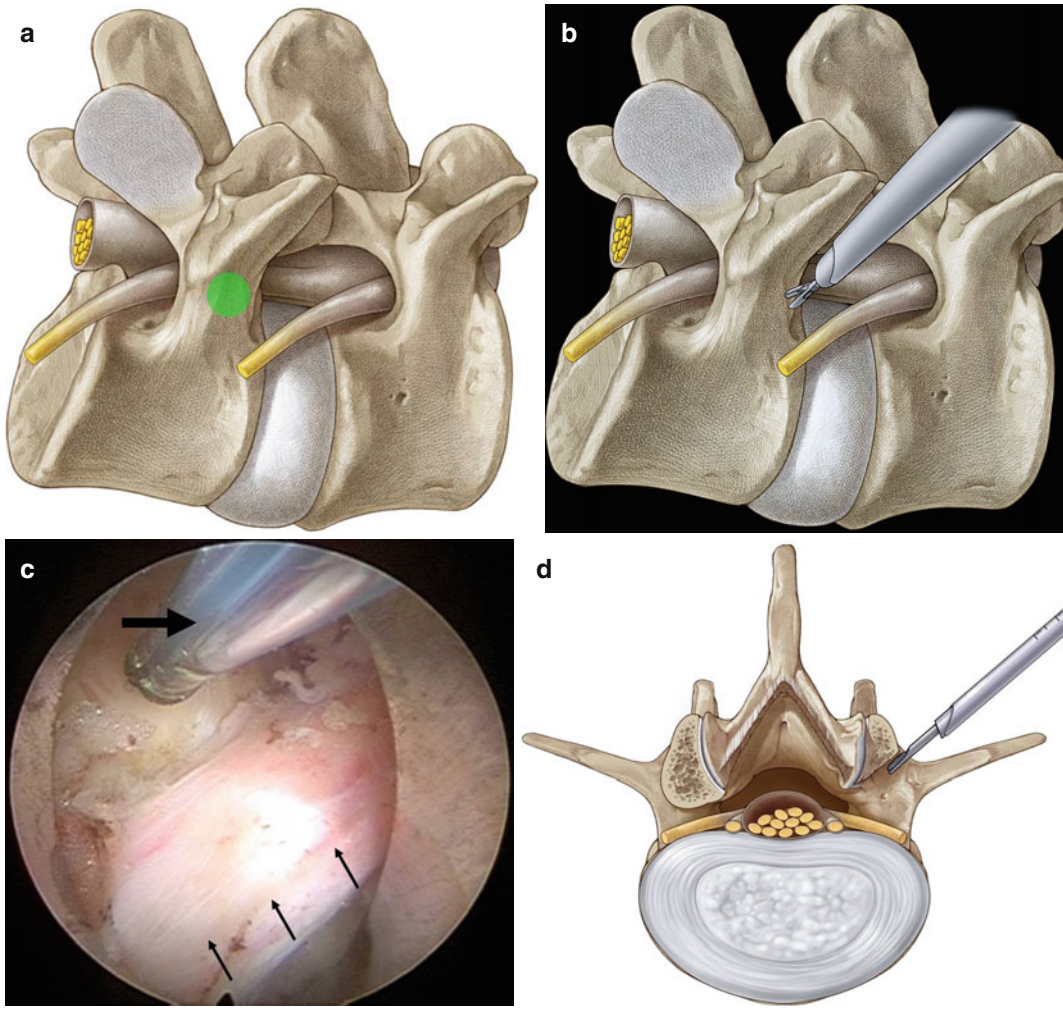

Fig. 34.6 (**a**) Target point (*green circle*) for the cannula in the extraforaminal approach. (**b**) The extraforaminal operation starts at the caudal pedicle. (**c**) Intraoperative view after intraforaminal decompression (*thin arrows*, exiting nerve; *bold arrows*, radiofrequency electrode). (**d**) Bone resection to enlarge the foramen

3–5 mm. The subsequent procedure is enabled by the elasticity of the ligament. By rotating, the operation sheath with beveled opening can be used as a second instrument and serves, for example, as a nerve hook in shifting the neural structures in the medial direction.

The neural structures are identified prior to operating on the primary disk herniation, in particular the lateral boundary. If the recess cannot be visualized laterally to the traversing spinal nerve, medial portions of the ascending facet can be resected with the punch. If adequate space is available in the recess, the operating sheath can be introduced with the opening aligned medially on the floor of the spinal canal in order to shift the neural structures in a medial direction. The sheath is rotated with continuous contact to the base of the spinal canal. If the operating sheath cannot be introduced directly in the recess, the maneuver can be carried out with the aid of the dissector. A partial decompression through the axilla must be carried out prior to the maneuver involving sheath rotation. At the same time, this prevents parts of the disk herniation from being displaced medially together with the neural structures. The protruding disk herniation material is dissected and

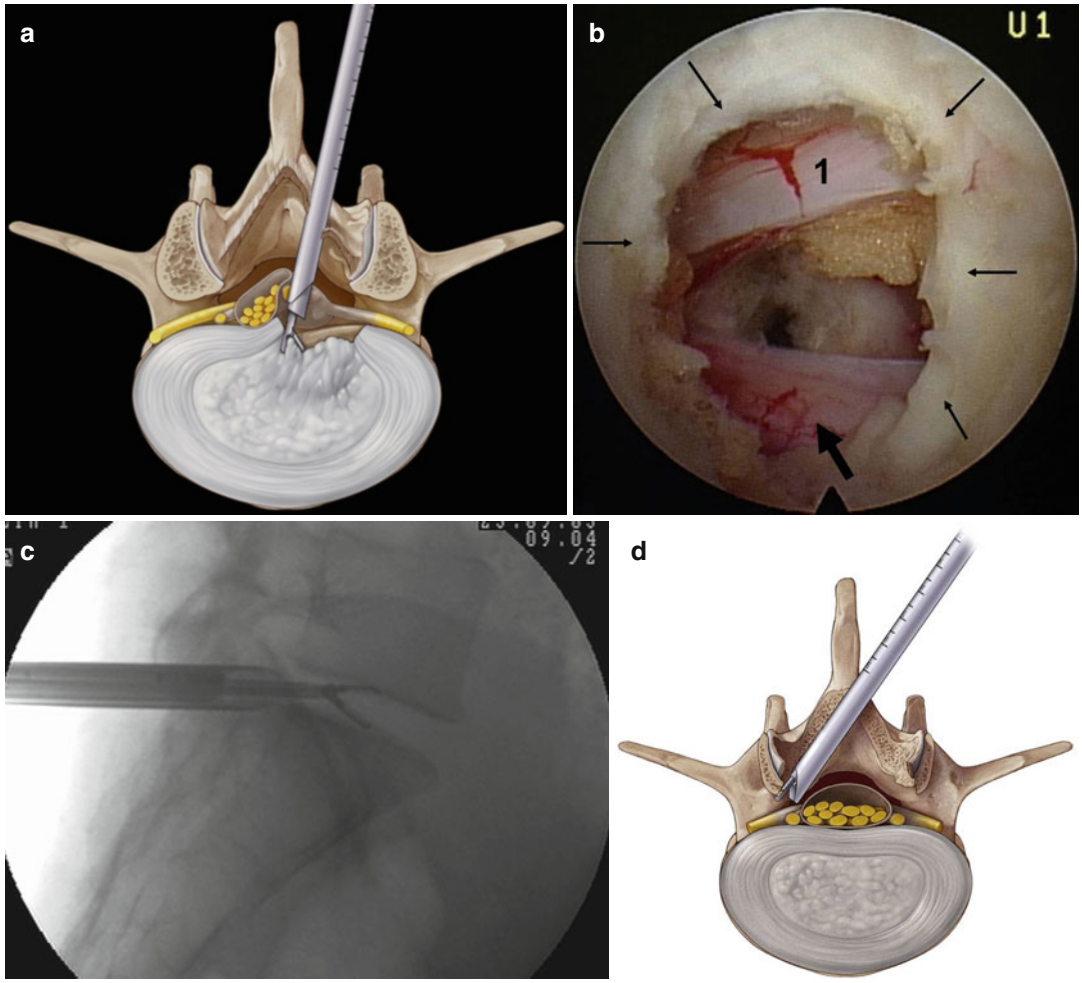

Fig. 34.7 (**a**) Interlaminar operation inside the spinal canal. (**b**) Intraoperative after decompression (*thin arrows*, flavum ligament; *bold arrow*, traversing spinal nerve; *1*, dura of cauda equina). (**c**) Intraoperative radiographic view. (**d**) Bone resection on the contralateral side in over-the-top technique

resected. The intervertebral space can be cleared (Fig. 34.7a–c).

If the bony diameter of the interlaminar window does not permit passage or for large sequestered herniations, the window is enlarged using a burr and instruments. The descending facet joint is dissected and the medial edge and caudal pole are exposed. An incision is made on the surface leaf of the ligamentum flavum along its process at the medial edge of the descending joint facet. Bone resection begins at the caudal pole of the descending facet and continues along the medial part of the descending facet and toward the cranial lamina. Since the ligamentum flavum is inserted caudally, directly at the bony edge of the lamina, burrs are used to thin the lamina here and the intervention is then continued with resection using a punch.

When revision operations are performed, no assessment on the implication of the ligamentum flavum can be made in advance of the operation – so that the dilator and operating sheath are introduced directly at the descending facet joint. The ongoing approach varies with each individual and depends on the degree of scarring and the type of operation carried out previously. If there is significant scarring, dissection directly along the edge of the bone and the descending facet in

a ventral direction has proved effective. If direct entry to the recess is not possible, the medial edge of the ascending facet joint is dissected and the approach is carried out strictly at the bone in the direction of the spinal canal. Once the recess has been adequately dissected, the operating sheath is introduced. Depending on the degree of scarring, the maneuver involving rotation of the operating sheath displaces all the tissue en bloc medially. The neural structures may be fixed depending on the scarring. There may be an increased risk of damage as a result of manipulation. The force applied when displacing the neural structures therefore needs to be carefully moderated. If it is not possible to enter the recess, bone resection described above has to be carried out in advance.

As described above, bone resection has to be performed for operating on a recess stenosis. The medial portion of the descending facet joint or parts of the cranial lamina have to be resected as part of the standard procedure until the cranial tip of the ascending facet is reached. Experience indicates that bone resection caudally is adequate if it extends to the middle of the caudal pedicle. The ligamentum flavum is frequently involved in the pathology and then has to be resected in the lateral area over the entire craniocaudal extension. Depending on the characteristics of the pathology, the medial bony edge of the ascending facet is resected using a punch or burr until the recess has been exposed. The maneuver involving rotation of the sheath is used to shift the neural structures medially. If compression is caused by a protruding annulus or ventral osteophytes, they must be resected.

If a single-sided port is used for the central spinal canal stenosis, the approach used in the lateral stenosis of the ligamentum flavum has to be expanded by resecting medially up to the midline. In the case of contralateral decompression in the over-the-top technique with a single-sided approach, bone is already removed medially up to the spinous process during dissection of the caudal lamina depending on the characteristics of the pathology. After ipsilateral decompression has been completed, the operating sheath is inserted contralaterally and the contralateral ligamentum flavum, the contralateral bone of the lamina, and the descending facet and the medial edge of the ascending facet are resected until the spinal canal and the recess are exposed (Fig. 34.7d). As in microsurgical interventions, the central spinal canal stenosis can also be sufficiently decompressed contralaterally in the over-the-top technique. The detailed decompression of the recess in the cranial and caudal area is frequently subject to ipsilateral decompression. A bilateral approach with independent ports on both sides should therefore be considered in cases of bilateral recess stenosis with radicular symptoms. This enables the complete median area of the spinal canal and its structures to be retained, which is not involved with the pathology in recess stenosis.

The intraspinal cyst of the zygapophyseal joints generally occurs on one side and leads to symptoms of lateral or central spinal canal stenosis depending on the extent and localization. In addition to cyst resection, it may be necessary to carry out spinal canal expansion as described above. After opening the ligamentum flavum, this is resected until the cyst can be dissected and completely visualized. If possible, the cyst wall is separated from the dura. The cyst is opened, the material inside is removed, and the cyst wall is resected as far as possible. If necessary, a burr can be used on the joint side in order to resect all the parts of the cyst in contact with the joint.

34.7 Postoperative Care

The length of stay in hospital depends on the surgical measures carried out. Pure diskectomies or simple decompressions are treated with brief hospitalization or, if patient care at home is adequate, on an outpatient basis. Mobilization is immediate, as soon as this is possible following recovery from anesthesia. No medication is required for pain following the operation. Apart from patients with neurological deficits, no rehabilitative measures are necessary. Isometric and coordinative exercises can be performed without supervision once they have been learned. A passive lumbar brace is prescribed during the day for

about 6 weeks. The level of exercise can be increased depending on the pathology and the patient's subjective sense of well-being. Return to work and sports are possible under the same conditions after the wound has healed. Limitations are imposed only to the extent that there should be no increase in pain during any activity. After more complex operations, the postsurgical treatment regimen is usually more restrictive and depends on the individual and the interventions carried out.

34.8 Complications and Avoidance

Possible complications during microsurgical procedures are known and there is a wide body of literature on this subject. A minimally invasive procedure is able to reduce the complication rate, although statistically this cannot be completely avoided. In principle, all the complications from conventional operating procedures may occur. These include the following:

Intraoperative complications: surgery on the wrong segment, epidural bleeding, insufficient decompression, injuries to the dura, injuries to neural structures, injuries to vessels, injuries to organs

Direct postoperative complications: persistent or preexisting radicular symptoms, cauda equina syndrome, urinary retention, consequences of injury to vessels or organs

Delayed postoperative complications: soft tissue infection, spondylodiskitis, CSF fistula, delayed consequences of injury to vessels or organs, further radicular symptoms, surgically induced symptoms (failed back surgery syndrome)

As far as full-endoscopic procedures are concerned, it is important to emphasize that a one-sided or two-sided switch to an open procedure may be necessary to carry out therapy in the event of a complication. In particular, endoscopic suture of a dural injury is not technically possible. Theoretically, if operating times are extended and blockage for outflow of irrigation fluid is overlooked, the consequences of increased pressure within the spinal canal and the attached and neighboring structures cannot be completely ruled out. Operations should therefore be performed leaving the system open such that the irrigation fluid can overflow.

With the interlaminar approach, a long-lasting and uninterrupted excessive retraction of the neural structures with the working sheath in the medial direction must be avoided or made only intermittently in order to avoid the risk of neurological damage.

In the transforaminal approach, the risk of injury to the exiting nerves cannot be completely eliminated. The highest risk occurs while performing the approach itself. If the risk is to be avoided, it is necessary to remain strictly within the caudal aspect of the foramen (Fig. 34.8). Alternatively, if the foramen is narrowed, an extraforaminal approach should be performed if necessary. When the lateral access is used, it is important to ensure that abdominal organs do not block the access path. It is particularly important to take account of this at the levels cranial to L4–L5. If the findings are not entirely clear, a single abdominal CT scan should be made through the

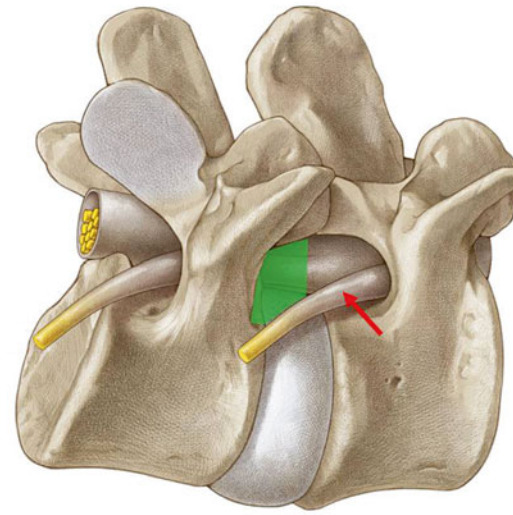

Fig. 34.8 Remain strictly within the caudal aspect (*green plane*) of the foramen during the approach to avoid damaging the exiting nerve (*red arrow*)

disk for purposes of evaluation, preoperative planning, and measuring of the approach. An important factor for the outcome is the correct indication for the procedure itself and the proper approach.

Especially during the learning curve, there is an increased risk of complications occurring in the initial surgeries, as with any new technique. Prior observation of and assisting in procedures and workshops involving practice on cadavers might be instructive. Strict adherence to the indication criteria for the appropriate full-endoscopic approach is necessary. In the first instance, operations should be carried out on "simple" cases where no difficulties are to be expected in view of the anatomical situation. The possibility of an intraoperative switch to a standard procedure is helpful if problems are encountered. Nonetheless, it is important to remember that difficulties can never be ruled out during the learning curve.

34.9 Critical Evaluations

The objective in the development of surgical therapy for radicular compression syndromes caused by disk herniations or spinal canal stenoses is to provide adequate decompression under optimum visualization conditions with minimal trauma induced by surgery and the resulting negative consequences of such trauma. When new techniques are introduced, the clinical results of conventional standard procedures must be attained as a minimum criterion. At the same time, advantages in surgical technique and/or clinical variables must be the objective.

The development of new rod-lens endoscopes with a large intraendoscopic working channel and appropriate instrument sets has provided the technical platform for full-endoscopic operation on all lumbar disk herniations, inside and outside the spinal canal, and on spinal stenosis [32–36, 40–42]. In order to ensure complete decompression with certainty, operations on disk herniations and spinal canal stenosis must also be carried out using a full-endoscopic technique and under continuous visualization. The development of the lateral transforaminal approach optimizes and facilitates access to the spinal canal and working under continuous visualization [32–34]. This eliminates problems associated with the posterolateral approach. However, the lateral approach also entails clear inclusion and exclusion criteria and hence also constraints [32–34]. Today, the interlaminar approach can be used in cases that are inoperable using the transforaminal approach for technical reasons [33, 34, 36, 40–42]. The full-endoscopic techniques that have been developed can now produce results where the clinical outcome coincides with the conventional microsurgical procedure. Simultaneously, significant advantages are evidenced that remain consistent over subsequent follow-up periods of examination [32–36, 40–42].

Despite the developments over the past 10 years, there are clear limits to full-endoscopic techniques. Open and maximally invasive procedures are necessary today and will remain so in the future. Surgeons must be able to perform such operations, not simply so that they are in a position to offer patients the most appropriate procedure for their particular circumstances but also to enable them to deal safely with any problems and complications that may emerge during full-endoscopic interventions as in any other invasive procedure. The development of full-endoscopic techniques should not be evaluated as a replacement for existing standard operations, but as a complementary procedure and alternative within the overall concept of spine surgery.

34.9.1 Indication for Disk Herniation

Possible negative consequences of conventional operations on the lumbar spine are well known and documented in the literature [43–53]. A comparison of the literature and the underlying studies reveals that the full-endoscopic procedure reduces operating times, tissue trauma, and complications [34, 54–58]. This corresponds to the published benefits of a minimally invasive intervertebral and epidural approach. The current state of knowledge indicates that it is possible to avoid instabilities as a result of the ability to reduce or eliminate bone and ligament resection

combined with atraumatic curettage of the intervertebral space. The full-endoscopic technique minimizes the annulus defect and this appears to exert a protective influence [43, 59–68]. Rehabilitation measures following an operation are not necessary and comparatively high return to the performance level required for job and sporting activities is achieved [69]. There is no evidence of increased morbidity resulting from accompanying factors [55, 57]. The rate of recurrence demonstrates no significant differences with the conventional approach in a comparison of the literature and within the studies [70–74]. Revisions can be carried out using the same technique. The form of the disk herniation and the annulus defect appear to exert a greater influence on the rate of recurrence than the extent of curettage of the intervertebral space [5, 71, 75]. No relevant disadvantages for the application of the full-endoscopic technique when operating on disk herniations have been identified overall [32–34, 36]. At the same time, there is evidence of advantages in operating technique and reduced trauma in the area of the access path to the structures of the spinal canal. The transforaminal approach is evaluated as inducing less trauma on account of reduced bone and ligament resection. It is therefore assessed as the approach of first choice. However, the anatomical and pathological prerequisites entail significant restrictions so that the interlaminar approach has the greater spectrum of application.

34.9.2 Indication for Recurrent Disk Herniation

Recurrent disk herniations following diskectomies can never be completely excluded. The rate of relapse is described in the literature as being between 5 % and more than 20 % depending on the fragment type and annulus defect [5, 70–74]. When operating on recurring disk herniations, the risk of dura and nerve injuries is increased if there is already epidural scarring [57, 76–78]. Extensive dissection generally needs to be carried out in the operating area in order to reduce such injury and the resulting increase in trauma has to be taken into account. As a result, conditions such as segmental instability following surgery, progressive degeneration, increasing epidural scarring, or arachnoiditis may occur [43, 46–50, 53, 79–82]. This may induce clinical symptoms and create difficulties for further revisions. The scarring connection between dura and paravertebral musculature may cause so-called tethering of the cauda equina [83–86]. The increasing resection of stabilizing structures is conducive to instability following surgery [43, 46–50, 53]. The trauma caused by the access pathway in the innervation area of the dorsal branch of the spinal nerve may exert a negative effect on the stabilizing and coordinative system [44, 87]. The aim is, therefore, to use techniques designed to preserve tissue when carrying out revisions, as in the case of primary operations [88, 89]. When using the full-endoscopic procedure, the parameters determining the results and the benefits are comparable with those evinced by the indication of primary spinal disk herniation in respect of reduced operating times, tissue trauma, and complications [34, 42, 54–58, 90, 91]. No relevant disadvantages have been identified by comparison with the conventional microscopically assisted technique [34, 42]. The same inclusion and exclusion criteria are applicable. The transforaminal access is particularly effective because it completely circumvents the existing epidural scarring caused by the previous operation.

34.9.3 Indication for Spinal Canal Stenosis

The same problems are discussed in relation to operations on spinal canal stenosis as in diskectomy [43–49, 52, 53, 76, 92, 93]. Resection of joints and soft tissue structures in the lateral and ventral area is generally more extensive on account of the pathology. Hence, any instability induced as a result of surgery always needs to be taken into account [43, 46–50, 53, 94]. Extensive decompressions, or additional instabilities and deformities, may require additive fusion. Attempts to reduce trauma are made through the

use of various tissue-conserving techniques [86, 95–101]. A key prerequisite for using full-endoscopic techniques was the development of appropriate abraders that permit bone resection under visualization. This provides the technical capability for adequate decompression of spinal canal stenosis [33, 34, 42]. When using the full-endoscopic approach, the parameters determining results and the benefits are comparable with those evinced by the indication of primary or recurring disk herniation in respect of complications, tissue trauma, and reduced operating times [34, 40–42, 54–58, 90, 91]. Also in this case, no relevant disadvantages have been identified by comparison with the conventional microscopically assisted technique [40, 41]. Only a small number of these stenoses meet the inclusion criteria for a transforaminal approach on account of anatomical and pathological constraints. This approach is therefore restricted to a small number of individual cases.

34.10 Other Areas of Application

The transforaminal and interlaminar approaches are possible in the area of the thoracic spine depending on pathology and anatomy. The main indication is constituted by thoracic spinal disk herniations without significant spinal cord compression that continue to induce symptoms despite conservative therapy. Generally, only pathologies in a lateral position are operable, since manipulations of the spinal cord have to be avoided due to the risk of lesion and a lateral transforaminal approach is precluded by the organs located in the thorax. Technical implementation of both ports is equivalent to the lumbar procedure and is possible from the cervical-thoracic to the thoracic-lumbar junction. Other indications may be posterior pathologies like facet cyst, epidural abscess, or spinal stenosis. Contrary to the lumbar spine, in the case of thoracic spine, there is a higher overall risk of injury to neural and surrounding structures and, on account of these constraints, in the implementation of the ports and during the surgical procedure. In borderline cases relating to anatomy, pathology, and symptoms, an operation using the conventional procedure may be the only appropriate option.

The anterior transdiskal and the posterior foraminotomy techniques are available in the area of the cervical spine [88, 93, 102–106]. Only relatively small endoscopes with more restricted visualization relations and small intraendoscopic working channel can be used for the anterior transdiskal procedure. Some specific work stages have to be carried out in the absence of direct visualization under radiographic control, mobility in the spinal canal may be restricted, and adequate bone resection is limited. Greater mobility is provided dorsally as well as the possibility of carrying out all work stages in vision. The spinal disk is retained. Surgery focuses primarily on lateral pathologies due to the risk of damage to the spinal cord during manipulation, as known from standard posterior foraminotomy. Other indications may be posterior pathologies like facet cyst, epidural abscess, or spinal stenosis.

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35 Minimally Invasive Lumbar Disk Herniation Surgery with Tubular Retractors: Indications and Technical Aspects

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35.1 Introduction

Removal of herniated lumbar disk material is one of the most common procedures performed by spine surgeons, with the ultimate goal of alleviating radiculopathy through decompression of the nerve root [1]. Surgical treatment of patients with neural element compression due to lumbar disk herniation was first described in the American literature in 1829 by A. G. Smith [2, 3]. While the goals of surgery have not changed, surgical technique has seen considerable evolution. In the early twentieth century, full laminectomy with transdural approach was abandoned in favor of a hemilaminectomy-extradural approach [4]. In the 1970s, Yasargil, Caspar, and Williams introduced microsurgical technique to the treatment of lumbar disk disease, applying principles of minimal and careful dura and root manipulation to spine surgery, initially envisioned for application in cranial surgery [5]. The principles of manipulation of neural elements were mostly laid out at that time, and accordingly, neurological morbidity has remained stable since then. Further technical advances would basically try to minimize soft tissue and osseous trauma: Faubert and Caspar introduced tubular retractors in 1991, which allowed the development of the microendoscopic technique in 1997 by Foley and Smith [6, 7]. These technical advances have allowed minimally invasive surgery (MIS) to become increasingly popular with spine surgeons.

Lumbar diskectomy through a tubular retractor allows the surgeon to address the vast majority of disk herniations (Fig. 35.1) while minimizing collateral damage to superficial structures. Multiple randomized prospective trials comparing MIS diskectomy to the established open diskectomy have produced similar results in regard to outcomes [8–12]. Other studies have found muscle-splitting tubular retractors to reduce postoperative pain, limit blood loss, decrease rate of infection, and minimize damage to the paraspinal musculature and ligaments [12–14]. A reduction in damage to surrounding anatomy is not only vital in determining satisfactory outcomes in the immediate postoperative period but may also avoid long-term complications such as iatrogenic spondylolisthesis. In this chapter, we describe a minimally invasive lumbar microdiskectomy/foraminotomy technique via tubular retractors that provides access to the neural foramen, preserves the midline structures, and results in minimal muscular injury.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_35

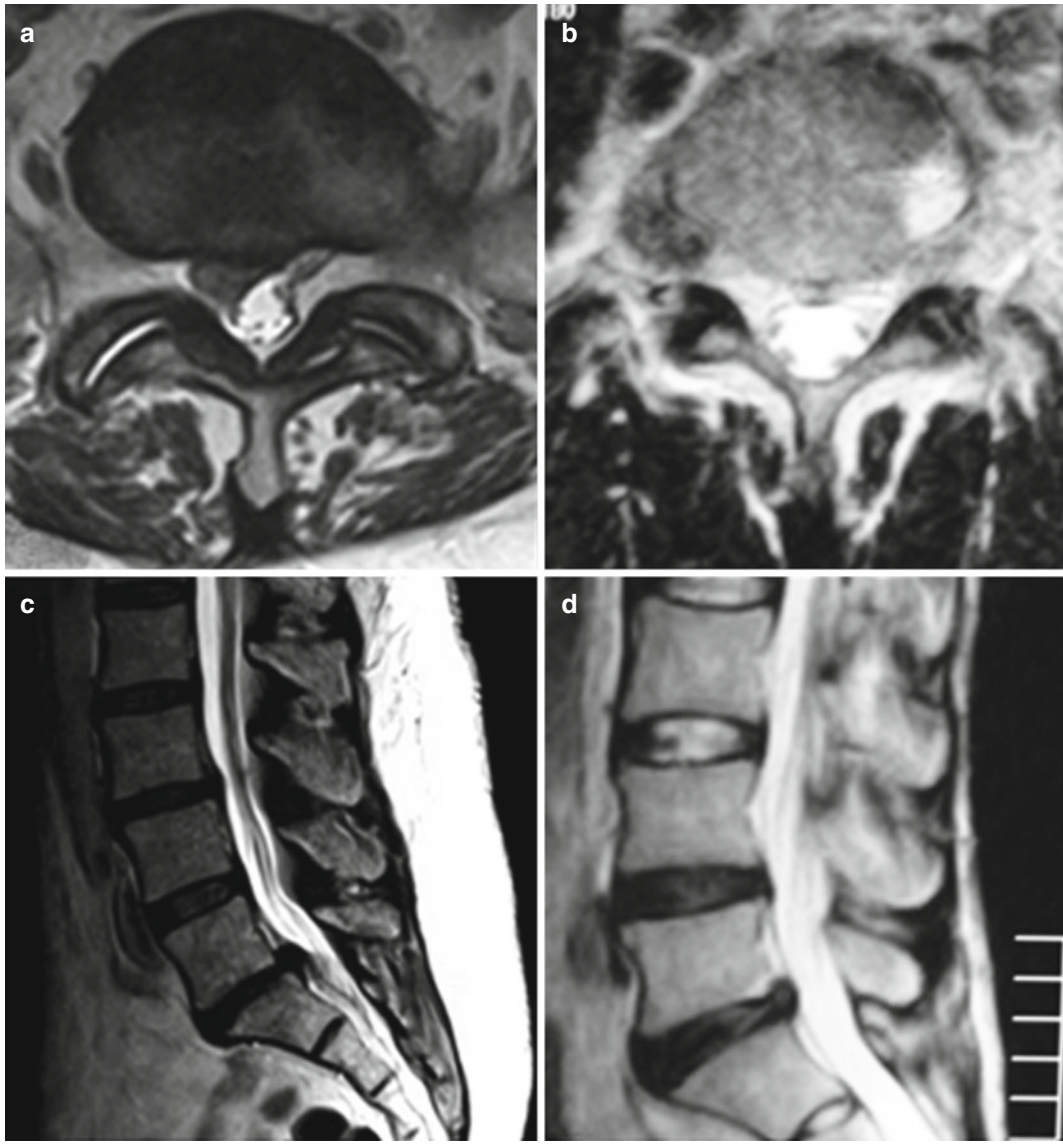


Fig. 35.1 Right-sided paramedian L5–S1 disk herniation with nerve compression amenable to tubular diskectomy (**a**, **b**). (**c**, **d**) Demonstrate a foraminal herniation that can be addressed through the far lateral technique described in the chapter

35.2 Surgical Technique

Once diagnosis is established and a decision to undergo surgical treatment is made, patients should be examined to assess the access site and the body habitus. Obese patients may particularly benefit from the use of the tubular retraction systems [15, 16]. With standard open techniques, obese patients often require an incision two to four times the standard length to provide adequate exposure, whereas with tubular retractors the incision is the same for all patients. Patients should have a complete medical work-up prior to surgery and meet the criteria for general anesthesia. The majority of patients can be safely treated as outpatients. Age in isolation should not be a contraindication to surgery; the senior author has performed the procedure successfully on multiple

patients in their 90s. Depending on their level of independence in the community and their home situation, elderly patients or patients with other comorbidities may benefit from an overnight hospital stay for observation.

35.2.1 Equipment

A tubular retractor system such as the MetRx system (Medtronic Sofamor Danek, Memphis, TN) is required. Systems should include all of the necessary instruments for retractor placement such as the dilators, retractors, and retractor arm, but also provide extra-long, anti-glare-coated instruments including a variety and sizes of curettes, disk punches, and rongeurs. If utilizing the conventional microscope, bayonet-shaped instruments and an angled drill attachment are also helpful.

While the tubular retractor can be used with an operating microscope or a 30° angled endoscope, it is our belief that endoscopic diskectomy provides better visualization of the surgical anatomy over that provided by conventional microscopy. The coupler provided with the MetRx kit allows for the use of a variety of different endoscopes with either the 16 or 18 mm working channel. Lateral fluoroscopic guidance is required for localization and during the dilation phase and electrophysiological monitoring is not routinely utilized.

35.2.2 Anesthesia and Positioning

This procedure can be safely performed under general, local, or spinal anesthesia [17, 18]. If being performed under general anesthesia, non-depolarizing neuromuscular blockers are avoided to allow for improved feedback from nerve root manipulation during surgery. Any position/frame/bed combination that allows for a free-hanging abdomen is acceptable so pressure is not transmitted to the epidural veins and causes bothersome bleeding during surgery (Fig. 35.2). The surgeon should stand on the same side as the patient's pathology and a rail attachment placed on the opposite level for the table-mounted arm; typically, this is aligned with the patient's hip. Video monitor for the endoscope is also placed across the table so the surgeon can face it directly. If a microscope is to be used in lieu of endoscopy, the microscope base can be brought in from the side opposite to the C-arm base. In either case, it is usually easiest to position the C-arm monitor at the foot of the operative table.

35.2.3 Surgical Technique: Paramedian Disk Herniation

The whole lumbar area is prepped and draped. The fluoroscopy C-arm is also draped in sterile fashion in an under-table position to enable quick radiological confirmation throughout the case. Localization of the level of interest is performed under lateral fluoroscopy counting cranially from the sacrum, noting vertebrae with transitional morphology. Specific adjustments may be made for migrated fragments. When the radiopaque marker is in the correct location, incision is planned 1.5 cm off midline on the side of the intended approach.

The operative site is then infiltrated with local anesthetic, while the assistant secures the clamp and retractor arm to the operative table (Fig. 35.3). An 11-blade scalpel is used to make a small 20-mm incision exposing the subcutaneous fat. A stainless steel guide pin or Kirschner wire is passed through the stab incision and soft tissues on to the underlying bone. Fluoroscopy should be used to confirm location of the guide pin during such passage to avoid penetrating the interlaminar space and causing a dural leak, especially if positioned on a Wilson frame. The safest approach is to direct the guide pin perpendicular to the entry point, so that the pin will contact the zygapophysial joint or even the transverse process rather than the lamina. Once the pin is docked on the zygapophysial joint, the first dilator is passed over the pin and removed; with the dilator, it is safe to angle medial and dock at the spinous process-lamina junction, directly over the disk space (Fig. 35.3). The remaining dilators are then passed sequentially and lastly, the

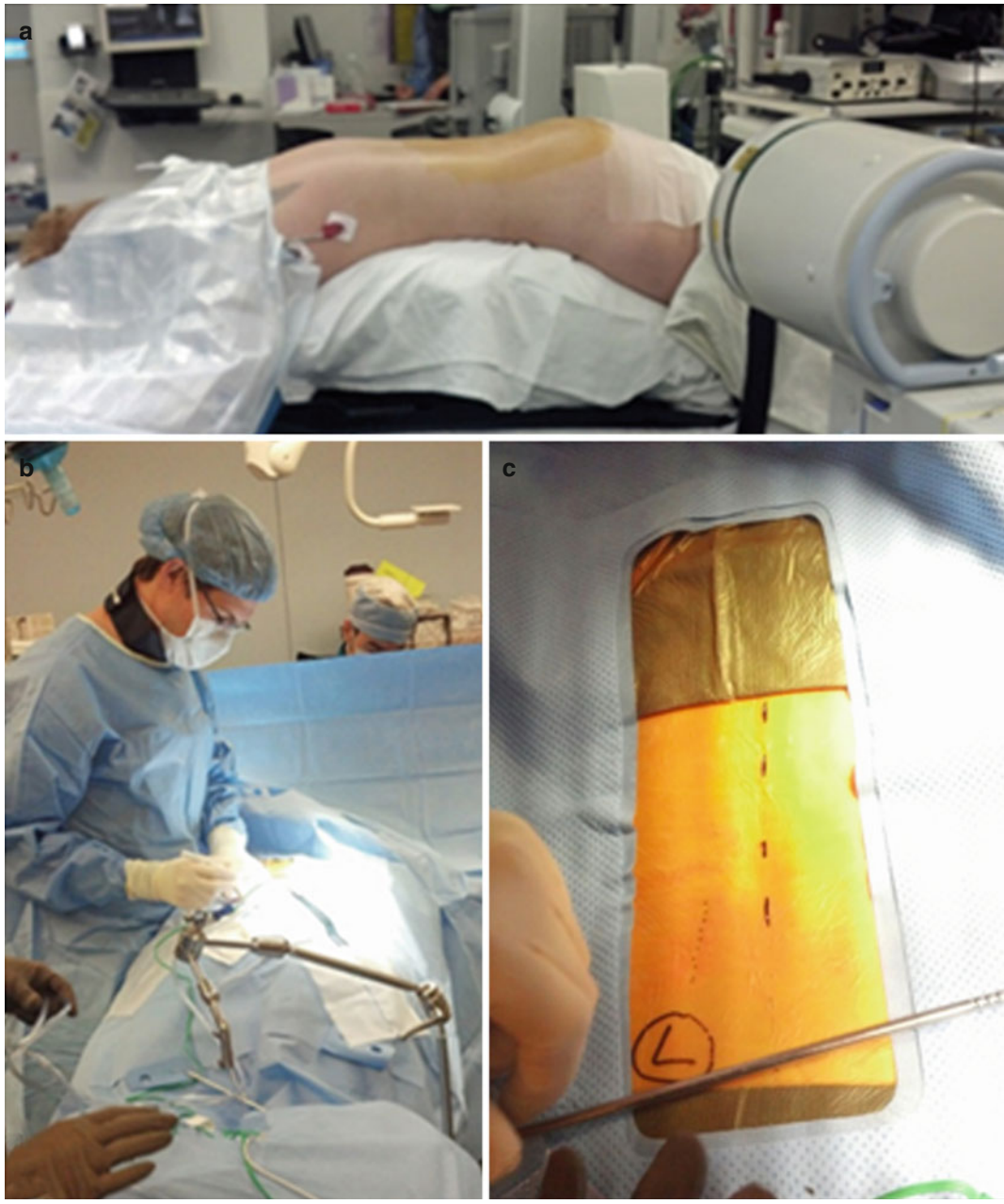
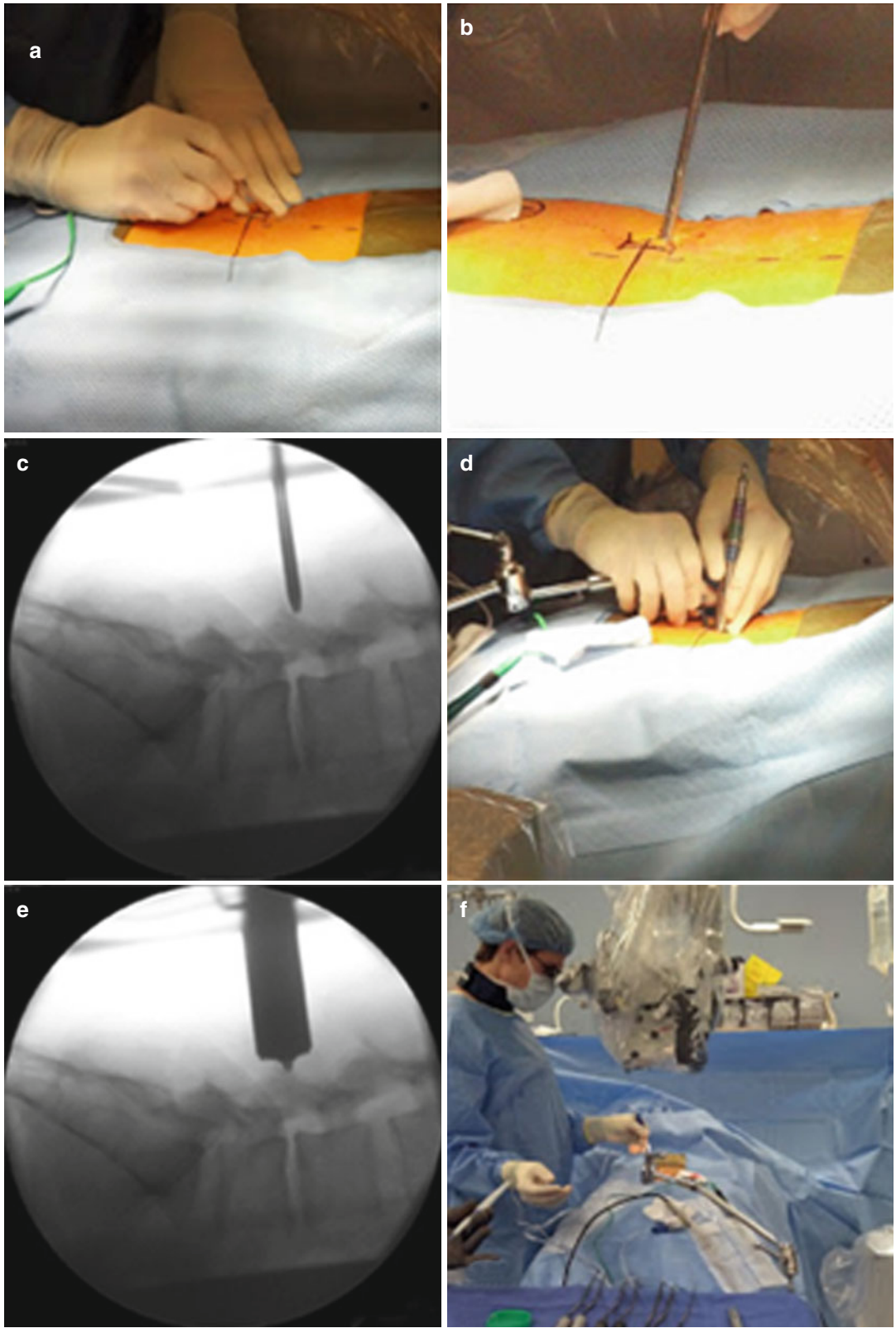


Fig. 35.2 Patient positioned on a Wilson frame (**a**) which distracts the lamina at the level of interest. The articulating arm is attached contralaterally at hip level (**b**) and the 2-cm incision is marked 1.5 cm off-midline (**c**)

Fig. 35.3 The incision is carried through the lumbar fascia (**a**). The guide pin is inserted and contacts the lamina (**b**, **c**). Subsequent dilators are placed one over another, followed by the tubular retractors (**d**, **e**). The articulating arm is attached and the microscope or endoscope is brought into the field (**f**)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working channel. These devices are introduced with a twisting motion so the dorsal lumbar fascia and underlying musculature are split along their fibers rather than torn. It is important to utilize fluoroscopy during this stage to confirm the trajectory and that the dilators are resting against the bone; this minimizes the amount of tissue that needs to be removed later. A working channel of 16 or 18 mm may be utilized for endoscopic applications and up to 22 mm for use with the microscope. In either case, it is connected to the table-mounted arm and secured in position, and the dilators are removed from its interior. Following a final fluoroscopic position check, the endoscope is attached to the working channel. Should the working tube be repositioned during the procedure, it is also recommended that fluoroscopy be used: even a seemly small adjustment may prove enough to aim at the wrong disk space.

Monopolar cautery and pituitary rongeurs are used to clear the remaining soft tissue off the lamina and inferior articular process, taking care to start the dissection over solid bone laterally. All muscle tissue should be detached completely along the circumference of the tube prior to attempting removal of the muscle (Fig. 35.4). Failure to do so can result in excessive bleeding and pulling more muscle into the field beneath the edges of the working channel. The "cut" setting on the cautery appears to be more effective than "coagulation" during initial exposure. Once the muscle has been cleared, a straight curette is used to identify and clear any residual soft tissue from the caudal edge of the lamina. The surgeon's view should be centered on the spinous process-lamina junction and the tubular retractor may need to be readjusted at this point. Straight and up-angled curettes are used to detach the ligamentum flavum medially from the overlying lamina and then work laterally under the lamina. Fluoroscopy should be used to confirm the location under the lamina dorsal to the desired disk space. Once an adequate plane has been established, 3 and 4 mm Kerrison rongeurs should be used in a rostral direction to perform a laminotomy. The up-angled curette is routinely utilized to confirm separation between the ligamentum flavum and lamina, in order to prevent injury to the underlying dura and nerve roots. In general, the laminotomy should extend the length of the neural foramen, from pedicle to pedicle; the rostral insertion of the ligamentum flavum normally marks the cranial extent and exposed dura is seen adjacent to it. At the junction of the lamina and facet complex, it is usually necessary to use a high-speed drill to perform a medial resection of the inferior articular process until an up-angled curette can be passed easily into the neural foramen. It can be useful at this point to aim the tube slightly lateral and to utilize fluoroscopy with a probe or up-angled curette in the foramen to confirm the extent of the laminotomy and foraminotomy. With these maneuvers, a medial foraminotomy is performed, which can be a stand-alone procedure or a routine, initial part of every paramedian diskectomy. Bony bleeding is easily addressed by the use of bone wax. In most cases, the bony opening exposes the ligament superficial to the shoulder and lateral margin of the traversing nerve root that exits at the foramen one level caudally.

Attention is then directed toward removal of the ligamentum flavum. A blunt, delicate dissector is used to elevate the rostral end of the flavum from the dura. If another opening has been made elsewhere, it can also be used. A curved curette is then used to establish a plane between the dura and ligament and can be used to detach the ligament from the bone along the edges of the laminotomy. Right-angle rather than 60-degree-angled punches are useful for removal of the ligamentum. The ligament can be detached laterally from the superior articular process with an up-angled curette. In cases of disk herniation, the nerve root may be distorted by the disk herniation and it may be necessary to carefully resect more of the medial zygapophysial joint in order to adequately visualize the shoulder of the nerve root. Once the shoulder of the root is exposed, gentle medial retraction usually reveals the disk fragment in extruded cases or the protruding annulus with a contained fragment. This step may be difficult if a tethering fragment is present at the axilla; careful dissection at the axilla and initial partial removal of a fragment there may be required. A combination nerve root retractor and sucker is

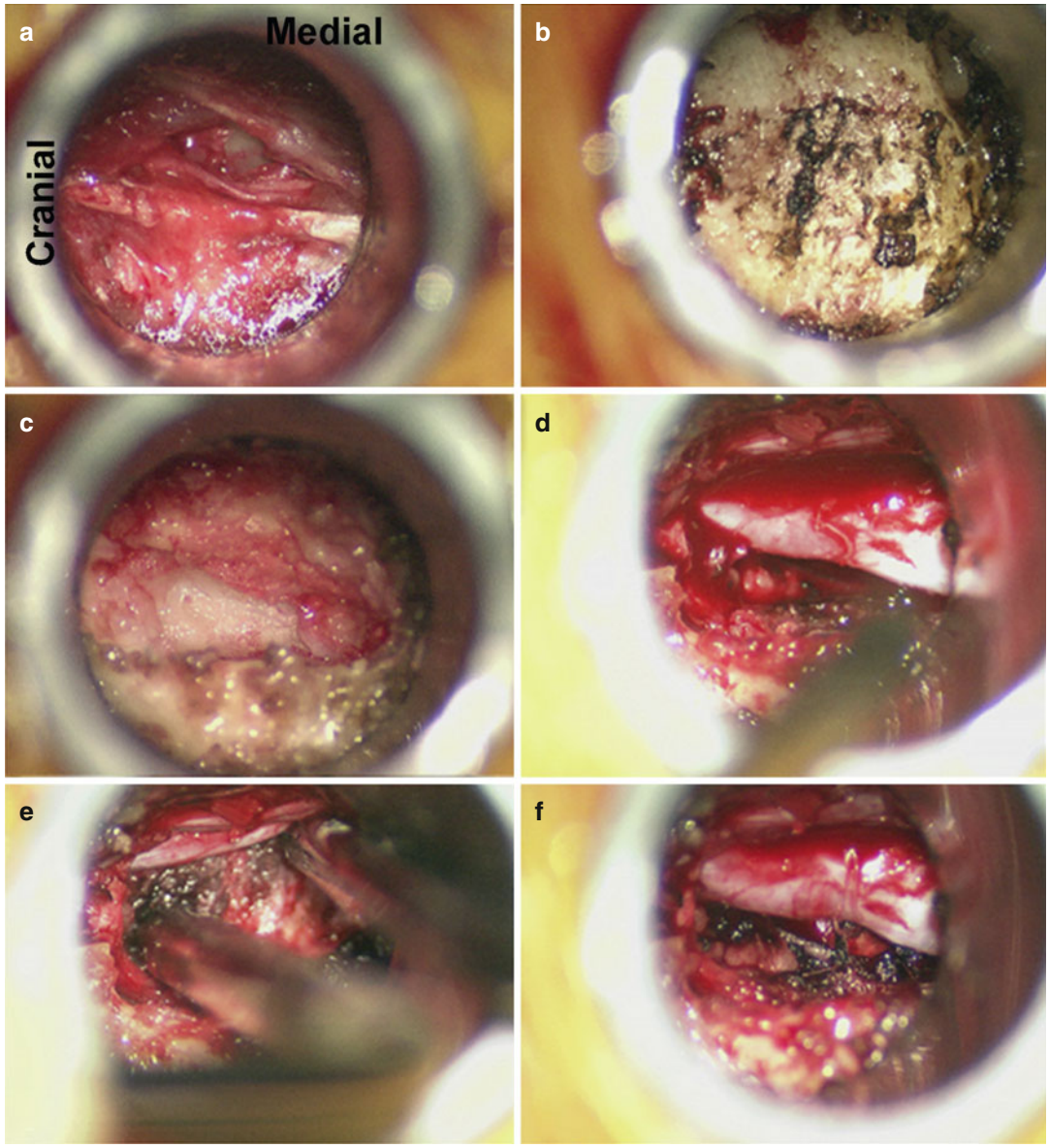

Fig. 35.4 Residual muscle is removed with cautery and rongeurs (**a**, **b**). A laminotomy is performed with bone punches and/or a drill (**c**). Removing the ligamentum flavum exposes the nerve root (**d**) which is then retracted medially (**e**). Diskectomy and foraminotomy fully decompress the root (**f**)

used to retract the thecal sac medially, or a gentle, blunt-tip suction may be utilized. Extruded fragments are removed with a variety of disk punches. In case an extruded disk fragment is expected but not initially visualized, a spatula or blunt hook can be used to explore the ventral aspect of the dura and the level should be checked with fluoroscopy.

If the nucleus fragment is still retained under the posterior longitudinal ligament and annulus, once the root is retracted, epidural veins may be coagulated with the bipolar forceps in a low setting. Coagulation should be minimized around the root, as well as manipulation through the axilla. The annulus is incised and nucleus fragment removed with a disk forceps. It is our

routine to not aggressively explore the interspace and remove contained fragment but just the disk material that is loose and removed easily. If the 30° endoscope is used for the procedure, the endoscope can be directed medially to help with decompression of more medially located disks, a maneuver not possible with the operating microscope. When dealing with calcified annulus or large osteophytes adjacent to the disk, a down-angled curette can be utilized to fracture the osteophyte into the annular opening and decompress the root. At the end of the decompression, a ball tip probe should be passed into the foramen to confirm adequacy.

Hemostasis is achieved while minimizing coagulation; simple tamponade with a number of different agents may be performed. We do not advocate closing the annular defect. The retractor arm is unlocked and the tube is removed under direct vision: bipolar cautery is used to coagulate more significant muscle arteries. Closure is performed in the usual fashion with fascial and subcuticular suture layers.

35.2.4 Surgical Technique: Foraminal Disk Herniation

A tubular MIS approach is particularly useful in the management of foraminal or "far lateral" disk herniations as it obviates a very large muscular dissection. In this situation, the incision is made 5–6 cm lateral to midline rather than the 1.5 cm used for paramedian herniations. Dilation is performed as described above. Desired site for docking of the initial dilator is at the caudal edge of the medial transverse process or, alternatively, the lateral margin of the pars interarticularis. The monopolar cautery cannot be utilized in this setting as the root is exposed: a straight curette is utilized to detach the muscle fibers from the transverse process and sweep it in a lateral-caudal direction. Once the lateral limits of the neural foramen are defined, a lateral foraminotomy can be performed with the high-speed drill and Kerrison punches. The exiting nerve root can be identified at the cranial part of the foramen just caudal to the foramen. It is then retracted cranially, thus exposing the disk and diskectomy proceeds in the usual fashion. A greater or smaller degree of foraminotomy may be performed as desired based on the amount of disk expected to be removed (e.g., soft disk herniation versus calcified disk bulge with adjacent osteophytes).

35.2.5 Tips and Tricks

Working through the tubular retractor is not inherently different than standard microsurgical technique. If the endoscope is being utilized, it is important to attempt to maintain the working instrument and the suction tip in parallel and avoid "crossing" instruments.

- Frequent repositioning of the tubular retractor

The small working area of the tubular retractor can be multiplied by sequentially unlocking the retractor arm or adjusting or "wanding" the tubular retractor as necessary to visualize another area. This can be more effectively done with the last dilator inserted within the tube, to create a longer moment arm, while the assistant unlocks and locks the retractor arm. In this manner, the surgeon can better visualize relevant anatomy and address neural compression. It is important to repeat fluoroscopy imaging after each adjustment in order to avoid migration to an adjacent level.

- Use of the bipolar cautery for soft tissue and ligamentum flavum retraction

Once the tubular retractor is positioned, soft tissue may "creep under" the retractor and reduce visualization. We utilize the bipolar cautery with a special angled tip to coagulate and retract this soft tissue under the tube. This may also be utilized for remnants of the ligamentum flavum or annulus fibrosus that may be protruding into the spinal canal.

- Wide exposure for very large disk herniations

For cases with large, extruded disk fragments, a wide exposure with complete hemilaminectomy

is recommended. We strongly advise to obtain visualization of the normal anatomy cranial and/or caudal to the fragment before attempting to retract the nerve root medially. Partial removal of whatever fragment is evident and loose may also be performed before root retraction.

- Additional partial facetectomy

While instability is a concern in open cases, the surgeon must always be aware the visualized field is minimal when working through a tube (16 or 18 mm in diameter). Therefore, lateral angulation of the tube and additional removal of 2–3 mm of the facet is unlikely to result in instability, as discussed below. In 14 years performing this procedure, the senior author has only one case of delayed, clinically significant instability following a microdiskectomy. We thus advocate for additional removal of facet when the root cannot be clearly identified as opposed to blindly retracting the root and/or dura.

- Use of a suction-retractor

In open microdiskectomy, a root retractor is normally utilized and the assistant may also utilize suction. In the restrained environment of the tubular retractor, the assistant is unable to assist with both these tasks. A combined root retractor-suction tip can be found in many commercially available sets of tubular systems and is particularly useful, as the assistant is then able to perform both tasks. The surgeon may then work two dissecting instruments, which may be particularly useful when trying to separate the root and dura from the herniated disk.

35.3 Postoperative Care

Patients are allowed to ambulate immediately after the procedure: 80–90 % of all our diskectomies are performed in the outpatient setting. Patients are discharged on mild narcotics and analgesics and seen in clinic two weeks postoperatively. NSAIDs and steroids may be utilized at the surgeon's discretion.

35.4 Potential Complications and Avoidance

Acute radiculopathy may occur in cases with large disk herniations requiring aggressive mobilization of the nerve root. In these patients a rapid methylprednisolone taper has proven quite useful. If suspected during surgery, deposit steroids may be utilized in situ. Although painful, the symptoms usually resolve within 7–10 days. Persistence of radiculopathy at the 6-week follow-up in well-indicated cases should raise the suspicion of incomplete decompression or retained fragment. Similarly, initial improvement and recurrence of symptoms may be an indicator of acute re-herniation. Both conditions are assessed with repeat MRI, and re-exploration is a consideration versus continued pain management. We have found that patients with acute disk re-herniations are likely to experience the same improvement with re-exploration they had initially.

Clinical instability requiring fusion is a recognized complication of lumbar diskectomy that occurs in 6–9 % of open cases [19, 20]. Preservation of the ligaments, intervertebral disk, and facet joints that compose the posterior tension band is vital to prevent destabilization. Facetectomy may be necessary to access lateral disks; however, this should be done sparingly and be less than 40 % to avoid significant mobility [21]. Although prospective data is lacking, case series demonstrate that MIS techniques allow for similar outcomes with lower iatrogenic instability rates, while biomechanical data support this affirmation due to preservation of the posterior tension band and smaller degree of facet removal [22, 23]. Ulterior arthrodesis of the operated segment may also be required due to persistent back pain. *While aggressive removal of the disk significantly decreases the likelihood of recurrence, loss of disk height is directly related to subsequent instability and poor outcomes*, but in this case, this complication is inherent to both open and MIS techniques [24, 25]. Therefore, diskectomy should focus on fragment removal and should stop once the nerve root is adequately decompressed.

Accidental durotomy is a known complication of diskectomy and happens in 4–9 % of cases. The incidence of such complication may actually be higher for MIS techniques due to the constraints of operating within a narrow channel and the learning curve [26, 27]. Paradoxically, the incidence of symptomatic pseudomeningocele requiring reoperation is far smaller with MIS techniques due to the absence of dead space and perfect apposition of soft tissue layers at the end of the procedure. Although intradural surgery is commonly performed through tubular channels including direct dural repair, it is a very challenging task through the 16–18-mm-diameter tubular retractors and ultimately unnecessary [28]. In durotomies of small to moderate sizes, we have been lately simply covering the defect with muscle, fat, blood-soaked Gelfoam (Pharmacia and Upjohn, Kalamazoo MI), or a dural substitute along with a layer of fibrin glue or dural sealant (Fig. 35.5). The patient is maintained on overnight bed rest in the hospital and ambulation is resumed the following morning. For larger dural tears, this strategy is complemented by 2–3 days of lumbar cerebrospinal fluid drainage to allow for healing of the surgical site. In addition, a larger tear may allow placement of one to two sutures to oppose the dural edges [26, 27].

Vascular and intra-abdominal injury is a potential complication of the MIS diskectomies during the localization and diskectomy phases. The incidence of arterial injury has been estimated at 5 per 10,000 diskectomy cases with a mortality rate reaching 65 % [29]. Fluoroscopy is essential during the dilation step to confirm the depth of the guide pin and ensure it never reaches deeper than the transverse process. During the diskectomy portion of the procedure, fluoroscopy can be used to confirm the depth of the instruments within the disk so that the anterior annulus is not violated, but the general rule of "minimal necessary diskectomy" outlined above should be enough to prevent anterior penetration. Arterial bleeding from the wound is frequently not seen because of a "self-sealing" effect of the anterior annulus [30]. Suspicion of an anterior breach along with hemodynamic instability should thus immediate and aggressive volume resuscitation and abdominal exploration. With prompt action, these injuries are survivable [30].

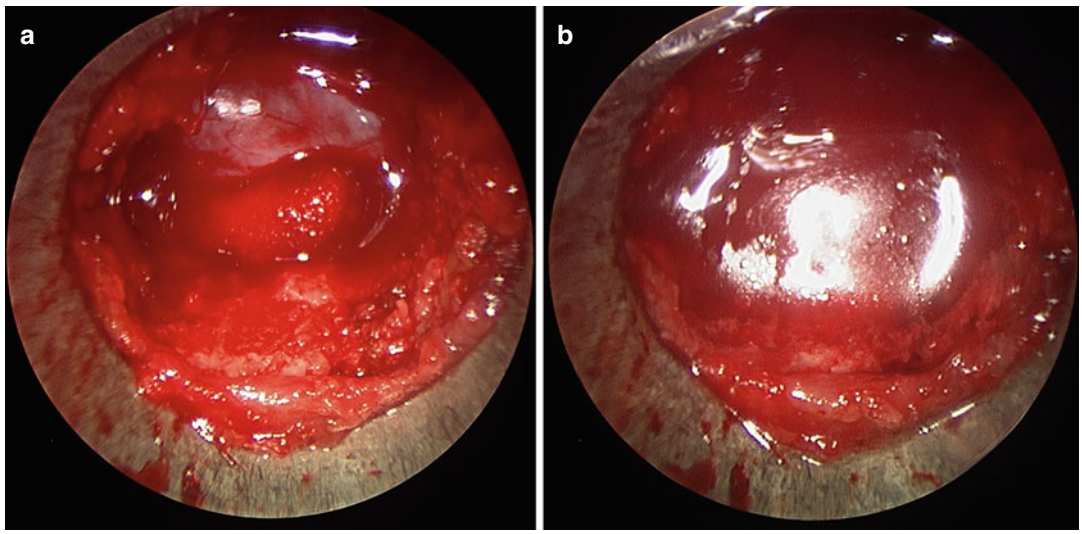

Fig. 35.5 Following an unintended durotomy, a piece of Gelfoam is placed over the defect (**a**) followed by dural sealant (**b**) and closure of the wound

Conclusion

Minimally invasive spinal surgery has rapidly been adopted by surgeons throughout the world as a philosophy to minimize unintended trauma to surrounding tissues. Tubular retractors are valuable tools within this context to adequately perform the end-procedure; lumbar diskectomy is just the simplest of them. There are multiple factors driving the acceptance of minimally invasive diskectomy including ease of use for the surgeon, patient demand, and the improved outcomes from minimizing exposure-related damage. Most surgeons in training today receive more or less extensive training in minimally invasive techniques. Those that have mastered open techniques are able, and encouraged, to apply that valuable knowledge to mastering lumbar diskectomy through tubular retractors and, in so doing, offering their patients the best care possible.

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36 Minimally Invasive Transforaminal Lumbar Interbody Fusion (TLIF): Indications and Techniques

Richard Assaker, Fahed Zairi, and Mohamed Allaoui

36.1 Introduction

In the past two decades, the development of spinal instrumentation devices and of minimally invasive approaches and the understanding of spinal biomechanics have lead to dramatically increase the use of spinal fusion procedures [1]. It is estimated that almost 300,000 spinal fusion procedures are performed annually in the United States alone. In the present time, approximately 75 % of cases are performed for spinal degenerative changes especially in the lumbar spine [2]. Of all available techniques, transforaminal lumbar interbody fusion (TLIF) is very popular as it allows the surgeon to achieve a 360° fusion using a single posterior approach. TLIF has gained popularity because of some advantages such as minimal epidural dissection or its efficacy in revision cases [3]. The main disadvantage of this technique is directly related to the morbidity of the approach, which requires a midline incision and a wide soft tissue retraction. Detachment and retraction of the paraspinal muscles are associated with increased blood loss, postoperative pain and muscle necrosis, which may alter the kinematics and stability of the motion segment [4–6]. In order to avoid these drawbacks and especially to preserve the muscle anatomy, minimally invasive TLIF has been introduced [7] and has become an increasingly popular technique in recent years. We describe the indications, the technical aspects and complications of the minimally invasive TLIF.

36.2 Indications and Contraindications

Minimally invasive TLIF is generally performed for the same indications than open procedure [8]: low-grade isthmic or degenerative spondylolisthesis, degenerative disk disease and failed back surgery syndrome requiring revision surgery with fusion and instrumentation [9]. However, there are some limitations to the minimally invasive approach, which must be screened by an exhaustive radiological evaluation. Preoperative radiological evaluation, as with an open procedure, includes full-spine standing X-rays, CT scan and MRI. The pelvic parameters should be evaluated on standing X-rays. One should ensure that the pedicles are well identified on lateral and AP views. The foramen should be carefully evaluated on MRI, including its size and the exiting nerve root. The facet complex is better evaluated on the

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_36

CT scan. Limitations of the minimally invasive approach can be classified as follows:

- *Number of levels*: Most often, minimally invasive TLIF is achieved to treat one level [10]. However, many reports have demonstrated the feasibility of performing TLIF on two adjacent levels using the minimally invasive approach [11]. Indeed, expandable retractors allow exposing two adjacent foramina without altering the paraspinal musculature. Contemporary, available instrumentations do not allow performing more than two levels of fusion.
- *High-grade spondylolisthesis*: Many tools allow the surgeon to perform reduction manoeuvres, making minimally invasive TLIF an effective treatment option for the management of low-grade (1 or 2) spondylolisthesis [12]. Currently, a high-grade spondylolisthesis that require significant reduction manoeuvres remains a contraindication to the minimally invasive approach.
- *High pelvic incidence*: It is mandatory to detect preoperatively, on full-spine standing X-rays, patients with high pelvic incidence, which require the restoration of a significant lumbar lordosis. Such a situation is not a real contraindication, but the risk of causing a flat back must be well known. If this approach is still preferred, we recommend to insert the cage as anteriorly as possible and to perform a bilateral arthrectomy in order to enhance the posterior compression and then to increase the lordosis.
- *Anatomical considerations*: We should ensure preoperatively that the pedicles are well visible on plane X-rays especially on the AP view. In such cases, an open procedure is more suitable. However, when available, the new navigation technologies guided by CT scan make it possible to overcome this limitation [13]. Nerve root abnormalities, such as a conjoined root, are also a contraindication for TLIF in general. In our experience, in one case we decided not to insert the interbody fusion device because of a conjoined root that obstructed the route for disk access. As it was not detected preoperatively, we converted to minimally invasive posterior fusion and instrumentation. If needed, the cage should be inserted through an anterior approach.

36.3 Surgical Technique

36.3.1 Patient Positioning

The patient should be positioned prone on a radiolucent table, allowing AP and lateral fluoroscopy (Fig. 36.1). Radiolucent rolls are placed on the chest and the iliac crest to ensure the physiological placement of the lumbar spine. Note that excessive lordosis can narrow the foramina and makes the transforaminal disk approach more difficult. The abdomen and the chest must hang free to avoid elevation of the thoracic pressure or vena cava compression. Before draping the patient, AP and lateral fluoroscopy are obtained to ensure proper visualisation of the pedicles. Needles can be placed percutaneously to locate more precisely the pedicles and the disk space. Landmarks are drawn to locate the projection of these structures of interest (midline, pedicles).

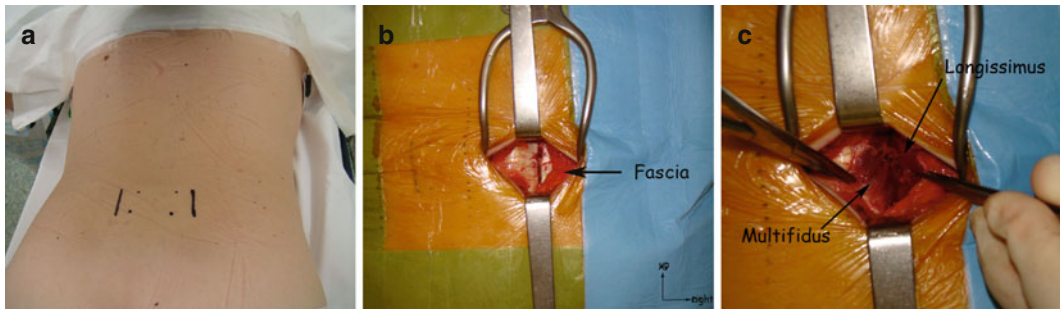

Fig. 36.1 Minimally invasive approach. The skin incisions are marked lateral to the projections of the pedicle entry points (**a**). Opening of the thoracolumbar fascia (**b**) and muscle-splitting approach (**c**)

36.3.2 Screw Placement

Pedicle screws can be inserted in a true percutaneous manner as described by Foley et al. [14] or through an expandable tubular retractor. When a purely percutaneous technique is chosen, it is essential to have a high-quality fluoroscopic guidance, with properly aligned images (Fig. 36.2). The surgeon should place the C-arm in order to obtain a true AP view with no shadow on the superior end plates. The pedicles should be well seen and located at the cranial part of the vertebral body, and the spinous process observed must be strictly in the midline. The lateral view should be obtained with strictly superimposed pedicles and single posterior vertebral body wall. Once the surgeon ensured the reliability of AP and lateral views, a Jamshidi needle can be introduced in the pedicle. Under fluoroscopic guidance, the needle is introduced through a 2 cm skin incision and docked gently on the lateral margin of the pedicle. On AP view, the tip of the needle is at the lateral cortex of the pedicle while it appears at the posterior edge of the pedicle on the lateral view. The Jamshidi needle is then hammered deeper in the pedicle, targeting its centre on the AP view and the posterior wall of the vertebral body on the lateral view. Once the Jamshidi needle is correctly placed, a K-wire is then introduced in the vertebral body through the needle. The needle can be removed and a cannulated tap is used over the wire to prepare the placement of a cannulated screw. Once the screws are inserted on one side, the rod can be placed but not locked, before the placement of the interbody cage.

36.3.3 Placement of the Expendable Retractor

The major principle of the minimally invasive approach is to minimise muscle trauma by

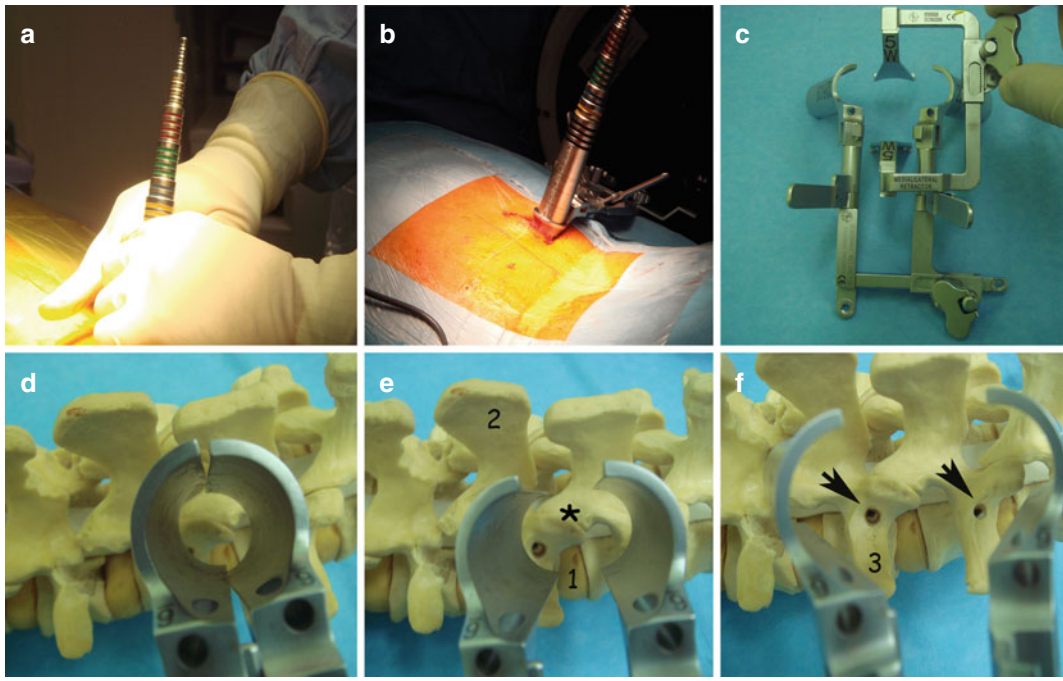

Fig. 36.2 Optimal placement of the Jamshidi needle on AP (**a**) and lateral (**b**) fluoroscopy. K-wires are introduces through the needles into the vertebral body (**c**, **d**). After taping (**e**), the polyaxial screws are introduced over the guide wire (**f**)

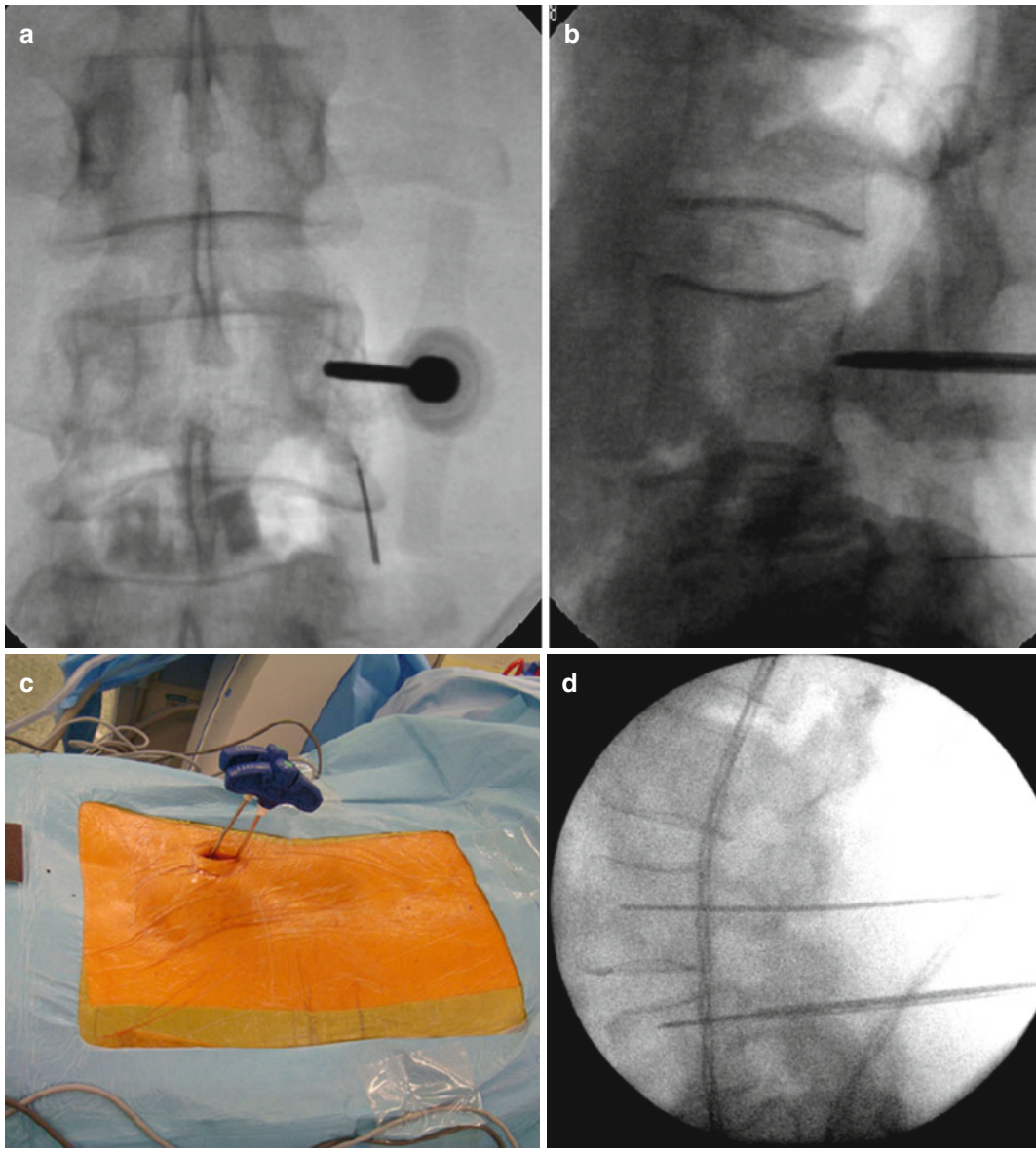

Fig. 36.3 Introduction of the expandable retractor. Introduction of the dilatators (**a**, **b**). A mediolateral retractor (**c**) allows a better lateral exposure. Photographs (**d**–**f**) showing the anatomical exposure after progressive opening of the retractor. The different anatomical structures were identified (*, facet joint; *1*, disk space; *2*, spinous process; *3*, transverse process; *arrows*, pedicle entry points)

lessening the soft tissue dissection and retraction (Fig. 36.3). It is crucial to properly place the retractor to ensure adequate exposure, creating a "working corridor" for safe disk access with minimum muscle injury. On the other hand, this "working corridor" limits the anatomical exposure. There are two technical points to become familiar with: first, handling and placing properly the retractor and, second, identifying the global anatomy with minimum bone exposure. The side of the transforaminal approach is based on the side of the radiculopathy, in order to achieve a large decompression of the affected nerve root. The site of the skin incision must be identified on

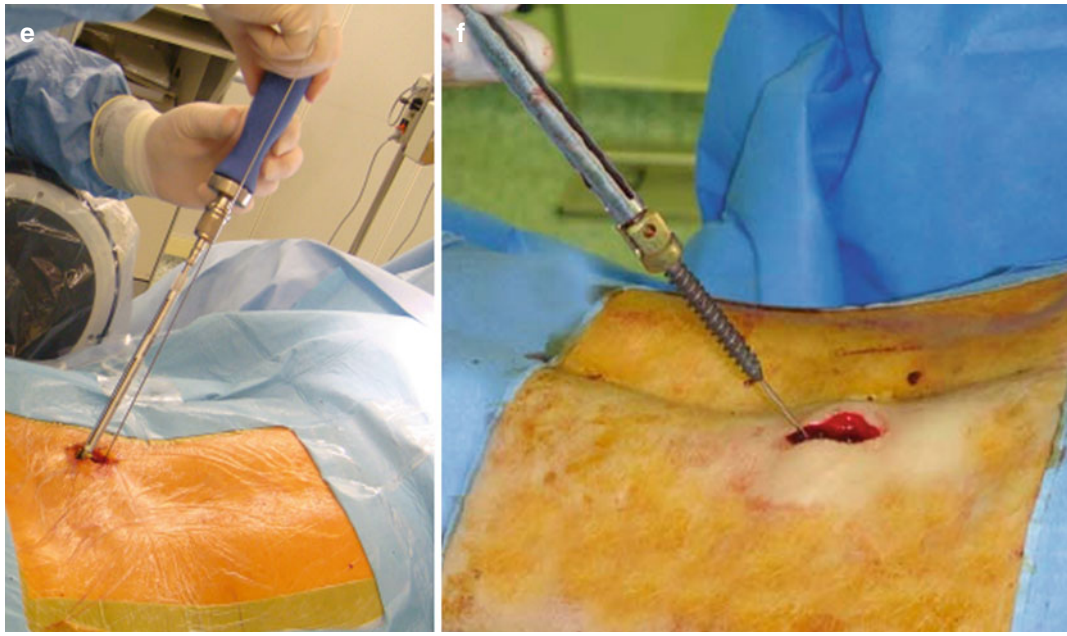

Fig. 36.3 (continued)

AP fluoroscopy. A 3 cm skin incision is done 1–2 cm to the lateral margin of the pedicles. Notice that the incision may be more lateral in overweight patients, to maintain an adequate obliquity. The lumbosacral fascia is opened sagittally, and a blunt dissection is carried on in the plane between the multifidus and the longissimus, as described by Wiltse et al. [15]. The paraspinal muscles are split parallel to their fibres, creating a route to the junction between the transverse processes and the facet joint. The entry points of the cranial and caudal pedicles, overlying the disk of interest, are then identified. Using this plane, serial dilatators are introduced in the direction of the disk and centred on the facet joint. An appropriate length retractor is introduced over the dilatators and secured against the facet joint. Many retractors dedicated to this procedure are currently available. We recommend expandable retractors that can accommodate to the patient's anatomy and expand the exposure when needed. The retractor is secured to the operating table via a flexible arm. A mediolateral retractor can be used in combination to widen the exposure of the segment of interest. This mediolateral retractor maintains the muscle split during the procedure. It is recommended to loosen this mediolateral retractor every 30 min to release the pressure and to limit the risk of muscle trauma and necrosis. One of the main advantages of the expandable retractor is the direct visual access to the pedicle's entry point. In this setting and according to the surgeon's preference, an operating microscope or operating loupes could be used. We prefer the microscope for the improved visualisation, the quality of the light, the possibility of video transmission and teaching purposes.

36.3.4 The Transforaminal Approach

The dorsal and lateral surfaces of the facet complex are exposed using electrocautery and forceps (Fig. 36.4). Typical exposure includes both pedicle entry points and the transverse processes achieving posterior fusion. A total facetectomy is then performed using high-speed drill or osteotomes. During this step, the resected bone must be saved as bone graft. That is why osteotomes should be preferred rather than the drill. The inferior facet of the above vertebra is completely removed. The lamina can be partially drilled or opened using

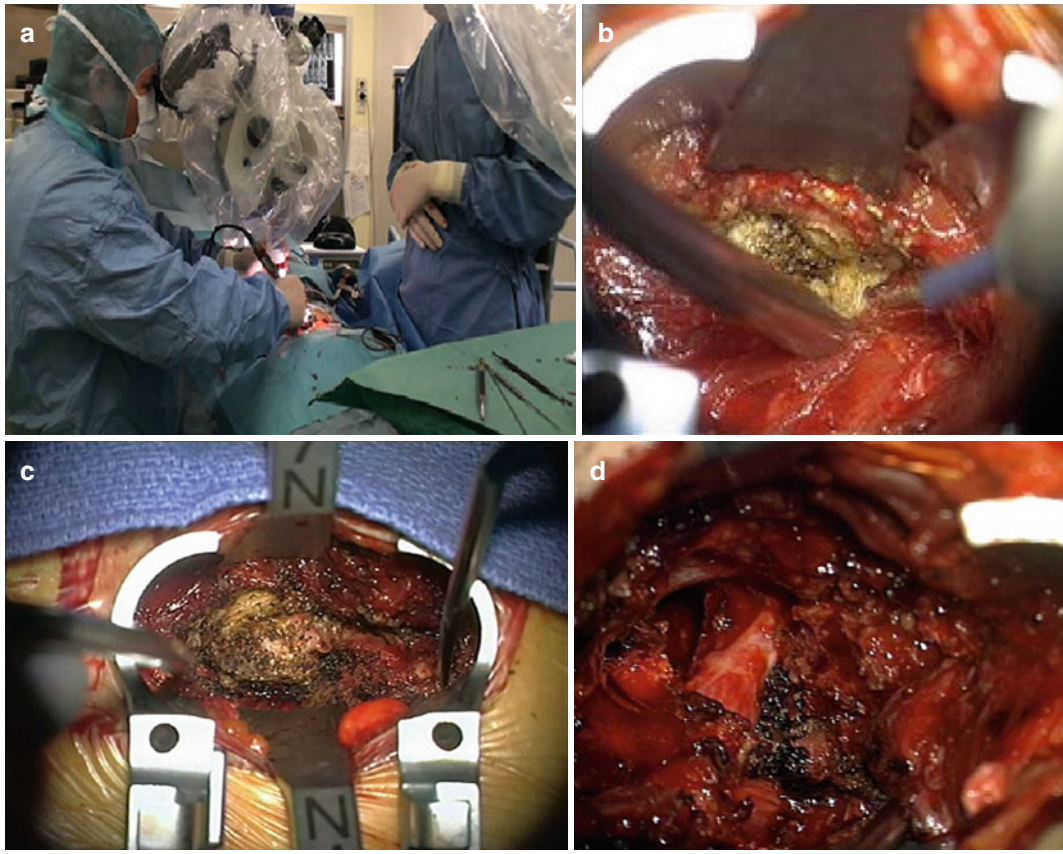

Fig. 36.4 Operative settings. The microscope is used to perform the muscle splitting and to expose the right facet complex using electrocautery (**a**–**c**). We performed a wide diskectomy between the dura and the exiting root (**d**)

Kerrison rongeurs to expose the canal. In case of spinal canal narrowing, it is also possible to perform a wide laminectomy using this approach. The superior facet of the below vertebra is also cut or drilled without breaching the caudal pedicle to not alter the screw anchorage. For better identification, the pedicles should be located and tapped first. Once the foramen is opened, ligaments are carefully removed to expose both exiting and passing nerve roots. The surgeon should be aware of the location of both nerve roots and especially the exiting root. Epidural dissection can be carried on using bipolar cautery and spatulas. At this step, bayoneted instruments are required for optimum visualisation with microscope, in a small working channel. Step by step, the surgeon ensures enough space between the lateral margin of the dural sac and the passing root and the medial margin of the exiting root. This is mandatory to have a safe and wide exposure of the disk and mobile roots to be manipulated safely. The disk is then incised to perform an ipsilateral diskectomy using bayoneted forceps and curettes.

36.3.5 Cage Placement and Grafting

The interbody space is gradually distracted using sequential distractors until reaching the optimal reduction and suited height (Fig. 36.5). Sometimes, an osteophyte must be resected first using osteotomes to access the disk space. Once the desired distraction is obtained, it is maintained by locking the rod on the other side. The distractor is removed and the diskectomy can be completed. The end plates must be carefully

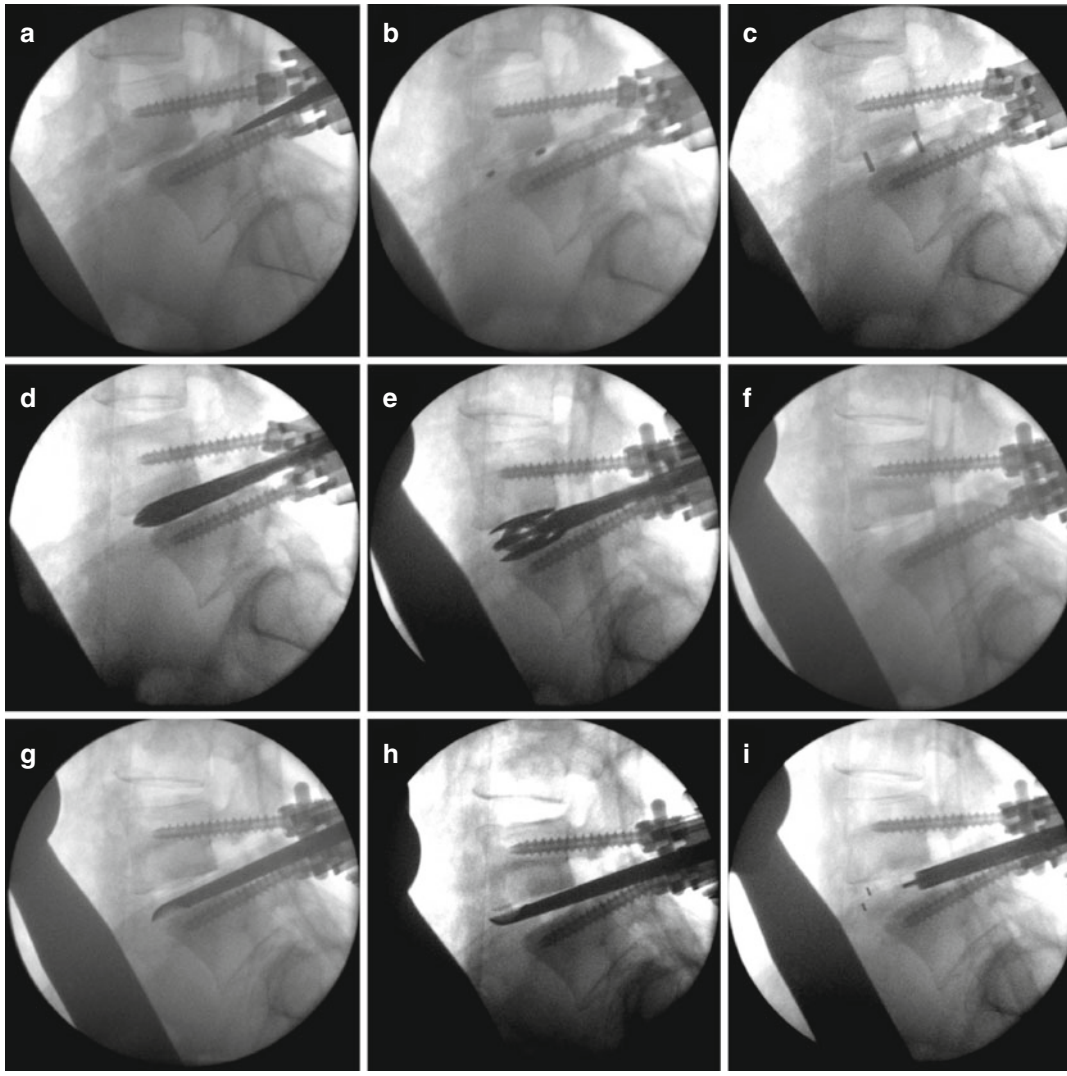

Fig. 36.5 Different steps for disk distraction and interbody grafting. A bone chisel can be used to cut an osteophyte for disk access (**a**). Progressive distraction of the disk space (**b**–**e**). The distraction is maintained by locking the contralateral construct (**f**). Preparation of the end plates by using forceps and scrapers (**g**, **h**). Insertion of the graft and of a wide PEEK cage as anteriorly as possible (**i**)

prepared using dedicated straight and angled curettes and scrapers. The disk space is filled with the graft material. In our experience, the graft is performed using resected bone expanded with BCP (biphasic calcium phosphate). The fusion rate reported using such graft material is up to 90 %. Currently some teams use rh-BMP-2 (bone morphogenetic protein) and report a fusion rate of 100 % [16]. However, many complications have been reported such as postoperative radiculitis, bone osteolysis and symptomatic ectopic bone formation. As its use is not without risk, the reader should be aware of the reported complications related to the off-label use of rh-BMP-2 in minimally invasive TLIF [17]. Once the graft is inserted in the disk space, a straight or shaped TLIF cage is introduced after proper sizing. During the cage insertion, care should be taken on the roots especially the exiting root. A nerve root retrac-

tor might be needed to protect the root during this step. Finally, the ipsilateral screws and rod are placed under direct vision. Before locking, a posterior contraction is needed to secure the cage and to increase the lordosis. The posterior graft is placed and a drain is suitable on the side of the transforaminal approach.

36.4 Outcomes/Advantages of the Minimally Invasive Approach

36.4.1 Clinical Results

Numerous studies have demonstrated that the two techniques can achieve similar clinical outcomes. In these studies, the back and leg pain and functional scores were not significantly improved by the minimally invasive approach in comparison with the standard approach [10, 18, 19]. This means that there is no tangible evidence that muscle preservation may lead to improve the functional status of patients. Additional randomised trials with a longer follow-up are needed. However, recent works have demonstrated that the minimally invasive approach reduces postoperative pain and analgesic consumption. The reduced surgical invasiveness is also associated with a shorter hospital stay [18].

36.4.2 Complications

The main advantage of the minimally invasive approach is the significant reduction of the overall complication rate [20]. The minimally invasive approach reduces dramatically the blood loss, making use of blood transfusion very rare. Moreover, the risk of infection is also reduced, which is an important concern especially for high-risk patients [10, 18–20]. Many other complications can be reported during and after such a procedure. Misplacement of pedicle screws is not uncommon at the beginning of the surgeon's experience [21]. Usually this is due to inadequate fluoroscopy or lack of experience. The quality of the C-arm and its manipulation are crucial for the safety of pedicle screw placement in a minimally invasive fashion. Many studies demonstrated that in trained hands the accuracy of screw placement is at least as safe as an open technique. Dural tears may be encountered. It is difficult to close such tears through a tube. The use of collagen, biological glue and fat-tissue flap is recommended for small tears. However, this complication is rarely reported in the published series and also in our experience [10]. The oblique and lateral access, the little needed exposure of the dura and the use of the microscope may be sufficient explanations. However, to limit the risks related to the transforaminal approach, especially with the nerve exposures, it is mandatory to respect a learning curve. We recommend starting the minimally invasive experience by transmuscular tubular approaches for lumbar diskectomies and decompressions. It may be also suitable to have training in anatomical labs.

36.5 Perspective

The main drawback of this technique is the radiation exposure. It is an important concern not only for patients but also for surgeons. The insertion of the pedicle screws and the cage and the manoeuvres of reduction are performed under strict AP and lateral fluoroscopic control. The radiation exposure for patient and surgeon is much more important in minimally invasive approach than in open surgery [22]. Surgeon exposure is significant and requires strict protection and careful monitoring. Annual dose limits for the eyes and the thyroid can be exceeded if a large number of these minimally invasive procedures are performed. Many new protocols and navigation-assisted fluoroscopy systems have been developed in order to overcome this drawback [23, 24]. The CT navigation system is the most recent one [25]. It provides an excellent accuracy and a very low radiation exposure, especially for the surgical team (Fig. 36.6). The recent development of these tech-

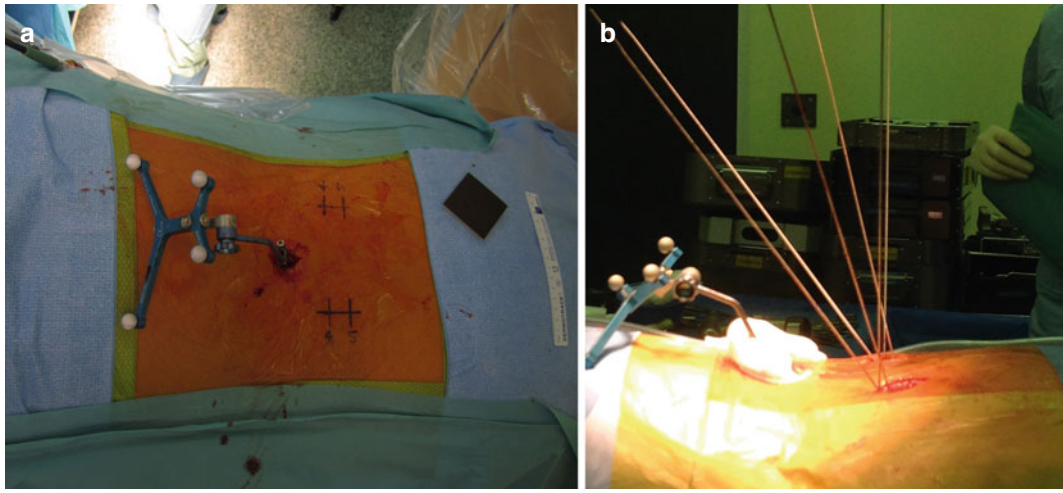

Fig. 36.6 CT navigation system. The frame is fixed to the upper spinous process (**a**). Placement of the K-wires under navigation system without fluoroscopic control (**b**)

nologies is likely to improve the safety of the procedure while decreasing operative time and radiation exposure.

Conclusion

Minimally invasive TLIF is a safe and effective technique to achieve circumferential fusion for the treatment of various degenerative diseases at the lumbar spine. The limits of this technique must be well known by surgeons who should comply with a learning curve for patient's best care.

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37 Minimally Invasive Operation for Lumbar Fusion, Canal Stenosis, Degenerative Scoliosis, and Spondylolisthesis. Is It Possible?

Christopher C. Gillis and Richard G. Fessler

37.1 Introduction

Minimally invasive spinal surgery (MISS) is one of the most recent revolutions to occur in the treatment of the spine. Minimally invasive techniques compared to "open" techniques are considered those which use smaller skin incisions, spare the muscle and ligamentous complexes, and often utilize a tubular muscle retractor [1–3]. Using these principles as guidelines, it is definitely possible to perform minimally invasive techniques to achieve lumbar fusion, to decompress lumbar canal stenosis, and to correct or stabilize degenerative scoliosis and spondylolisthesis. The efficacy in comparison to open techniques will be discussed, as well as a brief description of techniques that can be implemented.

The idea of using smaller incisions and less tissue disruption has been present in all branches of surgery and has expanded rapidly in spinal surgery over the past 50 years [4, 5]. The majority of evolution in technique occurred concurrently with rapid expansion in technology allowing for intraoperative spinal imaging, improved microscopic and endoscopic video imaging techniques, and the development of the tubular dilation and retraction system. The majority of MISS techniques use a progressive muscle dilation and tubular retraction technique. From the basic indication of the microendoscopic diskectomy, the indications for MISS have rapidly expanded to a wide variety of procedures and pathologies. MISS has been developed for the cervical, thoracic, and lumbar spine in both anterior and posterior approaches. Over the past decade, the field has been rapidly advancing as more surgeons train and become experts in these techniques to the degree that MISS approachable pathology now includes intradural spinal tumors and even spinal deformity. In this chapter, we focus on the literature and techniques as they pertain to the lumbar spine.

This topic will be subdivided into three general sections discussed in the order of their evolution as minimally invasive techniques: (1) decompression of lumbar canal stenosis, (2) treatment of spondylolisthesis, and (3) lumbar scoliosis correction.

37.1.1 Decompression of Lumbar Canal Stenosis

Lumbar stenosis is a recognized and well-described etiology of neurologic disease, usually resulting from a combination of hypertrophied facet joints, ligaments, disk herniation, osteophyte overgrowth, and underlying

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_37

spondylolisthesis. This combination of degenerative arthritic changes is termed spondylosis and is prevalent in the relatively mobile cervical and lumbar spines. Decompression for lumbar stenosis is the most common surgery for patients over age 65 [3, 6]. The resultant narrowing of the spinal canal can cause compression on nerve roots or the cauda equina leading to neurogenic claudication with intermittent symptoms, or intense radiating pain into the buttocks or legs. Often patients are trialed on nonsurgical options which can include narcotic, anti-inflammatory and neuropathic pain medications, epidural steroid injections, and physiotherapy. Patients who experience progression of symptoms, severe symptoms, and no resolution of their symptoms with conservative measures or are greatly limited in their activities leading to a decreased quality of life then are considered for surgical management.

The Spine Patient Outcomes Research Trial (SPORT) [7] demonstrated statistically significant improvement in patient outcomes with surgical management and continued long-term improvement of the beneficial effect. The traditional approach for lumbar stenosis has been through an open, decompressive laminectomy with or without facetectomies. The difficulty with open approaches is the inadvertent creation of iatrogenic spinal instability, subsequently leading to additional procedures to stabilize the spine. Radiographic and cadaver studies have illustrated both the decompressive effectiveness of open procedures and the disruption of the native anatomic support structures, including the paraspinal musculature, the supraspinous ligament, the intraspinous ligament, and the facet joints. It is believed that the muscle atrophy from dissection and loss of posterior supporting ligaments lead to long-term instability [3, 4]. Knowledge of these issues led to the development of minimally invasive spine procedures. Through the use of muscle splitting serial tube dilators and retractors, the musculature is left intact and subsequent atrophy minimized. Through a more lateral approach, the midline posterior ligaments are also left intact. Anatomic maintenance and tissue sparing is the main goal of the minimally invasive approach, leading to decreased long-term instability. Traditionally, MISS approaches were associated with a higher rate of cerebrospinal fluid (CSF) leak than the open approaches, and controversy has persisted about the ability to decompress the contralateral side when a unilateral approach has been taken. Both of these points have been disproven as the techniques have improved and long-term literature has been reported. MISS techniques are increasingly used, and lumbar decompression is one of the most frequent indications.

The historical efficacy of open laminectomies is quoted as 64–83 % of patients achieving clinical improvement with durotomy rates as high as 18 % [3, 7]. We can compare this number to the review of Polikandriotis et al. [6] looking at 320 patients treated with an endoscopic lumbar laminotomy and foraminotomy and evaluated out to an average of 18 months postoperatively. The surgical technique used was very similar to that preferred by the senior author, and the surgeries all done on an outpatient basis. The rate of surgical complications was 2.2 %, with all the complications being CSF leaks (c.f. 18 % open laminectomy).

37.1.1.1 Technique Description

The favored minimally invasive technique of the senior author is described as the microendoscopic decompression for stenosis (MEDS). Fluoroscopy is used to identify the surgical level and an 18 mm incision made paramedian to the midline. A stab incision is made with a scalpel, and a Kirschner (k) wire or guide wire is used to further localize the level at the facet region of the vertebral body that has the stenosis. Once the level is correctly identified, serial dilators are placed over the k wire until enough space is created for insertion of the tubular retractor to an 18 mm diameter. The retractor is fixed to the surgical table by a fixed articulating arm (Fig. 37.1). Once the retractor is inserted, some surgeons prefer to use a microscope or loop vision to continue the dissection; however, the senior author prefers to use a specially designed endoscope which fits in the medial side of the retractor (Fig. 37.2). The trajectory to the lamina is lateral, and once a hemilaminectomy is made on the side of entry, the

Fig. 37.1 Photograph of equipment used for MIS procedures. Shown are a series of dilator tubes, used for the muscular dissection over a K wire, and the 18 mm retractor tube. The retractor tube has a forked attachment arm to secure to the articulating arm affixed to the operating room table

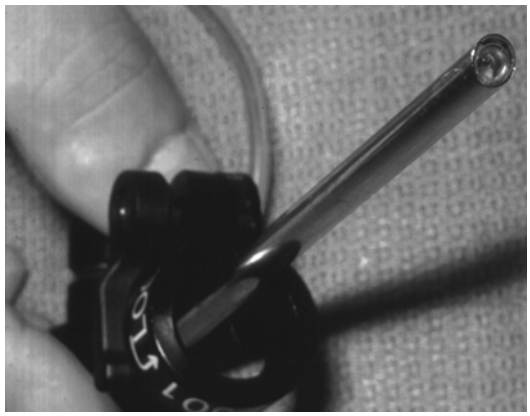

Fig. 37.2 Photograph of the special endoscope used for MEDs procedures. This endoscope fits within the retractor tubes (As illustrated in Fig. 37.1)

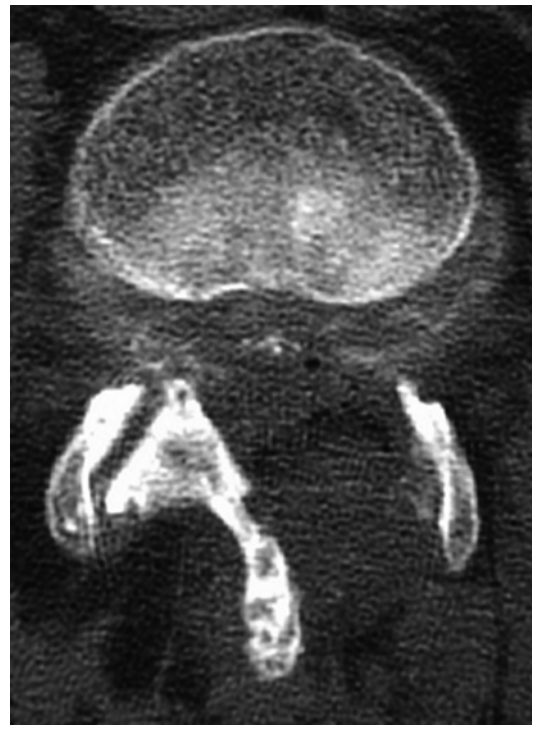

Fig. 37.3 Axial computed tomography scan (CT) demonstrating a left-sided MEDS procedure and the bony decompression achieved

tube can be angled medially, and through a specially designed drill with a retractable single-sided guide, the contralateral lamina can be drilled from underneath the spinous process. The visual angle to the contralateral lateral recess is excellent and can be well decompressed from the unilateral approach (Fig. 37.3).

Rosen et al. [8] described the effective treatment of lumbar spondylosis and stenosis in patients greater than age 75 in a retrospective database review. The results were documented on VAS, ODI, and SF-36 showing great improvement over baseline. Due to disparate measurements, age groupings, and clumping of decompression and fusion patients together, it is difficult to compare this particular patient group outcome to open techniques. The result of this

paper is critical to the concept of MISS techniques for lumbar disease due to the correlation of spinal stenosis and degenerative disease with increasing age and with the increasingly aging patient population we are all faced with. It is interesting to note that there were better results for the older patients compared to the younger patients, the reoperation rate was only 2 %, and the hospital stay was significantly shorter than that in other "open" technique series (29 h vs 3.9–11.6 days). Overall the follow-up for this paper was short at mean 7 months, but the prevailing theory is that MISS technique benefit will only increase over time with preservation of anatomic structures leading to decreased instability, adjacent segment disease, and thus delayed reoperation.

Smith et al. [4] evaluated the biomechanical effects of the unilateral MISS lumbar decompression using cadaver specimens in comparison to bilateral decompression and a wide facetectomy. Evaluated was the range of motion in flexion and extension, axial rotation, and lateral bending. The findings of statistically significant increased range of motion in flexion and extension, ipsilateral lateral bending and axial rotation in those treated with a traditional unilateral decompression compared to MISS, point toward the relative destabilization of the open approach. This was further apparent with the wide facetectomy procedure, which caused significant hypermobility in all tested movements, especially in axial rotation.

37.1.1.2 Interspinous Devices

A brief discussion of interspinous devices and decompression of lumbar stenosis is warranted given the popularity of these devices. Gazzeri et al. [9] discussed the controversies related to these devices and their ability to provide relief of degenerative lumbar disease. Although not an entirely minimally invasive procedure, the insertion of an interspinous device follows the principle of minimal anatomical disruption. These devices are used to treat a range of lumbar pathologies including canal stenosis, segmental instability, facet pain syndrome, and discogenic low back pain. Reported benefits to use of an interspinous device include local anesthetic, preservation of bone and soft tissue, reduced risk of epidural scarring, reduced risk of CSF leak, and even reversibility of the procedure [9]. Looking more closely at the use of the interspinous devices simply for lumbar decompression, the selection criteria are specific to those patients who have relief of their stenotic pain with flexion of the lumbar spine. The mechanism of flexion of the lumbar spine is believed to stretch the redundant ligamentum flavum, which causes posterior compression and stenosis. Once the ligamentum is stretched by the continuous flexion of the interspinous device, there is increased canal diameter and enlargement of the neural foramina, relieving lower extremity symptoms. As reviewed by Gazzeri et al., mean expansion of the spinal canal with insertion of a device is reported between 18 % and 22 % and neural foramina area increased by approximately 25 %. The interspinous devices can be inserted through small, tissue-sparing midline incisions, or even percutaneously. There are a multitude of different devices on the market. The only device with level 1 data is the X-Stop (Medtronic, Tolochenaz, Switzerland; Formerly St. Francis Medical Technologies, Alameda, CA). Looking at published literature the short-term results with the use of the X-Stop device had a significant benefit over nonoperative therapy. Compared to open decompression, the X-Stop showed no significant difference in symptoms or function at 24 months; however, there was a significant increase in reoperation rates for those in the X-Stop group (26 % vs 6 %) [9]. Overall the current evidence does not support a benefit to an interspinous device over surgical decompression, either open or minimally invasive.

A major consideration in the use of MISS is the learning curve encountered when beginning the use of the technique [3, 10–12]. All surgical techniques have a learning curve, and in advanced neurosurgical fields such as complex spine and skull base surgery, there are often a higher incidence of complications encountered during the initial phase of a surgeon's application of a new technology. Depending on the similarity of a technique to one already in use or familiar to the

surgeon, it can be understood that some techniques have steeper curves than others. Generally it is believed that familiarity of a surgical technique occurs after approximately 30 cases, while mastery of a technique may continue for some number of cases after. Complications encountered early in the learning process include unintentional durotomy, nerve root injury, inferior facet fracture, wrong level surgery, infections, and new neurologic deficits. Looking at Ikuta et al.'s [12] retrospective review of 114 patients, they found that the incidence of neurologic complications in the first 34 patients was 18 %, whereas it was down to 6.3 % in the last 80 patients.

Minimally invasive spine surgery can be done for lumbar spinal stenosis. The literature confirms that MISS is equivalent or better than open procedures in clinical patient outcome measures [3, 7, 10, 12, 13]. It allows for less blood loss, shorter overall operative time, shorter hospital stay, decreased postoperative narcotic use, decreased rate of infection, decreased incidence of symptomatic CSF leak, and a decrease in the time required for the patient to return to work [3]. As well, as was illustrated in Smith et al.'s biomechanical study [4], MISS has the advantage of less tissue disruption allowing for decreased rates of spinal instability and subsequent requirement for future procedures. One may thus conclude that MISS decompression is a superior technique to a traditional open approach, once the technique has been mastered.

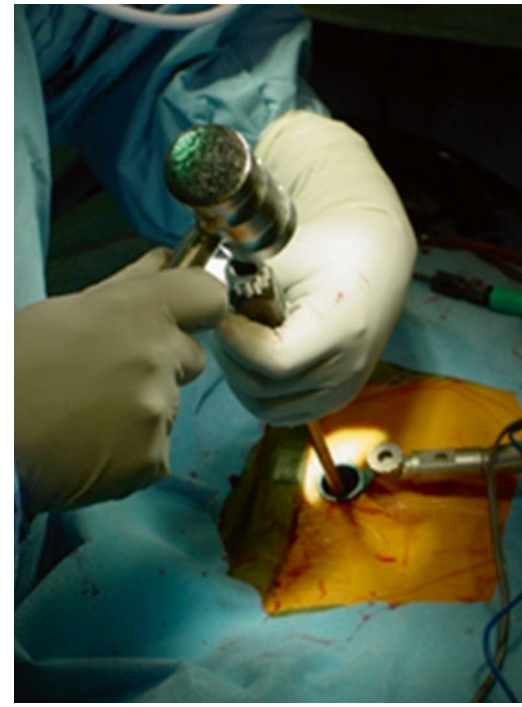

Fig. 37.4 Intraoperative photograph of osteotomy being performed through retractor tube for MISS TLIF

37.1.2 Treatment of Spondylolisthesis

Minimally invasive TLIF is covered extensively in another chapter, and it is a TLIF that has emerged as the current gold standard treatment for spondylolisthesis. We provide a brief summary of the literature outlining the efficacy and feasibility of MISS TLIF (Fig. 37.4).

MISS TLIF is being increasingly performed and has shown reduction in perioperative complications with comparable clinical and radiological outcomes. Compared to an open technique, the benefits of MISS TLIF are decreased postoperative pain, decreased intraoperative blood loss, shorter postoperative hospital stay, faster return to normal activity, and reduced reoperation rates for adjacent segment disease [6, 14]. In example, Parker et al. [15] demonstrated a significant benefit to MISS TLIF with only 2.6 weeks of postoperative narcotic use compared to 6.5 weeks in open cases and a return to work at 8.3 weeks compared to 16.3 weeks. Lee et al. [16] showed a mean operating time of 166 min for MISS TLIF compared to 181 min with open. The mean blood loss was 50.6 mL compared to 447.4 mL and mean hospital stay 3.2 days compared to 6.8 days.

Quality of life in MISS TLIF was studied prospectively by Perez-Cruet et al. [14] with mean 47 months of follow-up in 304 patients. It was found that MISS TLIF provided statistically significant improvement in clinical outcome for patients with symptomatic spondylolisthesis and degenerative disk disease with or without stenosis. There was a high rate of fusion (>95 % majority achieved by 6.8 months) with the technique and very low rate of interbody device failure

(1 %) and very low rate of adjacent segment disease requiring reoperation (2 %). Looking at quality-of-life scores: visual analog scale (VAS) improved by 35.7 % in the immediate short-term and this benefit was maintained long term; the Oswestry Disability Index (ODI) also demonstrated immediate and long-term significant improvement as did the SF-36 physical and mental component scores.

Concern about obtaining bilateral decompression with a unilateral approach was discussed by Kim et al. [17] via magnetic resonance imaging (MRI) analysis. Sagittal T1 MRI was used to calculate the foraminal stenosis at the level of the mid pedicle both quantitatively and qualitatively and central canal stenosis examined both qualitatively and quantitatively on axial T2 MRI. They found significant improvement in all measurements following unilateral TLIF. Contralateral decompression is achieved during the procedure by angling of the retractor medially providing access to the contralateral lateral recess and indirect decompression of the neural foramen by placement of a distracting intervertebral cage. By restoring disk height with an interbody cage, it is believed the disk bulge is reduced and unfolding of the ligamentum flavum occurs which provides central stenosis decompression.

In refinement of technique, the idea of using unilateral versus bilateral percutaneous instrumentation was examined by Dahdaleh et al. [18]. This study was done as a single-center randomized controlled trial with follow-up out to approximately 1 year. Results demonstrated no significant difference between the groups in terms of clinical outcome (measured on validated outcome scores) lordosis correction or in fusion rate. Biomechanical studies have demonstrated superiority of bilateral pedicle screws in both open and MISS constructs, but unilateral fusion may be sufficient for measurement of clinical and radiographic improvement and outcome. Unilateral fusion after TLIF is an option, however, only for single level disease.

The cost benefit of MISS TLIF compared to open was examined by Perez-Cruet et al. and Parker et al. [14, 15]. Parker et al. calculated a 2 year treatment mean cost difference of $8,731 in favor of MISS TLIF compared to open. Wang et al. [19] showed that hospital stay cost was $2,106 less per patient with two-level MISS versus an open approach, but no significant difference with one level approaches. Surgical site infections were examined by McGirt et al. [20] and with 6.1 % for open compared to 4.5 % in MISS procedures there was a direct cost difference for investigation and treatment of infections at $3,593,862 for open and $1,024,950 for MISS.

37.1.2.1 Reduction of Spondylolisthesis

In treatment of spondylolisthesis, reduction is a consideration in those patients with Meyerding grade 1 or greater. The decision of whether to reduce or fuse in situ remains an often discussed issue with benefit of reduction believed to be restoration of spinal anatomy leading to improved sagittal alignment resulting in improved neurologic decompression and fusion rate. Disadvantages of reduction are believed to include neurologic deficits and prolonged operative time. A recent paper by the senior author [21] looked at MISS TLIF in 282 patients, 162 with reduction, and 120 without reduction with at least 1 year follow-up. The authors found found no statistically significant difference in operative time, length of stay, or complication rate. The estimated blood loss and the rate of fusion (84.5 % vs 70.8 % $p<0.05$) was significantly higher in those patients with reduction. Reduction is achievable through an MIS approach, led to a higher fusion rate in the study, and was not associated with a higher rate of neurologic complications. If reduction cannot be achieved, fusion in situ is an acceptable alternative.

Thus, MISS TLIF is an accepted and useful technique and can be employed for reduction of spondylolisthesis. Outcome measures are least equivalent for open and MISS procedures. There are lower rates of intraoperative complications, a more rapid return to baseline patient functioning and recent studies show a possible benefit in terms of cost benefit analysis.

37.1.3 Lumbar Scoliosis Correction

Adult degenerative scoliosis is an increasingly identified condition presenting to spine surgeons for consideration, usually along with lumbar spondylosis and varying degrees of radiculopathy or spinal stenosis. Given the aging population in developed nations, the incidence is only expected to increase in the near future. The correction of lumbar scoliosis is traditionally performed with open surgical approaches involving significant rates of complication and blood loss.

The latest in MISS techniques covers those surgeries that are often the maximally invasive of open procedures: the scoliosis deformity correction. MISS deformity correction has arisen over the past decade and is a field that is continuously evolving. With these developing procedures, it is possible to correct a variety of coronal and sagittal lumbar deformity with percutaneous screws and hybrid MISS techniques for osteotomies and TLIF at appropriate levels. Early versions of the technique, despite being internally tissue sparing of the fascia and muscle, would often leave multiple small incisions which could be cosmetically displeasing. This has evolved to a midline incision for cosmetic reasons with suprafascial dissection and a far lateral muscle splitting (similar to a Wiltse approach) approach to the facet joints which allows for multi-level osteotomies and interbody cages. This is augmented with percutaneous screws placed in a muscle splitting fashion and through lateral trans-psoas approaches (DLIF, XLIF, LLIF etc.) which allow for direct coronal plane correction through manipulation of the anterior column. Some surgeons have also advocated for release of the anterior ligamentous structures which allow for more extensive manipulation of the anterior column. We will briefly discuss these techniques and the evidence to support their use.

The main goal of lumbar scoliosis correction is pain relief with the secondary goals of neural decompression, creating or maintaining coronal and sagittal balance, and stabilization of the construct. Deformity correction progresses from the discussion of MISS TLIF. The basic building block of lumbar deformity correction and fusion is the complete removal and fusion reconstruction of a single motion segment; this is achieved with MISS TLIF or as we will discuss, lateral lumbar interbody fusion (LLIF). This involves a single level central and foraminal decompression of the local neural elements, fusion, and placement of a cage after disk removal and depending on instrumentation used can stabilize or improve deformity present at that level. It stands to reason, then, that expanding upon the basis of the minimally invasive (MISS) TLIF, we can achieve multi-level decompression, fusion, and correction of a variety of lumbar spine disease.

Anand et al. [22, 23] described their extensive long-term experience with MISS correction of scoliosis in 187 patients. This paper was in both thoracic and lumbar deformities but has the longest published follow-up experience and serves as our starting point. They found that the technique was possible and useful but limited in the ability to achieve normal sagittal vertebral angle (SVA; SVA less than 47 mm optimal) in patients who had a preoperative value less than 100 mm, and limited in the ability to correct pelvic incidence to lumbar lordosis mismatch (PI-LL $\pm 10^{\circ}$). The maximum SVA correction achieved was 89 mm and the PI-LL could only be normalized in those patients with starting values of 38° or less. The average curve reduction achieved was 61 %. They also noted five of their patients developed L5-S1 pseudoarthrosis. The conclusion by Anand et al. was that their circumferential technique was effective on patients who had preoperative deformity measurements within the confines of the limitations of the technique, based on the values given above. In moving forward from this, it is important to note the techniques used included direct lateral trans-psoas approaches for interbody fusions and MISS percutaneous pedicle screw and rod placement. In those patients requiring L5-S1 fixation, transsacral axial lumbar interbody fusion was used. The limitations in the lateral trans-psoas approaches are likely the limitation in sagittal correction found in this study, similar to Acosta et al. [24], who found that lateral trans-psoas approaches did not improve lumbar lordosis.

As mentioned, some surgeons advocate for release anterior longitudinal ligament (ALL) when performing lateral trans-psoas interbody techniques. In deformity correction, it is often necessary to release anteriorly to achieve greater deformity correction, and it can be conferred that without this release, a limitation in the ability to achieve maximum correction is reached. In MISS deformity correction, a direct anterior approach is replaced by the lateral trans-psoas approach, and some surgeons believe that depending on the degree of correction required, the release of the anterior longitudinal ligament may be needed to achieve this. However, the release of the ALL is associated with significant intraoperative complications, specifically injury to the great vessels and/or anterior dislodgement of the cage after placement, as a result this can be considered a higher-risk maneuver. Due to the risks associated with ALL release, it is likely best avoided for those unfamiliar with its use. Another newer technique allowing for greater deformity correction from the lateral approach is the approval of increasingly hyperlordotic interbody cages. Using these devices, which have far greater angulation than the usual TLIF or PLIF interbody device, increasing severity of sagittal deformity is able to be corrected through lateral approaches alone. In some cases, the lateral approach alone may be all that is required to achieve the correction. The senior author prefers to perform the lateral interbody procedure and then obtain upright postoperative imaging before progressing to a posterior approach. Overall, lateral interbody techniques continue to evolve and add to the toolbox of the MISS deformity surgeon. As technology continues to progress, so will the level of achievable deformity correction.

In Dahdaleh et al.'s review of the literature [11], the lateral trans-psoas approaches and their role in deformity correction are examined in detail. The technique involves a small incision with a lateral window created through the psoas muscle (Fig. 37.5). A retraction device is mounted to the operating room table, and cages of sizes up to the anterior-posterior diameter of the vertebral body can be placed for lumbar interbody fusion. Coronal deformity can be corrected from 3.0 to 5.9° and sagittal correction from 2.2 to 3.3° per level [11]. Lateral interbody fusion also allows for indirect decompression of the foramina and central canal [11], and the lateral approach allows for a superior result compared to TLIF for lordosis. Complications of the lateral trans-psoas approach include injury to the lumbar plexus in its path through the psoas muscle. This can present as groin and anterolateral thigh sensory symptoms and muscle weakness in ipsilateral

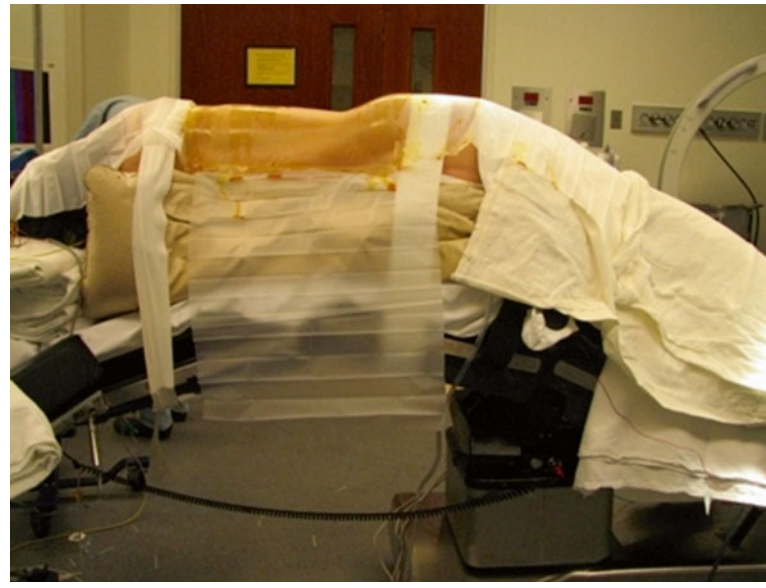

Fig. 37.5 Patient positioning for LLIF procedure. Patient is positioned lateral, on a bean bag support with the break in the operating room table just below the iliac crest, where it is used to maximize the space between the iliac crest and ribs to provide maximum lateral exposure

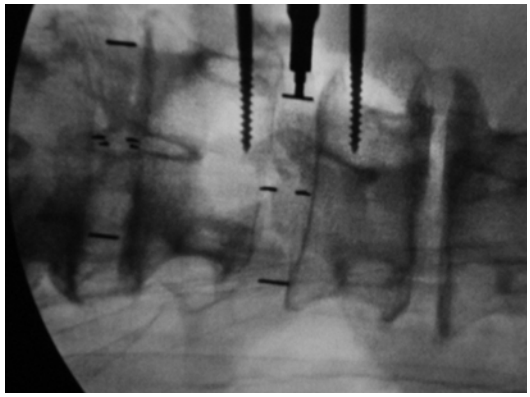

Fig. 37.6 Intraoperative fluoroscopic image illustrating the insertion of the lateral interbody cage through the LLIF approach. There are pins in the vertebral body above and below to stabilize the tube retractor over the lateral disk space. The subjacent level has already had an interbody cage placed

psoas or quadriceps. The published rates of numbness vary from 18 to 40 % postoperatively and the rates of weakness range from 25 to 55 %; the majority of these symptoms are resolved by 6 month to 1 year follow-up (Fig. 37.6).

In patients with appropriate sagittal balance and pure coronal scoliosis symptoms, a lateral interbody fusion technique with percutaneous screws alone can be used. When more extensive sagittal correction is also required, depending on the degree of deformity, as discussed previously, more extensive posterior work is required than percutaneous screws alone. This more extensive posterior work can be performed through essentially a MISS TLIF approach, allowing for access to the lamina, the disk and posterior ligamentous elements, and the facet and foraminal zone. This allows for facet osteotomies as well as Smith-Peterson facet osteotomies for achieving greater degrees of sagittal deformity correction.

To illustrate what we have surmised from the literature, Dangelmajer et al. [25] performed a meta-analysis comparing differences in patient selection and outcomes between MISS lumbar scoliosis correction and open surgery. They included 12 studies for analysis, of which 8 used lateral interbody fusion or XLIF technique and 4 studies did decompression without fusion. The analysis showed that the patients selected for MISS were older with more medical comorbidities than those offered open surgery. Those patients with more severe deformity as measured by greater Cobb angles and greater sagittal imbalance had open surgery, with a higher rate of reoperation. Overall there were no significant differences between complications between the two groups, but given the differences in patient selection, this cannot be taken as a direct comparison between MISS and open deformity surgery. Given what we have discussed, these results are not unexpected; MISS deformity correction has a limitation and open surgery is favored in the case of severe deformity, as well as those patients who are likely unable to tolerate a large open surgery (elderly, medical comorbidities) will better tolerate MISS procedures and with acceptable complication rates.

Currently, MISS techniques are not as versatile as open deformity techniques, and some reports detail suboptimal correction or pseudoarthrosis with sagittal plane deformity, despite the ability to achieve excellent coronal correction. To examine the current consensus of what can be corrected by MISS, Mummaneni et al. [26] created a decision-making algorithm for MISS deformity correction. They tested the reliability of their algorithm by presenting 20 representative cases to 11 fellowship trained spine surgeons at two separate time points. There was very good intraobserver reliability and moderate good interobserver (intraobserver kappa 0.86, interobserver 0.58 and 0.69) reliability with their survey. Overall the agreement was echoed almost identical to Anand et al. [23] in that open approaches were required for the most severe deformities, with the values given as SVA >7 cm, with a rigid curve; LL-PI mismatch greater than 30° with a pelvic tilt greater than 25°; and/or thoracic hyperkyphosis greater than 60°. Deformity with values less than this can be considered for MISS procedures ranging from one- to two-level TLIF with minimal deformity and for those with moderate deformity more extensive MISS including lateral interbody fusion and muscle sparing minimally invasive or mini open posterior procedures combined with percutaneous pedicle screws.

MISS scoliosis correction is a newly developed technique, which currently has technical limitations in the degree of deformity that can be corrected. As techniques, especially the lateral interbody fusion, continue to expand and develop, the limit of deformity that can be corrected slowly diminishes. Within these limitations, MISS deformity correction is an accepted and possible surgical option. Both MISS techniques alone or in a hybrid procedure with osteotomies are an emerging tool in the field of spinal deformity correction.

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38 Spine Injections for Persistent Lumbar and Radicular Pain After Lumbar Spine Surgery

Lee R. Wolfer, Richard Derby, and Jeong-Eun Lee

Patients with persistent lumbar pain and/or radicular leg pain after lumbar surgery pose significant diagnostic and therapeutic challenges. Patients who do not improve after lumbar surgery are commonly labeled with a diagnosis of "failed back surgery syndrome (FBSS)." The term "FBSS" was coined before by spine surgeons prior to 1970 when reporting surgical outcomes [1, 2]. Some nonsurgical specialists have served only to obfuscate the etiology of persistent lumbar and/or leg pain after lumbar surgery by stating that FBSS is "easy to recognize but hard to define" [3]. FBSS is "a euphemistic term used for a heterogeneous group of disorders in patients complaining of back and leg pain" [4]. Burton et al. [5], lacking MRIs and diagnostic/therapeutic spine injections, incorrectly attributed persistent pain after spine surgery to prima facie psychological comorbidities and secondary gain. Based on his collective experience of treating over 800 FBSS cases per year, Burton et al. [5] stated: "Patients with this condition can rarely be 'cured' because FBSS is actually a spectrum of organic disease processes complicated by secondary financial gain and learned chronic pain behavior." Unfortunately the label implies (is often equated with) both psychological pain exaggeration and a centralized self-sustaining pain process in which further diagnostic tests are inappropriate and treatment options directed at a specific structural cause are useless. Patients with persistent pain after surgery do not have a primary psychological problem, responsible for their pain; however, psychological comorbidities are present in this population, some premorbid, and others likely reactive to the life circumstances of persistent pain. With increasing number of physicians and societies devoted to pain management and musculoskeletal spine and sport medicine, the diagnosis and nonoperative/noninterventional treatment algorithms used in these practices have evolved to include conservative care modalities such as aggressive pharmacologic pain management, functional restoration, behavioral modification, and psychological counseling; however, in a subset of patients, these treatments may at best be adjunct treatments or may in fact miss the opportunity to diagnose and treat pain generators definitively.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_38

The FBSS of 30 years ago was nonspecific and non-diagnostic (Slipman et al. [6]); however, we can now state that "failed back surgery syndrome" (FBSS) is an outmoded, inaccurate, and pejorative term. A current, more accurate definition of FBSS is: "persistent or recurrent pain, mainly in the region of the lower back and legs, even after technically, anatomically successful lumbosacral spine surgeries" [7]. The primary label used by the authors of this chapter is "post-lumbar surgery syndrome" (PLSS) [8]. PLSS is defined as a disease entity representing "a cluster of nomenclature and syndromes following spine surgery wherein the expectations of the patient and spine surgeon are not met, with persistent pain following lumbar surgery" [9]. With modern imaging innovations, as well as refined diagnostic and therapeutic spine interventions including spine injections and re-operation, more than 90 % of patients can be given a specific diagnosis and treatment for their persistent low back and/or leg pain after lumbar surgery.

The postsurgical patient with persistent lumbar pain and/or leg pain poses diagnostic and therapeutic challenges unlike those of the patient with chronic low back pain. The most common causes of persistent pain after lumbar spine surgery currently are: recurrent/residual or new disk herniation, painful internal disk disruption, sacroiliac pain, facet joint pain, instability, fibrosis (epidural, perineural, or intraneural), neuropathic pain, acquired stenosis, and adjacent segment disease. Rare patients may have a surgical complication or technical failure.

The goal of this chapter is to inform the reader about the most common spine injections currently used to diagnose and treat PLSS. Due to the influence of payors and policymakers on surgical decision-making, PLSS will also be briefly presented within an epidemiologic, historic, and socioeconomic context. Payors, policymakers, researchers, and other stakeholders have sounded an "alarm" over the increase in spine surgeries. They have sounded the same alarm over the proliferation of interventional procedures in nonoperative spine practices. Detractors argue that some of these procedures are dubious, risky, and scientifically unproven and do not lead to long functional improvement. Some interventions have stood the test of time, e.g., epidural injections, diagnostic facet and sacroiliac joint blocks, and medial branch neurotomy, but other treatments such as pulsed radiofrequency treatments of spinal nerves or various intradiscal therapies are recent interventions and may or may not be in common use in the future. With the meteoric rise in spine injections over the last decade, often without appropriate indications, spine interventionalists have come under intense scrutiny to justify the medical necessity of their procedures. Ultimately, both patient and the physician are the losers with performance of medically unnecessary spine injections. Because spine interventionalists did not utilize rigorous indications for successful diagnostic and therapeutic interventions in the last decade, payors and policymakers intervened.

Interventional procedures are directed at specific peripheral sources of pain originating within the posterior, middle, or anterior columns, and for the most part, their use requires the identification of an ongoing nociceptive/neuropathic source via diagnostic lumbar spine injections. The most important task of the surgeon evaluating a patient with persistent lumbar pain and/or radicular pain after surgery is to provide a diagnosis based on history, physical exam, imaging, and diagnostic/therapeutic spine injections. The role of diagnostic and therapeutic spine injections is to assist the surgeon in precision identification of pain generators to optimize surgical outcomes. Once a diagnosis is obtained, the spine surgeon can consider the best treatment options, as presented in this chapter, based on the most up-to-date, evidence-based review of the spine literature on PLSS currently available [10, 11].

As with any surgery, spine surgery has risks and may not completely eradicate pain and functional impairment. Ideally, patients undergoing primary or revision surgery should have exhausted noninterventional, conservative care modalities, as well as interventional spine care treatments. For example, in patients with primary chronic axial low back pain, spine injections performed per the International Spine Intervention Society criteria for facet pain, sacroiliac pain, and provocative discography should be considered

before lumbar fusion if the patient meets appropriate criteria [10, 11]. If spine interventionalists drop the bar by adopting less stringent diagnostic criteria for diagnostic blocks, outcomes suffer and payors and policymakers will continue to decrease reimbursements. If the diagnostic bar is set high for facet blocks, SIJ blocks, epidural steroid injections, and so forth, both patients and physicians will benefit. If the bar is set high with more stringent definitions of a successful lumbar surgery, as well as more rigid surgical indications, the incidence of PLSS should also decrease.

The esteemed spine surgeons Burton et al. [5] presciently stated the following – which still rings true today to guide spine specialists to the best possible outcomes:

> The answer to the problem is not better FBSS salvage, but avoiding the causes of failure of lumbar spine surgery. It relates to the prevention of induced iatrogenic disease; it also relates to adequate diagnosis and treatment based on that diagnosis. Moreover, it relates to preventive care and early, aggressive, comprehensive, conservative management of low back pain. Conservative treatment is often inadequate and employed for insufficient periods of time. Finneson [12, 13] pointed out in a survey of surgical patients that '80 % should not, in our opinion, have been brought to surgery'…When surgery is indicated, adequate diagnostic tests and the execution of appropriate procedures based upon this information should largely prevent the failed back surgery syndrome.

38.1 Epidemiology of Chronic Low Back Pain

To understand the etiology of persistent lumbar and/or radicular pain after lumbar surgery, it is critical to briefly review the epidemiology of low back pain. According to the Global Burden of Disease study from 2010: "*Low back pain causes more global disability than any other condition*." Disability weights were applied to overall prevalence to obtain overall disability expressed in years lived with a disability (YLD). The years lived with a disability (YLD) increased from 58 million in 1990 to 81 million in 2010 [14]. All agree that these patients represent a tremendous social and financial burden. In the United States, it was estimated that direct healthcare expenditure for back pain was $90.7 billion in 1998 [15]. A significant percentage of chronic low back pain patients will fail conservative care and seek out diagnostic and therapeutic spine injections. A small percentage of chronic low back patients will fail both conservative care and interventional spine treatments and undergo surgery.

Among the US adult population, the prevalence of chronic pain ranges from 2 % to 40 %, with a median point prevalence of 15 %. Chronic spinal pain is the most common source of chronic pain [16]. The lifetime prevalence of spinal pain has been reported as 54–80 % [16]. Some studies have reported an increased prevalence of "chronic, impairing low back pain" [17]. A telephone survey of greater than 4,000 North Carolina households showed a 3.9 % prevalence in 1992 and a 10.2 % prevalence in 2006.

Other researchers have looked at healthcare utilization as a surrogate marker for patients with chronic spine problems. Martin et al. [18] studied trends in healthcare expenditures, utilization, and health status among US adults with spine problems from 1997 to 2006. There was an increase in the estimated number (and treated prevalence) of people reporting care for spine problems in the United States from 14.8 million (10.8 % of the population) in 1997 to 21.9 million (13.5 %) in 2006. Per-user expenditures for spine-related inpatient, outpatient, pharmacy and emergency services were followed. From 1997 to 2006, a 49 % increase in the number of patients seeking spine-related care was the largest contributor to outpatient expenses. Among people with spine problems, a 660 % increase in expenditures for opioid medications was reported, from $246 million in 1997 to $1.9 billion in 2006 [18].

38.2 "Nonspecific Low Back Pain": A Closer Look

How a physician defines low back pain determines how they will treat a patient with low back pain. A physician, payor, or policymaker who has learned that 80 % of low back pain is "nonspecific" or "idiopathic" will be a minimalist and be

unlikely to endorse spine injections or surgery. A majority of healthcare professionals, insurance industry, and policymakers have been taught that the majority of low back pain has no clear cause and no compelling reason. Patients suffering from chronic low back pain also continue to be told their pain is psychogenic or due to secondary gain motives. In contradistinction, a spine surgeon or spine interventionalist, who has identified greater than 90 % of the causes of low back pain, will approach the treatment of chronic, disabling low back pain much differently.

A brief look origin of the statement that "80 % of low back pain is nonspecific" is not simply an academic epidemiologic tangent. This statement of "fact" has been used to frame and guide spine care for almost 50 years. This statistic continues to be used as "evidence" for limiting spine surgery, limiting spine injections, and perhaps causing unnecessary pain and suffering in patients with low back pain. Primary care physicians and many neurologists have learned this statistic as fact and patients are principally given only conservative care options. This statistic from one isolated study has also contributed to the creation of a climate of fear of back surgery, quite unlike attitudes toward other orthopedic surgeries.

In 1982, prominent spine surgeon, Augustus A. White quoted a study in which the authors found that in 79 % of first attacks of low back pain in men (and 89 % in women), the "specific cause was unknown" [19, 20]. From this time on, it became generally accepted that 80 % of low back pain was idiopathic or nonspecific. This statistic came to be broadly misapplied to all patients with low back pain, acute and chronic. Taking a closer look, the original study published in the 1960s included patients with less than 2 weeks of low back pain; diagnostic tools included only history and physical exam [19]. The conclusions of this 60-year-old observational study continue to be inappropriately applied to the diagnosis and treatment of patients with prima facie chronic low back pain and post-lumbar surgery persistent pain. The evidence for treating chronic low back pain can almost always be divided into two polarized camps, each camp continuing to provide evidence for its position. Much of our current division has its historic roots in the acceptance of the view that the etiology of low back pain cannot be determined in 80 % of patients.

Beginning in the late 1970s, the use of fluoroscopic imaging and contrast during injection procedures allowed for the development of more precise localized injection techniques [21] in which pain reproduction and local anesthetic pain relief could be used to help confirm that the target structure was a source of pain. These techniques have evolved and culminated in the International Spine Intervention Society (ISIS) Practice Guidelines for injection standards for diagnosing and treatment of chronic spinal pain [10, 11]. Based on Schwarzer's studies [22–27] using precision diagnostic injection as the criterion standard for diagnosis, Bogduk [28] postulated that a definite diagnosis could be made in 70–80 % of patients with chronic lumbar pain. Schwarzer et al. [23, 27] identified the z-joint (9 %), SI joint (15 %), or disk (39 %) as the primary sources of pain. Although arriving at a different percentage prevalence of specific pain sources, Manchikanti et al. [29] using the same techniques in 120 consecutive patients with spinal pain was able to identify the z-joint (40 %), SI joint (2 %), or disk (26 %) as the primary source of pain in 68 % of patients. High-quality, randomized controlled trial studies, particularly in last 20 years, using diagnostic spine injections (facet, sacroiliac blocks, and provocative discography) have definitively disproven the general statement that 80 % of low back pain is nonspecific or idiopathic. These same diagnostic techniques have been refined and utilized to determine specific etiologies of persistent lumbar and/or leg pain after surgery. Advances in imaging have also contributed significantly to our understanding of low back pain. In the 1950s, the only imaging tool was x-ray. MRI, especially in the post-lumbar surgery spine, has proven to be an indispensable tool for diagnosis.

The "literature legends" of "nonspecific" and "idiopathic" low back pain have been passed from publication to publication for over 50 years without critical review of the original study. The study from which these terms are derived applies narrowly to patients presenting with acute

(<2 weeks) low back pain in the 1950s, not to patients with chronic, disabling low back pain presenting in the twenty-first century. In 1966 Dillane et al. published a study entitled, "Acute low syndrome: A study from general practice" [19]. The incidence of *acute low back pain episodes lasting less than 2 weeks* was collected in a general practice setting from patients seen between 1957 and 1960. X-rays were not performed because of their reported unreliability for diagnosing disk herniations [30]. According to Troup [30], x-ray evidence of a "disk" problem is known to be unreliable. At this time discogenic pain and painful internal disk disruption were not well understood as a cause of low back pain; only herniated disks causing radiculopathy were recognized. Dillane et al. [19] reported that the cause of low back pain was not evident in 79 % of males and 89 % of females (see Table 38.1). The report of 79 % of males with a "cause not evident" was rounded up to 80 %, thus giving rise to the claim that 80 % of low back pain is idiopathic or nonspecific. Female patients were even more mysterious, with 90 % of women having a "cause not evident." The reader can see how this data could be misused with many physicians attributing low back pain to an organic psychogenic problem or the attitude that the patient will recover if given enough time. Dillane et al. [19] reported that a majority of patients (62 %) recovered in 2 weeks. (Of note, no follow-up was undertaken on the 38 % of patients who did not recover in 2 weeks.) Forty-five percent (45 %) of patients experienced a reoccurrence within 4 years.

Table 38.1 Cause of index attack [19]

Cause of index attack	Males (%)	Females (%)
Cause not evident	79.3	88.9
Strain	10.9	4.3
Proved disk[a]	7.6	5.6
Ankylosing spondylitis and neoplasms	0.5	0.6
Direct trauma	0.5	–
Others	1.1	0.6

[a]A diagnosis of prolapsed disk was accepted only if there was objective evidence of nerve root pressure – paralysis or wasting of muscle of an area of anesthesia

The population reported on by Dillane et al. [19] is not the population routinely seen by spine surgeons; however, the notion of nonspecific low back pain has persisted and remains a common retort for those against spine interventions for both chronic low back pain patient and patient with persistent low back or leg pain patient after surgery. Many physicians persist in offering only pharmacologic management, cognitive behavioral therapy, functional restoration, and/or physical therapy under the belief that the spinal pain is primarily psychogenic in origin or that the pain has become centralized, and therefore the search for a pain generator is futile and unsupported by evidence. Interesting, as briefly noted above, an important historic study by Rowe [31] was published in 1969 shortly after the Dillane study, but has been ignored from an epidemiologic perspective. Rowe (1969) studied 500 employees with chronic low back pain for 7 years at the Kodak factory [31]. Rowe states the reasons for his 7-year observational study best: "Studies based upon short-term observation of patients with low back disability have yielded information nearly as tunnel-sighted as that gleaned from the single etiology approach. Experience indicates that backache is characteristically intermittent, episodic, and recurrent and can meaningfully be studied only as a continuum which stretches through the active years in a man's life." Rowe [31] reported a diagnosis in approximately 80 % of his patients, including disk pain (54 % both intrinsic discogenic pain and pain due to disk herniation), inflammatory backache (14 %), and miscellaneous causes (10 %). Rowe did not have use of CT scans, MRI, or diagnostic spine injections to identify facet or sacroiliac joint pain. The use of provocative discography is not reported. Furthermore, in the late 1960s, discography had fallen out of favor based on the negative discography study by Holt [32]. Holt's study was later discredited as he utilized a nonstandard technique on prisoners receiving incentives for study participation.

In summary, the statements on low back pain being almost entirely "nonspecific" and "idiopathic" are based on a single, general practice study on *acute low back pain* (less than 2 weeks)

in the late 1960s [19]. The terms "idiopathic low back pain" and "nonspecific low back pain" then reentered the literature with the 1982 Symposium on Idiopathic Low Back Pain publication by eminent spine surgeons Augustus White and Alf Nachemson [20]. Research published at the same time as the Dillane study was ignored [31]. While Dillane et al. [19] accurately reported his experience as a general practice doctor (in 1950s Boston, MA USA) caring for patients with less than 2 weeks of low back pain, his results should not be applied beyond that time or narrow clinical setting. However, the statistic continues to be taught in medical school and utilized by many authors, payors, and policymakers to apply to all causes of low back pain and most importantly to patients with *chronic low back pain*. The statistic is an example of a "literature legend" wherein the original study, clinical setting, and relevance have been lost over time. "Nonspecific low back pain" and "idiopathic low back pain" are terms used primarily by detractors of spine surgery and spine injections. Just as the majority of etiologies of failed back surgery syndrome have been elucidated, so have the etiologies of "nonspecific low back pain." The terms "idiopathic" and "nonspecific" low back pain are not supported by the current published evidence.

38.3 History of "Failed Back Surgery Syndrome (FBSS)"

It is useful to examine the history of failed back surgery syndrome (FBSS) or persistent pain after lumbar surgery (post-lumbar surgery syndrome) before looking to the present state-of-the-art in diagnosis and treatment of the condition. Patients with persistent pain after lumbar spine surgery represent a heterogeneous group which has changed over the years due to advances in surgical techniques and diagnostic/therapeutic spinal injections. Until the early 1980s, largely single-surgeon or single-institution case series results were reported, but no evidence-based, critical quantitative studies. A brief historical review demonstrates the significant advances achieved in both diagnosis and treatment of low back and leg pain before and after lumbar surgery. Reviews of spine surgery outcomes published in the 1980s [5, 33] lacked MRIs and diagnostic/therapeutic spine injections and were unable to diagnose a significant percentage of PLSS patients. The authors attributed PLSS in many patients to psychosocial comorbidities and secondary gain as primary pain drivers. Long et al. [33] were unable to find a cause for the patients' pain in up to 44 % of patients: 21 % of patients were classified as "normal," and 21 % were diagnosed as having expected postoperative changes/mild spondylosis – not consistent with their persistent pain. A majority of patients were instead diagnosed with primary psychiatric and addiction problems as well as prominent motivations for secondary gain. Pain medicine specialists, also lacking diagnostic tools at that time, diagnosed a majority of patients with persistent pain after lumbar surgery as having a "centralized pain syndrome," as opposed to ongoing, correctable peripheral nociceptive lesions. Patients with centralized pain syndromes and "learned chronic pain behavior" were relegated to functional restoration, medication management, and cognitive behavioral therapy interventions.

Seven seminal quantitative studies are reviewed here (see Table 38.2). In 1981, Burton et al. [5] published the first quantitative study on the etiologies of "failure of surgery in the lumbar spine." Collectively, this paper reflects the experience of surgeons who treated an average of "800 FBSS cases per year." The authors summarize the status of patients with persistent pain after lumbar surgery, circa 1970s: "The FBSS entity represents a highly complex challenge to the physician. Patients with this condition can rarely be "cured" because FBSS is actually a spectrum of organic disease processes complicated by secondary financial gain and learned chronic pain behavior. While many of these patients can be "salvaged" to varying degrees by comprehensive rehabilitation programs, it is uncommon to achieve complete pain relief by any combination of therapeutic measures. This is due in part to the great difficulty in quantitating pain and associated psychologic, occupational, social, monetary, intellectual,

Table 38.2 Comparison of studies on failed back surgery syndrome (reported as %)

	Burton et al. [5]	Burton et al. [5]	Long et al. [33][c]	Bernard [34][d]	Fritsch et al. [2]	Waguespack et al. [35]	Slipman et al. [6]	DePalma et al. [36][i]
Surgical								
Spinal stenosis, total	64	72	5	29	–	–	21.5	–
Stenosis, foraminal	–	–	–	–	–	–	12.4	–
Stenosis, central[a]	7	14	–	29	–	–	5.9	–
Stenosis, lateral	57	58	–	–	0	29	3.2	0
Internal disk disruption/ disk degeneration	–	–	–	29	12	25[f]	21.5[h]	11[j]
Severe spondylosis	–	–	5	–			–	
Instability	–	–	–	2	12	5	0.5	0
Spondylolisthesis	–	–	–	4			1.6	
Recurrent or retained HNP	12	16	1	33	62[e]	11[g]	12.4	0
HNP at a new level	–	–	–	7	22	–	–	–
Scoliosis	–	–	1	–	–	–	–	–
Pseudoarthrosis	<5	–	–	29	–	14	–	–
Foreign body	<5	–	–	–	–	–	–	–
Surgery performed at the wrong level	<5	–	–	–	–	–	–	–
Traumatic meningocele	–	–	1	–	–	–	–	–
Tarsal tunnel syndrome	–	–	1	–	–	–	–	–
Fractured hip	–	–	1	–	–	–	–	–
Compression fracture	–	–	1	–	–	–	–	–
Synovial cyst	–	–	–	–	–	–	1.1	–
Vascular claudication	–	–	–	–	–	–	1.1	–
Pseudomeningocele	–	–	–	–	–	–	0.5	–
Nonsurgical								
Arachnoiditis	6[b]	16[b]	13	11	–	1	0.5	0
Epidural or intraneural fibrosis	6[b]	8[b]	14	–	4	–	14.6	0
Nerve injury during surgery/battered root	<5	–	6	–	–	–	1.6	–
Chronic mechanical pain	<5	–	–	–	–	–	–	–
Transitional syndrome	<5	–	–	–	–	–	–	–
Unknown	<5	–	–	–	–	6	5.6	0
Normal	–	–	21	–	–	–	–	–
Expected postop/minor spondylotic	–	–	21	–	–	–	–	–
Cancer	–		4					
Musculoskeletal abnormality	–	–	3	–	–	–	–	–
Degenerative spondylosis	–	–	–	9	–	–	–	–
Mechanical low back pain	–	–	–	–	–	–	9.1	–
Radiculopathy	–	–	–	–	–	–	5.4	–
Radicular pain	–	–	–	–	–	–	4.8	–
Deconditioning	–	–	–	–	–	–	3.8	–
Facet syndrome	–	–	–	–	–	–	2.7	18

(continued)

Table 38.2 (continued)

	Burton et al. [5]	Burton et al. [5]	Long et al. [33][c]	Bernard [34][d]	Fritsch et al. [2]	Waguespack et al. [35]	Slipman et al. [6]	DePalma et al. [36][i]
Sacroiliac joint syndrome	–	–	–	–	–	–	1.6	43
Complex regional pain syndrome	–	–	–	–	–	–	0.5	–
Fibromyalgia	–	–	–	–	–	–	0.5	
Diskitis/infection	–	–	–	–	–	1	0.5	–
Hardware/soft tissue irritation	–	–	–	–	–	–	–	14
Neuropathic pain	–	–	–	–	–	9	–	0
Psychological	–	–	–	–	–	3	–	–

[a]Stenosis, central: includes fusion overgrowth
[b]Burton et al. [5]: Arachnoiditis or epidural fibrosis not defined
[c]Long et al. [33]: 78 patients; 64 underwent surgery
[d]Bernard [34]: 19 patients had more than one diagnosis
[e]Fritsch et al. [2]: 40 % recurrent HNP; 22 % recurrent HNP and new HNP
[f]Waguespack et al. [35]: 17 % IDD; 3 % within fusion; 5 % IDD with stenosis
[g]Waguespack et al. [35]: 6 % recurrent HNP; 5 % recurrent HNP and stenosis
[h]Slipman et al. [6]: Internal disk disruption syndrome is included in surgical diagnoses although nonsurgical intradiscal thermal and orthobiologic treatments are being researched
[i]DePalma et al. [36]: Patients presented with primarily axial low back pain
[j]DePalma et al. [36]: 3 cases, 2 cases adjacent to surgical level and 1 case removed by one level from surgical level

motivational and educational factors" [5]. During the 1970s, diagnostic imaging was limited to x-ray, CT scan, CT myelography, and selective use of discography. MRI (particularly with and without gadolinium postoperatively) has contributed significantly to understanding the etiologies of PLSS.

In the first substantive review on FBSS, Burton et al. [5] reported (see Table 38.2) almost 75 % of the patients with persistent pain had correctable lesions caused either by lateral stenosis (58 %) or retained/recurrent disk herniation (12–16 %). Nonsurgical etiologies diagnosed (without MRI) included: arachnoiditis (6–16 %) and epidural fibrosis (6–8 %). With the introduction of MRI (with and without gadolinium) and diagnostic spine injections, diagnostic sensitivity and specificity improved markedly over the next three decades. Surgeons also responded to this early data with improved surgical techniques or revision strategies to eliminate or reduce certain persistent postsurgical pain problems, such as residual lateral/foraminal stenosis, re-herniation/residual disk herniation, "battered root syndrome"/traumatic neuritis, epidural fibrosis, and arachnoiditis.

Long et al. [33] studied 78 patients admitted to the inpatient Johns Hopkins multidisciplinary pain clinic program for an average of 18 days. Of 1,541 admitted to the pain clinic, two-thirds were noted to suffer from disabling low back and leg pain. The "typical patient" had undergone three spine surgeries and six myelograms and was "misusing narcotics and psychotropic agents." Approximately one-third of patients were diagnosed with primarily iatrogenic complications from spine surgery. A prospective study of patients admitted from 1979 to 1981 was performed. The average age was 43 years old (range of 19–67 years). The average duration of pain was 7.2 years. The first surgery occurred in the early to mid-1970s. Fifty-three patients (68 %) were involved with disability litigation or receiving disability compensation. This study is the only PLSS study obtained from a pain clinic. Patients were independently evaluated by both a neurosurgeon and orthopedic surgeon. Demographically, this patient cohort represents the "worst of the worst" in terms of persistent pain after lumbar surgery. The authors summarized their findings, noting that *67 % of patients did not meet generally accepted surgical criteria*

per neurosurgery. Twenty-six patients (33 %) met clinical criteria for surgery. Second surgery criteria were met in 18 patients (40 %). The authors found that 52 patients (67 %) had "persistent pain" of with normal preoperative imaging or showed "nonspecific DDD." These patients also had significant "underlying psychiatric abnormalities." Sixteen patients (21 %) had no physical abnormalities to explain their complaint and were classified as normal. Another 16 patients (21 %) had "minor postoperative changes insufficient to cause disabling pain." Twenty-seven patients (35 %) had a complication from the previous surgery. (Sixty-four patients underwent 171 surgeries; patients underwent an average of 2.6 surgeries.) Thirteen patients (17 %) had spondylotic disease and six patients (8 %) received a new diagnosis. The authors found significant psychiatric pathology to which persistent pain after lumbar surgery was attributed: 10 patients (13 %) had a definitive psychiatric diagnosis, 34 patients (44 %) had a maladaptive personality disorder, and 34 patients were normal. Thus 57 % were classified with significant psychiatric disorders. Sixty-seven patients (86 %) experienced reactive depression. In terms of pain medication used, the authors reported extensive aberrant pain medication usage: 58 patients (74 %) "misused narcotics," 9 patients had (12 %) "drug addiction," and 54 (69 %) patients had withdrawal symptoms. In summary, the most common diagnoses given were "normal" in 16 patients (21 %) and "expected postop changes/minor spondylosis" in 16 patients (21 %) and various primary psychiatric disorders. Expected postop changes were defined as: "insufficient to warrant any interventional procedure and did not necessarily explain intractable pain." Therefore in 42 % of patients, no primary diagnosis and/or no "objective physical cause" was identified to explain pain. The remaining most common diagnoses (total 33 %) were attributed to surgical complications: localized epidural scar, 11 patients (14 %), arachnoiditis, 10 patients (13 %), and traumatic neuritis 5 patients (6 %). (The surgical complication rate among this 78 patient cohort was 12 %.) Six patients had an unexpected source of back/leg pain which was incorrectly diagnosed. Viewed historically, Long et al.'s [33] ability to diagnose the cause of persistent pain suffered greatly from lack of advanced imaging (MRI) and diagnostic spine injections; moreover, many of these patients were given an incorrect primary psychiatric diagnosis for pain and labeled as addicts or substance "misusers."

Bernard [34] reported on etiologies of PLSS in 45 patients in a single-author practice audit. His diagnostic workup of the etiology of persistent pain was extremely robust – with extensive diagnostic imaging and an average of 2-year follow-up after surgery for correctable causes of pain. The author reported that intrathecally enhanced CT, MRI, and provocative discography with CT scan were critical to obtain a diagnosis; a single imaging study revealed surgical abnormalities in only 61 % of cases. The following are variables found to be statistically significant in predicting a successful repeat surgery: noncompensable injury ($p<0.04$), return to work ($p<0.002$), and achieving a solid fusion ($p<0.0012$). Variables not statistically significant ($p>0.05$) are as follows: age, absence of litigation, number of previous operations, psychological diagnosis, and postoperative diagnosis. Bernard's study made significant contribution in terms of the role of diagnostic imaging to obtain a specific diagnosis. CT myelography was conclusive in 40 % of cases; however, it missed contained disk herniation at 21 adjacent levels. Diagnosis of contained disks can only be shown by provocative discography with CT scan. Intrathecally enhanced CT scanning picked up lateral recess stenosis and small disk herniations overlooked with CT myelography. MRI use in this study was limited due to the recent introduction in the technology. MRI with gadolinium is highly sensitive and specific for distinguishing scar tissue from disk herniations. MRI did show decrease in T2-weighted signal in patient disks; however, provocative discography was necessary to determine if the disk was a true pain generator. Provocative discography disclosed 25 symptomatic contained disks. Lumbar discography was conclusive in 32/34 patients. The author did not find that a "poor psychological profile" predicted an unsuccessful surgical outcome. The author

stated: "patients with poor psychological profiles who are experiencing pain may improve when the pain is alleviated" [34]. Thirty-six out of 45 patients underwent fusion for their persistent pain. Fusion was undertaken when the workup revealed recurrent disk herniation, contained painful discogenic disease (with positive discogram), or instability. A solid fusion was achieved in 34/36 patients. Achieving a solid fusion predicted a successful outcome ($P<0.0012$). Diagnostic facet blocks or SI joint blocks were not done. It is likely that some degree of symptomatic facet arthropathy was present in this cohort. Fusion addresses more than one pain generator: disk, facet, and instability of the index segment.

Fritsch et al. [2] retrospectively reviewed 182 revisions on FBSS from 1965 to 1990. The authors previously reported a reintervention rate of 10.8 % in 1,500 lumbar diskectomies. A total of 182 revisions were performed on 136 patients; 44 patients (34 %) were revised multiple times. Imaging was used to assist in diagnosis as follows: CT myelography in 54 patients (40 %), CT scan 41 patients (33 %), and MRI 4 patients (4 %). Clearly, MRI now provides much greater diagnostic information than CT scan; moreover, with the dyes previously used in CT myelography, the risk of arachnoiditis was not trivial. Re-intervention was primarily for recurrent or un-influenced sciatic pain and neurologic deficiency. A total of 84 % patients were diagnosed with: true re-occurrent disk herniation (44 %); true reoccurrence and new herniation (22 %); and new herniation (22 %). Four percent (4 %) of patients had epidural fibrosis as a primary diagnosis. The other reason for reoperation was "instability," reported in 12 % of patients based on history, x-ray, CT, and physical exam findings. Laminectomy performed in the primary surgery was reported as the only factor leading to a higher rate of revisions. Epidural fibrosis and instability increased to greater than 60 % in multiple revision patients.

The next quantitative study on the etiology of long-term failures from lumbar spine surgery was published by Waguespack et al. [35]. This study was the first to employ diagnostic spine injections to precisely identify pain generators. A total of 181 patients with persistent pain after lumbar surgery between 1995 and 1997 underwent extensive diagnostic testing including: high-resolution CT scan, MRI, standing flexion-extension x-rays, discography, additional diagnostic spinal injections, and a psychiatric evaluation. With the advent of MRI and improvements in surgical techniques, the incidence of residual stenosis dropped to 29 % (from 58 % in Burton et al. [5]). Four other etiologies were identified as causes of persistent pain: retained/recurrent disk (7 %), painful disk (17 % at surgical level, 3 % at nonoperated level), neuropathic pain (9 %), and instability (5 %). Recognition of the adverse effects of dyes (i.e., iophendylate (Pantopaque®)) used in CT myelography and the introduction of MRI reduced the incidence of arachnoiditis to very rare. Painful internal disk disruption was increasingly recognized as a significant contributor to persistent axial low back pain through the use of discography (albeit controversial).

Two additional quantitative studies, performed by interventional spine physicians, have since been published. Slipman et al. [6] studied 197 patients and identified 23 various diagnoses. He found that 55 % of patients with persistent pain after lumbar spine surgery had a surgical etiology and that 95 % of patients could be provided a diagnosis. The most common diagnoses were: residual stenosis (21.5 %), retained/recurrent disk (12 %), painful internal disk disruption (22 %), and neural fibrosis (14.5 %). DePalma et al. [36] used modern zygapophyseal joint blocks, sacroiliac joint blocks, provocative discography, and hardware blocks to evaluate 28 patients presenting with primarily persistent axial pain after lumbar fusion. Given this referral population bias, certain types of pain patients were likely referred to other centers for treatment of persistent nonsurgical leg pain with spinal cord stimulators. Evidencing improved diagnosis and treatment of PLSS, DePalma et al. [36] did not diagnose any patient with PLSS from residual stenosis, retained/residual herniation, or epidural fibrosis. He reported the following etiologies of PLSS: sacroiliac pain (43 %), painful internal

disk disruption (IDD) (25 %), facet pain (18 %), and hardware pain/soft tissue irritation (14 %). All patients (100 %) received a diagnosis. The early studies by Burton (1981) [37] and Waguespack et al. [35] did not report the sacroiliac joint (SIJ) as a potential pain generator; Slipman et al. [6] reported a 1.6 % incidence of SIJ pain vs. 43 % by DePalma et al. [36]. Painful internal disk disruption incidence stayed relatively stable from 17 % in Waguespack et al. [35], 22 % per Slipman et al. [6], to 25 % with DePalma et al. [36]. All these investigators used provocative discography to diagnose painful internal disk disruption. Facet joint pain also took greater prominence, from no report of this pain generator in the earlier surgical studies to 2.7 % by van Wijk et al. [38] and then 18 % reported by North et al. [39]. Fortin et al. [40] also reported more hardware-related pain than prior investigators (14 %).

38.4 Spinal Fusion and Spine Injections: The Socioeconomic Controversy

To estimate the number of patients per year with persistent pain after lumbar surgery, accurate numbers on the how many spine surgeries are performed per year as well as surgical success rates are needed. In 1997, there were more than 293,000 spine surgeries performed [41] with costs at ~$5 billion dollars. In 2002, not long after the introduction of pedicle screws and the "cage rage" (based on data derived from proprietary sources on the spine industry), more than one million spinal surgeries were being performed per year: 600,000 uninstrumented and 400,000 instrumented cases, respectively [37, 42, 43]. In 2002, orthopedic industry data sources reported a yearly growth rate 3–5 % for uninstrumented cases and 6–8 % for instrumented cases [44–46]. In 2002, the spine market was forecast to compound at 22 % annually due to increased use of spinal instrumentation and aging of the baby boomer generation [37, 46]. By 2004, spinal fusions costs alone generated $16 billion dollars. Researchers critical of the rise in spine surgery noted that the United States had the highest rates of lumbar fusions in the world (see Fig. 38.1), two to five times higher than Sweden, the Netherlands, Australia, and the United Kingdom [47].

Deyo [48] reported a 220 % increase in lumbar fusions between 1990 and 2000 without an apparent improvement in clinical outcomes [49, 50] (see Fig. 38.2). This 2007, "anti-fusion" publication was widely read and disseminated by the US national media, thus placing spinal fusion under intense scrutiny and apparently single-

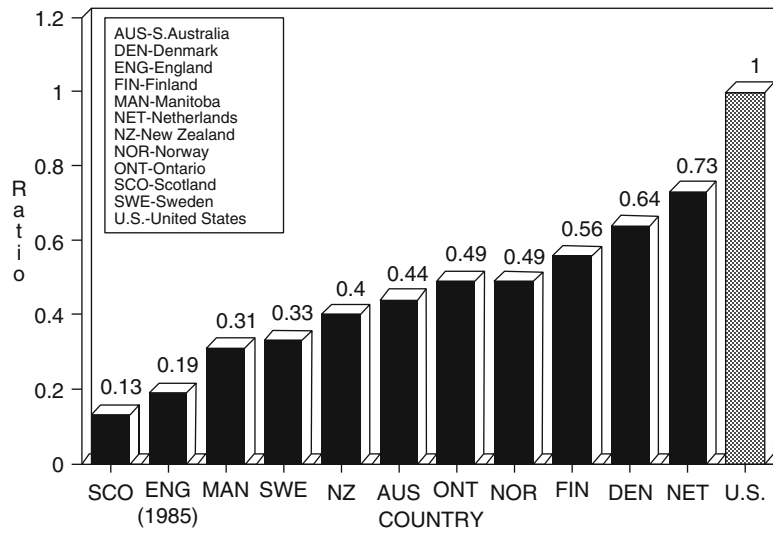

Fig. 38.1 Ratios of back surgery rates in selected countries to back surgery rate in the United States (1988–1989) (Adapted from Cherkin et al. [47])

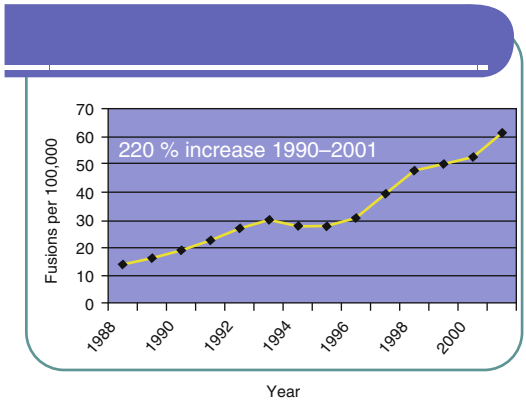

Fig. 38.2 Lumbar spine fusion rates, US National Inpatient Sample (Adapted from Deyo and Mirza [50])

handedly leading to decrease spinal surgery rates in the United States.

Responding to the increase in spinal fusion rates and costs, policymakers and payors began scrutinizing the medical necessity of lumbar fusion, particularly for degenerative disk disease. In 2010, the insurer CIGNA set a new policy for lumbar fusions: to obtain a lumbar fusion, patients had to first participate in a 6-month, physician-directed functional restoration program with behavioral modification and physical therapy [51]. Policymakers and payors are also looking more closely at the risks of spinal fusion. One researcher reported increased mortality after spinal fusion. Juratli et al. [52] examined mortality after spinal fusion among Washington state injured workers from 1994 to 2001. A total of 2,378 patients underwent lumbar fusion; 103 (4.3 %) were deceased by 2004. Analgesic-related deaths were the number one cause of death among this patient group, responsible for 21 % of all deaths. The risk of analgesic-related death was highest in men ages 45–54 years with degenerative disk disease (rate 7.45) who received instrumentation or intervertebral cage devices. Further investigation is needed into this report of increased mortality after lumbar fusion and to determine if patients receiving instrumentation indeed were at increased risk of analgesic-related death versus patient receiving bone grafts alone.

In 2008, beginning with the Great Recession and a confluence of other factors, the number of spine surgeries began to decline. Factors affecting the decline in number of spine surgeries include multiple publications critical of lumbar fusion [48, 50], increased scrutiny from payors and policymakers on spine surgery rates, costs and outcomes, and increased scrutiny on physician-owned distributorships. By 2011, a total of ~465,000 fusion operations were reported according to the Agency for Healthcare Research and Quality [51]. The research firm GlobalData reported that about 87 % of spinal procedures in 2013 were fusions [51].

According to spine industry analysts, a continued reduction in the number of spinal fusions per year is projected. The Sunshine Act (2013) is expected to inhibit collaboration and innovation between spine surgeons and industry [53]. GlobalData lowered its predicted compound annual growth rate for spinal fusions from 10 % annually to 5 % through 2020 due to multiple factors [54]: stricter reimbursement policies with surgeons reporting more denials for fusion, healthcare reform with mounting economic pressures, loss of physician autonomy over patient care, and a shifting focus to motion-preserving spinal technologies and intradiscal biologics. In January 2014, the Millennium Research Group reported that the global market for spinal *non-fusion* technologies is expected to triple in size through 2022, surpassing $1.6 billion, driven by emerging markets in Asia Pacific, Brazil, India, and China [54].

Spine interventionists have also come under increasing scrutiny and control due to dramatic increase in spine injections over the last decade. Interventional pain management (IPM) techniques for chronic spinal pain increased markedly from 2000 to 2011 based on data from the CMS (Centers for Medicare & Medicaid Services) [55]. IPM techniques overall increased by 228 % over this interval or 177 % per 100,000 Medicare beneficiaries (see Fig. 38.3). The population growth of this demographic during this interval was 18 %. The highest increases were noted for facet injections and sacroiliac blocks with a total increase of 386 % and 310 % per 100,000 beneficiaries, respectively. Other types of injections reported the following percent increases (total and per 100,000 Medicare beneficiaries): 168 % and 127 % for epidural and

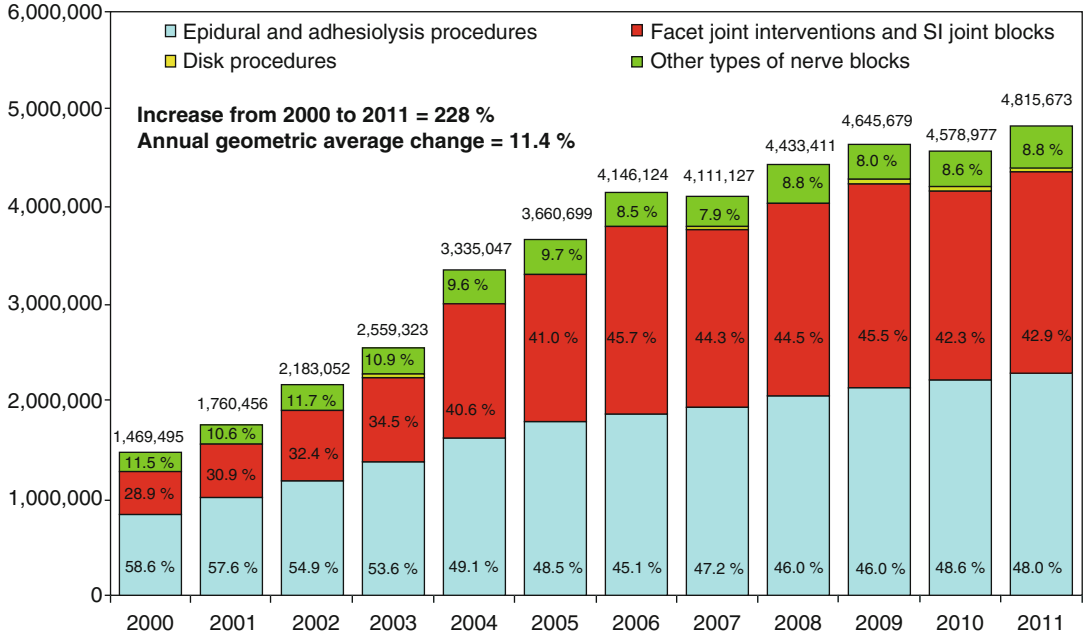

Fig. 38.3 Illustration of distribution of procedural characteristics by type of procedures from 2000 to 2011 (Adapted from Manchikanti et al. [55])

adhesiolysis procedures, 150 % and 111 % for other types of nerve blocks, and 28 % and 8 % for percutaneous disk procedures. The geometric annual average was 11.4 % for all IPM procedures with facet injections showing the highest increase at 13.7 % per year.

In 2008, the Office of the Investigator General (OIG) of the US Department of Health and Human Services focused its attention on this explosive rate of growth. Sixty-three percent (63 %) of injections did not meet criteria for medical necessity. Subsequently, facet joint injections have declined by 6 % since 2008. A recent audit by Noridian reported 60–95 % of facet joint injections to be medically unnecessary [56]. The United States Office of Inspector General (OIG) in 2008 [57] reported that Medicare paid over $2 billion in 2006 for IPM procedures. These investigators reported that 63 % of facet joint injection services and 34 % of transforaminal epidural injections did not meet the medical necessity criteria, leading to a total of $175 million of improper payments between 2003 and 2007.

The spinal interventionalist faces many of the same challenges as spine surgeons from payors and policymakers. IPM physicians have to take into account the risks and technical difficulties of with each procedure while keeping in mind the external payor pressure from CMS and the current healthcare cost reform environment. One of the goals of this chapter is to provide the high-quality evidence from the literature for the appropriate and efficacious use of diagnostic and therapeutic spine interventions in the PLSS patient.

38.5 Lumbar Spinal Surgery Outcomes: A Brief Review

Spine surgeons and spine interventionalists are under increased scrutiny for spine surgery and spine injection indications and outcomes. Increasingly, payors and policymakers are dictating how surgeons should diagnose and treat chronic low back pain patients. Spine specialists and their patients will be best served by an

evidence-based diagnostic and therapeutic approach to spinal pain to rebut critics. Spine surgeons and interventionalists must independently establish transparent, rigorous indications for spine surgery, continue technical refinements, and publish high-quality literature – or spine care will be increasingly withheld from patients. The lower the reported success rate for primary and revision surgeries, the less likely payors and policymakers will pay for spine surgery. A self-critical look at the definition of success rates is also needed among spine specialists. It is no longer sufficient for an author to personally ask if a patient is satisfied with their surgery. A surgeon's or spine interventionalist's results are considered more robust and therefore unbiased, if independent assessment of success is undertaken, along with inclusion of a range of primary outcomes, including: functional status (ODI), reduction in medication use, and return to ADLs/work. Evidence now is also weighted by type of study: retrospective reviews are ranked much lower than randomized controlled trials. In plain terms, to a payor or policymaker, a patient who is not a success is a failure; thus, that term is used in this chapter. However, among spine specialists it is well known that even partial pain relief, when a patient suffers from intractable pain, is meaningful.

Based on literature from the 1960s to 1980s, FBSS is quoted to affect up to 40 % of patients undergoing lumbar spinal surgery [39]. Based on recent data using the most stringent criteria for success, reports of persistent lumbar and/or leg pain after lumbar surgery can range from 20 % to 67 % for microdiskectomy and lumbar fusion, respectively [58, 59]. Patients undergoing microdiskectomy for primary leg pain have the best outcomes. Fusion outcomes vary considerably. Reports of success also vary considerably according to the "view" of the publishing authors, i.e., whether the authors are considered to be "pro-spine surgery" or not. Some surgeons also are very conservative in their use of fusion for DDD. Each study must be scrutinized carefully, particularly in terms of how the authors define "success." The true prevalence of PLSS is difficult to assess because of the heterogeneous nature of the syndrome, variable definitions of success, and access to public and proprietary data sources for the number, types, and outcomes of surgeries performed each year. Both chronic spinal pain and persistent pain after lumbar surgery present huge individual and societal costs. In an era of increasing healthcare restructuring and "reform," spine specialist are "awash" in "guidelines" and increasing restrictions on spine surgery and spine injections.

Regarding surgery outcomes, all interested parties question spine surgery studies which report greater than 90–95 % success rates. When Asch et al. [58], a neurosurgeon, used more rigorous criteria for assessing success after microdiskectomy among his patients, he reported leg pain relief (per VAS) at 80 % and low back pain relief at 77 % (success per VAS score defined as pain 0–4; VAS failure pain 5–10). These figures mean 20–23 % of microdiskectomies could be classified as unsuccessful. Santiago-Dieppa et al. (2014) reported on outcomes in older patients with spinal stenosis after non-instrumented arthrodesis, finding a ~60 % incidence of persistent back pain and leg pain with 31 % of patients requiring reoperation over the 7-year follow-up [60]. Regarding lumbar fusion, Fritzell et al. [61] reported a 63 % success rate with 37 % of patients who were unchanged or worse. Using very strict success criteria, from surgeons who perform fusion for DDD as a last resort, success rates are reported as low as 33 % and 43 % [59, 62].

The definition of success after spine surgery remains controversial, with marked variation in criteria applied often lacking independent review. Currently "success" in spine surgery is primarily being defined by authors well known for taking a conservative approach to fusion for DDD. Carragee and Cheng [63] performed a study on 165 patients undergoing spinal fusion to determine a preoperatively determined, patient-acceptable definitions of minimally acceptable outcomes for success. In summary, the patient-acceptable, minimal clinical important difference (MCID) was: at least a 3/10-point decrease in pain, an improvement in Oswestry Disability Index (ODI) of 20 or more*, discontinuation of opioid medication, and return to some occupational activity. Of note, increasing the definition of a successful functional outcome

from an 11-point ODI increase to a 20-point increase is appropriate. Historically, spine surgery studies have only set the bar at an 11-point change, which is not a meaningful functional improvement. A 20-point change in ODI is also the most likely to improve a patient by at least one disability grade. The ODI scoring system includes a description of degrees of disability relating to scores. Scores from 0 % to 20 % indicate minimal disability; 20–40 %, moderate disability; 40–60 %, severe disability; 60–80 %, crippled; and 80–100 %, bedbound or exaggerating [64]. Both the Asch and Caragee's studies are commendable for increasing the bar for a successful functional improvement by raising the ODI to a 20-point change.

Using the most rigorous composite definition of success to date in the surgical literature, Mirza et al. [59] reported success rate of 33 % for spinal fusion for painful internal disk disruption/discogenic pain, thus obtaining a failure rate of 67 % [59]. Published lumbar fusion failure rates range from 30 % to 67 % [60–62, 65–68]. Reports of surgical success rates have come under increasing scrutiny for setting the bar to low [58]. As the bar for success is raised, often by opponents of spinal fusion, published success rates fall. It is generally accepted that success rates for spinal fusion are best for spondylolisthesis (78–91 %) as opposed to degenerative disk disease [62]. Mirza et al. [59] are well known for taking a more "conservative" approach to spinal fusion for DDD. A statistical "composite" definition of success was defined as 30 % improvement in Roland Score, 30 % improvement in pain, and *no* opioid medication use and *working* (if relevant). This definition for success appears to be the most stringent presented to date in the spine literature. However, despite the high-bar, surgical intervention was superior to nonsurgical intervention at 1-year. Nonsurgical treatment obtained a 15 % success rate. A more detailed survey of additional lumbar surgery studies is discussed later in the chapter.

The authors of this chapter report the data from the literature with an attempt to provide a "balanced" view of current evidence, from the spectrum of both "positive" and "negative" spine surgery publications, as well as publications between these extremes. This is not a critical review or systematic review of the evidence. Every attempt has been made to identify the group publishing the report as knowing the authors' surgical approach typically predicts the outcomes they will report. Across the board, outcome reporting obtained by the operating surgeon from the patient underreports pain; therefore, careful attention has been paid to the demographics of the study and the definition of success. Throughout the orthopedic community, surgical outcome reporting has become more stringent out of medical necessity and increased scrutiny and external pressure from non-physician stakeholders in the age of healthcare reform. It is now standard to include functional outcomes (Oswestry Disability Index), medication intake, and return to work. Ultimately, this expansion of the definition of success will benefit both patient and surgeon. To estimate the number of patients with persistent low back and/or leg pain, current outcome data on the most commonly performed surgeries in the lumbar spine are reviewed for: microdiskectomy, spinal stenosis decompression, lumbar fusion, and lumbar total disk arthroplasty. To arrive at best estimates of success after lumbar surgery, this brief focused review of the literature includes recent systematic reviews, randomized controlled trials, and large cohort studies.

38.6 Lumbar Microdiskectomy: Success Rates

For lumbar microdiskectomy, patient satisfaction rates in the literature have varied from 40 % to 98 % [69] with microdiskectomy having an 88–98 % satisfaction rate over open diskectomy. However, in this same study, patient outcomes are not as robust when reported by grade. Patients reported the following outcomes after microdiskectomy: excellent (39 %), good (34 %), satisfactory (19 %), and failed (9 %). Moreover, the longer patients are followed up after spine surgery, the greater decline in satisfaction. Fritsch et al. [2] reported on results of 182 patients undergoing revision diskectomy between 1965 and 1990. In 80 % of the patients, the results were satisfactory in short-term evaluation,

decreasing to 22 % in long-term follow-up (2–27 years).

Asch et al. [58] were critical of publications reporting greater 90–95 % success rates after microdiskectomy. The authors concluded that outcome success rates of 75–80 % are more "realistic" than studies claiming greater than or equal to 90–95 % improvement. A prospective study of surgical outcomes in 212 consecutive patients was performed. Independent examiners collected and analyzed outcome data. The author points out that potential bias may be introduced into the literature when outcomes are reported by the operating surgeons and not an independent examiner. Results obtained from independent observers are typically less favorable. More recently, important functional outcome measures have been added to strengthen postsurgical assessments. Asch et al. [58] reported the following: leg pain relief, 80 %; back pain relief, 77 %; improvement in Oswestry Low Back Disability Index, 78 % (ODI <40); satisfaction with surgery results, 76 %; return to normal daily activities, 65 %, and, return to work, 61 %. Worker's compensation status and increasing age had negative effects on outcome. Based on this data, 20–25 % of patients would have persistent pain after microdiskectomy. Asch et al. [58] estimates are consistent with some of the most recent figures on outcomes after microdiskectomy as reported by other authors. Klessinger [70] reported a 25 % (120/479) prevalence of persistent axial low back pain after lumbar microdiskectomy. A 9 % reoperation rate was reported for recurrent lumbar disk herniation.

McGirt et al. [71] performed a meta-analysis of 54 studies with 13,359 patients comparing incidence of short-term and long-term (2-year) low back or leg pain after aggressive (AD) versus limited diskectomy (LD) between 1980 and 2007. After 2 years the reported incidence of recurrent back or leg pain was 11.6 % for LD versus 27.8 % for AD or a 2.5-fold decrease in persistent pain among patients undergoing limited diskectomy. Aggressive diskectomy involves aggressive removal of the herniated disk material with curettage of the remaining disk. The limited diskectomy technique involves removal of the disk fragment only with minimal incursion into the disk space. The AD technique has been criticized as leading to accelerated disk degeneration with loss of disk height and increased incidence of persistent low back and/or leg pain. Conversely, the LD technique has been criticized for an increased incidence of recurrent disk herniation (RDH). Overall, this paper suggests that ~10–30 % patients may have persistent axial low back pain or leg pain based on the type of microdiskectomy. Repeat surgery is less successful, and according to several studies, only 60–82 % of patients with recurrent disk herniation improve after surgery. In patients who have only epidural scar tissue, the success rate of reintervention is as low as 17–38 % [72, 73]. Recently, Lurie et al. (2014), known to belong to a conservative care spine research group, reported 8-year follow-up results from the Spine Outcomes Research Trial (SPORT) for surgical versus nonsurgical treatment for lumbar disk herniation. Researchers found superior outcomes for pain, physical functions, and ODI in the surgical group [74].

38.7 Non-instrumented Lumbar Fusion for Spinal Stenosis: Success Rates

Santiago-Dieppa et al. [60] reported long-term (median follow-up 7.7 years) outcomes of 376 patients undergoing non-instrumented lumbar arthrodesis at a single institution over a 20-year period. The primary outcomes were: symptom resolution, development of adjacent segment disease (ASD), and need for reoperation. The patient's mean age was 61 years at presentation with neurogenic claudication due to multi-level spinal stenosis. At follow-up, the presence of back pain decreased from 91.5 % to 61 %; radiculopathy decreased 81–58 %. The cumulative rate of ASD was 18 % (69 patients). The reoperation rate due to non-improvement or worsening of symptoms was 31 % (115 patients), necessitating additional stabilization techniques. Overall, 60 % of patients continued to have back pain,

42 % of patients continued to have leg pain, and 31 % needed reoperation.

38.8 Lumbar Fusion: Success Rates

Studies vary widely regarding lumbar fusion success rates. Rates of success also vary widely based on diagnosis and on the definition of success. Complications after lumbar fusion include: instrument failure (7 %), iliac crest bone-donor site pain (11 %), neural injuries (3 %), and pseudoarthrosis (15 %) [75]. Secondary surgeries for persistent pain or surgery-related complications are reported in 20 % of patients after lumbar surgery [76]. Lumbar spinal surgery success rates drop to 30 % after a second spine surgery, 15 % after a third surgery, and approximately 5 % after the fourth surgery [77].

Philips et al. [65] published a systematic review of 3,060 patients undergoing lumbar spine fusion for CLBP due to degenerative disk disease (DDD). The weighted average improvement in back pain was 37/100, Oswestry Disability Index (ODI) 22, and 12 points on the SF-36 physical component scale. Patient satisfaction averaged 71 %. These results indicate that ~30 % of patients were not satisfied. The reoperation rate was 12.5 %, with 9 % at the index level.

Caragee et al. [62] compared outcomes of fusion for lumbar DDD versus unstable spondylolisthesis. In the spondylolisthesis group, 23 of 32 patients (72 %) met the highly effective success criteria compared to 8 of 30 (27 %) of the presumed discogenic pain cohort. The minimal acceptable outcome was met in 29 of 31 patients (91 %) in the spondylolisthesis group versus 13 of 30 (43 %) of the discogenic pain group. From this data approximately 10 % of patients would be considered a failure after fusion for spondylolisthesis versus 57 % for presumed discogenic pain.

In a randomized controlled trial with 2-year follow-up, Fritzell et al. [61] reported fusion to be superior to usual physical therapy care directed by a family practice doctor in patients with severe axial low back pain of an average of 8 years. All primary outcomes measures favored surgical intervention with statistically significant improvements. Back pain was reduced by 33 % (64–43) or 19-point/~decrease of 2-point VAS in the surgical group vs. 7 % (63–58) in the nonsurgical group. ODI score was reduced 25 % (47–36) or 11 points. In the surgical group, a total of 63 % of patients rated themselves as "much better" (29 %) or "better" (34 %) vs. 29 % in the nonsurgical group. Among fusion patients 29 % rated themselves as "much better" vs. 14 % in the nonsurgical group. The net back to work rate was in favor of surgical treatment versus usual care group, 36 % vs. 13 %, respectively. In total, 37 % of surgical patients failed to respond to the intervention and rated themselves as unchanged (24 %) or worse (14 %). On every metric, surgical patients did better than nonsurgical patients. In patients with an average of 8 years pain, cure is not likely; the objective instead is to meaningfully reduce the amount of the patients' pain. In summary, substantial improvement was seen in 25–33 % of surgical patients vs. 4–8 % of nonsurgical patients. In addition, depression was reduced by 20 % in the surgical group vs. 7 % in the nonsurgical group. Of note, 28 % of patients randomized to usual care ultimately decided to undergo surgery at 2 years. This study reported surgical treatment of DDD as superior to usual care, 63 % of patients reported being "much better" or "better," leaving 37 % of patients with no improvement or worse pain. Success in this study was a VAS decrease in 2 points (i.e., from six to four) and an ODI decrease of 11 points. The criteria for success were minimally based compared to more rigorous independent outcome measures. Overall, 29 % of patients rated themselves as much better, 34 % better, 24 % unchanged, and 14 % worse. This data suggests a 38 % failure rate. Three other RCTs, comparing fusion to intensive rehabilitation [78] and cognitive behavioral therapy with exercise [66, 68], did not show fusion to be a superior intervention.

Brox et al. [66] compared lumbar fusion with posterior transpedicular screws (not anterior/posterior fusion) to cognitive behavioral therapy

(CBT) and exercise at 1 year, using the ODI as the primary outcome. Patients were ages 25–60 years with low back pain lasting longer than 1 year, imaging evidence of disk degeneration at L4–5 and L5–S1, and ODI score of at least 30 points. The average age of subjects was ~43 years, and duration of low back pain ~10 years; working was 24 % fusion group and 22 % CBT/exercise group; and 70–80 % of patients were either on sick leave, in rehabilitation, or on a disability pension. In the Norwegian healthcare systems, individuals on sick leave more than a year are entitled to a rehabilitation benefit or a disability pension. Approximately 50 % were taking analgesics and ~40 % were smokers. In terms of medical comorbidities, approximately ~70–80 % of subjects had comorbidities not specifically described. We know from the SPORT study that subjects with comorbidities such as diabetes and depression have inferior surgical outcomes [66]. Subjects were randomized to fusion or cognitive behavioral therapy. No difference was observed in ODI between groups at 1-year follow-up with only a 3 % lost to follow-up rate. ODI was reduced from 41 to 26 (15 points) after surgery which was not statistically significant from cognitive behavioral therapy (CBT) and exercise 42–30 (8 points). An independent observer rated success, reporting 70 % after surgery and 76 % after CBT/exercise. The early complication rate in the surgical group was 18 %. Seventy percent (70 %) success would give a 30 % failure rate. Brox et al. [68] also studied the 4-year follow-up results. Fifteen (23 %) patients assigned to surgery underwent reoperation. ODI decreased from 14 points, from 44.1 to 29.7 which was not statistically significantly different between groups. Both randomized groups reported less pain and better function at 9 years vs. baseline; more operated patients were on pain medication and not working. In 2006, Brox et al. [67] published another study comparing instrumented fusion with cognitive behavioral therapy plus exercise in patients with CLBP greater than 1 year. Patients had already undergone a diskectomy and had persistent pain. The primary outcome measure was a reduction in ODI. The fusion group averaged a 9-point ODI decrease from 47 to 38 versus the CBT/exercise group with a 13-point decrease from 45 to 32. At 1-year follow-up, such small ODI decreases represent an unimpressive outcome measure for defining success. The authors reported ~50 % success rate in both groups. This would give a 50 % rate of patients with persistent pain after instrumented lumbar fusion for persistent pain after diskectomy. At 11 years, Mannion et al. [79] were to perform long-term follow-up at 11 years and no difference was found in ODI (−0.7 vs. −0.8) or patient self-reported outcomes between fusion and CBT/exercises groups, respectively. The study had a very high lost to follow-up rate of 45 %. Of note, by 4 years, 25 % of surgical patients underwent reoperation. In summary, in the various RCTs by Brox et al., their early study reported 1-year failure rates or unchanged/worsened pain rate of 30 %; the midterm study reported a "failure rate" of 50 %.

Recently, a community-based study comparing surgical versus nonsurgical treatments for discogenic back pain was published by Mirza et al. [59]. This research group is well known for opposition to the increased rates of lumbar fusion and the use of fusion to treat discogenic pain [50]. Mirza et al. [59] enrolled 495 patients; 86 patients (17 %) underwent surgery. Grading success with a never-before utilized composite criteria (30 % improvement in Roland score, 30 % improvement in pain, no opioid pain medication use and working – if relevant), the 1-year success rate was 33 % for surgery and 15 % for nonstructured conservative care. Longer-term follow-up is critical to assess outcomes in the surgical group. Based on 1-year follow-up, 33 % of patients had a successful outcome and 67 % of patients did not meet success criteria.

38.9 Lumbar Disk Arthroplasty: Success Rates

Our data on total disk arthroplasty is limited. Summarized here are two RCTs comparing TDR to circumferential fusion and two different TDR implants. Zigler et al. (2012) reported 5-year results of a prospective, randomized trial compar-

ing circumferential arthrodesis to the ProDisc L for single-level DDD [80]; TDR was noninferior to fusion by a 12.5 % margin. Seventy-seven (77 %) patients in both groups were satisfied with surgery. Both groups had a 48 % decrease in VAS scores and similar ODI decreases [80]. These outcomes suggest similar outcomes between TDR and fusion patients. Patients' satisfaction was reported as 77 % among both groups. Eighty-three percent (83 %) of TDR patients vs. 68 % of fusion patients stated they would have surgery again.

Guyer et al. (2014) compared two different disk arthroplasty implants with a 2-year follow-up [81]. Success was defined by decrease in VAS, 15-point decrease in ODI, no complications, and lack of reoperation. Success rates were similar: 68 % for the Kineflex L-disc versus 67 % for the Charité Disk. At 2-year follow-up, greater than 90 % of patients in each group were satisfied with outcome. Reoperation was performed in 10.3 % of the investigational group versus 8.4 % of the Charité group. A total of 32–33 % of patients did not meet criteria for success. Likely, the disparity between the high self-reported satisfaction rate versus traditional outcome metrics is due to the novelty of the artificial disk. This phenomenon is not uncommon with the introduction of new drugs or medical devices.

38.10 An Algorithmic Approach to the PLSS Patient

An algorithmic approach to working up residual pain after lumbar spine surgery is useful. The spine surgeon or interventionalist utilizes history, physical exam, imaging, and diagnostic/therapeutic spine injections to identify and treat persistent pain after lumbar surgery. Increasingly, spine and pain specialists are also carefully scrutinizing patient's comorbidities as treatment of these conditions may help optimize patients for better surgical outcomes.

There are various approaches to diagnosing the cause of PLSS: time from surgery, predominance of back versus leg symptoms, and the three-column approach. Briefly, Crock [82] described two postsurgical failure patterns: "outright failure" and "failure following initial temporary relief." He emphasized that outright failure is usually related to wrong diagnosis. Immediate failure can also be due to technical error, instrumentation failure, or residual disk. There is temporary relief followed by pain within a few weeks: recurrent disk herniation or infection. There is onset of pain more than 6 months after surgery: re-herniation/new herniation, posterior column pain (facet/SI joint), or epidural fibrosis. Longer-term failures are as follows: loss of stability or stenosis at the surgical site or adjacent site, adjacent facet pain, SIJ pain, painful internal disk disruption (IDD),

Table 38.3 Causes of failure after spinal fusion

Time	Back pain predominates	Leg symptoms
Early (weeks)	Infection	Nerve impingement by fixation device or cement
	Wrong level fusion	
	Insufficient levels fused	
	Psychosocial distress	
Midterm (months)	Pseudoarthrosis	Fixation loose
	Disk disruption	Early adjacent disk degeneration
	Early adjacent disk degeneration	Graft donor site
	Inadequate reconditioning	
	Graft donor site	
Long term (years)	Late pseudoarthrosis	Disk with pseudoarthrosis
	Adjacent level instability	Adjacent level stenosis
	Acquired spondylolysis	Adjacent level disk
	Abutment symptoms	Stenosis above fusion
	Compression fracture above fusion	

Adapted from Kostuik's failures after spinal fusion 1997b [83]

Table 38.4 Algorithmic approach to the most common causes of residual lumbar and/or leg pain after lumbar surgery by column

Column	Posterior	Middle	Anterior
	Facet joint	Radicular pain/	Discogenic pain: painful IDD at surgery site or adjacent level
	Sacroiliac joint	Radiculopathy	Recurrent/residual disk herniation
	Soft tissue: "fusion disease"	Epidural fibrosis	Pseudoarthrosis
	Myofascial pain	Transition syndrome/vertical disease	Adjacent segment disease
		Arachnoiditis	

and pseudoarthrosis. Kostuik [83] (see Table 38.3) summarizes the causes of failure after fusion by time and predominance of back versus leg symptoms. Another straightforward approach is to divide the spine into three columns: posterior, middle, and anterior (see Table 38.4).

38.11 History

Accurate history can help identify the cause of pain in many cases. The patient should describe their pre- and postoperative pain in great detail (best to worst pain rating, intermittent versus constant pain, nocturnal pain, pain aggravating or relieved by certain positions, etc.), particularly if there is a change in quality or location. The qualities of nociceptive nerve pain and neuropathic pain are well known to the surgeon. With the 2013 publication of Hannah Albert's work on Modic type I changes [84], greater attention is being paid to patient's description of constant, compelling, deep, aching axial pain that does not respond to or is aggravated by usual conservative care such a physical therapy. Dr. Albert asserts that Modic type I changes on MRI are due to disk and endplate infection with *Propionibacterium acnes* which may be treated with 100 days of oral amoxicillin-clavulanate three times a day.

The examiner should determine whether the patient has primarily axial lumbosacral pain or leg pain or a combination. The workup for primary persistent lumbar pain is different for primary leg pain. The emerging standard for persistent leg pain (with no correctable surgical cause) is referral for spinal cord stimulator. Some consider spinal cord stimulation a first-choice treatment in PLSS due to lumbosacral fibrosis [85]. The reader is referred to outside sources for a more detailed description of this technology. In the United States FBSS is the most common reason for the use of spinal cord stimulation therapy [86]. The analgesic efficacy ranges from 52 % to 72 % and a recent analysis of the national Italian register of implantable systems found that 81 % of the patients reported a positive assessment for pain control with a lowering of drug needs in 71 % of the positive responders [87].

If axial back pain is the principal complaint, the disk, facets, and SI joint must be considered; painful hardware may also be an issue. Revel's criteria has not been validated or reproduced for predicting facet pain based on correlation with diagnostic facet blocks. Revel's criteria for facet pain (5/7) are: age greater than 65 years and pain not exacerbated with coughing, not worsened with hyperflexion, not worsened by forward flexion, not worsened when rising from forward flexion, not worsened with extension-rotation, and well relieved by recumbency. Revel's results have never been duplicated; moreover, to validate his history questions specific to facet pain, he only performed a single diagnostic anesthetic block [88]. The false-positive rate for a single facet block in this setting is 49 % [89]. The gold standard for the diagnosis of facet pain is dual, comparative diagnostic blockade. However, the finding of axial lumbosacral pain below L5 is a sensitive finding on history and is specific for sacroiliac pain and validity by dual-controlled SI joint diagnostic blocks [90]. The examiner should therefore endeavor to identify lumbar versus sacral pain when evaluating axial pain.

Medical comorbidities should be reviewed. Anecdotally, the first author of the study evaluates all chronic low back pain patients, potential primary lumbar surgery patients, and PLSS patients for presence of obesity, prediabetes/type 2 diabetes mellitus, visceral adiposity, metabolic syndrome, subclinical hypothyroidism, hypovitaminosis D, hypogonadism, andropause, menopause, and osteopenia/osteoporosis. If hardware is being considered for a fusion or if the patient has pseudoarthrosis, a recent DEXA scan for bone density is useful to assess bone health. The lower the bone density, from osteopenia to osteoporosis, the less the bone will be able to protect the disk and the greater risk for increased axial loading on the disk and posterior column as well as soft tissues (muscles, fascia, and ligament dysfunction). Hardware is also more likely to fail in osteopenic/osteoporotic patients, both women and men. Many women undergoing back surgery have entered menopause and no longer have the bone protection afforded by estrogen. Surgeons should take a careful history to see if their female patients have undergone surgery and entered surgical menopause or normal menopause. The average age for women to enter menopause is 51 years old. Estrogen is a key hormone for bone metabolism for men and women. Menopause is associated with a loss of bone mineral density (BMD): 10-year cumulative loss was 11 % in the lumbar spine. Serum estradiol (E2) concentrations predict fractures. Older women with total E2 levels <5 pg/ml have a 2.5 increased risk of hip and spine fractures independent of age and body weight; similar associations are found in men [91].

Similarly, we now appreciate that men also experience an age-related decrease in testosterone. Surgeons may consider asking their male patients about loss of vigor, depression, reduced sexual function, and muscle weakness to assess if their male patients have entered andropause. From a lab standpoint, hypogonadism is defined by some authors as a total testosterone less than 400 ng/dL; total testosterone less than 275 ng/dL is frank hypogonadism. Men with suboptimal testosterone also appear to be more prone to osteopenia/osteoporosis. Reduced muscle mass may also impair spine stability and efficacy of postoperative rehabilitation. We are awaiting the 2015 publication results of the Testosterone Trial which is testing the hypothesis that testosterone treatment of men in unequivocally low total serum testosterone (<275 ng/dL) will increase bone density of the spine [91–93].

Surgeons already make sure that their patients stop smoking for at least 6 months or quit altogether; NSAID use is also discouraged. New research shows that there is much more surgeons and bioidentical hormone specialists can do to help achieve optimal outcomes in surgery. This is clearly an emerging field of research. Koerner et al. [94] identified patient factors associated with the best outcome after diskectomy from the Spine Outcomes Research Trial (SPORT). Patient factors associated with the largest improvement in ODI at 4 years with either surgical or nonoperative treatment included: higher baseline ODI, body mass index (BMI) < 30, not being depressed, being insured, having no litigation or worker's compensation claim pending, and having symptoms for <6 weeks. Patients with diabetes did not benefit with surgery versus nonoperative care. Knowledge of these factors is useful to both patient and surgeon whether further surgical interventions are undertaken or not. Psychosocial issues, depression, anxiety, and so forth should be identified and treated as they can make the primary organic problem more difficult to diagnose and treat. When treating persistent lumbar and/or radicular pain after lumbar surgery, it is prudent to identify and modify as many risk factors as possible: abnormal lab values, obesity, prediabetes, type 2 diabetes, alcohol intake, smoking, depression and hormonal imbalances, and depression. Anecdotally, the first author's preference is the use of bioidentical hormones instead of synthetic hormones. Some surgeons may consider checking labs to help stratify and optimize their patients for surgical success or sending their patients to a specialist in bioidentical hormone replacement (a full discussion of the pros and cons of bioidentical hormone replacement versus synthetic hormones or traditional agents used to increase bone density is beyond the scope of this chapter). Briefly, some of the most interesting

findings in terms of vitamin and hormone function will be presented. The face validity of optimizing hormonal health and thus tissue health, bone strength, and healing capacity (especially under surgical stress such as fusion) would seem to make sense in terms of decreasing the incidence of persistent pain after lumbar surgery. Anecdotally, when potential primary surgery as well as postsurgical candidates present to the first authors' practice, they undergo a complete hormone and lab panel, to attempt to remove any barriers to healing. The first author has found the abovementioned medical comorbidities to be much more common in spine patients, especially patients with persistent pain after lumbar surgery. This is an area of research in which little research has been published.

Chronic pain patients, including low back pain patients, are known to have insufficient vitamin D 25-hydroxy (vitamin D3) [95, 96]. Severe to moderate deficiency of vitamin D25-OH, defined as <10 ng/mL, was statistically significantly associated with Modic type I changes, with an odds ratio of 0.30 (95 % CI 0.12; 0.75). The other two-thirds of patients had vitamin D25-OH >20 ng/mL which these authors considered "normal." Many authors disagree with this as the cutoff for normal, let alone "optimal" for bone and muscle healing. Dissenting authors have defined optimal as >50 ng/mL [97].

Briefly, we will discuss vitamin D3 as it is linked to bone health, falls prevention, immune function, cancer protection, and type 2 diabetes. However, controversy remains about the definition of insufficient versus optimal; thus the normal range is defined from 20 to 100 ng/mL. Deficient is based on the author ranging from <20 to <50 ng/mL. Great interest is emerging in having an "optimal" versus "normal" level of vitamin D. Anecdotally, some physicians work to optimize modifiable factors such as vitamin D3 level and prevention of type 2 diabetes, so patients can achieve the best outcomes if undergoing spine surgery. The optimal level for bone health is >50 ng/mL. According to the Third National Health and Nutrition Examination Survey, 61 % of white and 91 % of black Americans suffer from vitamin D insufficiency (25[OH]D <32 ng/mL). Recent studies have demonstrated that a minimum 25(OH)D level of 32 ng/mL is necessary for optimal protection from fracture and intestinal absorption of calcium. Calcium supplements for bone health will be ineffective if a patient is vitamin D deficient [98]. If a patient has cancer or heart disease, some studies recommended obtaining a blood level of 70–100 ng/mL. An intake of 2,000 IU of vitamin D3 will raise the blood level by 20 ng/mL over several months. Some patients may need to take 5,000–8,000 IU of vitamin D3 to obtain these blood levels. The current US Recommended Daily Allowance (USRDA) of 600 IU of vitamin D3 per day is considered inadequate by many; the RDA in Canada is 800–2,000 IU/day [99]. It may be prudent for surgeons considering fusion to optimize vitamin D 25-hydroxy levels to at least 50 at least 3 months before surgery. Lastly, the combination of any low sex steroid hormone (estrogen/testosterone) and 25-hydroxy vitamin D is associated with an increased fracture risk [91].

The majority of patients with PLSS are also on opiate medication which depresses the hypothalamic-pituitary-adrenal (HPA) axis. Valverde-Filho et al. (2014) studied chronic spinal and oral-morphine induced neuroendocrine and metabolic changes in non-cancer patients referred to a pain center [100]. The authors compared three groups, patients with intrathecal morphine pumps (0.2–10 mg/day), patients on oral opiates (60–120 mg/day), and patients receiving non-opioid analgesics. All patient groups experienced improvement in pain scores. Libido, reduced potency, hot flashes, and menstrual cycle dysfunction occurred more often in opiate groups vs. the non-opioid group. Low total testosterone (hypogonadotrophic hypogonadism) was significantly more prevalent in the morphine groups (58 % and 70 %, respectively) vs. non-opioid group (17 %). This group reported clinical symptoms concordant with lab findings. Total cholesterol >200 mg/dL and high-sensitivity CRP (C reactive protein) was significantly more frequent in opiate groups. Lastly, total bone mineral density was below normal in men receiving spinal morphine ($p = 0.014$). Growth hormone, thyroid-

stimulating hormone, and adrenocortical hormones were also suboptimal, but did not reach the same degree of statistical significance.

This author does not recommend statins due to the negative effects on nerve and muscle. At a minimum, statin doses should be the lowest possible "effective dose." In meta-analyses of RCTs, muscle adverse effects (AEs) are greater with statins versus placebo. Factors such as metabolic syndrome, thyroid disease, and genetic mutations linked to mitochondrial dysfunction can amplify AEs of statins. There is emerging evidence of additional statin-induced AEs such as neuropathy and cognitive impairment [101]. The reader is encouraged to read emerging literature in this area to obtain optimal surgical outcomes in patients, especially patients with persistent neuropathic or radicular pain after lumbar surgery.

38.11.1 Physical Exam

For the PLSS patient, the surgeon repeats a detailed preoperative spine exam with a few additions. Comparison of pre- and postoperative exam findings is essential. New pain generators and possible overlooked pain generators are sought. In some cases the patient may have an entrapment of the superior cluneal nerve (amenable to local surgical release), which travels through an osteofibrous tunnel over the medial iliac crest, approximately 7–8 cm lateral to midline at L4–5. Infrequently, osteoarthritis of the hip can refer to the low back, shin, and calf areas [102]. The presence of low back pain was also statistically more common in patients with longer duration of symptomatic end-stage hip osteoarthritis. Rarely, hip labral tears can also refer to the ischial tuberosity or anterior thigh regions [103]. Hip exam maneuvers for osteoarthritis (i.e., decreased internal rotation) and labral tears/femoral acetabular impingement tests (i.e., flexion-adduction-internal rotation – FAIR test) are critical both preoperatively and postoperatively to screen for less typical hip pain referral patterns. A neurologic exam must be performed to assess for focal deficits, particular residual impairment after disk herniation. If patients have symmetric hypoactive or absent ankle jerks, they likely have a comorbid peripheral neuropathy (most likely due to type 2 diabetes, alcohol, or subclinical hypothyroidism). Abnormalities in each of these areas adversely affect generally healing, especially nerve recovery. If the patient is diabetic, further surgical intervention can be expected to have a statistically significantly inferior outcome compared to nondiabetics. This finding also applies to efficacy of various pharmacologic and interventional spine treatments and is helpful in counseling patients regarding expectations for treatment [94].

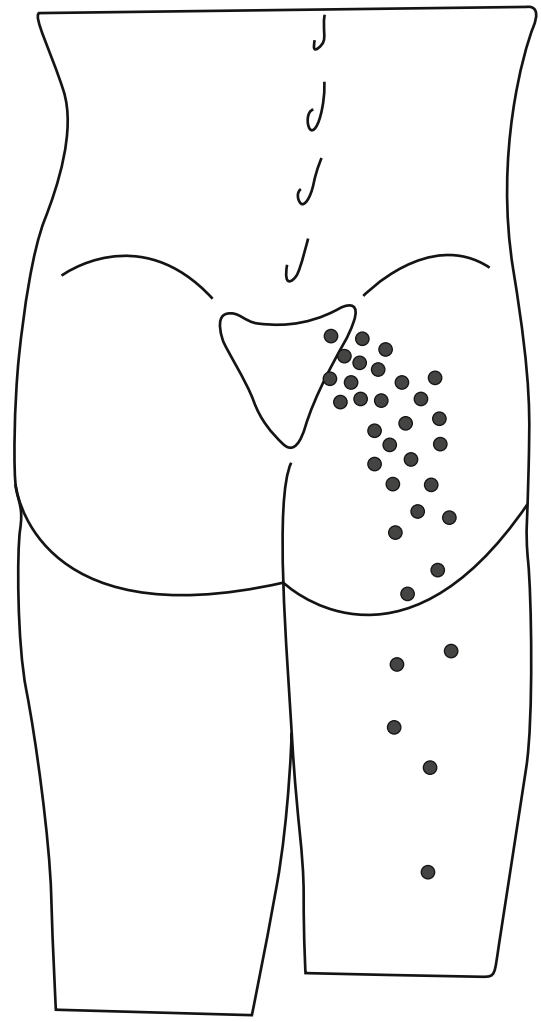

Fig. 38.4 The distribution of pain required for inclusion in sacroiliac pain study (Adapted from Maigne et al. [151])

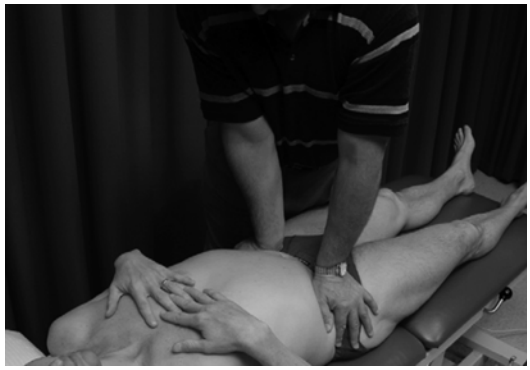

Fig. 38.5 The distraction test (testing right and left SIJ simultaneously). *Note*: Vertically oriented pressure is applied to the anterior superior iliac spinous processes directed posteriorly, distracting the sacroiliac joint

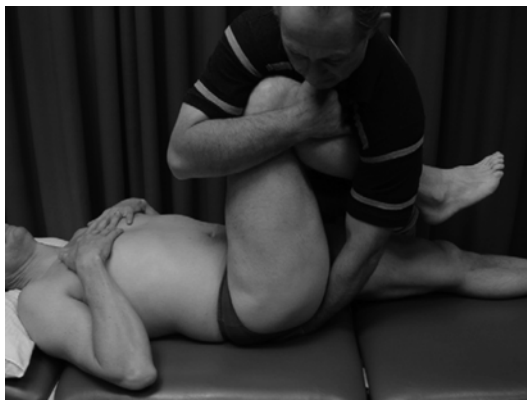

Fig. 38.6 The thigh thrust test (testing the right SIJ). *Note*: The thigh and sacrum are fixed against the table with the left hand, and a vertically oriented force is applied through the line of the femur directed posteriorly, producing a posterior shearing force at the SIJ

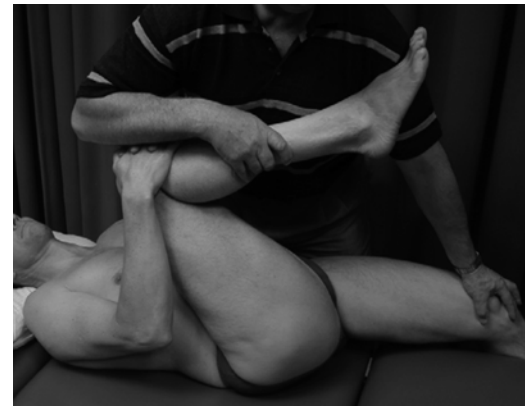

Fig. 38.7 Gaenslen test (testing the right SIJ in posterior rotation and the left SIJ in anterior rotation). *Note*: The pelvis is stressed with a torsion force by a superior/posterior force applied to the right knee and a posteriorly directed force applied to the left knee

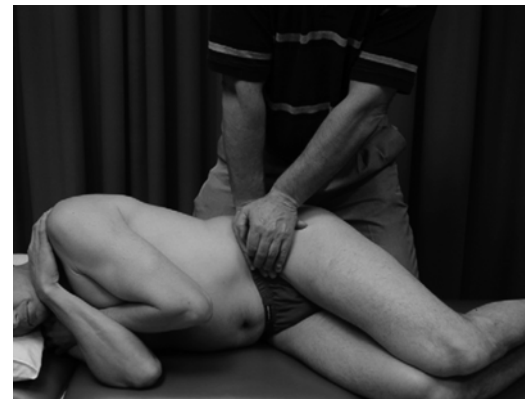

Fig. 38.8 The compression test (testing right and left SIJ). *Note*: A vertically directed force is applied to the iliac crest directed toward the floor, i.e., transversely across the pelvis, compressing the SIJs

Physical exam findings for spinal pain such as for facet pain are not reliable; diagnostic facet blocks are the gold standard. As the most recent quantitative study of PLSS reports the sacroiliac joint to be responsible for 43 % of persistent axial low back pain in PLSS [36], more attention is being directed to its precise diagnosis and treatment. The typical location of pain from the SI joint is 10 cm caudal and 3 cm lateral to the posterior superior iliac spine (Fig. 38.4). This referral pattern was obtained from asymptomatic subjects undergoing provocative arthrography [90]. Researchers have shown that a battery of ≥3/5 provocative SI joint tests are highly predictive of SIJ pain based on studies correlated with results from fluoroscopically guided, comparative SIJ blocks [104–106]. The five SIJ tests include: distraction, compression, thigh thrust, Gaenslen, and sacral thrust. The five SIJ tests are reproduced for the reader (Figs. 38.5, 38.6, 38.7, 38.8, and 38.9) [36].

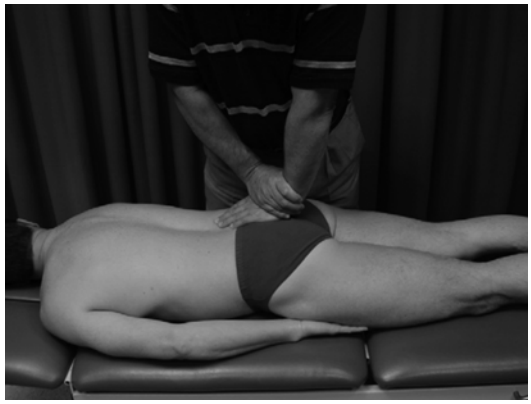

Fig. 38.9 The sacral thrust test (testing right and left SIJ simultaneously). *Note*: A vertically directed force is applied to the midline of the sacrum at the apex of the curve of the sacrum, directed anteriorly, producing a posterior shearing force at the SIJs with the sacrum nutated

38.11.2 Imaging

To help determine the cause of persistent pain after lumbar surgery, imaging is a useful first step to help guide evidence-based spine interventions. First, sagittal plane and standing, weight-bearing radiographs (AP/lateral/flexion-extension) are obtained to assess for stability of the fusion construct. Ideally they can be compared to preoperative x-rays. Most consider listhesis greater or equal to 4 mm to be indicative of clinically important instability. Thin-section CT scans (2–3 mm) with sagittal and coronal reformations are used to assess disk levels with hardware. High-resolution CT scan can detect pseudoarthrosis (absence of bridging bone), foraminal stenosis, misplaced bone graft or cement, and migrated/misaligned hardware. Hardware loosening is seen with stress fatigue and typically associated with a 2 mm halo around the hardware [107]. Complications associated with instrumentation are assessed by CT scan and need to be ruled out in the patient with leg pain. After transpedicular screw placement, the rate of nerve root irritation is 1 %, typically caused by inappropriately low and medial screw placement [108].

Postoperative MRIs are typically obtained if surgical outcomes are not achieved in a timely fashion. The optimal MRI is performed with *angled* T2-weighted sections from T12–L1 to L5–S1, with 1 mm stacked images through the fusion level. Metal artifact reduction sequences (MARS) can be used to better image fusion levels. Post-contrast (gadolinium) T1-weighted images are particularly useful for residual/recurrent disk herniation, new herniation, enlargement/enhancement of spinal nerves, perineural/epidural fibrosis, and/or arachnoiditis; however, postoperative MRIs with GAD must be interpreted with caution and guided by relevant clinically concordant symptoms. Caution against overinterpreting fibrosis is particularly critical in the early (< than 6 months) postoperative period. The extent and degree of scar tissue enhancement decrease within the first 6 months. In a study of MRI in 34 *successful* diskectomy patients, intrathecal nerve root enhancement was present in 6 (18 %) patients 6 weeks after surgery, facet joint enhancement was seen in the majority of subjects at 6 months (63 %), and eight patients (20 %) had residual mass effect on neural elements with an enhancement pattern suggesting a disk fragment [73, 109]. Grane et al. [110] reported a 19 % prevalence of residual/recurrent disk herniation in asymptomatic, post-diskectomy patients. Epidural scarring is typically more pronounced if patients receive an MRI before 12 months [110].

The label "segmental or mechanical instability" has been used much too loosely to diagnose the source of pain in patients with degenerative spondylolisthesis (DS) and rotational translation (RT). Lattig et al. [111] reported that facet joint effusion on conventional MRI (mean effusion size 2.15 mm) indicated abnormal motion in DS and RT. The authors identified 160 post-surgical patients status post either decompression alone or decompression with fusion. Mean age of patients was 69 years old. Twenty-five percent (40/160) of patients had no facet joint effusion with the % slip on upright x-ray and supine MRI ≤ 3 %. In 77 % (108/140) of patients, % slip between x-ray and MRI was >3 % (mean 10.6 %, range 4–29 %) and was associated with a mean facet effusion size of 2.15 ± 0.85 mm). Extent of facet effusion

was significantly associated with increased slippage on standing x-ray versus supine MRI ($p<0.001$); moreover, the extent of right/left difference in effusion was associated with the presence of rotational translation (RT 1.31 ± 0.8 mm vs. no RT 0.23 ± 0.17 mm, $p<0.0001$). If patients have evidence of % slippage >3 %, facet effusion >2.15 mm, or asymmetric facet effusion, diagnostic facet medial branch blocks would be useful in determining if these are pain generators. More study is needed to determine the role of facet effusion on MRI in surgical decision-making for optimal surgical treatment (decompression vs. decompression with fusion).

Modic type I changes are receiving great scrutiny since the publication of Hannah Albert's controversial work in 2013 [84]. Dr. Albert asserted that these Modic Type I changes are associated with an infection by *Propionibacterium acnes* infection of the endplates and/or disk. This is not a typical "diskitis" or osteomyelitis; thus patients will have normal white blood counts and sedimentation rates. Blood cultures are negative. Dr. Albert's work follows in the footsteps of Barry Marshall who discovered that ulcers were in fact caused by *H. pylori* which required treatment with antibiotics. At 1-year follow up, after completion of a 100-day course of antibiotics, Albert et al. [84] found that patients with Modic type I changes had a statistically significant reduction in back pain and disability. Recently, another group showed Modic type I changes to be correlated with low back pain outcome at 1 year. Patients with Modic type I changes on MRI had more pain, more disability, and greater incidence of an unsuccessful return to work at 1 year [112]. The Modic type I change was the only degenerative manifestation found on MRI to correlate negatively with clinical outcome.

Gates et al. [113] evaluated patients with SPECT scan after lumbar surgery. Sixty-three patients with persistent back pain after spine surgery were evaluated. Fifty percent of patients underwent scanning after at least 2 years and 25 % between 1 and 2 years. Bone scan can detect biomechanical stresses at the surgical level or above/below the operative level. Bone SPECT scan was used to detect pseudoarthrosis, abnormal facets uptake, disk pathology, and sacroiliitis. In the 63 patients, 132 bone scan lesions were detected. Overall, 75 of 132 lesions (57 %) were identified in the operative field, with 57 abnormalities (43 %) outside the field. Sixty percent of the abnormalities in the facets, disk spaces, and vertebral bodies were at the operative level with 29 % above the operative level (primarily facet) and 11 % below (facet and sacroiliac joint). The most common abnormalities were as follows: 37 % facet ($n=51$), 22 % disk space-centered conditions (degenerative disk disease, post-surgical reactive findings, no diskitis) ($n=29$), 15 % pseudoarthrosis ($n=20$), 14 % sacroiliac joint ($n=18$), and 7 % vertebral body lesions ($n=9$) and miscellaneous lesions. Sacroiliac joint uptake was seen in 15 patients for a total of 18 joints or 24 % of patients. Four fractures were uncovered and three in the vertebral bodies above the operative site. Many patients had more than one lesion.

Pseudoarthrosis causes continued motion at the operative site. Typically 6–9 months must elapse to see a solid fusion on x-ray. Two years is needed for a solid fusion to completely remodel. Based on studies with SPECT scans, increased tracer uptake at the fusion level at 1 year suggests raises possibility of pseudoarthrosis. All bone SPECT scans were performed at or beyond the usual window for surgical recovery. The SPECT scan can be a useful tool to add to the typical persistent lumbar pain patients after surgery. Additional diagnostic blocks can then be used to confirm or refute bone scan findings to distinguish between painless radiologic findings and actual pain generators.

38.12 Etiologies of PLSS: The Three-Column Approach

A three-column approach can be taken to diagnosis and treatment of the most common etiologies for persistent lumbar and/or radicular pain after lumbar surgery. The spine is divided into posterior, middle, and anterior columns. This approach assists the clinician with a straightforward algorithm for PLSS. In the remainder of the chapter, the primary etiologies of persistent pain are discussed, along with the current best evidence-

based approaches to treatment. This review will not cover intraoperative and perioperative complications as these areas are well reviewed in other chapters. Intrathecal pumps and spinal cord stimulators are not covered in this chapter. The authors present stringent diagnostic and therapeutic criteria for spine injections. If spine interventionalists adopt less stringent diagnostic criteria or use suboptimal techniques, outcomes suffer. Poor outcomes affect the patient, spine interventionalist, and surgeon adversely and make payors reluctant to pay for treatment.

38.12.1 Posterior Column: Facet Pain

Lumbar surgery changes the stresses on the posterior column and could result in new pain generators in the z-joints, sacroiliac joints, or muscles/ligamentous tissues. Such effects might include increased segmental motion above or below a spinal fusion or increased or abnormal segmental motion due to partial removal of the intervertebral disk. The most common pain generators are the facet and sacroiliac joints and soft tissues. According to DePalma et al. [36], posterior column structures comprised 75 % of pain generators in his series of 28 patients with persistent axial lumbar pain after surgery: facet 18 %, sacroiliac joint 43 %, and hardware/soft tissue 14 %. The remaining 25 % of patients were diagnosed with painful internal disk disruption by provocative discography.

In the patient with persistent axial lumbosacral pain, zygapophyseal joint arthropathy (ZJA) pain must be considered as a possible treatable source of persistent pain. Pathophysiologically, we know that after lumbar anterolateral interbody fusion, increased capsular strain is placed on the adjacent segment and index segment facet joint capsules. The facet joint has both nociceptors and mechanoreceptors. The mechanoreceptors are also thought to function in a proprioceptive role [114]. Little et al. [115] examined the effects of a single-level, L4–5 anterolateral interbody fusion on adjacent facets. Fixation increased the moment for all levels for all motions. Intervertebral angle and plane strains were increased at L3–4 and L5–S1 levels after fixation. The L4–5 facet capsules demonstrated decreased and increased strains ipsilateral and contralateral, respectively, in response to anterolateral interbody fixation.

Attempts to identify a clinical "facet syndrome" have largely been fruitless. Revel et al. [88] reported that patients with five of seven clinical variables distinguished 92 % of patients responding to a single lidocaine block with ≥75 % pain relief as positive response. Revel's criteria are as follows: age greater than 65 years and pain not exacerbated with coughing, not worsened with hyperflexion, not worsened by forward flexion, not worsened when rising from forward flexion, not worsened with extension-rotation, and well relieved by recumbency. The author's stated that these criteria could be used to select patients for facet injections; however, "these characteristics should not be considered as definite diagnostic criteria of lower back pain originating from the facet joint." Revel's study has never been duplicated; moreover, we know the single block false-positive rate to be unacceptably high (up to 49 %), thus making the claim of distinguishing 92 % of ZJA patients difficult to reproduce. Spine interventionalists fortunately solved the diagnostic dilemma with comparative blocks.

In patients with nonoperated, chronic low back pain, the prevalence of specific posterior column pain generators, i.e., painful zygoapophyseal joint arthropathy (ZJA), has been reported to range from 15 % to 40 % among persons with chronic low back pain [24, 26]. The first population studied had a prevalence of 15 % painful facet joint arthropathy. The study subjects were primarily male with a median age of 38 years and also receiving worker's compensation. The first study utilized a superior dual-block technique. The second study, which reported a 40 % prevalence of painful facet joint arthropathy, included primarily women with a median age of 59 years, using only a single intraarticular injection with a positive response defined as ≥50 % pain relief. Studies requiring at least 75 % pain relief reported prevalence rates of 27–45 % using controlled comparative local anesthetic medial branch blocks [116–119]. For a criterion of 90 % relief, the prevalence was 40 % in elderly female patients with no history of trauma [26].

Specifically to the question of prevalence of facet joint pain in patients with persistent axial low back pain after spine surgery, several studies have been performed. Prevalence ranges from 2.7 % to 33 % using varying criteria. Slipman et al. [6] reported a 2.7 % prevalence of facet joint pain (positive response criteria not reported). Using the standard technique of dual comparative medial branch blocks (with ≥75 % relief) in post-lumbar surgery patients, facet-mediated pain was reported as 16 % by Manchikanti et al. [89] with a 49 % false-positive rate for single blocks. The surgical group was composed of patients status post lumbar laminectomy (61 %), fusion with bone (20 %), fusion with hardware (18 %), microdiskectomy (8 %), and others (33 %, including disk arthroplasty) [89]. Greater than 80 % pain relief threshold was defined as a positive response; a screening block yielded a false-positive rate of 49 % [89].

DePalma et al. [36] reported an 18 % prevalence of ZJA. Klessinger [70] using a dual-block ≥80 % relief criterion reported an 8 % prevalence of facet syndrome after lumbar microdiskectomy. Siepe et al. [120] report a higher prevalence, likely due to using ≥50 % cutoff for positive response to screening blocks. These authors studied post-TDR pain etiologies with single, fluoroscopically guided facet intraarticular injections with local anesthetic and corticosteroids (>50 % relief) finding a 12.6 % incidence of z-joint pain in patients with chronic pain after TDR (ProDisc II), predominantly at the index level (86.4 %). (Intraarticular facet injections, however, lack specificity and sensitivity and are not considered the standard for diagnosing symptomatic facet joints [11].) Worse outcomes and a greater incidence of posterior joint pain were seen for TDR at L5/S1 (21.6 %) and two-level TDR (33.3 %). TDR may compromise the index segment while endeavoring to reduce adjacent segment degeneration [120].

Several studies of etiology of persistent pain after lumbar surgery show a lower prevalence of facet syndrome than in the nonsurgical patient literature; however, further study is needed. It is known that more stringent positive response criteria reduce prevalence.

To provide their patient with the best in spine care, today's spine surgeon is well served by making certain their patient's facets are evaluated using the evidence-based criterion standard for diagnosing ZJA, using at least a ≥75–80 % relief with dual comparative anesthetic medial branch blocks to be considered a positive response. Practice guidelines for facet evaluation have recently been updated from the International Spine Intervention Society [10, 11]. False-positive rates are unacceptably high with single blocks reported at 37 % [121], 41 % [117], and 47 % [29] and 49 % [89]. When appropriate technique is utilized, medial branch blocks are target specific with a low false-negative rate of 8 %, due to unrecognized intravascular injection of local anesthetic [122]. Many surgeons will also have potential surgical patients undergo facet blocks prior to surgery.

38.12.1.1 Radiofrequency Ablation (RFA) of Medial Branches

Multiple clinical guidelines and systematic reviews have been published with unfavorable conclusions regarding the efficacy and utility of radiofrequency ablation (RFA) [123–132]. However, these reviews included studies with technically incorrect electrode placement and inadequately inclusion criteria to diagnosis zygoapophyseal pain [10, 11]. Correct technique for RFA of the lumbar medial branch is paramount. Bogduk et al. determined that the radiofrequency techniques used by Shealy in the 1970s [133, 134] and additional researchers through the 2000s [135–137] were inadequate due to lack of knowledge of medial branch nerve anatomy [138, 139]. Moreover, researchers demonstrated that thermal RF electrodes coagulate radially around their tip, not distal to the tip [140]. This discovery led to improved success rates for researchers who coagulated medial branch nerves by placement of RF electrodes "parallel" versus perpendicular to the target nerve. The RCT of RFA of lumbar facet joints by Van Wijk et al. [137] showed no difference from sham; however, the RF electrodes were placed perpendicular to instead of parallel to medial branch nerves, thus creating a small, ineffective

ablative lesion no better than sham treatment [10, 11].

Many of the recent RFA clinical guidelines and systematic reviews also suffer from the inclusion of patients without facet-mediated pain. Recall that false-positive rates for a single block technique (with ≥50 % pain relief as positive response) can be as high as 50 % [89]. In many studies the bar for a positive response was set too low. The degree of diagnostic confidence is directly proportional to treatment outcome. If the dual comparative block approach is utilized, with ≥70 % pain relief or complete pain relief and appropriate electrode placement, the patient is much more likely to benefit from RFA [117, 141]. Operational and technical guidelines for optimal performance of RFA are set forth in the recent edition of the International Spine Intervention Society Practice Guidelines [10, 11].

In a narrative review of papers utilizing correct indications and technique, medial branch neurotomy was determined to be clinically effective [142]. In summary, the studies using a positive response criterion of 50 % pain relief achieved an approximate 40 % success rate (defined as 50 % relief of pain) [143]. However, if the criterion for a positive response is elevated to complete relief after diagnostic blocks, 56 % of patients achieve complete pain relief for a median duration of 13 months per treatment [144]. Dreyfuss et al. [145] reported outcomes using strict operational criteria with 60 % of the patients obtaining 90 % relief of pain at 12 months and 87 % of patients obtaining at least 60 % relief. Derby et al. [141] reported favorable RF neurotomy outcomes with a 70 % cutoff value for subjective relief after dual blocks. Klessinger [70] reported on the efficacy of RF neurotomy for facet pain in post-diskectomy patients. Using a ≥80 % diagnostic dual-block criterion to receive RFA, 59 % of patients reported at least 50 % pain relief for 6 months post neurotomy.

Recently increasing interest has emerged in treatment with pulsed radiofrequency (PRF). The mechanism of action of PRF is undergoing intensive investigation. Classic RF achieves temperature of 70–90 °C to achieve thermal coagulation of neural structures. PRF appears to work by both nonthermal electromagnetic field effects and very brief heat spikes, from 45 to 50 °C. Very little tissue destruction occurs beyond 0.5 mm from the tip. In general PRF produces markedly stronger electromagnetic fields than RF. A recent review included six RCTs using PRF: PRF versus epidural steroid injections, PRF versus sham, and the remaining studies PRF versus conventional RF [146]. The best evidence of PRF is in the cervical spine, prior studies with RF to the DRG produced transient neuritis and motor dysfunction. Van Zundert et al. performed PRF to the cervical DRG in patients with chronic radicular pain [147]. At 3 months patients reported >50 % reduction in pain vs. sham and a 20-point reduction in VAS. Patients had PRF to the cervical DRG for complaints of radicular pain. A similar study in the lumbar spine was poor quality and could not be assessed for efficacy.

38.12.1.2 Sacroiliac Joint Pain

In evaluating 368 patients presenting to a single spine surgeon's office for pain, including 25 % with prior diskectomy [148], 14.5 % of patients were found to have sacroiliac pain (SIJP) based on evaluation with diagnostic blocks. As sacroiliac pain can present with axial, lumbosacral, and pseudoradicular patterns, it is a critical diagnosis to consider both prior and after lumbar surgery (see Fig. 38.4: SIJ pain referral map). Early studies of PLSS reported no sacroiliac pain (see Table 38.2); Slipman et al. [6] reported a 2.7 % prevalence of SIJP in a heterogeneous PLSS population. By 2011, studying a more homogeneous population of patients presenting with persistent axial low back pain only after surgery, DePalma et al. [36] reported a 43 % prevalence of SI joint pain.

Based on current research using diagnostic blocks, sacroiliac joint (SIJ) pain currently appears to be an underappreciated source of chronic axial low back pain both pre- and postoperatively. Schwarzer et al. [27] were the first to use diagnostic blocks for SIJ pain. Using a validated historical factor, patient's subjective report of pain below L5 [149], Schwarzer et al. [27] reported a 30 % prevalence of sacroiliac pain in patients with CLBP using a single block tech-

nique. Using a dual comparative technique, reported prevalence of SIJP in patients with chronic LBP varies: 2 % Pang et al. [150], 6 % Manchikanti et al. [29], and 18.5 % Maigne et al. [151]. Maigne reported 30–47 % false-positive rates with single screening blocks [151].

Studies in postsurgical patients using a single, screening block protocol reported a 32–35 % prevalence of SIJ pain after lumbar fusion. Katz et al. [152] reported the SI joint as the cause of persistent pain after lumbar fusion in 32 % of patients; however, the authors utilized a single injection with local anesthetic and corticosteroid which would have an unacceptably high false-positive rate. A positive response was defined at >75 % pain relief from local anesthetic and at least 10 days of continued relief. Maigne and Planchon [153] reported a 35 % prevalence, using a single block technique with >75 % relief. Of note, however, they also found that the only historical factor predictive of SIJ pain was pain of different character than preoperative pain, typically arising greater than 3 months postoperatively. Sacroiliac joint pain was not related to iliac crest donor site or presence of fusion to the sacrum or not. The authors did not find that iliac crest bone harvesting close to the joint was a risk factor, as was suggested by Ebraheim et al. [154]. Studies using a dual-block protocol, by Liliang et al. [155] and DePalma et al. [36], reported a 40 % and 43 % prevalence of SI joint pain, respectively. Both investigators studied patients with persistent pain below L5 after lumbar fusion.

An in-depth look at Depalma's recent work evaluated [36] 28 patients with CLBP after lumbar fusion; SIJs were symptomatic in 43 % (12/28) of the fusion cases. In DePalma's workup of patients with chronic axial lumbosacral pain after fusion, SIJD was the most common etiology for pain, followed by painful IDD 25 % (7/28), painful ZJA 18 % (5/28), and soft tissue irritation by fusion hardware 14 % (4/28 cases). More than 80 % (10/12) of positive SIJD cases had lumbar fusion to the sacrum versus L5 ($p=0.0032$). DePalma concluded that inclusion of the sacrum into the fusion construct appears to be a risk factor for subsequent development of SIJ pain. Biomechanical studies of the sacrum after fusion show increased angular motion and stress across the SIJ increase after lumbar fusion [156].

Liliang et al. [155] evaluated 130 patients with persistent lumbar and/or radicular leg pain after lumbar fusion. Fifty-two patients [52] met inclusion criteria: pain below L5 and at least three positive provocative SI joint maneuvers. Triple block criteria, requiring >75 % relief, were utilized. A false-positive rate of 26 % was reported if patients did not undergo a third diagnostic block. Twenty-one patients [21] or 40 % of patients met criteria for SIJ pain. Of the initial 130 patients referred, this represented 16 % (21/130) of patients with persistent pain after lumbar fusion. Liliang et al. [155] reported the following predictive factors: unilateral pain (76 %) versus bilateral (24 %), positive responses to more than three provocative physical exam maneuvers, and pain with characteristics different from preoperative pain. Number of levels fused or fusion across L5–S1 did not predict SIJ pain.

After lumbosacral fusion, Emani et al. [157] reported that 15 % of 60 patients with long fusions to the sacrum required removal of painful implants, primarily iliac as opposed to sacral screws. In some patients, pain after fusion to the sacrum is mechanical; in other cases it appears to be a soft tissue hyperinflammatory reaction to the wear particles from implanted materials [158, 159]. In a study of causes for persistent axial low back pain after total disk replacement (TDR) with fluoroscopically guided injections, the SI joint was identified as a cause of pain in 12 % of cases [120].

There are varying hypotheses for the etiology of SIJ pain after fusion. Frymoyer et al. [160] reported that the SI joint was essentially noncontributory to persistent pain after posterior fusion based on an imaging-only comparison of lumbar fusion patients (with and without donor site pain) versus diskectomy patients. The authors could find no difference in terms of flexion-extension mobility or degenerative changes on x-rays of the SI joint. Subsequent researchers have found increased degeneration on CT scan in post-fusion patients. Ebrahim et al. (2000) performed CT scans of 22 patients with persis-

tent pain in 24 sacroiliac joints, after posterior iliac crest bone graft harvesting, and found that disruption of the synovial part of the joint led to severe degeneration [154]. Of 16 joints with disruption of the inner table at the ligamentous part of the joint, 10 had mild degenerative findings and 6 showed moderate degenerative finding. Three joints with disruption of the synovial portion of the inner table showed severe degeneration. Five joints had disruption of the inner table without degenerative changes. In summary, the authors concluded that there is a high prevalence of inner table disruption after posterior iliac crest harvesting, with more severe degeneration seen with disruption of the synovial portion of the inner table. Graft harvesting was recommended in only zone 1, versus 2 or 3, to avoid any inner table disruption. The shortcoming of this study was the lack of correlation with diagnostic SI joint blocks. Ha et al. [161] followed the CT scans in patients 5 years post-lumbar fusion, with and without sacral fixation. Seventy-five percent (75 %) of patients developed degeneration of the joint versus the control group. Greater SIJ degeneration was seen in the group with fusion to the sacrum.

Investigators have reported increased SI pain post-fusion (SIJ pain diagnosed by ≥75 % pain relief after SIJ block) when there are a decrease of the sacral slope (resulting in a more vertical sacrum) and an increase of pelvic retroversion [162]. This sacral position replicates a sitting position for which the individual compensates with a loss of lumbar lordosis and increased hip stress. Post-fusion pain is significantly more likely in patients with a more vertical sacrum (less sacral slope) and more pelvic tilt [163]. Mechanically, the lumbar paraspinal muscles have to exert greater force to maintain upright sagittal alignment, theoretically leading to increased posterior column pain in muscles "fusion disease" and in the facet and sacroiliac joints. Over time, this constellation of findings can lead to increased axial loading on the disk [163].

In these studies on the sacroiliac joint as a cause of persistent pain after lumbar fusion, the Duval-Beaupère criteria are used to assist sagittal spine alignment (Fig. 38.10) [164]. The lumbopelvic

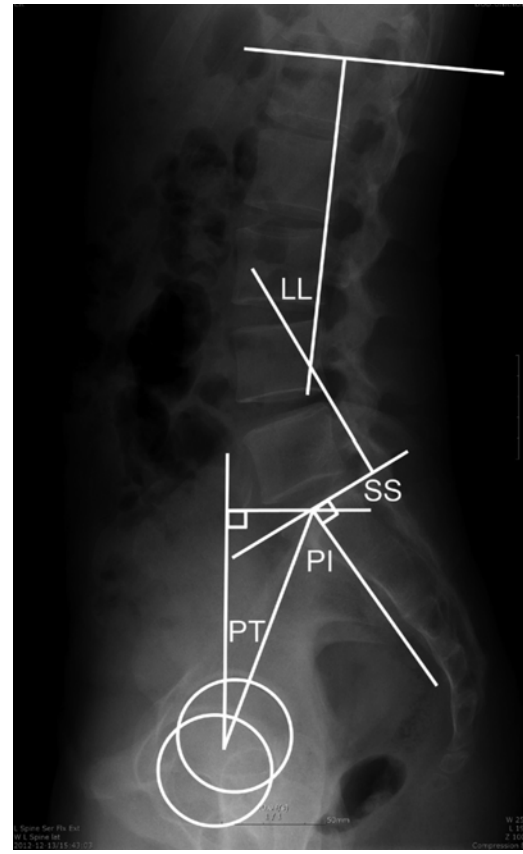

Fig. 38.10 Lumbopelvic spine, lateral x-ray parameters. *LL* lumbar lordosis, *PI* pelvic incidence, *PT* pelvic tilt, *SS* sacral slope [162]

parameters include lumbar lordosis (LL), pelvic incidence (PI), pelvic tilt (PT), and sacral slope (SS) on the standing radiographs (Fig. 38.10).

Anatomically, the sacroiliac joint has both synovial and ligamentous components. The anterior inferior one-half to two-thirds of the SI joint is a classic synovial joint with adjoining hyaline cartilage surfaces, whereas, in the upper part of the joint, the sacrum and ilium are not in direct contact and are bridged by anterior and posterior interosseous ligaments. One other intriguing theory about SI joint pain addresses the ligamentous structures of the joint as pain generators.

SIJ pain may be more complex than first appreciated. Controversy remains over primarily dorsal versus mixed dorsal and ventral innervations of the joint. Fortin et al. [40] dissected SIJs and reported that the joint was wholly supplied

by sacral loops from the dorsal rami from S1 to S3 (S4). These loops also innervate the interosseous ligaments and short and long dorsal SI ligaments; therefore potential extra-articular sources of SIJ pain cannot be ignored as noted by Murakami et al. [165]. Horwitz [166] reported that the long and short posterior SI ligaments are to contain dorsal rami branches from S1 to S2. Studies have shown that both the synovial portion and ligamentous portion of the SI joint have nociceptors [167].

Murakami et al. [165] screened for patients using a pain provocation test; then patients received either a fluoroscopically guided intraarticular or periarticular SI joint injection with lidocaine. The periarticular injection was effective in all patients, while the intraarticular injection was effective in only 9/25 patients. All of the intraarticular injection patients then responded to a periarticular injection. (For a more detailed description of the technique, the reader is referred to the article.) Vertical loading on the SI joint is primarily through the posterior and interosseous ligaments, where the posterior capsule is rudimentary or absent [168, 169]. The authors also found that the fluoroscopic injection into the middle one-third section of the SI joint had the highest yield, relieving more than 50 % of the pain. In a comprehensive review of SI joint pain [170], the authors reported evidence supports both intra- and extra-articular causes for SIJ pain, with clinical studies demonstrating intermediate-term benefit for both intra- and extra-articular steroid injections.

If the sacroiliac joint is determined with dual diagnostic blocks to be the pain generator, SI joint neurotomy can be considered for longer lasting relief. Cooled RF lateral branch neurotomy has also been shown to provide significant relief both short term [171] and long term for up to 2 years [172]. Hansen et al. [173] performed a systematic review of therapeutic interventions for sacroiliac pain; 11/56 studies met inclusion criteria. The evidence was fair in favor of cooled radiofrequency neurotomy and poor for short-term and long-term relief from intraarticular steroid injections, periarticular injections with steroids or botulinum toxin, pulsed radiofrequency, and conventional radiofrequency neurotomy.

38.12.1.3 Myofascial Pain/"Fusion" Disease

Myofascial pain may predate surgery as part of the patient presentation. Myofascial pain or "fusion disease" may also result from extensive muscular/fascial dissection and prolonged retraction with increased intramuscular pressures. "Fusion disease" may also result from post-fusion compensatory hyperextension and a more vertical sacrum leading to increased firing of the erector spinae muscles and increased loading to the posterior column [163]. Straightforward myofascial pain with trigger points may be amenable to trigger point injections, botulinum toxin injection, or dry needling; however, "fusion disease" is unlike to respond to usual myofascial treatments.

38.12.1.4 Miscellaneous Causes of Posterior Column Pain: Superior Cluneal Neuropathy

Superior cluneal neuropathy was first described by Strong and Davila in 1957 [174]. In the rheumatology literature, an "iliac crest pain syndrome" (ICPS) was reported in 30–50 % of patients with chronic low back pain in general practice [175]. Iliac crest syndrome is described by rheumatologists as a legitimate, distinctive cause of chronic low back pain. It is diagnosed by physical exam with tenderness over the medial iliac crest, 6–8 cm from the midline at L4-5. Detection of this sign is reliable with a kappa score of 0.57 for inter-rater reliability. In 1999, Bogduk in regard to ICPS stated that "there is no evidence of its mechanism or cause" and that it constituted no more than a single clinical sign. Bogduk [176] posited possible causes of ICPS (but not substantiated at the time) to include: sprains of the lumbar intermuscular aponeurosis or iliolumbar ligament; multifidus muscle or gluteus maximus muscle strain; trigger point activity in the quadratus lumborum muscle; or, entrapment of the lateral branches of dorsal rami in the fascia attached to the iliac crest. In 2005, Akbas

et al. [177], reported a case of a man admitted to the hospital after 6 months of severe right-sided low back pain post ipsilateral decubitus ulcer surgery. On exam he had two exquisite tender points at 6.5 and 7.5 cm lateral to midline over the medial iliac crest. Local injections with anesthetic and corticosteroid were performed and the pain dissipated in minutes. Recent researchers have since shown that the iliac crest pain syndrome is in fact entrapment of the superior cluneal nerve in a rigid osteofibrous tunnel penetrating the thoracolumbar fascia at the medial iliac crest. Prevalence was reported as 10 % [178]. The SCN provides sensory innervation to the posterior iliac crest and upper buttocks. The SCN originates from the L1 to L3 nerves and also penetrates the psoas major. Ermis et al. [179] diagnosed 25 patients with medial superior cluneal nerve entrapment via ultrasound and used local anesthetic with steroid for treatment. Recently, Morimoto et al. [180] reported on the surgical treatment of SCN neuropathy. A microinvasive release was performed of the osteofibrous tunnel containing the SCN in 34 patients. The patients presented with pain 7 cm lateral to midline over the iliac crest. Average duration of pain was ~5 years. Pain was both unilateral and bilateral. After a diagnostic block with lidocaine with >75 % relief, and failure of blocks with corticosteroid, surgery was performed. All patients reported immediate and total relief of pain once the SCN was released from its osteofibrous tunnel. At 10 months, all patients reported complete pain relief; none experienced recurrence of pain.

38.12.1.5 Technical Note: Diagnostic Blocks, Performed with or Without Sedation

A recent study has brought into sharp focus the effect of sedation on the validity, accuracy, and treatment outcomes after diagnostic injections. Based on the results of this randomized controlled study [181], it is recommended that conscious sedation (including agents such as propofol, midazolam, and fentanyl) should not be used because of the statistically significant probability of obtaining a false-positive diagnostic block. To properly diagnose facet-mediated or sacroiliac joint pain, dual comparative anesthestic blocks are needed. Patients with false-positive results are likely to be subject to misdiagnoses and unnecessary procedures. Patients receiving blocks with sedation reported statistically significant greater mean reductions in pain diary scores and less procedure-related pain. Critically, a higher proportion of patients receiving sedation obtained >50 % relief (70 % vs. 54 %, $p = 0.039$).

38.12.2 Middle Column

38.12.2.1 Etiologies of Persistent Leg Pain After Surgery

The most common causes of middle column pain are: recurrent/residual disk herniation, new herniation at a new level, epidural fibrosis, and, over time, adjacent segment disease. Historically, residual lateral stenosis, far lateral herniations, sequestered fragments, and arachnoiditis were more prominent causes of PLSS in early surgical outcome studies. In the first quantitative study of PLSS by Burton et al. (1981), CT myelography with pantopaque was still common, and the authors reported an incidence of 6–16 % of arachnoiditis [5]. Once dye use was discontinued and MRI became available, the incidence of arachnoiditis became rare. Chronic leg pain is one of the most disabling sources of pain after lumbar surgery. Radicular leg pain/radiculopathy pain needs a critical analysis with a search for a correctable cause due to the significant morbidity and mortality of FBSS with primary neuropathic leg pain.

Post-diskectomy re-herniation, either ipsilateral or contralateral, ranges from 5 % to 15 % of cases at the surgical level [182–186]. MRI with gadolinium is the study of choice postoperatively; however, it must be carefully correlated with the clinic presentation. Many surgeons also recommend an epidural steroid injection to attempt to manage the pain without need for revision surgery. In a study of MRI in recurrent sciatic patients 1 year after surgery, 42 % of

symptomatic patients had a disk herniation and 19 % of asymptomatic patients had a disk herniation [110]. Many patients with persistent or residual leg pain after surgery, without an obvious correctable lesion, simply need adequate time for the nerve to recover from prolonged compression and inflammation. Battered root syndrome can occur with prolonged and aggressive retraction and presence of a conjoined nerve root and/or excessive bleeding [187]. Persistent postsurgical leg pain can in rare cases result from arachnoiditis (3 %), not including lesions caused by prior myelography [188]. Three patterns are described for arachnoiditis, which albeit rare should be recognized (on T2-weighted MRI): nerve root clumping (type I, mildest type), "empty sac" with peripheral adhesions of nerve roots to thecal sac (type II, moderate severity), and an intermediate signal mass filling the subarachnoid space below the conus (type III, severe). The onset of the leg symptoms after an approximately 6-month pain-free period can also suggest possible epidural fibrosis. Complications may also arise from hardware migration or misalignment. X-ray and thin-section CT scan can assess hardware position. Rare reports have also found pars interarticularis fracture after instrumentation. Iliac crest graft donor site has been reported as a cause of diffuse leg pain; however, iliac crest bone harvest techniques have improved markedly to spare the superior cluneal nerve. Hardware placement and iliac crest graft donor site have also improved to avoid disrupting the sacroiliac joint and accelerated degeneration which could present with lumbosacral pain as well as "pseudoradicular" leg pain. Leg pain occurring over the long term may represent adjacent segment disease (ASD) post-fusion.

When a correctable cause of persistent leg cannot be found, the etiology is typically attributed to epidural fibrosis (including intraneural and perineural). There is controversy about the true incidence of epidural fibrosis. Advocates of an anti-adhesion barrier gel and the lysis of adhesions procedure tend to report literature with a higher percentage of clinically significant epidural fibrosis, whereas the quantitative reviews noted in Table 38.1 report a range of epidural fibrosis from 4 % to 15 %, which is currently a more reliable epidemiologic estimate. Thomson and Jacques [189] reported on the demographics of a subset of PLSS patients with severe neuropathic leg greater than back pain who were undergoing treatment with spinal cord stimulators. These patients have higher pain levels, increased disability/inability to work, poorer quality of life than patients with complex regional pain syndrome, rheumatoid arthritis, and fibromyalgia. This group likely constitutes the patients with the worst outcomes after fusion and is not representative of all patients with persistent pain after fusion. As compared to other chronic pain patients with complex regional pain syndrome (CRPS, previously called reflex sympathetic dystrophy or RSD) or rheumatoid arthritis, FBSS patients are severely disabled with an ODI of 56 (which is considered near "crippled" by pain) vs. 27 (low moderate disability) [189]. Demographically, these patients report an average back pain of 5/10 with leg pain 7.5/10 versus RA patients with pain ranging from 3.4 to 6.0/10. Quality of life by the EQ-5D is 0.16 or very poor. Seventy-eight percent (78 %) of FBSS are unable to work versus 31 % of CRPS patients.

In this study, patients were recruited from Canada, Western Europe, and Australia with severe neuropathic pain after PLSS. The prevalence of this PLSS subgroup was reported as 0.61 %, similar to rheumatoid arthritits (0.5 %) [189]. To estimate prevalence in the United States, we have to look at international spine surgery rates. Cherkin et al. (1994) presented an international comparison of back surgery rates from the mid to late 1980s [47]; see Fig. 38.1. The US rate of spine surgery is double the rate of surgery in Canada, Western Europe, and Australia and five times the rate in the United Kingdom [47, 51]. The estimated figure PLSS with severe neuropathic leg greater than back pain would be 1.2 %. Based on census data from 2012, with 314 million people in the United States, the number of Americans living with this subtype of PLSS would be ~3.8 million.

Burton et al. [5] reported a 6–8 % incidence of epidural fibrosis as a cause of persistent pain. Waguespack et al. [35] reported 4 % incidence of epidural fibrosis the primary cause of persistent leg pain; however, the authors noted that 44 % of

PLSS patients had some degree of epidural fibrosis noted at reoperation. Slipman et al. [6] reported 8.1 % epidural and 6.5 % intraneural fibrosis. Depalma et al. [36] did not attribute any cases of persistent axial low back pain to epidural fibrosis. Early evaluation of PLSS from the 1970s, when there was a known high incidence of residual lateral stenosis, arachnoiditis, and lack of MR imaging, published reports of up to 24 % of PLSS cases caused by epidural fibrosis [190, 191]. All spine specialists, however, agree that the more surgeries undertaken, the greater likelihood of significant scar tissue formation. Fritsch et al. [2] reviewed 182 surgical cases and reported a primary rate of 4 % of epidural fibrosis after primary diskectomy progressing to a 60 % rate of epidural fibrosis and instability after multiple revisions. Repeat neurolysis or fibrinolysis attempts to remove the scar tissue were largely unsuccessful. The authors concluded that in severe diskotomy syndrome with epidural fibrosis, local arachnoiditis, and progressive instability, fusion provided a better option than multiple fibrinolyses. Revision surgeries performed for peridural fibrosis have unfavorable long-term outcomes [192, 193].

While researching an anti-adhesion barrier gel, Ross et al. [194] investigated the presence of a correlation between recurrent radicular pain 6 months post-diskectomy and the amount of lumbar peridural fibrosis on gadolinium-enhanced MR imaging. The authors reported that a patient with extensive peridural scar is 3.2 times more likely to experience radicular pain (extensive peridural scar was defined as scar >75 % of the affected quadrant). A later study by same group, Petrie and Ross (1996), then reported reduced peridural scaring and improved patient clinical outcomes with use of anti-adhesion barrier gel [195]. As a follow-up to the possibly biased barrier gel studies, Vogelsang et al. (1999) reviewed post-diskectomy MRIs and found only rare cases of fibrosis and no correlation with radicular pain [196].

For the relatively infrequent cases of epidural, perineural, or intraneural fibrosis, we have pathophysiologic data to suggest mechanisms for persistent pain; however, the etiology is likely multifactorial including effects from the primary disk herniation (both mechanical and chemical effects) and intraoperative surgical factors (tissue manipulation, bleeding, etc). The application of nucleus pulposus (NP) to pig spinal nerves, *without compression*, reduces nerve conduction velocity [197]. The NP may also damage axons and myelin sheaths, increasing vascular permeability and intravascular coagulation and reducing intraneural blood flow [198]. Once perineural fibrosis exists, it interferes with normal cerebrospinal fluid mediated nutrition, making the nerve roots hyperesthetic and hypersensitive to compression [199]. We also know that the nerve root obtains as much as 50 % of its nutrition through cerebral spinal fluid within the dural cuff [200]. Postsurgical fibrosis of the dural cuff could potentially cause nerve root ischemia and neuropathic pain. Peridural scarring can also tether the nerve roots and dura compromising axoplasmic transport, increasing neural tension, and disrupting arterial and venous blood supply. In a subgroup of PLSS patients with arachnoiditis, defects in fibrinolytic activity with fibrin deposits are described [201]. Scar tissue reduces nerve vascularization, resulting in deafferentation pain [202].

As noted above, the nerve itself does not have to be compressed to become fibrotic. If the nerve becomes ischemic, fibrosis can result. In a cadaveric study of 160 lumbar foramens (range 35–91 years), distention of the venous plexus was more common than direct nerve root compression; furthermore, subjects with direct nerve compression from a disk herniation *did not develop nerve fibrosis*. In the absence of direct nerve compression, the most severe neural pathology was observed with compression, congestion, and dilatation of foraminal veins. The nerves demonstrated peri- and intraneural fibrosis, edema, and focal demyelination. Inflammatory cells were absent. The authors proposed a mechanism of venous obstruction with ischemia, thereby leading to perineural and intraneural fibrosis.

38.12.2.2 Epidural Steroid Injections (ESIs)

Epidural steroid injections (ESIs) are the most commonly used type of spine injection postoperatively in patients with persistent leg pain for both diagnostic and therapeutic purposes. Both negative and positive responses to ESIs have

prognostic value. Low-volume, local anesthetic-only, selective nerve root blocks can be utilized; however, most spine specialists add corticosteroid for potential temporary partial pain relief. An ESI has critical diagnostic and prognostic value for determining whether a patient has reversible cause of persistent leg pain versus neuropathic pain. A patient with ongoing leg pain without any correctable surgical lesion should have at a minimum one ESI although this is not an acceptable long-term management strategy. Patients diagnosed with persistent neuropathic leg pain are typically referred for a spinal cord stimulator trial if an ESI provides no relief.

In the nonoperated spine, epidural injections are routinely used to manage primarily leg pain associated with lumbar disk herniation or spinal stenosis. Epidural steroids can be delivered via the transforaminal, interlaminar, or caudal routes. General systematic reviews on the subject report moderate evidence for short-term relief and fair evidence for long-term relief. MacVicar et al. [203] performed a recent systematic review of the data on use of transforaminal epidural steroid injections (TFESIs), reporting that 70 % of patients achieve 50 % pain relief at 1 or 2 months and 30 % achieve complete relief. Over the last decade, the prevailing wisdom has been that the transforaminal route is superior to the interlaminar route for treating radicular pain, ostensibly to bring the steroid closer to the herniated disk/nerve root interface. As such there has been a tremendous rise in utilization with an annual 20.4 % growth rate of TFESIs [204–206] vs. 2 % for caudal and ILESI procedures [205] (Fig. 38.3). However, recently, a systematic review reported equal efficacy for both transforaminal epidural steroid injections (TFESIs) and interlaminar epidural steroid injections (ILESIs) in reducing pain and improving function for unilateral leg pain. There is evidence that a parasagittal ILESI provides comparable pain relief and functional improvement versus TFESIs [207]. Parasagittal ILESIs can achieve 100 % ventral flow versus midline ILESIs with 36 % ventral flow on epidurography. Further research is warranted, given the known serious complications of TFESIs in the lumbar spine which have included paraplegia and permanent neurologic injury [208]. Only a minor 15 % superiority was seen for TFESIs at 2 weeks, but in 1 months and 6 months, outcomes were not statistically significant difference in terms of pain relief, 43 % vs. 54 %. Functional improvement was >50 % in both groups. It is not known if this effect would also be seen in post-lumbar surgery patients wherein interlaminar spine access may be distorted status post laminotomy or laminectomy.

Few studies have looked specifically at postsurgical patients and epidural steroid injections. Klessinger [209] studied TFESIs in patients with persistent or recurrent radicular pain after microdiskectomy. Of 1,009 diskectomy patients, 156 (15.5 %) had persistent radicular pain. Nine percent (91/1009) of patients required reoperation. Patients received a TFI if they have pain persisting >3 months. A positive response was defined as >50 % relief. TFIs were performed with triamcinolone 10 mg and 0.25 % bupivacaine. TFIS achieved at least 50 % reduction in 31 % of these patients. The odds ratio is 17.5. No patient with positive result after TFIS had to undergo a reoperation. Klessinger et al. [70] reported both diagnostic and therapeutic value in performing a TFI in patients with persistent radicular pain >3 months after radiculopathy. Diagnostically, a negative TFI was highly sensitive for recurrent disk herniation (true positive rate 94 %) with a 17.5 odds ratio and the need for reoperation. Therapeutically, 31 % of patients can achieve at least 50 % reduction in pain which makes patient and surgeon less likely to consider a repeat surgery or further invasive procedures. The results also suggest performing the TFI during the first 3 month after the operation for better results (44.4 % good results early after operation versus 22.8 % later, $P=0.02$).

Derby et al. [210] also reported inferior surgical outcomes in patients undergoing an ESI after versus before 1 year. Derby et al. [210] findings suggest possible fibrotic remodeling over time with persistent pain, thereby making a nerve more difficult to treat the longer a patient's pain is unrelieved. Derby et al. [210] retrospectively studied a group of patients undergoing both primary and repeat lumbar spinal surgery for extremity pain and determined the correlation between >=50 %

relief of extremity pain for >1 week following selective epidural block with local anesthetic and corticosteroids to 50 % or greater relief of leg pain at 1 year post-spinal surgery. All patients had temporary relief of their leg pain for the duration of local anesthetic. The study found that when duration of leg pain was less than a year, both steroid responders and nonresponders had good outcomes; however when the duration of leg pain was greater than 1 year, nonresponders had a 5 % favorable outcome compared to 85 % who responded to corticosteroids. Derby et al. concluded that when leg pain was present more than a year in duration, especially in patients with previous surgery and underwhelming structural abnormalities, the chances of leg pain resolution following surgery were unlikely [210].

Manchikanti et al. (2010) evaluated caudal injections in post-lumbar surgery syndrome patients [9]. The RCT compared fluoroscopically guided caudal injections with local anesthetic (LA) versus local anesthetic plus Celestone. Postsurgical patients averaged ~50 years old with a mean of ~13 years of persistent pain. At 1 year, pain relief (≥50 %) and disability reduction were noted in 53 % LA group and 59 % LA plus steroid group, with no statistically significant difference noted. Subjects averaged three to four procedures per year with an average of 38 weeks of pain relief. Functionally subjects improved from moderate to mild disability per ODI. Patients also reported a statistically significant drop in opioid use. Average relief was 4–6 weeks per injection. In terms of pain relief, 70–75 % of patients reported significant pain relief, albeit short-lasting. For a patient with an average of 13 years of persistent postsurgical pain, a ~50–60 % reduction in pain and disability obtained by an average of 38 weeks relief with three to four injections with either LA or LA plus steroids is significant. This study in fact serves to highlight how difficult neuropathic pain is to treat. Given the choice, LA seems superior due to potential negative steroid side effects including adrenal and immune suppression. Yet reimbursement favors steroid injections currently. Local anesthetic, saline, and dextrose may have roles in treating radicular pain which are equal to corticosteroids. Smigel and Reeves [211] presented 1-year outcome data using 10 cc of D5W via fluoroscopically guided caudal injections for chronic low and/or leg pain. In a study of 25 patients, outcomes using D5W at 1 year were noninferior to results obtained using steroids.

Devulder et al. [212] studied patients with persistent leg pain status post diskectomy. Sixty post-lumbar surgery patients were diagnosed with "pronounced epidural fibrosis" around one to two nerve roots, confirmed by MRI, epidurogram, and positive EMGs. Three protocols were compared with transforaminal injections along nerves identified as fibrotic: Group A with 1 ml bupivacaine 0.50 % and 1,500 units of hyaluronidase and 1 ml saline, Group B with 1 ml bupivacaine 0.5 % plus 40 mg methylprednisolone, and Group C with bupivacaine 0.5 %, 1,500 units of hyaluronidase, and 40 mg of methylprednisolone. Patients received a total of two injections. A score of 3 indicated 50–80 % relief; and 4, complete relief. No statistically significant difference was found between solutions at 1 month, 3 months, and 6 months. Injections without corticosteroids were as effective as those without steroids. This study does not mean that steroids and/or hyaluronidase is ineffective; indeed it may more accurately characterize a group of postoperative patients with "pronounced epidural fibrosis surrounding the nerve root" unfortunately resistant to our best treatments. In this particularly intractable group with persistent radicular chronic pain group, a result of >50 % pain relief at 6 months is clinically and statistically significant.

Clearly, local anesthetic, dextrose 5 % in sterile water (D5W), and normal saline 0.9 % are not placebos; in fact they are all biologically active agents. In regional anesthesia blocks, both local anesthetic and normal saline affect the muscle twitch response; however, the current required for electrostimulation of the femoral or sciatic nerve is greater after injection of normal saline (NS) than D5W [213]. Many older studies assessing efficacy of steroid injections compared steroid to normal saline or local anesthetic (LA) as placebos, which are now understood to not be true placebos. Alternatively, these results suggest that the "active" agents (corticosteroid and hyal-

uronidase) offered no extra benefit versus local anesthetic and normal saline, perhaps due to a mechanical volume effect of lessening pain in affected fibrotic nerves by disrupting scar tissue such that local blood flow and axoplasmic flow could be improved. A systematic review examined the connection between volume of solution injection and relief of radicular pain during ESI. The authors found that the greater the volume injected, the greater relief achieved [214]. The proposed mechanisms of efficacy for additional volume include: washout of cytokines, lysis of adhesions, suppression of ectopic neural discharges, and enhanced blood flow to ischemic nerve roots.

In regard to radicular pain due to adjacent segment spinal stenosis, no primary studies have been done in this post-lumbar surgery syndrome subgroup. Recently, the efficacy of TFESIs for moderate to severe radicular pain in 400 patients with lumbar spinal stenosis has also been thrown into controversy. Friedly et al. (2014) performed a multicenter RCT [215]. The study was funded by the Agency for Healthcare Research and Quality (AHRQ). Epidural injection of glucocorticoid with lidocaine offered "minimal or no short-term" benefit vs. lidocaine alone. The editorial after the article recommended no ESIs for radicular leg pain and proceeding either with surgery or conservative care. This paper, published in the highly prestigious New England Journal of Medicine and widely publicized, has been criticized by Manchikanti et al. (2014), who stated: "The interventional pain management community believes that there are severe limitations to this study, manuscript, and accompanying editorial. The design, inclusion criteria, outcomes assessment, analysis of data and interpretation, and conclusions of this trial point to the fact that this highly sophisticated and much publicized randomized trial may not be appropriate and lead to misinformation" [216]. Reanalysis of the data shows that epidural local anesthetic with steroids was clearly superior at 3 weeks and potentially superior at 6 weeks.

Although this is a lumbar spine injection chapter, this is a straightforward, potential worthwhile "pearl" with a very low "downside" for physicians treating FBSS with primarily leg pain of all etiologies: strategic use of gabapentin as an adjunct to ESI and for postoperative pain control. For patients undergoing on ESI for FBSS due to epidural fibrosis, a recent study found that the addition of 1,200 mg of gabapentin TID resulted in a statistically significant reduction in pain compared to an alternate regimen and usual ESI care. The surgeon may consider a 1-month trial of gabapentin 1,200 mg TID for 1 month post ESI to potentially obtain significantly greater follow-up at 6 months. The study compared the addition of gabapentin for 1 month to the Group K versus Group G. Group K received 1 month of naproxen sodium 1,100 mg/day BID and 12 mg of tizanidine and vitamin B and C complex for 1 month versus 1 month of gabapentin. The gabapentin group did report increased mild sedation for the 1 month post ESI; otherwise no adverse effects were reported. An interlaminar, fluoroscopically guided ESI at L3–4 was performed in the midline with 80 mg of methylprednisolone. The average age of the group ranged from 42 to 47. The baseline pain in Group K and Group G was equal to VAS 7.70 and 8.05, respectively ($p = 0.142$). At 1-month, 3-month, and 6-month follow-up, Group K showed statistically significant and clinical significant reduction in pain: at 1-month follow-up, Group K and Group G reported VAS scores 1.90 and 0.70 ($p = 0.003$); at 3-month follow-up, Group K and Group K reported VAS scores 2.50 and 1.54 ($p = 0.004$); and at 6-month follow-up, Group K and Group G reported VAS scores of 5.60 and 2.60, respectively ($p < 0.001$). Gabapentin is a structural analog of γ-aminobutyric acid and acts on the α2δ1 subunits of voltage-dependent calcium channels. Gabapentin works via primary afferent neurons, dorsal root ganglia, dorsal horn neuron, and supraspinal sites [217]. Gabapentin also decreased movement associated pain in animal models of neuropathic pain and peripheral inflammation [218]. Surgeons may also seriously consider preoperative gabapentin in a single dose of 900 or 1,200 mg administered either pre- or post-incision. In a RCT on patients undergoing laminectomy receiving gabapentin, these required statistically signifi-

cant less morphine for postop pain control post-laminectomy. Note: the 600 mg dose of gabapentin did not achieve significant pain relief [219]. Theoretically, patients should obtain the same results undergoing microdiskectomy or fusion; however, this has not been studied yet.

38.12.2.3 Lysis of Adhesions

Whether or not fibrosis is a source of pain remains controversial because fibrosis is often seen in both patients with and without continued spinal pain following surgery. Fritsch et al. [2] report epidural fibrosis as the primary cause of FBSS in 4 % of patients; however, its presence was noted in 44 % of FBSS cases. Surgical neurolysis of adhesions has generally shown poor long-term results [2] which prompted the investigation and use of various percutaneous neurolysis procedures via the caudal route, with and without catheter use. Lysis of adhesions has also been used for patients with lumbar spinal stenosis. Various agents have been injected including hyaluronidase, hypertonic saline, local anesthetics, and corticosteroids. Hyaluronidase was observed to markedly reduce post-laminectomy peridural fibrosis in animal studies [220]. However, as noted early, the data are mixed on the subject. Devulder et al. [212] compared transforaminal epidural injections of hyaluronidase, local anesthetic, and corticosteroid. All groups in this RCT showed approximately a 30 % success rate (>50 % pain relief) at 1-, 3-, and 6-month follow-up.

Another neurolysis method is the forceful injection of a volume of fluid through a needle placed into the caudal epidural space. Using this approach, several randomized comparative studies have investigated the efficacy of providing pain relief in postoperative patients with back and leg pain without an obvious structural source other than epidural fibrosis. Using fluoroscopic and contrast verified injections, both Revel et al. [221] and Meadeb et al. [222] study compared the efficacy of the forceful injection of saline with or without added corticosteroids (40 and 20 ml, respectively) versus low-volume corticosteroid alone. At 6 months, Revel et al. [221] reported a success rate of 45 % vs. 19 % for relief of leg pain ($p=0.03$) with and 29 % vs. 6 % relief of back pain comparing forceful injection of saline with and without steroids. At 18 months post-injection protocol, forceful injection remained superior showing statistically significant pain reduction of 39 % of patients with sciatica and 31 % of patients with back pain compared to the steroid alone group. The Meadeb study [222] used a smaller volume of 20 ml and did not have enough cases to reach statistical significance, but a modest decrease of 15 % or greater was seen in 47 % of the forceful injection group at 4 months following three injections performed at 1-month interval. No complications were reported.

A more aggressive approach involves fluoroscopically guiding an epidural catheter to the site of fibrosis and using both injected fluid pressure and mechanical disruption by the catheter to lyse adhesions. The caudal approach has been advocated and pioneered by first by Gabor Racz and Holubec [223] and advocated more recently by Manchikanti et al. [224]. Originally Racz followed a 3-day in-hospital protocol using repeat treatments and included in addition to normal saline and corticosteroids the injection of a hypertonic (10 %) saline solution which presumably decreased edema and attenuated small pain fiber activity. In a randomized comparative study to compare the efficacy of hyaluronidase versus hypertonic saline in relieving spinal pain, the Racz group found a 25 % or more reduction in VAS scores in 83 % of the patients at 1 month and a 50 % reduction in VAS scores at 3, 6, 9, and 12 months. No difference in the outcomes was found between groups, although the groups receiving hypertonic saline with or without hyaluronidase required slightly fewer treatments.

Manchikanti et al. [224] performed a RCT in 120 post-lumbar surgery syndrome patients with presumed symptomatic epidural fibrosis. Patients were followed for 2 years. The control group received a fluoroscopically guided caudal injection with catheterization up to S3 with local anesthetic (lidocaine 2 %, 5 mL), nonparticulate betamethasone (6 mg, 1 mL), and 6 mL of 0.9 % sodium chloride solution. The intervention group received percutaneous adhesiolysis of the targeted area, with targeted delivery of lidocaine 2 % (5 mL), 10 % hypertonic sodium chloride solution (6 mL), and

nonparticulate betamethasone (6 mg). The intervention group was treated with the Racz catheter, guided to the regions of maximum fibrosis. At 2-year follow-up, 82 % of intervention patients versus 5 % of control patients experienced at least 50 % relief of pain. The intervention group received an average of 6 1-day injections with an overall total relief of approximately 78 out of 114 weeks.

38.12.3 Anterior Column

The primary structure in the anterior column responsible for continued or recurrent pain postlumbar surgery is the intervertebral disk. In the unoperated spine the prevalence of pain due to an internally disrupted disk, as evaluated by discography, has been reported as 26 % [29] and 39 % [22]. In the quantitative studies summarized in Table 38.2, the reports of painful internal disk disruption (IDD) and pseudoarthrosis are reported as a group by some authors, and other authors separate pseudoarthrosis from painful IDD at a nonoperated level. Burton et al. [5] reported <5 % pseudoarthrosis; Fritsch reported no cases; Bernard [34] reported 29 % painful IDD; Wageuspack et al. [35] reported 17 % psuedoarthrosis; Slipman reported 22 % painful IDD; and DePalma et al. [36] reported 25 % painful IDD (four cases pseudoarthrosis; three cases painful IDD).

If a patient has significant adjacent segment disease with discogenic pain or pseudoarthrosis, the standard is to extend the fusion and revise the index surgical level, respectively. However, potential new treatments are emerging for adjacent segment discogenic pain, including more effective thermal treatments and the injection of "regenerative" agents such as platelet-rich plasma, and growth factors, and "regenerative solutions" which include dextrose. Much more research is needed in these areas.

Because of nerve ingrowth into the pathologically painful degenerated disks or the postoperative disk, continued pain from the remaining disk tissue may be responsible for ongoing symptoms [225, 226]. While the existence of discogenic pain is now well accepted, the use of discography as the standard for identifying a painful disk remains controversial. The reader is also referred to a chapter devoted entirely to discography on this topic. The authors of this chapter recommend the current International Spine Intervention Society guidelines [10, 11]. Based on a meta-analysis of all of discography studies, if the International Spine Intervention Society guidelines and operational criteria are adhered to during discography [68], a false-positive rate of less than 10 % is attainable [227]. Regarding the question of whether discography causes disk degeneration [228], a critical review of this study has determined that the study is inconclusive, with significant statistical shortcomings, including the use of an atypical control group [229]. The control group had a much lower prevalence of Modic changes (11 % vs. 39 %) [230] and disk herniations [230, 231] than seen in the general population, which would have created an incorrect conclusion about discography accelerating degeneration or causing disk herniations. Moreover, there is a weak association between the mild degenerative findings seen in the study and the presence of back pain. If discography were indeed as damaging as the authors claim, we would be facing an epidemic of disk herniations after discography, which has not materialized [229].

38.12.3.1 Intradiscal Thermal Treatments

If pain following disk injury is in part due to the ingrowth of unmyelinated nerve fibers into the annulus, annular disk and nucleus pulposus may be prone to subsequent sensitization to mechanical and chemical stimuli. Pain reduction may occur by reducing or eliminating nociceptive input by destroying pain-sensitive fibers using heat. However, an early RCT of percutaneous intradiscal heating for 90 s to 70 °C was ineffective versus sham [232]. Helm et al. (2012) performed a systematic review of thermal annular procedures for the disk [233]. Forty-three studies were identified; however, only three RCTs and one observational study met inclusion criteria. The evidence for IDET was fair [234]. The evidence for disctrode was poor. Results of the most

recent biacuplasty study are reviewed below, suggesting good evidence thus far.

The first randomized, placebo-controlled study of transdiscal radiofrequency (biacuplasty) was recently completed by Kapural et al. [235]. A total of 1,894 patients were screened; 64 patients met inclusion criteria. Note: patients with prior lumbar surgery were excluded; this treatment may therefore be considered first for adjacent segment IDD. There are two cooled radiofrequency probes in a bipolar array to lesion nociceptors in the posterolateral annulus. The sham treatment was exactly the same except that the RF probes were not placed intradiscal nor was a RF current delivered. At 6 months, the biacuplasty group showed statistically significant reduction in pain ($p=0.006$), physical disability ($p=0.029$), and disability ($p=0.037$). Biacuplasty patients reported a trend toward decreased opioid use with a 16 mg reduction in opioid use. Other thermal treatments are discussed elsewhere in the book.

38.12.3.2 Intradiscal Injections

Intradiscal steroids have been shown to be ineffective for discogenic pain in a prospective, double-blind trial and have been abandoned [236]. A pilot study performed intradiscal injections with a solution containing agents thought to induce proteoglycan synthesis including: glucosamine, chondroitin, hypertonic dextrose and dimethylsulfoxide (DMSO) [237]. This pilot study was compromised of 30 patients with an average age of 45 years with intractable low back pain of an average 8.5 years duration [237]. On follow-up statistically significant improvement was found in pain, RMDQ. Fifty-seven percent of patients 17/30 improved markedly with 72 % reduction in disability scores and 76 % improvement in VAS scores. The remaining 43 % ([13] patients) had little or no improvement. Patients who did poorly had FBSS, spinal stenosis, and long-term disability. Further research is ongoing on this intradiscal therapy. This could be considered as a therapy in an adjacent pain disk to the surgical construct.

As noted above, the current standard of care for painful IDD or pseudoarthrosis is surgical intervention; however, there is emerging interest in intradiscal injections. On review of the latest business sites in treatment of spinal pain, there are 12 start-up companies working on intradiscal injections: including platelet-rich plasma/growth factors, stem cells, growth factors, etc. [238]. Terry et al. [239] presented the first human study on PRP in the disk for discogenic pain as diagnosed by a positive discogram. PRP is currently being used with success for various tendinopathies, hamstring/rotator cuff tears, as well as osteoarthritis. PRP is made by concentrating the patients' platelets. Typically, the ideal concentration is 4–6× baseline so as to exceed a cell count of one million. Platelets house multiple anabolic growth factors that include: PDGF, FGF, IL-1, IL-2, IL-8, and VEGF. Inclusion criteria included pain present greater than 3 months, greater than 50 % disk height preserved on MRI, no grade IV tears, and a positive discogram. A total of 41 patients were initially randomized and 11 were excluded. A 2:1 patient recruitment strategy was utilized; thus a total of 19 patients received PRP and 11 patients received contrast as a placebo. At 1 year, the PRP group has a statistically significant decrease in pain, including current pain, best pain, and worst pain. Patients receiving PRP also reported superior satisfaction per the NASS survey. Other researchers believe that the growth factors released with PRP alone or as single growth factors alone cannot be effective because of the short half-life. Some researchers are injecting transfected intervertebral disk cells with genes encoding the active proteins into the disk. Researchers are also implanting stem cells with PRP or in biologic scaffolds to restore disk structure and function [240–242].

Conclusion

- Persistent lumbar and radicular pain after lumbar surgery can best be termed post-lumbar surgery syndrome (PLSS) which is defined as a cluster of nomenclature and syndromes following spine surgery wherein the expectations of the patient and the spine surgeon are not met with persistent pain following lumbar surgery.
- Failed back surgery syndrome (FBSS) 30 years ago was largely non-diagnostic of major etiologies of persistent pain after lumbar surgery.

With more rigorous surgical indications, advanced imaging, and use of diagnostic spine injections, 70–100 % of causes of persistent pain have been elucidated. A more acceptable current definition of FBSS is: persistent or recurrent pain, mainly in the region of the lower back and legs, even after technically, anatomically successful lumbosacral spine surgeries.

- Chronic low back pain is neither "nonspecific" nor "idiopathic;" the causes of chronic low back pain can be determined in the majority of patients with history, physical exam, imaging, and diagnostic/therapeutic spine injections.
- Spine surgery outcomes and rates are closely monitored by payors and policymakers. More stringent definitions for success across all orthopedic surgery disciplines are expected and should include pain relief, functional assessment, medication usage, return to activities, and return to work.
- Surgical outcomes are negatively affected by obesity (BMI >30), type 2 diabetes mellitus, and depression. Studies have not borne out psychiatric pathology as the primary reason for persistent pain after lumbar surgery. However, if patients have significant pre- or postoperative co-morbid psychopathology, their psychiatric wellbeing should still be addressed as part of a multidisciplinary treatment approach.
- Emerging research shows that chronic pain patients and patients who take opiates may suffer from low vitamin D, low testosterone, low estrogen, osteopenia/osteoporosis, and other medical comorbidities. In addition to addressing smoking and NSAID use prior to surgery, optimizing treatment for medical comorbidities with bioidentical hormones may further improve surgical outcomes.
- The most common causes of persistent axial low back pain after fusion (as diagnosed by controlled injections) are: facet arthropathy, painful internal disk disruption, sacroiliac joint pain, hardware irritation/soft tissue pain, and adjacent segment disease.
- The most common causes of persistent leg pain after lumbar surgery are: recurrent/residual disk herniation or new herniation, neuropathic pain, and epidural fibrosis.
- Conscious sedation (including agents such as propofol, midazolam, and fentanyl) should not be used because of the statistically significant probability of obtaining a false-positive diagnostic block. To properly diagnose facet-mediated or sacroiliac joint pain, dual comparative anesthetic blocks are needed. Patients with false-positive results are likely to be subject to misdiagnoses and unnecessary procedures. Patients receiving blocks with sedation reported statistically significant greater mean reductions in pain diary scores and less procedure-related pain.
- If spine interventionalists adopt less stringent diagnostic criteria or surgeons use less rigorous surgical indications, outcomes suffer. Poor outcomes negatively affect the patient, spine interventionalist, and surgeon and make payors and policymakers reluctant to pay for treatment.

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Cell Transplantation for Lumbar Spine Degenerative Disk Disease

39

Christian Hohaus and Hans Jörg Meisel

39.1 Introduction

Low back pain is a very common symptom, affecting nearly three-quarters of the population some point in their life. While 90 % of the population recovers within 3 months, in some patients, chronic back or leg pain leads to long-term physical disability and a reduced quality of life. Disk anatomy likely plays a pivotal role in the underlying pain, yet abnormal spine and disk morphology, including disk herniation, have been described as normal findings in the asymptomatic population [1]. Why is it that some patients remain asymptomatic, while some symptomatic patients with degenerative changes may be treated?

Given that disk herniation is thought to be an extension of progressive disk degeneration that attends the normal aging process, seeking an effective therapy that staves disk degeneration has been considered a logical attempt to reduce back pain. Previous studies have validated genetic factors [2–5] and implicated nutrition [6] as relevant to the degenerative process. However, the high prevalence across diverse populations suggests that a myriad of unidentified factors likely contribute to the symptom complex.

As no effective therapies to retard or reverse disk degeneration have yet been devised, a variety of surgical procedures have been developed to treat disk degeneration and back pain. Unfortunately, the procedures currently available fail to provide an outcome that is structurally sound and at the same time physiologic. Surgery tends to limit motion. Fusion in particular seems to shift excessive stresses to adjacent spinal segments. Equally concerning in selecting fusion as an option is the fact that non-unions have been reported in 5–35 % of patients [7, 8] and that patients undergoing a repeat fusion for lumbar spine failed surgery have a clinical failure rate as high as 40 % [9–11]. The advent of tissue engineering has broadened the options for considering treatments that tailor repair to distinct anatomy. In particular, the use of cell and gene therapy to provide specific properties or repair specific tissues is widely considered an emerging modality for effecting treatment.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_39

Numerous scientific studies have provided observations concerning the biochemistry and biomechanics of the disk, offering insights and theories into structure-function-failure relationships [3, 12, 13]. The most apparent cellular and biochemical changes attributable to degeneration include a decrease in cell density in the disk that is accompanied by a reduction in synthesis of cartilage-specific extracellular matrix components, such as Type II collagen and aggrecan. As the proteoglycan content of the disk decreases, the resulting loss of water-binding capacity by the disk matrix, coupled with a subsequent reduced capacity for dissipating spinal forces, is thought to lead to degenerative disk disease [7, 14, 15].

Collagen plays a key load-bearing role in the disk, and changes in its extracellular matrix content have been attributed to aging as well as to the pathology of degeneration [16]. In normal intervertebral disks, at least seven different types of collagen are present (i.e., Types I, II, III, V, VI, IX, and XI), although Types I and II are the most abundant [17–22]. The anulus fibrosus contains more Type I collagen than Type II, whereas the nucleus pulposus is composed mainly of Type II collagen.

Calcification of the vertebral endplates is another factor thought to be relevant to disk degeneration. The passage of nutrients and waste products across the endplate depends on fluid flowing into the disk (during the night at bed rest) and flowing out during the day when we walk about [23]. Thus, shortcomings of permeability would be expected to adversely effect chondrocyte metabolism [24–26].

While cells constitute only 1 % of the adult disk tissue by volume, their role in matrix synthesis and metabolic turnover is vital. Most assessments of intervertebral disk failure have focused on degenerative, morphologic changes in disk tissue morphology that affect the biomechanical performance of the motion segment [13, 27]. In this vein, mechanical failure is little more than a corollary of matrix structure, which in turn depends on balanced cell metabolism for efficient maintenance of the disk matrix. Given the value of cells to the metabolic health of the disk, one therapeutic strategy could be to replace, regenerate, or augment the intervertebral disk cell population, with the goal of correcting matrix insufficiencies and restoring normal segment biomechanics.

Recent work has shown that disk aging and degeneration are accompanied by a decline in the number of cells in the disk, a change attributable to both necrosis and apoptosis [28]. Perhaps a more important outcome of this work and that of others has been to demonstrate that disk cells retain an ability to respond to both genetic endowment and in vivo stimulation and that when returned to the disk under controlled conditions, integrate with the surrounding tissue [6, 28–30].

With this in mind, we designed a study using the dog as our model to investigate the hypothesis that repair of the damaged disk is technically feasible, autologous cells can be reproducibly cultured under defined and controlled conditions, percutaneous delivery is possible, and disk cells will integrate with the surrounding tissue, produce the appropriate intervertebral disk extracellular matrix, and potentially provide a functional solution to disk repair.

39.2 Canine Trial of Chondrocyte Transplantation

The goal of this study was to test the hypothesis that restoration of intervertebral disk morphology could be achieved by transplantation of cultured autologous chondrocytes into the nucleus pulposus. As a natural model of degeneration has not been described in a large mammal, this study was fashioned after established work demonstrating that degeneration can be stimulated by damaging the outer anulus [31]. Under institutional guidelines of the Institutional Animal Care and Use Committee (IACUC), 18 purpose-bred, 2-year-old female dogs, weighing between 20 and 25 Kg, were studied to see whether the introduction of cultured autologous disk-derived cells

would repair a damaged disk and inhibit degenerative changes. Prior to surgery, 125 ml of blood was obtained from each of the dogs to serve as a serum supplement for autologous cell culture. As blood loss was insignificant during the surgical procedure, this approximate 6–8 % loss of total blood volume was not considered an additional risk to the animals.

The dogs were divided into two basic groups: 4 animals receiving autologous cells containing bromodeoxyuridine (BrdU) as a nuclear marker and the other 14 receiving autologous cells without a nuclear marker. Animals were radiographed to establish a baseline for preexisting spine pathology. Under general anesthesia, a minimal invasive approach was made to the posterolateral aspect of the canine lumbar spine. Lumbar intervertebral disks at levels L1/L2, L2/L3, and L3/L4 were identified as study levels for the procedure and disk tissue was collected. Approximately 200 mg of tissue was collected from the lateral aspect of the anulus, 100 mg of anulus material, and 100 mg of nucleus pulposus material.

The sampled disk cells were expanded in culture through several passages, with a goal of establishing a population of disk cells capable of producing matrix and sustaining an expanded volume within the damaged disk. The average number of cells expanded and transplanted in each L3–L4 disk was approximately six million cells. This procedure was done by the Co.don AG Teltow/Germany.

In this study, tissue was removed from the L1–L2 intervertebral disk, but chondrocyte transplantation was not performed. The L2–L3 disk was approached but not violated, thus serving as a surgical control, while the L3–L4 level underwent disk material removal and underwent chondrocyte transplantation 12 weeks later. The wound sites were closed with resorbable suture and the animals returned to their holding area. None of the animals developed problems related to the surgery and all regained full function.

An important criterion for evaluating the success of cell transplantation for the disk repair procedure was identifying that matrix regeneration was attributable to transplanted cultured expanded disk cells, rather than a result of inherent disk capacity for self-repair. BrdU, an analog nucleotide of thymidine, was incorporated into the nucleus during DNA synthesis and could later be identified by immunohistochemical techniques. As such, it was possible to analyze morphology in situ after repair and delineate cells that were transplanted from those already present in the host tissue. To verify the source of disk repair and matrix regeneration, BrdU was used as a cell marker in four animals.

During the last 4 days in monolayer culture, the cells in passage 2 were tagged by adding a small concentration of BrdU (1:1000) to the culture medium. To perform growth curves, monolayer cells in passage 1 were cultivated in six-well plates and the cell number in each well was determined daily. Viability of the cells was assessed by staining with trypan blue.

Twelve weeks after the disk tissue had been harvested, the autologous disk cell cultures were transplanted at L3–L4 on each of the dogs. The intervertebral disk between L1 and L2 served as the control for untreated degeneration. Cells were shipped from Teltow, Germany, overnight at 4–8 °C for transplantation. Animals were anesthetized, placed in right lateral recumbence, and the L3–L4 level was located by fluoroscopic imaging. As the previous surgeries had been performed from the right lateral side, the cultured cells were introduced through the left side of the anulus.

The animals were humanely euthanized 3 months (3 dogs), 6 months (7 dogs), 9 months (4 dogs), and 12 months (4 dogs) following the cell transplantation. Immediately after the dogs were killed, their lumbar spines were removed and the tissue analyzed (Fig. 39.1), MRI and X-ray analysis and coronal slices of the spinal column were performed to interpret disk height.

Tissue analyses included light microscopy and immunohistochemistry for assessing BrdU content (Fig. 39.2) and collagen expression.

The canine study evaluated whether autologous disk cell transplantation might be an appropriate therapeutic treatment to repair disk

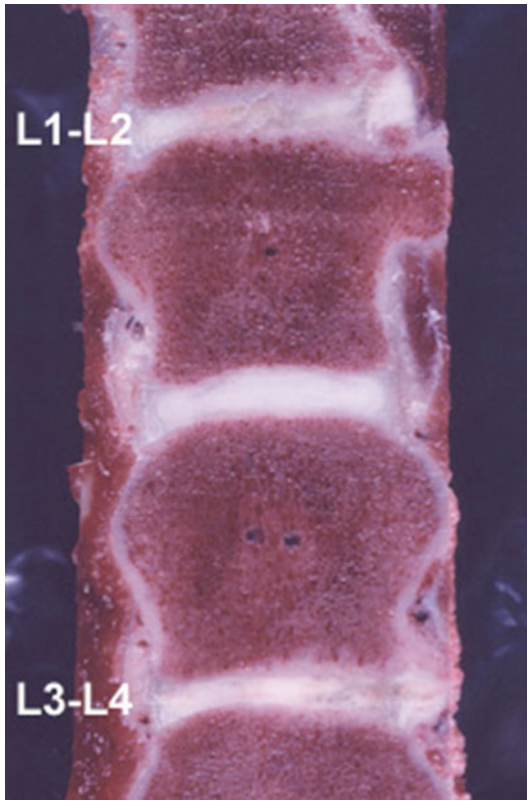

Fig. 39.1 Gross pathology 12 month follow-up after autologous chondrocyte transplantation in the Canine model. Level L3–L4 was transplanted, level L1–L2 received no treatment and displayed more scar tissue, L2–L3 was the control level with a normal intervertebral disk

damage and inhibit degeneration. In this context, several important observations emerged:

1. Autologous disk cells were expanded in culture and returned to the disk by a minimally invasive procedure after 12 weeks. Under defined conditions, it was possible to assure phenotype and assess metabolic capacity of the cells prior to transplantation.
2. Disk cells remained viable after transplantation as shown by BrdU incorporation and maintained a capacity for proliferation after transplantation as depicted by histology.
3. Transplanted disk cells produced an extracellular matrix that contained components similar to normal intervertebral disk tissue. Positive evidence of proteoglycan content was supported by accepted histochemical staining techniques such as safranin O-fast green.
4. Both Type II and Type I collagens were demonstrated in the regenerated intervertebral disk matrix by immunohistochemistry following chondrocyte transplantation.
5. There was a statistically significant correlation between transplanting cells and retention of disk height that was demonstrated at longer intervals following transplantation.

Although a morphotypic nucleus pulposus was not generated, cells that could appropriately be considered disk cells were identified in the intervertebral disks that had received disk cell transplantation. The observed matrix to cell ratio suggested strongly that these cells were elaborating a cartilage-specific matrix that was appropriate with respect to both collagen and proteoglycan components. No evidence of necrotic change was present, nor were there any active signs of tissue vascularization. Absence of bone in the intervertebral space and the productive matrix synthesis suggested that active remodeling and expression were guided by the demands of the anatomy and that cell response after transplantation was dependent on both the phenotypic identity of the cells and the biomechanical cues of the anatomy.

Cell viability and their capacity for matrix synthesis were particularly encouraging outcomes of this study. In the light of a 12-week interval between disk tissue sampling and cell transplantation, cells were placed into an environment that had fundamentally changed in both composition and function. Under the provision of central delivery and pressurized containment, the transplanted cells were prepared for the environment of the nucleus pulposus. The high cell to volume ratio of the transplanted cells, the deformable nature of the regional anatomy, and the inherent capacity of the cells to respond to new loading regimens all supported the vitality of the transplant conditions.

Extracellular matrix change, biomechanical variation, altered morphology, and cell viability are acknowledged steps leading to intervertebral disk degeneration. In the process of invigorating the population of vital disk cells and achieving matrix transformation, a positive observation regarding the morphology of the disk was made. The ability to control cell conditions, potentially to imbue the cells with additional genetic capac-

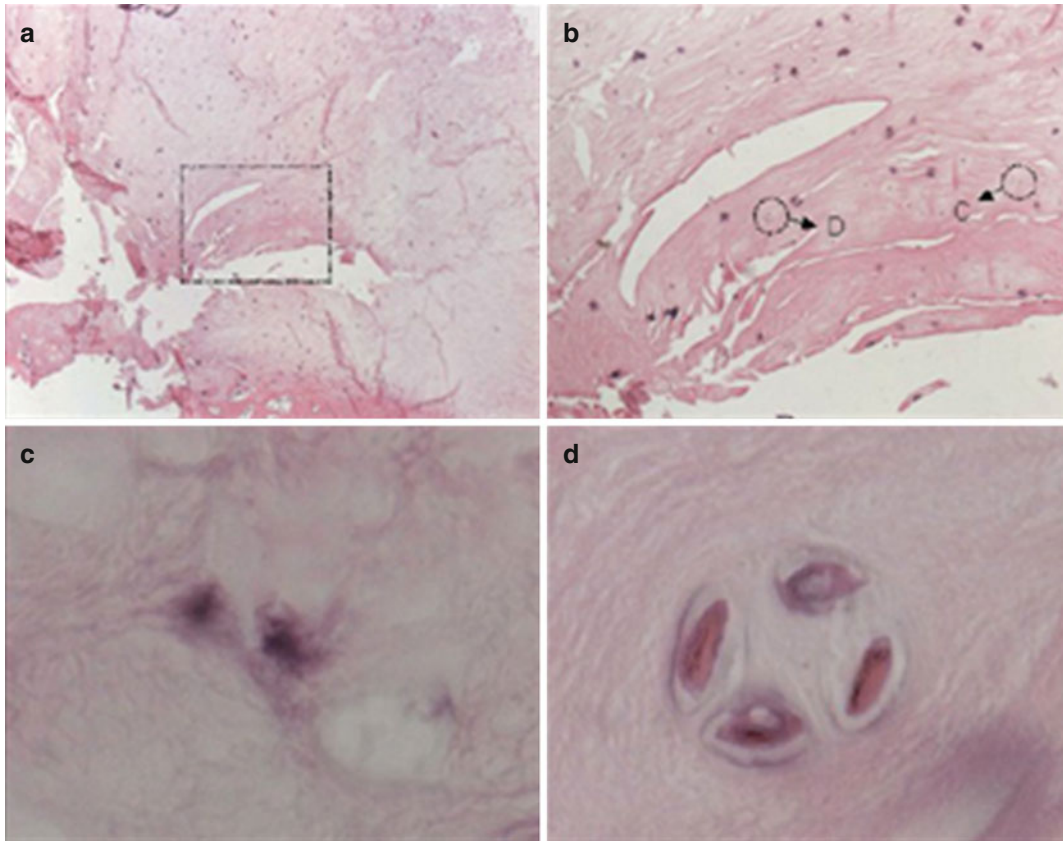

Fig. 39.2 Staining of paraffin sections of the regenerated intervertebral disk 6 months following cell transplantation. BrdU-containing chondrocytes were detected and stained by immunohistochemical procedures using DAB as the chromogen. Sections were counterstained by eosin. BrdU-positive cells are colored *black*. (**a**) Nucleus regenerates overview (25×); (**b**) BrdU-stained transplanted cells (200×); (**c**, **d**) single BrdU-stained transplanted chondrocytes, pericellular de novo synthesis of nucleus matrix (1,000×)

ity, and the availability of autologous tissue from diskectomy procedures make this technology both feasible and attractive.

39.3 EuroDisc Randomized Trial

After these positive and promising results, the EuroDisc Randomized Trial was initiated to embrace a representative patient group, examining not only the traumatic, less degenerative disk, but also to include patients with persistent symptoms that had not responded to conservative treatment and in whom a surgical treatment is considered.

Interventional surgery for disk herniation is one of the most widely used and effective treatments for back pain that emerges within the broad scope of disk degeneration. Successful removal of impinging tissue offers the individual patient substantial relief for associated pain. However, the reduction of tissue involved with the surgical procedure anatomically compromises the function of the affected disk and effects a load transfer to adjacent disks. Biological restoration with interventional cell therapy offers a potential for accentuating disk metabolism with an underlying intent to restore spine mechanics.

Patients who were to undergo surgical intervention at one level were eligible for participation in the trial; patients requiring treatment at more than one level were excluded from the study. Prior to their participation, all patients were advised of the potential risks and signed a letter of consent. No placebo group was commit-

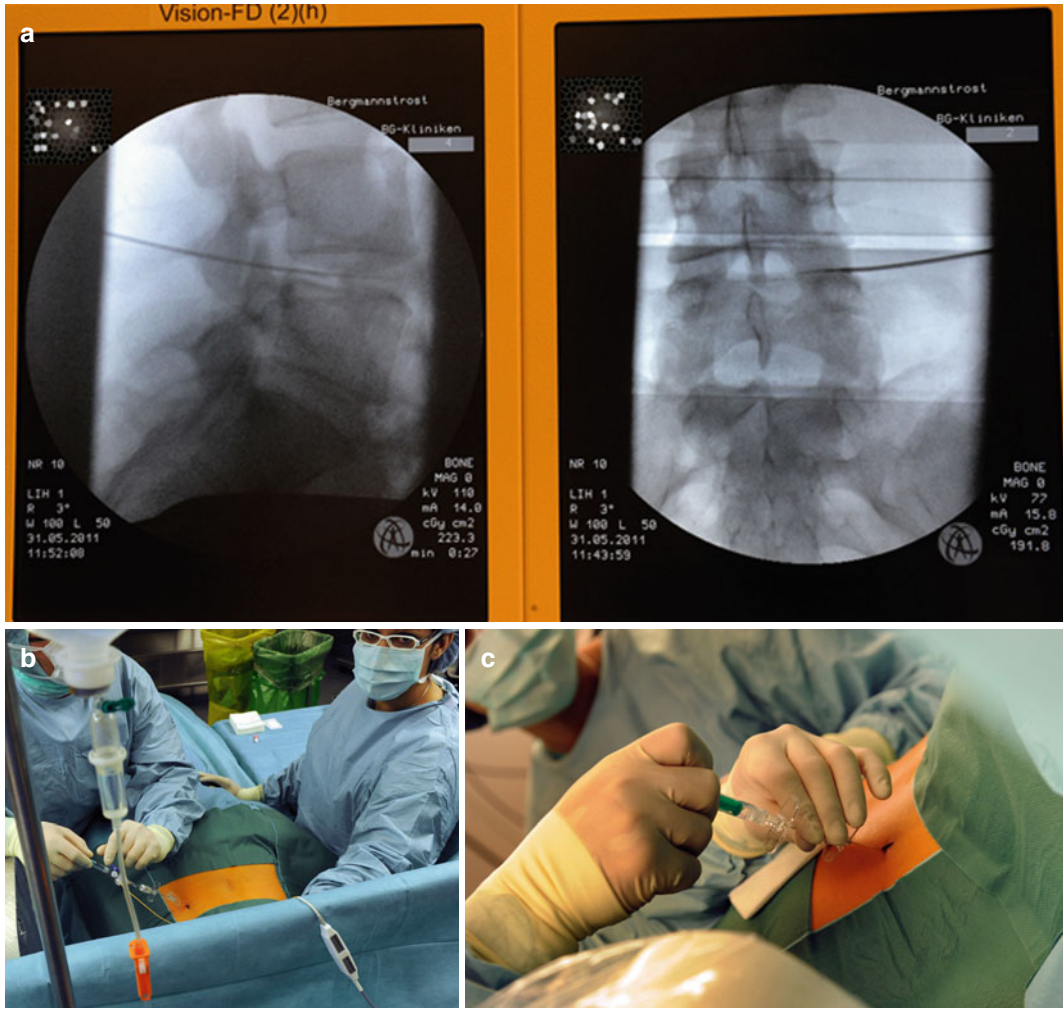

Fig. 39.3 Intraoperative setting. (**a**) Fluoroscopic-guided minimal invasive puncture of the intervertebral disk form the opposite side, (**b**) pressure-volume-test, (**c**) cell transplantation

ted to this study; each patient participating in the clinical trial was to undergo surgical treatment for their disk prolapse, and the prospective basis of cell transplantation separated the active treatment group from the control group. Patients were not blinded to their treatment. Randomization was done after the open microdiskectomy. Eligibility was limited to patients between 18 and 60 years of age, with a body mass index (BMI) below 28. Exclusion criteria for participating in the study included sclerotic changes, edema, Modic changes of Types II or III, and spondylolisthesis among other accepted criteria such as pregnancy, etc.

Operative procedures were performed as minimally invasive open sequestrectomies performed by an experienced neurosurgeon under general anesthesia. The harvested cells from the sequestered disk material were cultured by the Co.don AG Teltow/Germany under GMP conditions. More than five million living disk cells were included in the solution for transplantation.

A single puncture with a minimal caliber cannula was used to achieve a precise delivery with minimal trauma to the patient and to the anulus (Fig. 39.3). The technique was developed with respect to literature that has demonstrated a size-specific correlation between anular injury and

disk degeneration. A simple, minimal invasive technique was necessary to reduce the wound site trauma and effectively support cell injection without further injury to the anulus. Cells were transplanted approximately 12 weeks following sequestrectomy to assure that the anulus has healed and will contain the cells. Using a pressure-volume test prior to the delivery of any chondrocytes, cells could be placed with the confidence that they would be retained at the site of delivery.

One hundred and twelve patients have been enrolled in the EuroDisc Study; the primary criteria follow-up was intended to occur at 1 year, an interim analysis scheduled at 2 years, and the final analysis will be completed at 4 years. The primary clinical evaluation criterion was the Oswestry Low Back Pain Disability Questionnaire. Secondary criteria include the SF-36, Prolo Score [32], Quebec Back Pain Disability Scale, MRI, and X-ray evaluation. The use of the Oswestry disability questionnaire in clinical trials is recommended by the German Orthopedic Society (DGOT), demonstrating acceptable test quality and satisfactory test-retest reliability. The Quebec Back Pain Disability Scale, another self-rating scale, was professionally developed using factor analysis comprising high internal consistency, high item discriminability, and high test-retest reliability. Finally, the SF-36, an often used scale to assess patients' general condition and quality of life, and a VAS will be used to standardize measureable pain.

The interim analysis, made by a cut in January of 2006 to assess whether intervention correlated with positive clinical outcomes, forms the basis for this report. Within the analysis, successive 3-month, 6-month, 12-month, and 24-month assessments are stratified within the continuum of the study. The information within this study allows a broad interpretation of the general progress made over 2 years following a clinical intercession with autologous disk cells. Interim analysis was performed on the first 28 patients who reached 24-months follow-up with regard to autologous disk cell transplantation (ADCT). These first 28 patients were randomized in three different centers.

For descriptive analysis of efficacy, the total sum score as well as the disability index of the Oswestry Low Back Pain Disability Questionnaire (OPDQ) and the total sum score of the Quebec Back-Pain Disability Scale (QBPD) were taken into account from the initial presurgical presentation through the 2-year follow-up. The outcomes are depicted in Table 39.1. Based on the mean total sum score as well as the disability index of the OPDQ, differences in initial presentations between the control group and those receiving autologous cells were not minimal. Surgery as an intervention was a positive experience and, as expected, substantially reduced the patient's disability and pain. The trend in reduction of the total sum score continued to decrease in the patients whose treatment was supplemented by cell transplantation, while the control group did not sustain continual improvement. Two years following the therapeutic intervention with cells, both the total sum score and the disability index of the OPDQ were lower in the ADCT group compared with the control.

Descriptive analyses of the mean total sum score of the QBPD prior to sequestrectomy, prior to ADCT/control, and 3 months after ADCT/control demonstrated a decrease in mean and median sum scores in both groups. Although the mean and median values for both the ADCT and the control group decreased between 1 and 2 years, the assessments for the ADCT group were clearly lower (Table 39.2). Patient global assessment of pain demonstrated some fluctuation although both groups received substantial relief from the surgical intervention. However, as patients were tracked over the course of the 2-year follow-up, changes emerged that suggest that the ADCT-treated patients have a lower pain scores (Table 39.3).

MRI was used to assess the respective disk height along the course of the analyses from the date of the sequestrectomy until the 2-year follow-up (Fig. 39.4). In addition to the disk height, the content of the liquid component was evaluated as a means of assessing matrix content. Results of the analysis of the intervertebral disk height compared affected (treated with surgery, or with surgery and cells) with non-affected adja-

Table 39.1 Total sumscore and disability index of the OPDQ based on patients who had been followed for 2 years after autologous disk chondrocyte transplantation

Total sumscore									
		N	Mean	SD	Min	Lower quartile	Median	Upper quartile	Max
Visit -1	ADCT	12	28.42	9.30	13.00	20.00	29.50	36.00	45.00
	Control	16	26.88	9.99	14.00	18.00	25.50	34.00	46.00
Visit 0.5	ADCT	12	8.00	6.89	0.00	2.50	7.50	12.50	24.00
	Control	15	8.40	4.69	1.00	4.00	9.00	13.00	15.00
Visit 1	ADCT	11	6.73	8.56	0.00	0.00	5.00	12.00	28.00
	Control	14	7.14	6.36	0.00	1.00	5.50	13.00	19.00
Visit 2	ADCT	10	9.10	10.72	0.00	1.00	6.50	12.00	35.00
	Control	14	7.79	7.42	0.00	2.00	6.50	12.00	26.00
Visit 3	ADCT	11	7.82	8.46	0.00	2.00	4.00	15.00	25.00
	Control	14	7.07	5.94	0.00	1.00	7.00	12.00	19.00
Visit 4	ADCT	12	6.00	8.89	0.00	0.00	2.00	8.50	29.00
	Control	16	7.56	6.52	0.00	2.50	6.00	13.00	19.00
Disability index (%)									
Visit -1	ADCT	12	56.83	18.60	26.00	40.00	59.00	72.00	90.00
	Control	16	53.75	19.97	28.00	36.00	51.00	68.00	92.00
Visit 0.5	ADCT	12	16.06	13.73	0.00	5.33	15.00	25.00	48.00
	Control	15	16.80	9.37	2.00	8.00	18.00	26.00	30.00
Visit 1	ADCT	11	13.45	17.11	0.00	0.00	10.00	24.00	56.00
	Control	14	14.29	12.72	0.00	2.00	11.00	26.00	38.00
Visit 2	ADCT	10	18.64	21.53	0.00	2.00	13.89	26.67	70.00
	Control	14	15.62	14.80	0.00	4.44	13.00	24.00	52.00
Visit 3	ADCT	11	15.64	16.92	0.00	4.00	8.00	30.00	50.00
	Control	14	14.14	11.88	0.00	2.00	14.00	24.00	38.00
Visit 4	ADCT	12	12.00	17.79	0.00	0.00	4.00	17.00	58.00
	Control	16	15.19	12.99	0.00	5.50	12.00	26.00	38.00

Visit -1: Sequestrectomy. Visit 0.5: ADCT/control. Visit 1: 3 months after ADCT/control visit 0.5
Visit 2: 6 months after ADCT/control visit 0.5, Visit 3: 12 months after ADCT/control visit 0.5
Visit 4: 24 months after ADCT/control visit 0.5

Table 39.2 Total sumscore of the QBPD based on patients with at least 2 years follow-up after autologous disk chondrocyte transplantation

Total sumscore									
		N	Mean	SD	Min	Lower quartile	Median	Upper quartile	Max
Visit -1	ADCT	12	45.08	17.60	23.00	31.50	42.00	55.00	82.00
	Control	16	49.69	18.69	21.00	34.00	45.00	65.00	81.00
Visit 0.5	ADCT	12	14.75	16.07	0.00	4.50	8.50	17.50	50.00
	Control	15	18.27	11.04	1.00	6.00	19.00	25.00	38.00
Visit 1	ADCT	11	10.64	16.05	0.00	1.00	4.00	15.00	55.00
	Control	14	13.29	9.72	3.00	6.00	8.50	24.00	30.00
Visit 2	ADCT	10	15.00	20.77	0.00	1.00	10.00	19.00	70.00
	Control	14	13.93	11.76	1.00	4.00	12.50	18.00	41.00
Visit 3	ADCT	11	11.09	16.71	0.00	2.00	4.00	19.00	57.00
	Control	14	12.71	12.55	2.00	4.00	9.50	17.00	48.00
Visit 4	ADCT	12	9.33	15.33	0.00	0.50	3.50	12.50	55.00
	Control	16	13.94	12.61	0.00	5.00	8.00	22.50	41.00

Visit -1: Sequestrectomy, Visit 0.5: ADCT/control, Visit 1: 3 months after ADCT/control visit 0.5
Visit 2: 6 months after ADCT/control visit 0.5, Visit 3: 12 months after ADCT/control visit 0.5
Visit 4: 24 months after ADCT/control visit 0.5

Table 39.3 Global assessment of pain based on patients with at least 2-years follow-up after autologous disk chondrocyte transplantation

Global assessment of pain (100 mm VAS)									
		N	Mean	SD	Min	Lower quartile	Median	Upper quartile	Max
Visit -1	ADCT	11	59.45	22.76	15.00	48.00	60.00	76.00	96.99
	Control	16	57.31	28.51	0.00	27.00	70.00	79.50	88.98
Visit 0.5	ADCT	12	19.17	19.37	0.00	2.50	13.00	31.50	65.00
	Control	15	17.20	14.70	0.00	3.00	14.00	31.00	46.00
Visit 1	ADCT	11	12.82	19.37	0.00	0.00	3.00	24.00	61.99
	Control	14	14.36	10.59	1.00	4.00	15.00	22.00	33.00
Visit 2	ADCT	10	21.00	22.85	0.00	8.00	16.50	23.00	78.99
	Control	14	14.00	16.51	1.00	2.00	5.50	19.00	51.00
Visit 3	ADCT	11	18.00	18.73	2.00	3.00	9.00	25.00	56.00
	Control	14	15.07	12.16	0.00	3.00	12.00	29.00	37.00
Visit 4	ADCT	12	11.17	13.48	0.00	1.00	5.00	17.00	39.00
	Control	16	15.62	15.16	1.00	3.00	12.50	26.50	53.99

Visit -1: Sequestrectomy. Visit 0.5: ADCT/control, Visit 1: 3 months after ADCT/control visit 0.5
Visit 2: 6 months after ADCT/control visit 0.5, Visit 3: 12 months after ADCT/control visit 0.5
Visit 4: 24 months after ADCT/control visit 0.5

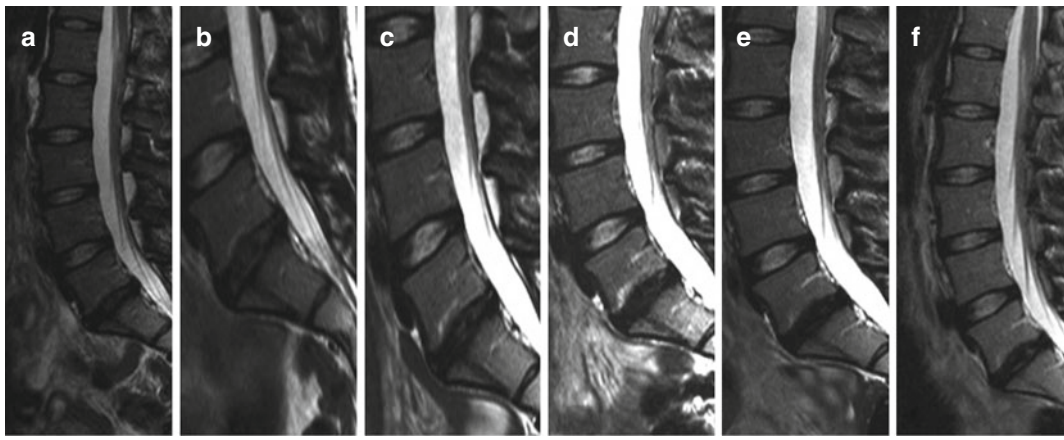

Fig. 39.4 A 28-year-old woman undergoing diskectomy in level L5–S1. The 60-month follow-up MRI displays increased signal intensity in the transplanted L5–S1 level. (**a**) Pre-transplantation. (**b**) 1 day post transplantation. (**c**) 3 month post transplantation. (**d**) 12 month post transplantation. (**e**) 24 month post transplantation. (**f**) 60 month post transplantation

cent segments in the same patients, and also measured the relative vertebral heights as a means of assessing patient demographics and morphologic variation. Comparison of the mean intervertebral disk heights and the vertebral heights revealed no differences between the groups.

An analysis of fluid content of the intervertebral disk at each visit demonstrated that more than 80 % of the affected segments showed decreased hydration 3 months following surgery (Table 39.4). In general, the proportion of affected segments with a diminished water content decreased over the course of the trial. Of particular interest was the outcome at 2 years, where the ADCT-treated group showed a substantially higher normalization as a group; 41 % normal fluid content compared with only 25 % normal content in the control group. Perhaps the most interesting of all the data to emerge from this study comes from inspecting disks either one or two segments from the treated intervertebral disk. Fluid levels at both of these segments

Table 39.4 Analysis of fluid content of the intervertebral disk with at least 2-years follow-up after autologous disk chondrocyte transplantation

Content of liquid								
		N	Affected segment		1. Non-affected segment		2. Non-affected segment	
			Normal (%)	Decreased (%)	Normal (%)	Decreased (%)	Normal (%)	Decreased (%)
Visit -1	ADCT	12	16.67	83.33	83.33	16.67	83.33	16.67
	Control	15	13.33	86.67	86.67	13.33	46.67	53.33
Visit 0.5	ADCT	12	25.00	75.00	81.82[a]	18.18[a]	50.00	50.00
	Control	14	0.00	100.0	78.57	21.43	28.57	71.43
Visit 3	ADCT	11	27.27	72.73	90.91	9.09	63.64	36.36
	Control	13	23.08	76.92	76.92	23.08	53.85	46.15
Visit 4	ADCT	12	41.67	58.33	91.67	8.33	66.67	33.33
	Control	16	25.00	75.00	86.67[b]	13.33[b]	56.25	43.75 %

Visit -1: Sequestrectomy, Visit 0.5: ADCT/control, Visit 3: 12 months after ADCT/control visit 0.5
Visit 2: 6 months after ADCT/control visit 0.5, Visit 3: 12 months after ADCT/control visit 0.5
Visit 4: 24 months after ADCT/control visit 0.5
[a] : only 11 values available
[b] : only 15 values available

showed a substantially higher percentage of normal fluid content despite the fact that they were distant from the surgical intervention site.

The interim analysis of the EuroDisc Study revealed the following:

1. Disk cells that had been removed as a normal part of sequestrectomy could be expanded in culture under GMP conditions and returned to the patient after the anulus had been allowed to heal for 12 weeks.
2. Disk cell transplantation could be delivered by percutaneous technique.
3. Patients who received autologous disk cell transplantation had greater pain reduction at 2 years compared with patients who did not receive cells following their diskectomy surgery.
4. Disks in patients that received cells demonstrated a significant difference, as a group, in the fluid content of their treated disk when compared to control.
5. Adjacent intervertebral disks, both at one level and two levels from the intervertebral disk that received the cell therapy also demonstrated a difference in fluid content.

The results of this study are encouraging from several perspectives. First morphologic outcomes mirrored that seen in our preclinical animal study [33]. Second, the pain relief seen in the pilot study which served as a basis for this clinical trial was sustained for the course of this 2-year interim analysis. This gives cause to the success of the cell-based intervention. Chondrocytes for transplantation into degenerated disks are limited in daily practice. Different cell types with regenerative capacity are required to treat patients with clinical symptoms but earlier levels of disk degeneration.

Adipose tissue provides such an alternative source of regenerative cells with little donor site morbidity. These regenerative cells are able to differentiate into a nucleus pulposus-like phenotype when exposed to environmental factors similar to disk and offer the inherent advantage of availability without the need for transporting, culturing, and expanding the cells [34, 35].

39.4 Canine Trial of Adipose-Derived Regenerative Cell Transplantation

In an effort to develop a clinical option for cell placement and assess the response of the cells to the postsurgical milieu, adipose-derived cells were collected, concentrated, and transplanted under fluoroscopic guidance directly into a surgically damaged disk.

For this study, 12 dogs 2 years of age, were obtained. Adipose cells were harvested from the super-scapular region of the neck (scruff) and adherent cells separated, collected, and labeled with DAPI. Adipose tissue has been known for some time to contain regenerative cells in addition to fat cells [36]. Three lumbar intervertebral disk levels in each dog underwent a partial nucleotomy; other levels served as nonoperated controls. Levels of intervention, as well as the regimen of treatment, were dually randomized. Three interventions were used in this study; adipose-derived cells in hyaluronic acid (HA) carrier, HA alone, or no intervention – all deliveries were guided by fluoroscopy. Assessments were made by MRI, radiography, microscopy, RT-PCR, and ELISA.

Six dogs were radiographed, received MRI scans (Fig. 39.5), and then were euthanized by 6 months. The disk tissue was harvested from the lumbar spine in each dog (Fig. 39.6). Cells were seen to be viable in the tissue (Fig. 39.7). Matrix composition was assessed; assays were made of aggrecan, Types I and II collagen by both RT-PCR and ELISA to assess and compare matrix regeneration. mRNA and protein from each level were presented with respect to normal values defined as the 100 % expression (Table 39.5).

Table 39.6 depicts the relative protein levels as measured by ELISA.

The data were calculated with two samples t-test, comparing control with interventions at $P<0.05$ and $P<0.01$. Statistical differences were found between the control and each intervention at $P<0.01$, whereas the difference between control and HA plus cells was only significant at $P<0.05$. No significant difference could be shown between HA alone and no intervention. These evaluations and other morphometric assessments support:

1. Cell viability follows implantation.
2. Supplementing adipose cells following injury supports regeneration.
   - Morphology was maintained.
   - Intervertebral disk height was not lost.
   - MRI signal remained similar to native control.
3. Hyaluronic acid was insufficient to prevent disk degeneration or desiccation.

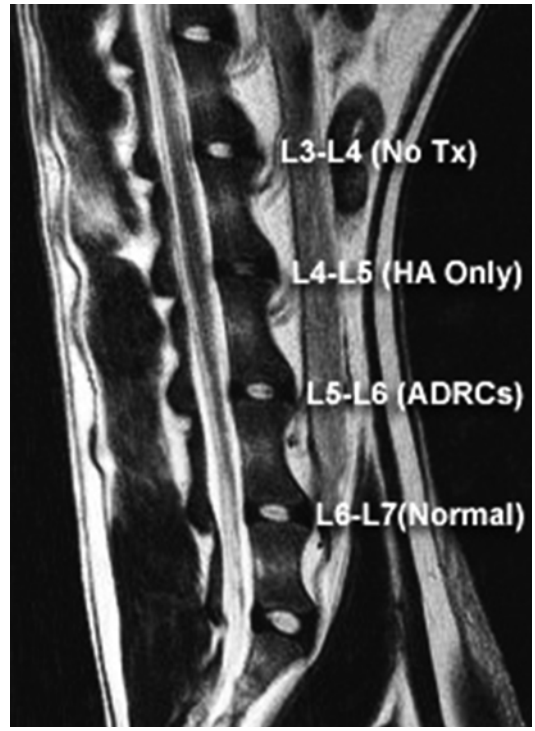

Fig. 39.5 Six-month follow-up MRI sagittal section (same dog as in Fig. 39.2)

4. Lack of intervention resulted in progressive degeneration.
5. A limited nucleotomy procedure, similar to that which would be experienced following clinical microdiskectomy, resulted in prolapsed anulus tissue into the central space of the nucleus pulposus.
6. No significant regeneration of cells or matrix occurred without treatment.

The results of the study provide evidence that cells harvested from adipose tissue might offer a reliable source of regenerative potential capable of bio-restitution. Such makes the case for using adipose-derived cells; first, cells can be transplanted percutaneously; and second cells survive and functionally adapt and produce an appropriate matrix. The span of this study was sufficient to show that freshly isolated cells will survive the trauma associated with postsurgical inflammation. The time to treat, the cell carrier, and the ability of the cells to integrate into the disk matrix were all certainly convincing.

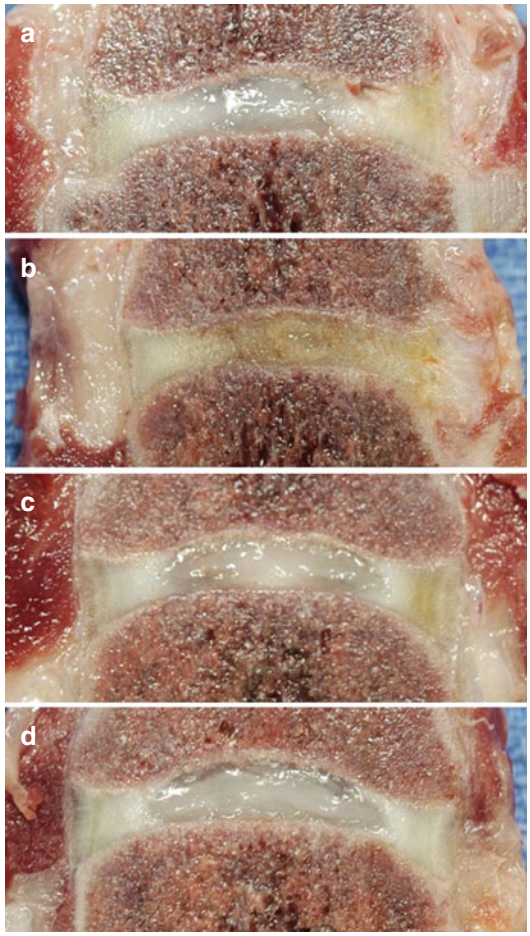

Fig. 39.6 Six-month follow-up gross section pathology. (**a**) L3–L4 no treatment. (**b**) L4–L5 hyaluronic acid alone. (**c**) L5–L6 adipose-derived stem cells in hyaluronic acid. (**d**) L6–L7 normal disk

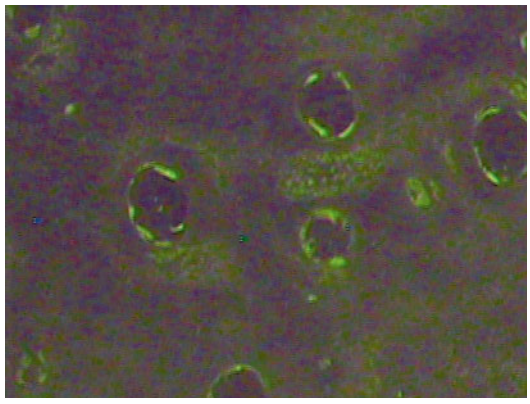

Fig. 39.7 Cell viability and cell sustenance were judged positive by DAPI-stained nuclei that were present 6 months following transplantation of the adipose-derived stem cells

39.5 Discussion

Cell transplantation for degenerative disk disease is possible, and the good results of the aforementioned clinical trial provide a promising outlook for the future treatment for patients with intervertebral degenerative disk disease.

Autologous disk cell transplantation after sequestrectomy is a safe and technical feasible procedure. Transplanted chondrocytes are viable in situ and create a functional matrix.

The first results of the EuroDisc Study give strong evidence for the safety and efficiency of the disk-derived cell transplantation applied following sequestrectomy to delay or inhibit ongoing processes of disk degeneration. After transplantation a statistically significant decrease in OPDQ, QBPD, and VAS in ADCT-treated patients for disability and pain is measured. In the MRI analysis, less decreased liquid content in affected intervertebral disks in the ADCT group could be displayed. A statement for the ideal group of patients who profits most from the autologous disk cell transplantation is at this time not possible.

The technique of autologous disk cell transplantation is only possible for patients who underwent a sequestrectomy. It might be better to transplant disk cells in the earlier stage of degeneration without any loss of matrix from the intervertebral disk, but this unfortunately requires an operation. Surgery to harvest cell material in the early stages of disk degeneration introduces the risk of infection to the disk and bone, the risk of nerve root injury, and other potential complications. Therefore, there is no ethical or medical foundation for this consideration.

In patients with symptoms of disk degeneration and MRI findings according to the Pfirrmann classification [37] of one to three along with symptomatic nerve root compression by a sequestered nucleus pulposus prolapse who plan to undergo a minimal invasive operative procedure, the possibility of autologous disk cell transplantation may now be entertained.

For patients with intervertebral degenerative disk disease who do not need to undergo operative treatment with sequestrectomy

Table 39.5 Relative mRNA for specific matrix proteins – comparison between treatments

	Control	Hyaluronic acid alone	Adipose-derived stem cells with hyaluronic acid	No intervention
Aggrecan	100	43.6	85.6	37.9
Type I col	100	73.2	87.1	67.2
Type II col	97.5	41.5	82.8	41.35

Table 39.6 Relative protein for specific matrix proteins – comparison between treatments

	Control	Hyaluronic acid alone	Adipose-derived stem cells with hyaluronic acid	No intervention
Aggrecan	100	62.3	83.0	58.4
Type I col	97.7	74.9	88.4	71.2
Type II col	99	55	85	53

concerning by root nerve compression with untreatable pain or neurological deficits, a therapeutic option could be the transplantation of adipose-derived stem and regenerative cells.

We have presented in the animal model the evidence that these cells can be transplanted at surgery using fluoroscopic guidance and that these cells can be injected directly into the intervertebral disk with the expectation that they will remain viable and produce appropriate, tissue-specific matrix [38, 39].

If the future results of the adipose-derived and regenerative cell study present demonstrate promising outcomes, this may represent a safe and easy technique of producing cells for minimal invasive transplantation into a symptomatic degenerative intervertebral disk without open operative intervention.

In a first clinical study using stem cells for treatment of intervertebral degenerative disk disease, Orozco et al. illustrate the technical feasibility and safety [40]. Ten patients with chronic back pain diagnosed with lumbar disk degeneration with intact anulus fibrosus were treated with autologous expanded bone marrow MSC injected into the nucleus pulposus area. The follow-up time was 1 year and there was no control group. Treated patients exhibited rapid improvement of pain and disability. The authors compare this favorably with the results of other procedures such as spinal fusion or total disk replacement. These positive effects should be studied further more and should transfer into a controlled randomized study.

Another option for these patients could be the transplantation of juvenile allogenic chondrocyte cells. Coric et al. could demonstrate in a small group of patients the technical feasibility and safety of this procedure by using juvenile allogenic chondrocyte cells harvested from the articular surface of cadaveric donor tissue [41]. These cells were transplanted using fibrin glue like carrier.

Conclusion

A total regeneration of the degenerated intervertebral disk is today not possible. The goals of regenerative medicine at this time are to prevent further progression of disk degeneration and its associated symptoms.

The now available, safe, and well-studied strategy for arresting and reversing degenerative disk disease is the autologous disk-derived cell transplantation after sequestrectomy [39].

Our own experience currently embraces more than 120 patients treated with autologous disk cell transplantation over the last 10 years. This is the largest number of patients with degenerated intervertebral disk disease treated with cell transplantation under strong study conditions. All patients profit from transplantation via reduced back pain and increased quality of life. All of the patients with an employment contract could return to work after transplantation. Over time, MR

images demonstrate a stable disk height in the transplanted segment. The reduction of the reherniation rate was by 52 % compared with the control group. We didn't see any inflammation in all these patients.

However, the use of autologous chondrocytes requires the ex vivo expansion of cells, which is costly, time-consuming, and highly regulated, making it an intricate procedure.

An alternative that might circumvent these disadvantages is the use of a one-step procedure, using stem cells obtained from autologous adipose tissue. Ongoing studies should provide more information about the possibility of using stem cells for regenerative therapies in intervertebral degenerative disk disease.

Pitfalls and factors for associated drawback of these regenerative therapies should include the alteration of regulatory frameworks as the European Union – Advanced Therapy Medical Products (EU-ATMP) regulation, as well as refined reimbursement strategies.

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Spinal Robotics: Present Indications and Trends

40

Konstantin Hockel, Gottlieb Maier, Marcos Tatagiba, and Florian Roser

40.1 Introduction: Image-Guided Surgery

The success of spinal surgery is highly dependent on accuracy. Surgeons are aware of the close local relations when manipulating the anatomical structures of the spine, i.e., vascular and neuronal structures, bone, ligaments, and joint space, which eventually determines the clinical outcome.

With conventional open-spine surgery, frequently consisting of decompression and stabilization, the target structures and trajectories are identified by exposure of the surface anatomy in combination with 2D fluoroscopy. Not only high-grade degenerative disease, spinal deformities, and revision surgery but also the increasing numbers of minimal invasive techniques create a challenge for the anatomical orientation, even for the experienced surgeon.

There exist several computer-assisted image guidance systems that help to visualize the anatomical relations in a 3D environment and facilitate the accurate placement of spinal instrumentation [1–3]. Such systems typically improve the accuracy of screw placement while reducing the need for extensive fluoroscopic imaging [4]. Several manufacturers have introduced computer-assisted navigation systems designed to increase implant placement accuracy in spine surgery.

A meta-analysis published by Kosmopoulos and Schizas, covering 37,337 pedicle screw implants in total, determined in a subgroup of in vivo implants a median accuracy of 95.1 % and 90.3 % with and without the assistance of navigation, respectively (15,358 screws) [1]. Verma et al. were determined to assess the actual functional benefit for the patient by applying computer-assisted navigation [3]. Their evaluation of 23 studies confirmed the superior accuracy of navigation over conventional pedicle screw placement. On the other hand, no statistical significant difference could be found for complication rates and the study was unable to make conclusion regarding functional outcome.

In recent years, the implementation of intraoperative imaging has further refined the possibilities and helped to overcome some drawbacks of

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_40

image-guided navigation for spinal instrumentation. Intraoperative 3D fluoroscopy and computed tomography (CT) increases accuracy of navigation system and facilitates the registration process [5]. While the benefits of intraoperative image-guided surgery are evident, there is further demand for alternative active assistance in the surgical workflow of spinal procedures.

40.2 Surgical Robots for Spinal Procedures

In many ways, spine surgery is ideally suited for the integration of robot-assisted surgical procedures. Although navigation assists the surgeon in display of trajectories in a complex 3D environment, the surgical task, e.g., cannulating the pedicle, has traditionally been carried out "free hand." This manipulation has to be performed in close proximity to critical structures that are more frequently accessed through minimally invasive approaches. A robotic interface actually represents the so far missing link between preoperative imaging, trajectory planning, and surgical execution. Thereby, it can significantly improve microsurgical dexterity and perform repetitive tasks with precision and reproducible results [6, 7].

A variety of surgical robots for different applications have been introduced, e.g., general surgery, cardiac surgery, urology, and spine surgery. Surgical robots can be classified into three broad categories, varying in their degree of automation [8]: (1) supervisory-controlled systems in which the surgeon plans the operation offline, specifying the motions that the robot must follow to perform the operation, and the robot then performs the procedure autonomously with the surgeon closely supervising; (2) telesurgical systems that allow the surgeon to directly control the surgical instruments held by the robot via a joystick or hand controls in which task execution can be either passive or active; and (3) shared-control systems that allow both the surgeon and the robot to directly control the surgical instrument at the same time.

Only a handful of robotic systems are specifically designed for spinal applications [9–15]. The Miro system (German Aerospace Center (DLR), Cologne, Germany), comprised of a robotic arm and an optical tracking system, positions a drill holder, through which the surgeon performs the procedure, has been evaluated for the placement of pedicle screws [10]. The Georgetown Robot (Johns Hopkins University, Baltimore, MD, USA), introduced in 2002, was designed as a percutaneous needle driver for minimally invasive spine procedures under biplane fluoroscopic guidance [15].

In addition, there are two readily commercially available robotic systems, i.e., the da Vinci (Intuitive Surgical, Sunnyvale, CA, USA) and the Renaissance/SpineAssist platform (Mazor Robotics Ltd., Israel). The teleoperated da Vinci enables the surgeon, who operates the control handles, to translate his hand movements via a robotic arm to the surgical field, facilitating complex manipulations, motion scaling, and tremor reduction. In spine surgery, it has been implemented in animal studies performing anterior lumbar interbody fusion, paraspinal schwannoma resection, laminotomy, disk incision, and dural suturing procedures [12–14, 16]. Thus far, this system was evaluated in humans for transoral odontoidectomy and for decompression of the craniocervical junction [11, 17]. The da Vinci system offers improved visualization and dissection of soft tissue structures [18] in deep cavities (e.g., transthoracic approaches) but lacks bone-handling instruments.

Today, the Renaissance/SpineAssist Surgical Guidance Robot available for routine clinical use in spinal procedures resembles a semiautonomous, shared-control system. The robot is a cylindrical (50 × 90 mm) device equipped with an end effector with 6° of freedom. The bone-mounting platform interfaces the robotic device with the patient's skeleton, and the robotic arm is positioned according to preplanned, image-guided trajectories, and the surgeon directs the instruments (e.g., drill guide, cannulas) along the predefined path. Applying this concept, the device is not only applicable for spinal instrumentation but also for collecting biopsies, tumor excisions, cement augmentations, and extraforaminal disk prolapses in distorted anatomic spaces [19–24].

40.3 Present Data for the Use of Robotic Systems in the Lumbar Spine

40.3.1 Instrumentation Accuracy and Radiation Exposure

So far, a clinical evaluation of surgical robots in treatment concepts of the lumbar spine has only been performed for the SpineAssist platform. Since 2005, numerous cadaveric and clinical studies on the SpineAssist system have been evaluating the technical feasibility, radiation exposure, and the accuracy of pedicle screw instrumentation at the thoracic, lumbar, and sacral spine [20, 23, 25–31].

A recent meta-analysis by Marcus et al. evaluated all available studies, including two randomized, two cohort studies, and one cadaver study [20, 21, 25–27], comparing pedicle screw placement with robot assistance vs. fluoroscopy guidance [32]. Among the total of 1,308 pedicle screws, 729 were instrumented robot assisted and 579 under fluoroscopy guidance with a satisfactory position of 94.1 % and 92.7 %, respectively.

A retrospective, multicenter evaluation of 3,271 SpineAssist-supported spinal implantations between 2005 and 2009, involving a large percentage of pediatric scoliosis patients, reported a clinically acceptable placement rate of 98 % assessed by intraoperative fluoroscopy [19]. Postoperative CT-based evaluation of a subset of patients included 646 pedicle screws and demonstrated an accuracy of 98.3 % according to Gertzbein and Robbins A and B criteria [33], with a mean axial and sagittal plane deviation of 1.2 ± 1.49 mm and 1.1 ± 1.15 mm, respectively. Only two screws deviated >4 mm from the pedicle wall, but without irreversible neurological deficits reported.

Pechlivanis et al. in their prospective study report successful integration of the device in 31 cases, with 98.5 % of screws demonstrating axial and longitudinal accuracy, i.e., deviations less than 2 mm [34]. Another case series evaluated a total of 960 pedicle screws in 102 patients, primarily presenting spinal deformities and or revision surgeries. Accurate positioning was determined for 98.9 % of the screws [22]. Eleven screws were considered misplaced, of which ten screws were manually corrected during surgery. One patient required implant removal within 3 days of surgery as a result of radiculopathy. Screw misplacement was presumably caused by tool "skiving," i.e., the tip of the drill holder or guiding tool skids off the intended entry point leading to an aberrant trajectory.

Similar aspects for inaccurate screw placement have been pointed out recently by Ringel et al. [25]. In contrast to all other comparative data, this randomized, prospective study assessed screw accuracy in favor of freehand fluoroscopy-guided over robot-assisted instrumentation with a satisfactory placement rate (Gertzbein and Robbins A and B on postoperative CT) of 93 and 85 %, respectively. They concluded that besides displacement of the entry point by soft tissue pressure, an unstable attachment of the robot to the spine may have contributed to the assessed inaccuracies.

During conventional fluoroscopy-guided pedicle instrumentation, the patient and the surgical team are exposed to a significant amount of radiation. Several clinical studies have shown that robot-assisted instrumentation decreases the occupational risk for surgeons and operating room staff members by significantly reducing intraoperative radiation doses, particularly in minimally invasive surgery (MIS) procedures [21, 27, 35].

A retrospective cohort analysis comparing conventional open to robotic-guided open/percutaneous pedicle screw insertions measured up to 70 % less radiation exposure in the robot-guided procedures, 64 % of which were performed using percutaneous approaches, when compared to 57 freehand surgeries, all executed using an open approach [21].

Similarly, in a prospective, randomized comparative trial of freehand, navigation-guided, and robotic-guided spinal procedures reports a two-fold reduction in radiation time and dose when integrating the robotic system to insert pedicle screws in a minimally invasive approach, as compared to freehand surgeries in a conventional open approach [20]. In another single-center

study of conventional versus robotic-assisted percutaneous spine fusion surgeries, a median 40 % lower radiation exposure was measured for the robot cohort [24].

Upon implementation of SpineAssist in a controlled, cadaveric implantation trial, overall radiation exposure among 87 % of the surgeons was below 1 mrem, versus a mean 136 mrem exposure when using traditional surgical approaches [27]. When calculating the average radiation per screw, a 98.2 % reduction in ionization exposure was observed in robot-guided procedures, with an average 0.2 mrem per screw, versus a mean 10.1 mrem per screw in the control group. Fluoroscopy time was reduced by a similar degree, from a mean 33.0 s per screw in the control group and 0.7 s per screw.

40.3.2 Surgical Robots for Minimally Invasive Surgery

The present experience confirms a high level of accuracy for robot-assisted pedicle instrumentation for both the conventional open and percutaneous approach. In "regular" open cases in which the anatomy is clearly exposed, the advantage is less significant and the extra input might not be justified. Whereas in high-grade degenerative disease, spondylolysis, revision surgery, and in deformity cases, visualization of surface anatomy alone may not be sufficient, and robotic guidance can be helpful. Therefore, the system has clear advantages in percutaneous or MIS procedures [21]. The multicenter evaluation of robot-guided cases by Devito, in which a significant subgroup had complex deformities, already showed that 49 % of the screws in their study were placed in a percutaneous approach [19].

In general, MIS procedures in spine surgery have gained more acceptance and are applied more frequently as they are associated with less postoperative pain, lower infection rates, less blood loss and less paraspinal muscle trauma, and reduced recovery period and tissue scarring [36–41]. On the other hand, MIS procedures are usually associated with increased operating time and have been reported to expose patients and surgeons to high radiation doses [21, 27, 35, 42, 43].

For instance, interbody fusion techniques represent a reasonable strategy for the management of lumbar degeneration, in isthmic spondylolisthesis, postlaminectomy situations, and pseudoarthrosis [44, 45]. Particularly the TLIF (transforaminal lumbar interbody fusion) is particularly suited for minimal invasive or percutaneous approaches due to its posterior, unilateral access to the spine [45]. Numerous comparative studies, MIS TLIF versus open TLIF, have been performed in recent years and results are fairly homogeneous [42, 43, 46–50]. The clinical outcome reported was generally favorable with special highlight on reduced postoperative pain, reduced intraoperative blood loss, and shortened hospital stay. A meta-analysis by Karikari et al. quantified the blood loss from 150 to 456 mL for MIS TLIF and 366.8–1,147 mL for open TLIF. The duration of postoperative hospital stay ranged in the MIS TLIF from 3.0 to 10.6 days and from 4.2 to 14.6 days for open TLIF [41]. The clinical outcomes are ranging from favorable to excellent (assessed by VAS and ODI), especially during the immediate postoperative course [48], but long-term outcome is not significantly better for MIS than for open TLIF in most studies [42, 47, 49]. Whereas studies from Peng et al. and Wang et al. found both operating time and radiation exposure to be increased in MIS TLIF procedures [42, 43]. Concerns whether equally solid bony fusion is feasible in MIS TLIF, in which preparation of the disk space through narrow corridors is more challenging, were invalidated by numerous studies [46, 47]. Recently, Wu et al. reported in a meta-analysis a fusion rate of 94.8 % and 90.9 % for MIS versus open TLIF [51].

Therefore, the integration of a robotic platform in a minimal invasive TLIF procedure is reasonable. We evaluated a heretofore unpublished case series of 28 patients with monosegmental lumbar disk disease, composed of either isthmic or degenerative spondylolisthesis (Table 40.1). The study was initiated after the authors had gathered experience with the

Table 40.1 Clinical characteristics in robot-assisted MIS TLIF ($n=28$)

Mean age	55 ± 10 year		
Sex	Female $n=16$	Male $n=12$	
Spondylolisthesis	Isthmic $n=15$	Degenerative $n=13$	
Meyerding	Grade 0 $n=3$	Grade I $n=16$	Grade II $n=9$
TLIF segments	L3/4 $n=3$	L4/5 $n=12$	L5/S1 $n=13$
Postop Meyerding	Grade 0 $n=15$	Grade I $n=12$	Grade II $n=1$
Clinical improvement (VAS 3–6 months)	Radicular pain 95 %	Back pain 60 %	

SpineAssist system in pedicle screw placement in about 50 cases. The primary objective was to integrate the robotic platform in a completely minimally invasive and more complex procedure with attention on surgical technique and workflow, operating time, radiation exposure, and clinical patient outcome.

40.3.3 Surgical Technique

The surgical workflow involves acquiring a CT of the patient's spine for the preoperative planning stage (Figs. 40.1 and 40.2). In the operating room, the robotic platform is attached to the patient's spine involving pins to the spinous process and to the iliac crest or to the OR table. Two fluoroscopic images (anteroposterior and 60° oblique to the lateral plane) of the spine and the robotic platform (marked by a 3D fiducial array) are used for registration and matching to the preoperative CT. Following 3D synchronization, the robot is attached to the platform and the robotic arm is dispatched to the calculated trajectories. After stab skin incision (1–1.5 cm) and robot-assisted k-wire insertion, the four pedicle screws are placed percutaneously followed by removal of the robotic system. In the majority of cases, the rod construct is inserted and temporarily tightened. A small midline incision (about 3 cm) is followed by subperiostal placement of the retractor system to gain access to the ipsilateral lamina and facet joint. Microsurgical facetectomy is performed using high-speed burr and rongeurs. Bone may be harvested for graft material. If indicated, ipsilateral and/or bilateral decompression of the dural sac and the exiting nerve root is feasible. Eventually, lateral exposure of the annulus allows for meticulous preparation of the disk space, and implantation of a TLIF cage was performed under fluoroscopic control. This is followed by compression of the screw-rod system and final tightening of the screw caps.

Postoperative CT scans were assessed for screw placement accuracy. Ninety-six percent of the overall 120 screws met Gertzbein and Robbins criteria A and B. Misplaced screws (grades C and D, three screws) were located at the lateral pedicle wall but were not associated with neurological deficits as deviance was to the lateral superior aspect of the pedicle. The overall mean operation time was 165 ± 30 min and mean blood loss was assessed to be 162 ± 99 ml, which are on the lower range of the previously reported MIS procedures. Under robot guidance, a mean of 17 ± 7 min was needed for k-wire placement and further 15 ± 8 min for final screw insertion. Radiation time per screw was assessed 4.1 ± 1.9 s and radiation dose was 3.4 ± 2.1 mGy per screw. Observed complications included one patient with postoperative epidural hematoma that needed evacuation and one patient with a L5 syndrome postoperatively that was not related to screw misplacement. No infections were observed.

40.4 Discussion and Future Outlook

The literature is replete with reports of spinal surgery outcomes, yet varies widely in the diagnostic criteria and methods employed to judge clinical efficacy. Image-guided navigation in spinal surgery has demonstrated its feasibility and qualities for spinal instrumentation in numerous studies, but lacks sufficiently powered data to prove the benefit on clinical outcome.

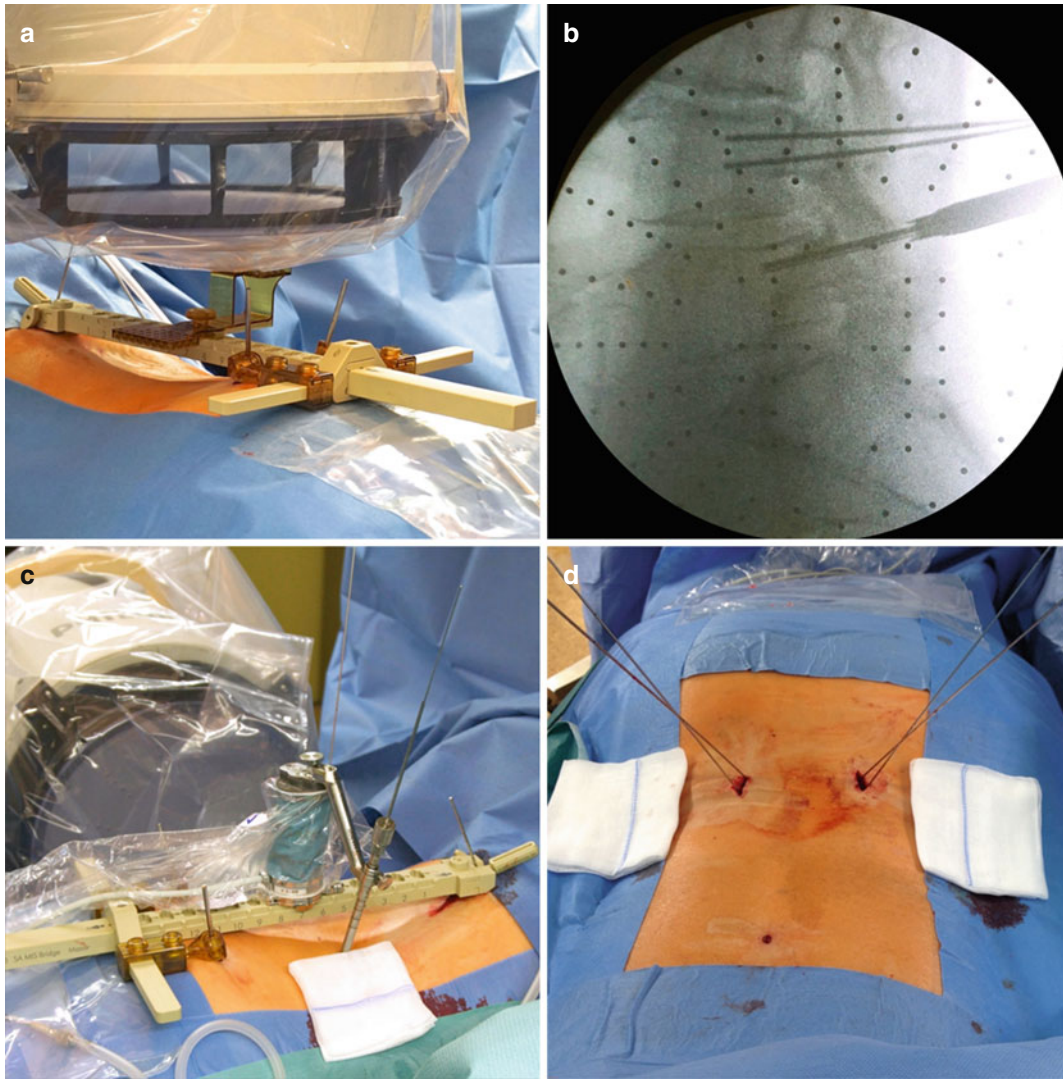

Fig. 40.1 Surgical workflow for SpineAssist. (**a**) Referencing of the spine-fixated platform prior to robot assembly with marker array and fluoroscopy. (**b**) Robot-guided trajectory of the percutaneous drill cannula. (**c**) Intraoperative lateral fluoroscopy with k-wires in L4 and drill cannula directed to L5. (**d**) Inserted k-wires before screw placement

Correspondingly, the available, mainly observational, data established a superior accuracy for robot-assisted pedicle instrumentation in the thoracic, lumbar, and sacral spine to conventional surgery along with a reduced radiation exposure. The only two RCTs, however, show inconsistent results [20, 25]. Here, further prospectively and randomized controlled data on accuracy and especially patient outcome is still needed for the evaluation of robotic guidance systems.

Besides, clinical studies have to identify treatment strategies and surgical procedures where robotic systems can realize their potentials best. Minimally invasive and percutaneous procedures represent a reasonable field of application. A growing number of technological advancements have been implemented in this field to enhance the possible benefits of MIS spine surgery, i.e., reduced soft tissue trauma and recovery period, reduced complication rates, and improved

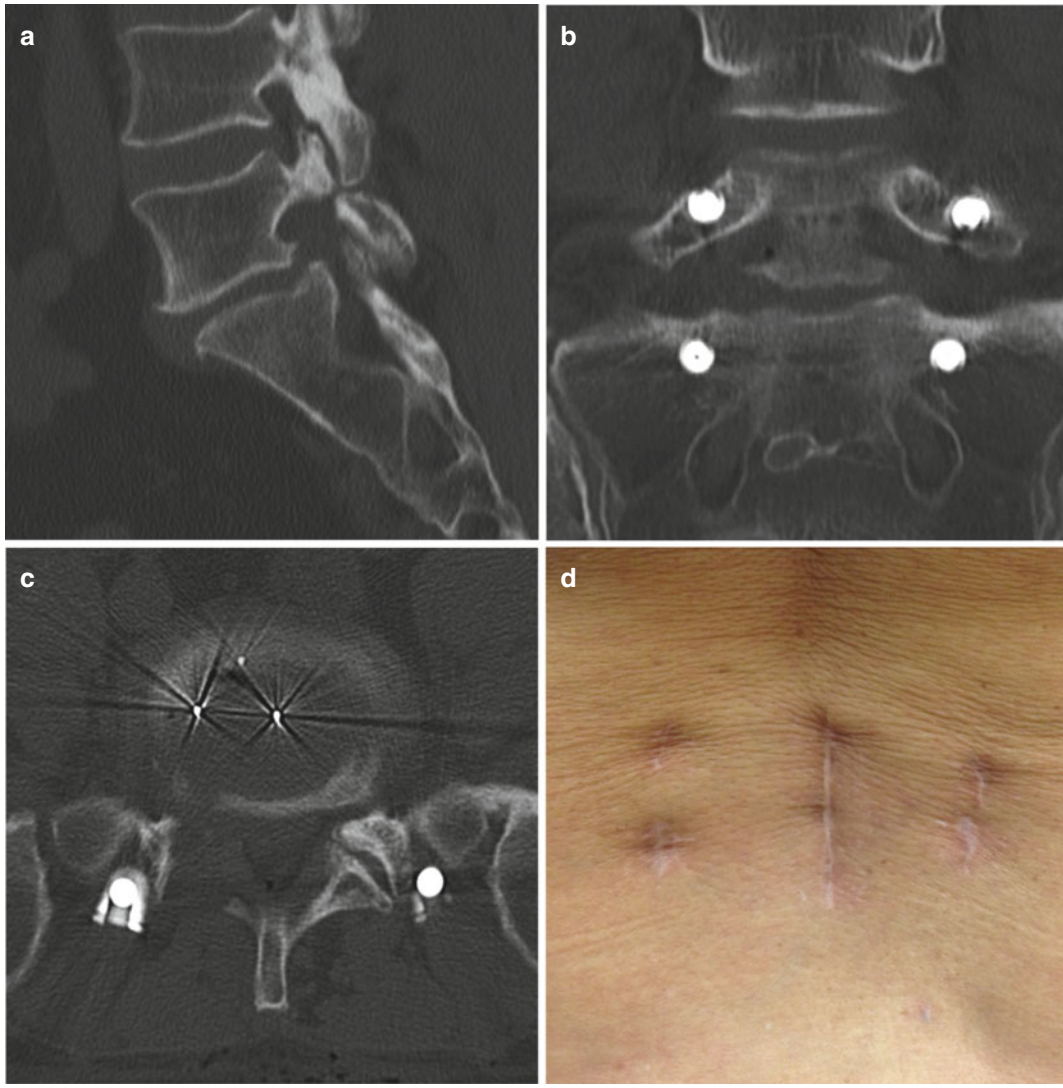

Fig. 40.2 Example case of a 54-year-old isthmic L5/S1 spondylolisthesis grade I for MIS TLIF using SpineAssist. (**a**) Preoperative sagittal CT scans. (**b**) Pedicle screws, placed via SpineAssist on coronal CT scan. (**c**) Postoperative axial CT scans showing the TLIF cage after right lateral decompression and facetectomy. (**d**) Postoperative (3 months) skin scarring of 3 cm midline incision and lateral stab incision for percutaneous pedicle screws

outcome. The integration of robotic systems could in addition reduce radiation exposure and accelerate the workflow.

Surgery of the cervicothoracic junction and cervical spine, in which the need for accuracy is crucial, is likewise dependent on fixation implants. The target bone volume is much more delicate and the critical anatomical structures, i.e., the vertebral arteries, the spinal cord, and nerve roots, are in close proximity and their violation is related with significant morbidity. The preliminary application of SpineAssist devices at the cervical spine clearly demonstrated the limitations as the cervical spine displays a high intersegmental mobility and even more vulnerable structures. However, robotic assistance may be helpful in revision cases, which will confront surgeons more frequently due to the increasing number of spinal instrumentation. The altered anatomy and scar tissue in a previously operated

situs make orientation more difficult and bears the risk for further complications.

Despite strong evidence for the accuracy of robotic systems, continuous refinement is necessary. For the SpineAssist system, for example, technical hardware and software solutions are meant to enhance the stability of the mounted platform, to minimize the influence of tool deviation due to skiving or soft tissue pressure and to reduce the rate of conversion to conventional manual instrumentation, which in some reports lies between 10 % and 16 % [19, 22].

Future advancements, e.g., including a range of different surgical tools, are conceivable and should be evaluated.

The available surgical robot technology does not only facilitate spinal instrumentation and guided bone work (SpineAssist) but has also demonstrated a high degree of dexterity for soft tissue dissection and preparation in non-openly exposed deep cavities (da Vinci). To combine these robotic philosophies would, at least in theory, potentiate their individual potential.

Integration in other upcoming technologies, e.g., intraoperative imaging modalities such as 3D fluoroscopy and intraoperative CT and MRI, would promote direct intraoperative planning and omit the preoperative preparation steps (imaging and planning), thus further condensing the workflow. Moreover, a gain in accuracy and direct onsite control over the robot-assisted procedures would be feasible.

To connect imaging studies, 3D anatomy, presurgical planning, and in vivo execution through a computerized platform create a new interface that gives essential support but also requires special attention. So far, in a shared-control and hands-on robotic system, the surgeon is the eventual executing factor of the process, which allows but also demands for a continuous reinsurance and validity check of each step. This dichotomy is further continued in the issue to what extent an extension of robotic automation is possible and justifiable. For instance, the tasks of drilling the pedicle and driving-in the screw implants into the sometimes fragile bony structures require tight control of the trajectory axis, which could certainly be performed with high accuracy and precision by a robotic arm. Whether surgeons should leave these critical steps, where the bony anchorage of the implant is prepared and perceived, to the robot computer is debatable.

The question whether the surgeon enables a robot to completely perform delicate positioning of screws remains unanswered. Even markedly reduced, there is an immanent risk of nerve lesion due to the robot, a responsibility bearded solely by the surgeon. The more robots are autonomous, the more likely it is that the responsibility seems to drift away from the surgeon. However, the decision-making process of the surgeon is completely different than that of the robot, as the surgeon additionally incorporates patient's history, his personal experiences, and intuition to the case.

The financial investment in a surgical robot or other computerized surgical systems is substantial. While navigation systems have been introduced over two decades ago and have proved to produce superior results, only 11 % of spine surgeons responding to a survey reported using such technology in their surgical protocols [52]. Cost-efficiency is a critical factor for the appraisal and adoption of new technologies in the clinical setting, and expectations will increase further. If the clinical value of computer-assisted spinal surgery, for example, in MIS TLIF surgery, which is promising but has to be further validated, consists in significantly reduced hospital stay, reduced reconvalescence and postoperative pain, and thus improved patient outcome, general acceptance and financial compensation will escalate.

Moreover, the growing acceptance of computer-assisted systems, to the degree of newly defined standards of care, will have medicolegal implications for spinal surgery as well. Although experienced spine surgeons achieve high accuracy and excellent results in conventional freehand techniques, the application of these technologies facilitates a detailed documentation of every single step of a surgical procedure, starting from preoperative imaging studies and planning, referencing of the virtual anatomy to the surgical situs, execution according to predefined pathways, and eventually confirmation by intraoperative imaging modalities.

It has become obvious that computer-assisted guidance technology, navigation, and robotics have a significant learning curve for surgeons and OR staff [53]. The preoperative planning, the robot assembly, and referencing do consume extra time that can only be minimized by sufficient training and experience. To reserve the application of these systems for the few really demanding cases seems not advisable. Only use on a daily basis, i.e., for standard instrumentation as well, will provide the necessary experience to enable rapid workflows, short operating times, low complication rates, and eventually satisfactory outcome.

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Part VII

Nonfusion Technologies

Disk Arthroplasty: A 30-Year History

41

Klaus John Schnake and Frank Kandziora

41.1 Introduction

While the first artificial disk was implanted just 30 years ago, the history of disk arthroplasty is already about 55 years old.

Arthroplasty has been quite successful for joints such as the hip and knee. In contrast, disk arthroplasty is far away from being the standard treatment in spine surgery. Degenerative lesions of the disk consist of a decrease in the hydrophilic properties of the nucleus as well as the appearance of annulus tears. Secondary, osteoarthritis of the facet joints and subchondral bone alterations occur. Thus, the entire functional spinal segment degenerates. While severe hip osteoarthritis can be treated with total hip replacement, successful replacement of a total spinal segment is still not possible.

In the past, surgeons attempted to develop arthroplasty-like implants in order to mimic physiologic motion. The primary purpose was to restore symptom-free biomechanical function. While there is almost no more indication to perform a hip or knee arthrodesis, it is still unclear if spinal arthrodesis will follow this pattern. Today, the increasing demands and expectations from the patients' side, and the medical desire to avoid fusion with its adverse side effects, have led to the development of multiple implants for disk arthroplasty.

Over the average human lifespan, the spine is exposed to more than 100 million cycles of motion. Per year, the lumbar spine is exposed to 2 million nonsignificant motions and 125.000 significant bends per year. The optimal lifetime for an arthroplasty spinal implant was therefore considered to be approximately 30 million cycles, or 10 million cycles in a fully loaded spine situation [1, 2].

The intervertebral disk is not a simple cartilaginous joint, but rather a complex anatomic structure allowing small movements along and around three main axes. In contrast to peripheral joints, whose stability is mainly achieved by ligaments, the disk on its own provides the major part of its stability. The configuration of nucleus and annulus allows high resistance to external forces.

The biomechanical requirements present quite a challenge for any implanted mechanical device, since the most elastomeric polymers will degrade, metals will wear, each will be exposed to the immune system, and open spaces will lead to tissue ingrowth. Continuous motion and stress

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_41

will lead to metal fatigue and potentially implant failure. Thus, the implants must be biocompatible and resistant to the stresses of the spine.

The development of disk prostheses was heavily influenced by design and engineering principles previously established for total joint arthroplasty. Strategies for immediate and delayed implant fixation have been taken from lessons learned with hip prostheses. The same is true for the use of cobalt chrome alloys and ultra-high-molecular-weight polyethylene in a majority of devices. Titanium provides excellent biocompatibility and the advantage of MRI compatibility. Knowledge transfer from joint arthroplasty to the spine certainly offers advantages. However, the disk space is a different biomechanical and biologic environment compared to other joints. To complicate matters, the origin of low back pain is not fully understood yet and appears to be more complex than in peripheral joints.

Two key principles can be differentiated for disk arthroplasty [3]:

1. Reproduction of the viscoelastic properties of the disk. Those implants are mostly manufactured from various silicones or polymers. Some rely on springs and/or piston systems and some are injected in monomer form and polymerised in situ. The main field of application is nucleus replacement.
2. Reproduction of the motion characteristics of the disk. Those implants are usually mechanical devices made from metal and/or polyethylene couples. The main field of application is total disk replacement.

Innumerable different designs for both principles have been developed and patented so far. However, only a few of them reached the level of clinical application, and even fewer were implanted in a bigger number of patients. The story began in Europe in the 1950s with preclinical studies and patents. While today the negative aspects of spinal fusion serve as a rationale for disk arthroplasty, the rationale in the last century was restoration of joint biomechanics.

In 1955, van Steenbrugghe patented a joint replacement for the disk consisting of two cushions [4]. In the late 1950s, Nachemson injected self-hardening liquid silicone rubber into cadaver disks [5].

However, the virtual clinical pioneer of disk arthroplasty was Fernström. He was the first to implant an "artificial disk" in the late 1950s. In fact, he was using a metal ball in an attempt to reproduce the "ball joint" mechanism of the disk [6].

The Fernström ball seems to have been used in about 250 patients. Because of poor results, the implant was withdrawn [7].

Probably the first attempt of a total disk replacement restoring the motion function was patented by Weber in 1978. The devices consisted of two polyethylene box-like structures anchored in the adjacent vertebrae. In between, a ceramic ovoid core was placed allowing motion. However, the device was never manufactured [8].

The modern history of disk arthroplasty began in the 1980s. Nucleus replacement strategies and total disk replacement were separated and both could reach clinical application in the subsequent course.

41.2 Nucleus Replacement

Nucleus replacement strategies reflect the earliest attempts to relieve pain and restore function of the degenerated spinal motion segment. The above-mentioned Fernström ball was one of the first replacements. All of those early techniques were neither mechanical nor biological promising.

The history of nucleus replacement suffered from many setbacks. Surgeons and engineers ingenuity lead to numerous devices. The majority of them were either tried and failed or were never tried clinically at all. The early designs were made of virtually any material (metal or polymer) having flexibility, especially elastomeric (rubbery) materials or metal springs and hinges. Literally all of the early designs were mechanical devices. Typical problems of most of the implants were: surgical implanting technique, attachment to the bone, resistance to expulsion, mechanical failure loads, longevity, and tissue compatibility. Despite those problems, nucleus replacements have been used since the late 1990s.

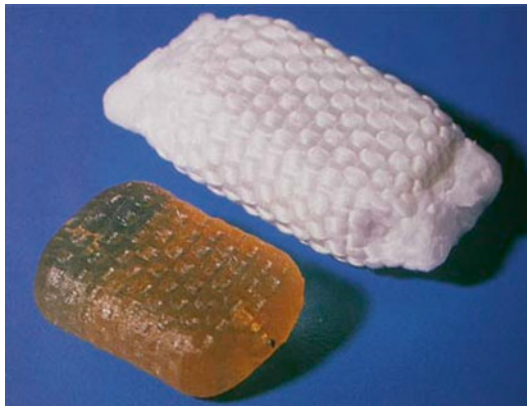

Fig. 41.1 PDN

This is probably due to the tremendous efforts of Charles D. Ray, the inventor of the prosthetic disk nucleus (PDN) (Fig. 41.1). He followed the idea to compare the degenerated disk with a flat car tyre. The nucleus loses water and shrinks and consecutively the disk height decreases like a tube of a tyre which deflates. As long as the annulus (respectively, the tyre) maintains its integrity, a restoration of function is possible if the pressure in the disk (respectively, the tube) can be increased again. Coming from this point, he developed a hydrogel which could be hydrated. The first prosthetic disk was patented in 1988 [9].

Ray gave his prosthetic disk nucleus a scientific background. To date, the most often used nucleus replacement is the PDN and PDN-SOLO (Raymedica, Bloomington, USA). The PDN consists of a hydrogel core and an ultra-high-molecular-weight polyethylene jacket. The hydrogel core is a polyacrylonitrile-polyacrylamide multi-block copolymer with memory capability. It can absorb 50–90 % of its dry weight in water to become fully hydrated. The woven jackets provide dimensional control of the swollen pellets. Two PDN devices are usually implanted next to each other after removal of the nucleus [10].

Indications that have been proposed are low back pain due to degenerative disk disease, with or without leg pain [11].

While the theory of nucleus replacement with a swelling implant sounds auspicious, early clinical reports revealed high complication rates. Typical complications were implant dislocations and subsidence into the adjacent vertebral body [12, 13].

Obvious problems led to a new implant design, the PDN-SOLO®. Thus, complication rate dropped to less than 10 %, which is, in our opinion, still too high [14, 15]. Only few data concerning the long-term outcome are available showing persistent favourable clinical results. However, quality and quantity of data are too poor [16].

In the past, many other nucleus replacement strategies have been developed and are currently under investigation. Today, nucleus replacement devices can be functionally categorised as elastomeric and mechanical. The latter are in clinical use but are confronted with many of the same problems encountered with the PDN implant [17]. The surgical approach to the nucleus harms the integrity of the annulus. Thus, implanted nucleus devices can be extruded through the primary approach. The sewing of the annulus as well as lateral approaches to the disk did not eliminate this problem [18].

Elastomeric devices are under clinical investigation with encouraging preliminary results. Most of the actual strategies follow the path of injectable materials that undergo in situ polymerisation.

However, up to now, there is no evidence that nucleus replacement offers any clinical benefit. Furthermore, the indications are not clear yet.

In conclusion, further clinical investigation with prospective, randomised pivotal trials is needed to determine the efficacy of nucleus replacement in the treatment of lumbar degenerative disk disease [19, 20].

41.3 Total Disk Arthroplasty

The Charité artificial disk was the first available total disk replacement (TDR) system. Three different types have been developed so far. While type I and II Charité artificial disks were manufactured in the former German Democratic Republic (GDR) and, therefore, was never commercially available, the type III Charité disk was

distributed by DePuy Spine (Raynham, Massachusetts, USA) until spring 2010.

The Charité type I was developed in East Berlin by Kurt Schellnack and Karin Büttner-Janz in the Charité Hospital in 1982. The idea was based on the biomechanically proven "low friction" principle, which had already been successful in total joint replacement. It consisted of two highly polished metal end plates with teeth for bony anchorage and an ultra-high-molecular-weight polyethylene (UHMWPE) sliding core. The device was intended to imitate the movement of the nucleus pulposus of the intervertebral disk within its annular containment. It is therefore considered to be an unconstrained type of total disk replacement. An unconstrained design incorporates a mobile-bearing core and provides independent rotation and translation about three axes. The so-called SB Charité Artificial Disk Mark I was implanted at the Charité Hospital in the years 1984–1985 [21, 22].

Due to axial plane migrations, the device was modified to the SB Charité II.

It was used between 1985 and 1987. In contrast to type I, end plates were enlarged and exhibited bilateral wings to avoid subsidence. Finally, problems of migration and metal fatigue fractures led to the abandonment of type II also [22].

From 1987 on, the Link SB Charité III was manufactured by Waldemar Link GmbH in Hamburg, West Germany. The end plates were changed to cobalt-chromium-molybdenum alloy (CoCrMo) and received a porous coating of plasma-sprayed titanium and calcium phosphate to enhance osteointegration. The free-floating biconvex sliding core is still made of ultra-high-molecular-weight polyethylene (UHMWPE), encased by a metal wire for radiological marking. Primary stability is achieved by press-fit implantation through the teeth on the end plate which anchor into the subchondral bone. Different sizes and angulations were developed later [21].

After being taken over by DePuy Spine (Johnson & Johnson) in 2003, the SB Charité III was called Charité artificial disk until its abandonment (Fig. 41.2).

One of the earliest and most comprehensive clinical review regarding the Charité III was published by LeMarie in 1997. After 51 months follow-up of 105 patients, he found 79 % excellent results and a return to work rate of 87 % [23].

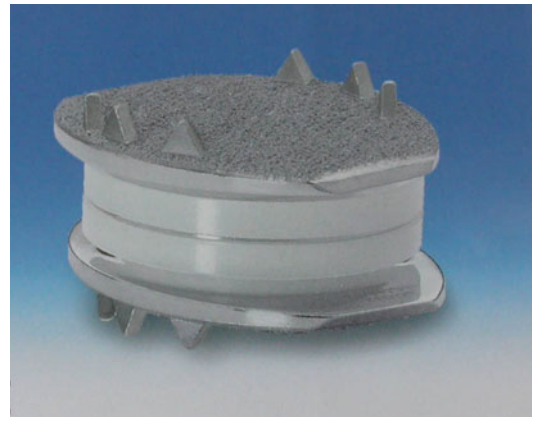

Fig. 41.2 Charité artificial disk

The American Food and Drug Administration (FDA) approved the Charité artificial disk in October 2004, the first of its kind, for use in treating pain associated with degenerative disk disease (DDD). The device is intended to replace a diseased or damaged intervertebral disk at either the L4–L5 or L5–S1 level.

In a multicenter study, the artificial disk was performed in 205 patients who had been diagnosed with DDD and had failed to have their pain relieved after 6 months of nonsurgical therapy and compared them to 99 patients who received the control device (stand-alone BAK spinal fusion cage using bone graft).

The study showed that 2 years after surgery, patients treated with the artificial disk did no worse than patients treated with intervertebral body fusion. However, patient satisfaction was higher in the artificial disk group. The rates of adverse events from use of the artificial disk were similar to those from treatment with fusion. In addition, the study showed that there was no statistically significant relationship between motion at the level where the disk was implanted and the patient's relief from pain [24, 25]. To conclude, the patients treated with the Charité artificial disk were as good as the patients treated with a stand-alone cage. However, the latter is considered to be an obsolete treatment in Europe due to unsatisfactory clinical results.

The SB Charité III has the longest clinical follow-up of any TDR. It has been implanted more than 17.000 times worldwide. Following the implantation, most of the authors stated 60–90 % satisfactory to excellent results [26–28].

Despite the good results published otherwise, Michael Putzier from the Charité Berlin published long-term results after an average follow-up of 17 years. The deflating results revealed spontaneous ankylosis in 60 % and a reoperation rate of 11 % [29].

Interestingly, the last Charité artificial disk was already implanted in the Charité hospital in Berlin in 1989. Despite the fact that the implant carried the name of the biggest university hospital in Germany, it has not been used there since then. In the USA, criticism increased over time, and numerous patients started to sue Johnson & Johnson alleging the pharmaceutical company knew or should have known about the serious complications of the artificial disk surgery. As mentioned above, the Charité artificial disk is not available anymore.

Another early type of artificial disk was the AcroFlex (DePuy Spine), designed by Arthur Steffee. The first implant type consisted of a hexen-based polyolefin rubber cushion attached to two titanium end plates. A pilot study with six patients was published in 1993. Due to concerns regarding potential carcinogenicity of parts of the implant, the clinical trials were suspended. The next generation was proposed by Steffee, Fraser and co-workers. Debris and implant failure were the typical problems of the AcroFlex series [30, 31]. A prospective non-randomised study with almost 10 years follow-up revealed a cumulative survival of only 61 %. The authors concluded that further use of this implant is not justified [32].

Two other types of TDR were developed in the 1990s and showed promising results: the ProDisc and the Maverick artificial disk.

The first ProDisc (Aesculap, Tuttlingen, Germany) was developed by Thierry Marnay in Montpellier in the late 1980s [33].

The ProDisc has two metal (titanium) end plates which are plasma sprayed with titanium and have two vertical fins for fixation to the end plates. The core is made of high-density polyethylene and fits firmly to the inferior end plate. The superior surface of the core is formed convex. The resulting centre of rotation is fixed and located inferior to the disk space. This semiconstrained design includes a fixed axis of rotation that limits translation. This leads to increased stress within the device and at the device-bone interface, resulting in a potentially increased risk of implant loosening.

Fig. 41.3 ProDisc-L

The first series of 64 patients were operated by Marnay between 1990 and 1993 with promising results. Follow-up ranged between 7 and 11 years with over 75 % excellent or good results. There was no outcome difference between 1 and 2 level implantations. All implants were still intact and functioning without signs of subsidence or migration [34].

The second generation of the ProDisc called ProDisc-L (Fig. 41.3) is distributed by Synthes (Paoli, Pennsylvania, USA). It was introduced to the market in 2000. Different end plate sizes and lordosis angles, different core heights and only one keel per end plate were the main design changes. It has been approved by the American FDA in August 2006 for one- or two-level implantation. The FDA IDE trial compared the ProDisc II with an anteroposterior fusion using femoral ring allografts anteriorly and pedicle screw fixation with autograft posteriorly. The clinical results in the ProDisc group were slightly better than in the fusion group [35].

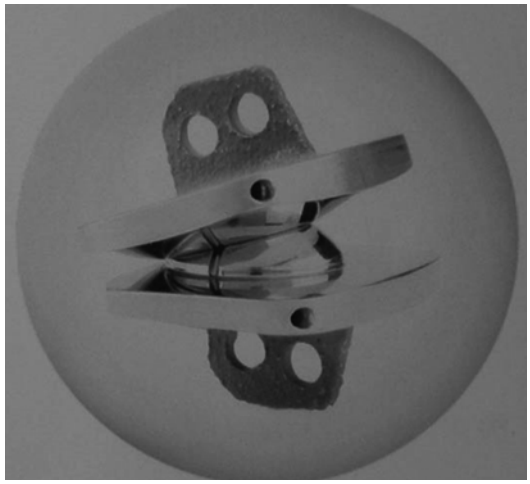

Fig. 41.4 Maverick

In uncontrolled clinical series, success rates up to 90 % are reported [27, 36]. Long-term data are sparse. In a prospective, single-centre investigation, 181 patients (90 % follow-up rate) could be examined after a mean follow-up of 7.4 years. Clinical results improved significantly after surgery and 87 % of patients were (highly) satisfied at final follow-up. Complication rate was 14 %, about half of which were device related. Reoperation rate was 16 %. The authors concluded that for a carefully selected cohort of patients, results compare favourably to results achieved with fusion [37]. Similar mid- to long-term results have been published by other authors [38–40].

Mathews, Le Huec and co-workers conceived the semiconstrained Maverick artificial disk (Fig. 41.4) (Medtronic Sofamor Danek, Memphis, Tennessee, USA), a metal-on-metal (chrome cobalt) interface implant with a posterior rotation axis [41].

Metal-on-metal disk prostheses have been developed to eliminate polyethylene wear and its potential risks. Although polyethylene debris and osteolysis have not been proven to be significant clinical issues with TDR, the long-term effects remain unclear. As known from hip surgery, metal-on-metal surfaces produce far lesser debris than polyethylene-on-metal surfaces [27].

The Maverick artificial disk is fixated to the end plates with a midline sagittal fin like the ProDisc. The end plates are hydroxyapatite coated. The overall biomechanical profile is similar to the ProDisc. However, the convex caudal component has a slightly smaller radius of curvature compared with the concave superior component.

Like in the other TDR, different sizes, heights and angles are available.

The first implantation was performed in 2002 and a randomised FDA clinical trial was begun in 2003, comparing the Maverick artificial disk to a fusion using cage combined with BMP. LeHuec and co-workers published a prospective study reporting the outcome of 64 Maverick devices implanted between January 2002 and November 2003. The Oswestry score improved for 75 % of patients [42]. Published midterm data 4 years after surgery showed 85 % of patients were again working and 79 % took up their normal sports activities [43].

In the last 6 years, a variety of new implants and techniques have been developed so that nowadays nearly all companies offer implants for disk arthroplasty. Despite extensive biomechanical studies, it currently remains unclear which type of constraint offers the most advantages in total disk replacement. Constrained implants offer stability but lead to high stress on fixation, while unconstrained implants are sensitive to surgical positioning. The normal axis of rotation of the lumbar spine is not fixed but varies. Although a constrained device in good position may provide more controlled motion and consecutive preservation of the facet joints, an unconstrained device may provide greater range of motion and be more forgiving in terms of surgical positioning.

In the recent past, results from multicenter and prospective randomised studies without any potential conflict of interest have been published. Data from 240 patients from a Swiss registry including different types of TDR showed significant, clinically relevant and lasting reduction of pain until 5 years after surgery. Adjacent segment degeneration occurred in 10 % of patients. Revision rate was 4.4 %. Almost 87 % of operated segments remained mobile despite the fact

that heterotopic ossifications could be detected in 44 % of patients [44].

In a Swedish prospective randomised controlled trial, 152 patients were either fused posteriorly or received TDR of different types. After 5 years, both groups still showed significant clinical benefit from surgery. However, all parameters were significantly better in the TDR group. No differences were found concerning complications and reoperations [45].

In a recent meta-analysis looking at results after 2-year follow-up, seven relevant RCTs with a total of 1,584 patients could be included. TDR was significantly more effective in ODI, VAS score, shorter duration of hospitalisation and a greater proportion of willing to choose the same operation again. All other parameters showed no significant difference [46].

Nevertheless, the authors of a Cochrane review judged the results slightly different: "Although statistically significant, the differences in clinical improvement were not beyond generally accepted boundaries for clinical relevance. Prevention of adjacent level disease and/or facet joint degeneration was not properly assessed. Therefore, because we think that harm and complications may occur after some years, the spine surgery community should be prudent to adopt this technology on a large scale, despite the fact that total disk replacement seems to be effective in treating low back pain in selected patients, and in the short term is at least equivalent to fusion surgery" [47].

Complications have been reported with all types of TDR and can be divided into two groups: those related to the surgical approach and those related to the prosthesis.

Access to the anterior lumbar spine includes potential injury to major vascular and visceral structures. Total complication rates range from 10 % to 23 %. Complications related directly to device implantation occur in 2.9–6.5 % of patients [26, 37, 44, 46].

Implant-related complications are design specific and appear as subsidence, dislocation and breakage of the prosthesis. Overall complication rates range from 2 % to 26 % of patients [26, 27, 37, 46, 48].

Conclusion

Thirty years of clinical application has not revealed a clear advantage of disk arthroplasty over fusion techniques. Even the prospective randomised FDA studies are arguable since the methods used in the control groups are considered to be arguably substandard treatment in some parts of the world. Conflicting results, increasing number of lawsuits and inconsistent demeanour of companies have lead to an increasing mistrust of both surgeons and patients in TDR. During the last decade, in the USA, surgical treatment for lumbar DDD has increased 2.4-fold. Although all fusion procedures significantly increased, TDR did not increase [49].

Therefore, some authors still consider total disk replacement as an experimental procedure [50].

On the other hand, much knowledge has been gained on TDR, and extensive database exist from numerous randomised and non-randomised studies. The results are as good as with fusion. Complications and reoperations are similar with both techniques. Disk arthroplasty has opened a new era in spinal surgery and has gained a firm place in the operative portfolio of many surgeons. Many patients beyond the clinical trials were treated successfully with disk arthroplasty. As often in spinal surgery, proper patient selection is more important than selection of implant.

Looking to the future, surgeons must be aware of the interests of the manufacturers, which spent billions of dollars for disk arthroplasty technologies. Nevertheless, the lessons we have learned from the past 30 years should lead us to the development of better implants for our patients.

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Biomechanics of Lumbar Disk Arthroplasty

42

Fanor Saavedra, Christopher A. Iannotti, Dani Bidros, and Edward C. Benzel

42.1 Introduction

Mechanical low back pain (LBP) from lumbar degenerative disk disease (DDD) is a leading cause of pain and disability for adults in this country with over $34 billion in annual health costs. Mechanical LBP has been problematic to both diagnose and treat. Nonsurgical treatment is successful in the majority of patients with LBP [1, 2]. Unfortunately, a significant minority of patients at various stages of the degenerative cascade remain debilitated with mechanical LBP. Surgical intervention is often recommended when conservative treatment fails to alleviate the symptoms. Surgical treatment for mechanical LBP has traditionally focused on segmental spinal fusion with concomitant loss of function of the motion segment(s). Traditional lumbar fusion techniques have evolved over the years, and with increasingly sophisticated spinal instrumentation and implants, increased fusion rates have been achieved. However, fusion rates do not reliably predict clinical success rates. While fusion rates have approached 100 %, clinical success rates that range from 60 % to 90 % have been reported [3–7].

Arthrodesis of the three-joint functional spinal unit (anterior disk and two posterior facet joints) results in loss of motion [8–11] with a known incidence of adjacent-level symptomatic degeneration, ranging from 10 % to 30 % [12–15]. Spine arthroplasty techniques allow for pain relief by eliminating presumed pain generators (e.g., the annulus and/or nucleus) while preserving motion and theoretically protecting adjacent levels from additional strains and stresses.

Partial disk replacement was performed as early as the 1960s, when Fernstrom implanted stainless steel balls into the cervical and lumbar spine [16]. The modern era of lumbar arthroplasty originated at Charité Hospital in Berlin when Butner-Janz and Schellnack developed the original Charité artificial disk in the early 1980s. In the late 1980s, Dr. Thierry Marnay, a French orthopedic surgeon, developed the ProDisc-L [17]. Subsequently, total disk replacement has seen a steady evolution with a proliferation of devices and concomitant refinements in implant design, surgical technique, and instrumentation.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_42

Lumbar arthroplasty can be divided into total disk replacement (TDR) and partial disk replacement (PDR) or nucleus replacement. TDR devices may be categorized according to their composite biomaterials (metal on metal or metal on polymer), biomechanics (unconstrained, semi-constrained, constrained), components (one-, two-, or three-piece designs), or fixation (spike or keel). Nucleus replacement devices represent an even more heterogeneous group of devices. Functionally, nucleus replacement devices can be divided into two broad classifications: elastomeric and mechanical.

The primary indication for both mechanical nucleus replacements and TDRs is mechanical low back pain due to DDD. Elastomeric nucleus replacement can also be utilized in the post-diskectomy setting. Generally, nucleus replacement represents a therapeutic intervention aimed at an early stage in the degenerative cascade, consisting of mild to moderate DDD. Advantages of PDR include minimally invasive and multiple approach options, including anterior retroperitoneal, lateral, and posterior approaches. The limited exposure required for insertion via annulotomy allows for multiple revision options, including TDR and fusion. Challenges of PDR include migration or expulsion risk since the devices generally are not fixed to the end plates and subsidence [18–27]. TDR is applicable for more advanced degenerative changes, as seen in moderate to severe DDD. Advantages of TDR include complete disk removal (which addresses pathology involving both the annulus and the nucleus), as well as reliable fixation to bony end plates. The challenges of TDR include avoidance of complications such as implant failure and expulsion, as well as longevity and wear debris.

42.2 Lumbar Fusion: Advantages and Disadvantages

The surgical procedure offered to patients with mechanical LBP due to DDD typically consists of arthrodesis of the painful motion segment, which may be combined with decompression for patients with radicular or neurogenic claudication symptoms. The rationale for spinal fusion is based on the assumption that it will eliminate painful nonphysiological motion across the destabilized or degenerated segment, preserve sagittal balance, and restore normal disk space height if combined with interbody spacers. Good to excellent results have been reported in 50–100 % of patients following anterior interbody or posterior spine fusion. Spinal fusion, however, is not a benign treatment. In a long-term study (>20 years), results of lumbar fusion demonstrated approximately 50 % of patients suffered recurrent symptoms requiring medication years after the original procedure, and approximately 15 % of patients reported undergoing additional surgery during the study period [13].

Fusion alters the normal biomechanics of the spine, transmitting forces to adjacent vertebral levels. The increased strain in the neighboring motion segments may accelerate disk degeneration, facet arthropathy, and promote osteophyte formation, all of which lead to recurrent back pain and symptomatic spinal stenosis at levels adjacent to the fusion site [13, 28–30]. Spine fusion also is associated with other complications, including alteration of muscular synergy, loss of spinal mobility, graft collapse resulting in suboptimal sagittal alignment, complications associated with the hardware implanted to achieve immediate stability, and the harvesting of iliac bone that is necessary for bone fusion [31].

42.3 Lumbar Disk Replacement

Due to concerns regarding detrimental long-term effects of spinal fusion procedures, there has been a search to develop a more physiological solution to mechanical LBP. It is theorized that the development of the lumbar artificial disk may revolutionize the treatment of lumbar spondylosis, similar to the manner in which hip and knee arthroplasty techniques have revolutionized the treatment of degenerative disease in those joints. Although it remains unproven, many believe that by reconstructing the normal biomechanics of the lumbar spine, complications associated with spinal fusion can be reduced.

Lumbar disk replacements have evolved from early designs, such as the Fernstrom ball, over a period of decades to the current designs present in the Charité SB III and the ProDisc-L. These implants have been offered as an alternative to spine fusion, with the overall goal of treatment of painful degenerated lumbar disks. The Charité was approved for single-level implantation for degenerative lumbar disk disease in the United States after FDA approval in October 2004. A second lumbar disk replacement, ProDisc-L (Synthes), was later approved in August 2006 for use in the United States. Since then, dozens of companies now have either plans or aspirations to market their own disk replacement in order to tap into the lucrative and growing market of disk.

The theoretical advantages of lumbar disk arthroplasty are prevention of adjacent-segment disease by preserving segmental motion, protection of neural elements by restoring disk space height, and shorter recuperation times since patients do not require a prolonged postoperative period to allow for fusion maturation. The current indications for lumbar disk arthroplasty include young, non-osteoporotic patients with one- or two-level symptomatic disk degeneration without severe facet arthropathy, segmental instability, or neural element compression requiring a posterior decompression.

42.4 TDR Implants

42.4.1 Operative Procedure

The general operative technique for various TDR devices utilizes a standard anterior retroperitoneal approach or standard mini-open approach for exposure of anterior disk space at the operative level, similar to the approach used for anterior lumbar interbody fusion (ALIF). In the United States, exposure is often accomplished with an access surgeon, typically either a general or vascular surgeon familiar with this approach. The patient is positioned in a supine, neutral position on a radiolucent operating table. Use of intraoperative fluoroscopy is mandatory. The midline should be preliminarily identified and marked using anatomic landmarks prior to extensive dissection. It is imperative to mobilize the iliac vessels in order to visualize the lateral margins of the anterior disk. Figure 42.1 shows a standard anterior retroperitoneal approach to the lumbar spine.

A total diskectomy is facilitated by mobilizing the disk with interbody distractors and releasing or resecting the posterior annulus and posterior longitudinal ligament (PLL), with possible removal of any posterior osteophytes. The lateral annulus is preserved on both sides. Disk removal is accomplished with standard technique utilizing curettes

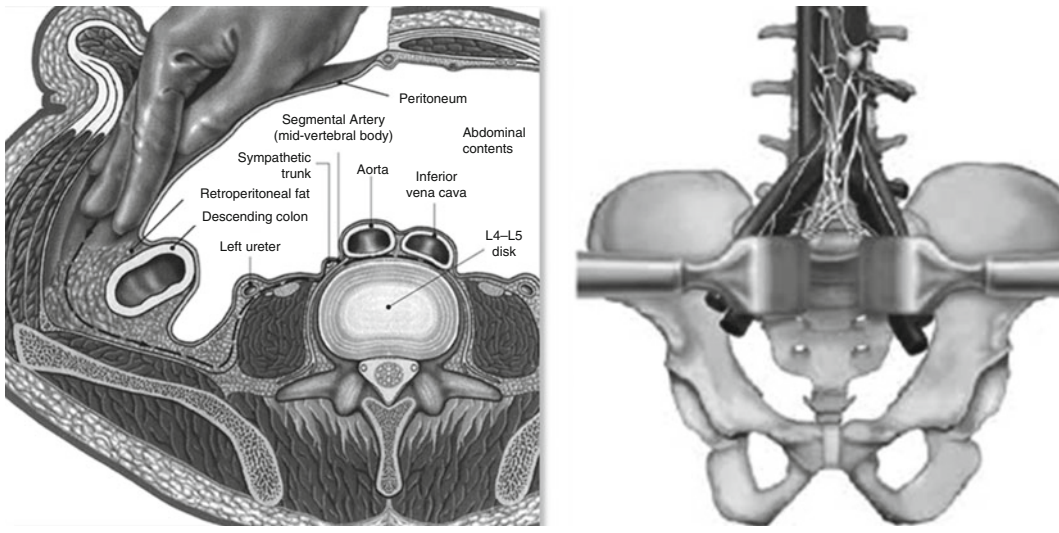

Fig. 42.1 Anterior retroperitoneal approach to the lumbar spine

and rongeurs. It is essential to establish a minimum width of 30–35 mm on the anterior part of the disk to perform the implantation safely. Care is taken to remove the cartilaginous end plates while preserving the bony end plates to minimize the risk of implant subsidence. Attention is paid to complete disk removal retaining only the lateral annulus bilaterally. Special care must be taken with lateral disk resection where any retained disk material can be pushed into the foramen during artificial disk placement. The artificial disk is then placed under AP and lateral fluoroscopic guidance using an individualized combination of sizing, trialing, midline verification, and disk placement.

42.4.2 TDR Devices

Concomitant with the Food and Drug Administration's (FDA) approval of the Charité artificial disk in October 2004, the era of spinal arthroplasty in the United States was born. Subsequently, the ProDisc-L (2006) received FDA approval. Several more devices have followed (Maverick, Kineflex, FlexiCore, and Activ-L). Cumulatively, these studies have produced a substantial proportion of class one evidence from prospective, randomized studies confirming TDR's efficacy in the treatment of symptomatic lumbar DDD (Table 42.1).

42.4.3 Charité (DePuy Spine)

The SB Charité III (DePuy Spine) is one of the most extensively studied intervertebral prostheses to date. The first two designs, SB Charité I and SB Charité II, were implanted in a small number of patients in East Berlin, Germany, and were never made commercially available [32]. These early designs included stainless steel end plates, which were prone to breaking and subsidence. The third-generation and current design (SB Charité III) was first marketed by Waldemar Link outside the United States in 1987, and DePuy Spine acquired the product rights to the Charité artificial disk in 2004. The Charité artificial disk consists of a three-piece design: two cobalt-chrome alloy end plates with spike fixation, with an intervening unconstrained, ultrahigh molecular weight polyethylene sliding core. This offers the theoretical advantage of allowing the spacer to shift dynamically within the disk space during spinal motion, moving posteriorly with flexion and anteriorly in lumbar extension. The primary attachment of the end plates is made possible by six "teeth" on the inferior and superior end plates, and a titanium/calcium hydroxyapatite coating promotes secondary fixation to the vertebral body by allowing bony ingrowth. Although this device was theorized to decrease facet joint arthropathy [32], the actual biomechanical effect of the device in vitro revealed a maximum local loading of facet joints approximately 2.5 times that of intact normal motion segments [26, 32, 33].

In 2009, Guyer et al. published a randomized, multicenter study comparing Charité artificial disk vs. anterior lumbar interbody fusion (ALIF) with BAK cages with a 5-year follow-up. From 160 patients, they did not found statistical differences regarding clinical outcomes between groups and concluded with a noninferiority report compared to ALIF [34].

Table 42.1 FDA-approved artificial disk devices

Artificial disk device	Company	FDA status
Charité III	DePuy Spine, Inc.	Approval date: October 2004
ProDisc-L	Synthes Spine	Approval date: August 2006

42.4.4 ProDisc-L Artificial Disk (Synthes)

The ProDisc was designed in the late 1980s by Thierry Marnay, a French orthopedic spine surgeon, and was approved by the US FDA in August 2006 for use at a single lumbar vertebral level. The polyethylene core is secured to the caudal end plate by a modular locking system. Each end plate has a central anchoring keel and two spikes to provide immediate stability. The end plates are coated with a titanium plasmapore surface to enable bony ingrowth for secondary stability. Specially designed instrumentation is used to create a midline groove in the vertebral end plates for implant

insertion and to lock the polyethylene core into the caudal end plate. There are two end plate sizes (medium and large), three heights (10, 12, and 14 mm), and two lordosis angles (6° and 11°).

Zigler et al. recently published a prospective, randomized, multicenter study with a 5-year follow-up comparing the ProDisc-L versus circumferential arthrodesis for the treatment of single-level lumbar degenerative disk disease. One hundred sixty-one patients underwent TDRs with the ProDisc-L and 75 patients underwent circumferential fusion. They found that both groups had sustained significant improvement from their preoperative status. No significant differences were found in clinical outcome scales (ODI, SF-36). They concluded that both fusion and TDR are reasonable surgical options [35].

42.4.5 Maverick Artificial Disk (Medtronic: Fig. 42.2)

The Maverick™ artificial disk consists of a cobalt-chrome, two-piece metal-on-metal design with keel fixation and a constrained ball-and-socket design. The center of rotation is fixed and located in the posterior third of the disk space. It is also a semi-constrained device that does not allow for pure translation. These features allow for unloading of the facet joints and reproduction of near-normal force transmission at the operated motion segment. Metal fixation into bone provides immediate stability, and there is no polyethylene wear issue.

Gornet et al. published in 2011 a 2-year follow-up randomized controlled study with 577 patients. Four hundred five patients received the Maverick disk device and 172 anterior interbody fusion (LT-cage). At the last follow-up, the overall success rate for the TDR group was 73.5 %, and for the control group (ALIF), the rate was 55.3 % with a noninferiority conclusion ($P<0.001$). Postoperative outcome scales (SF-36 and ODI) also favored the TDR group. There are no differences on adverse events between groups. There were two implant removals in the Maverick group; one was considered to be related to an allergic reaction. Longer follow-up with this two-piece metal-on-metal implant is needed, particularly in light of emerging complications (e.g., pseudotumor formation) with metal-on-metal hip implants. Despite completion of the investigational device exemption study in 2010, the Maverick™ is not currently marketed in the United States due to a patent dispute with another company [36].

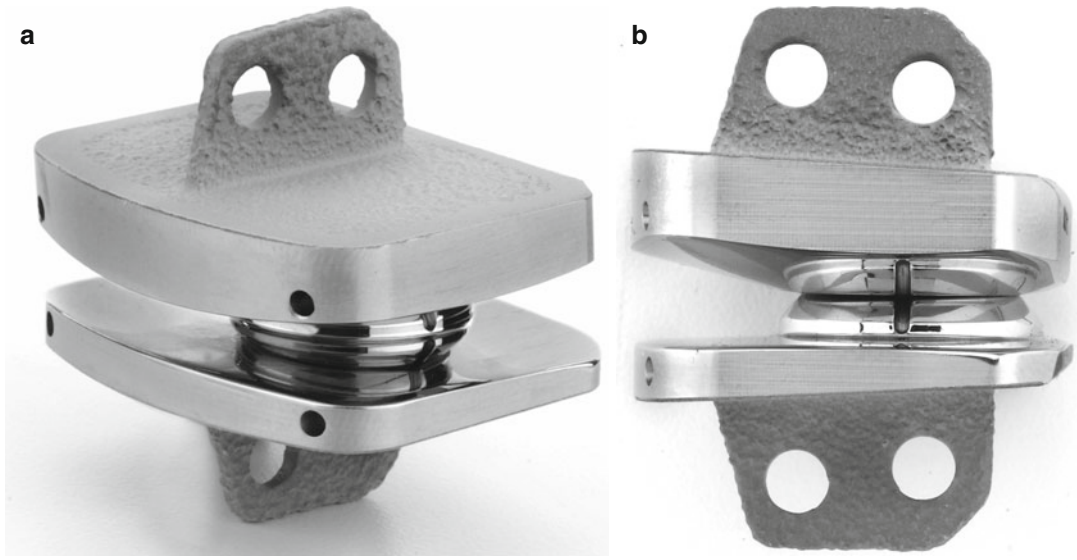

Fig. 42.2 (**a**, **b**) The Maverick artificial disk (With permission and image provided by Medtronic, Inc.) (The Maverick™ disk is not available or approved in the United States)

42.4.6 Kineflex Artificial Disk (SpinalMotion: Fig. 42.3)

The Kineflex artificial disk consists of cobalt-chrome, metal-on-metal design with a semi-constrained core. The mobile core is seated within a retention ring, and the superior and inferior end plates have multiple serrations, in addition to a central fin allowing for keel fixation and initial stability. On 2011 Kenneth Pettine published a randomized noninferiority trial comparing the Kineflex artificial disk versus the Charité. Sixty-four patients were randomized and followed for 24 months. Eighty-three percent of patients in the Kineflex disk group and 85 % of patients in the Charité group met FDA-defined criteria for clinical success, with no difference between groups ($P=0.802$) [37].

42.4.7 FlexiCore Artificial Disk (Stryker Spine: Fig. 42.4)

FlexiCore is a cobalt-chrome metal-on-metal device that is inserted as a single unit. The superior and inferior portions are linked by a captured ball-and-socket joint (constrained domed core). The FlexiCore can be implanted from a straight anterior or an anterolateral direction and offers the ability to manipulate the position of the implant within the intervertebral space. The FlexiCore features unique dome-shaped baseplate surfaces to approximate the concavities of the vertebral body end plates, with several small spikes or "teeth" for immediate bone fixation. These implants are also coated with titanium plasma spray to assist in delayed bony ingrowth for fixation. FDA IDE studies of the FlexiCore disk commenced in 2003 and enrolled and followed over 500 patients. It was also sold outside the United States beginning in 2005. The FlexiCore disk is not currently commercially available [38].

42.4.8 Activ-L Artificial Disk (Aesculap)

The Activ-L Artificial Disk is a next-generation intervertebral disk prostheses consisting of cobalt-chrome end plates with a semi-constrained, polyethylene core (ball-and-socket design). There are modular end plates available, in both spike and keel fixation. Low implant height (with a total height of 8.5 mm) may reduce disk space overdistraction. The convex-shaped end plate allows an ideal contact surface with the concave vertebral end plates. Importantly, the device allows for

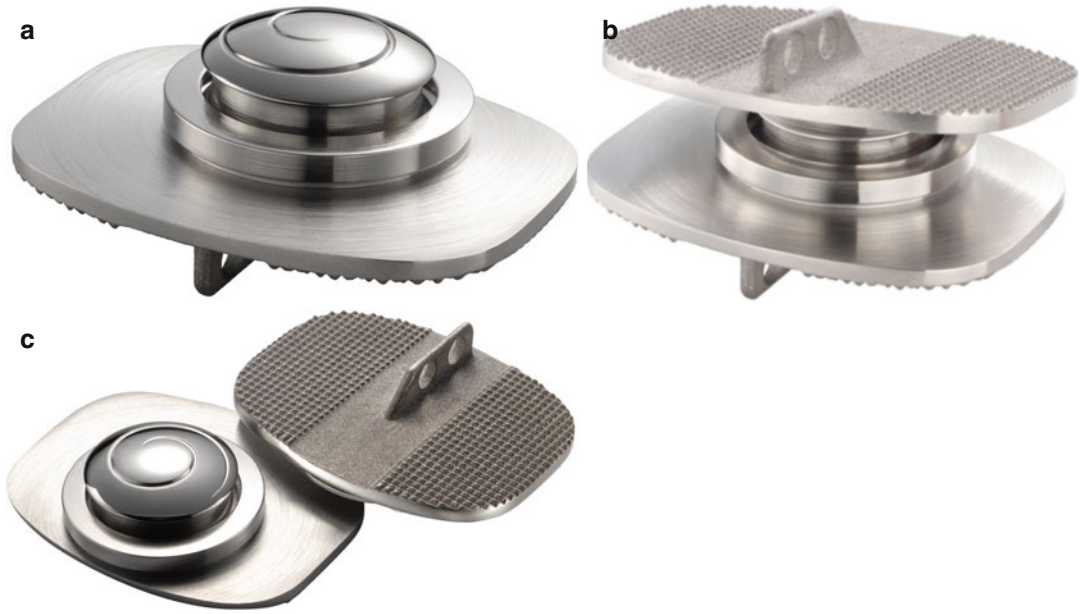

Fig. 42.3 (**a**–**c**) The Kineflex artificial disk (With permission and image provided by SpinalMotion, Inc.)

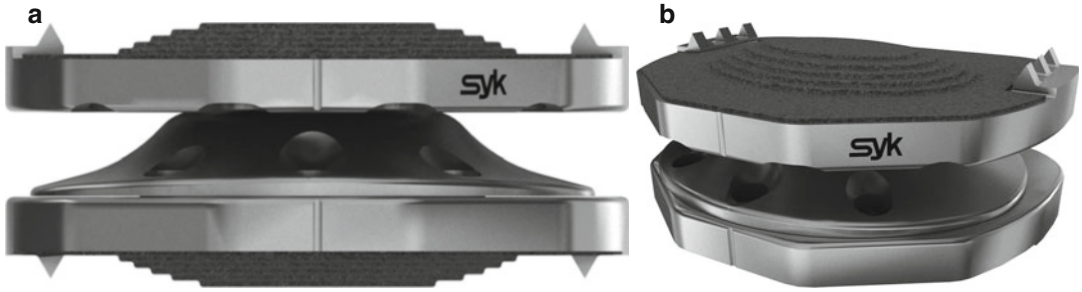

Fig. 42.4 (**a**, **b**) FlexiCore artificial disk (With permission and image provided by Styker)

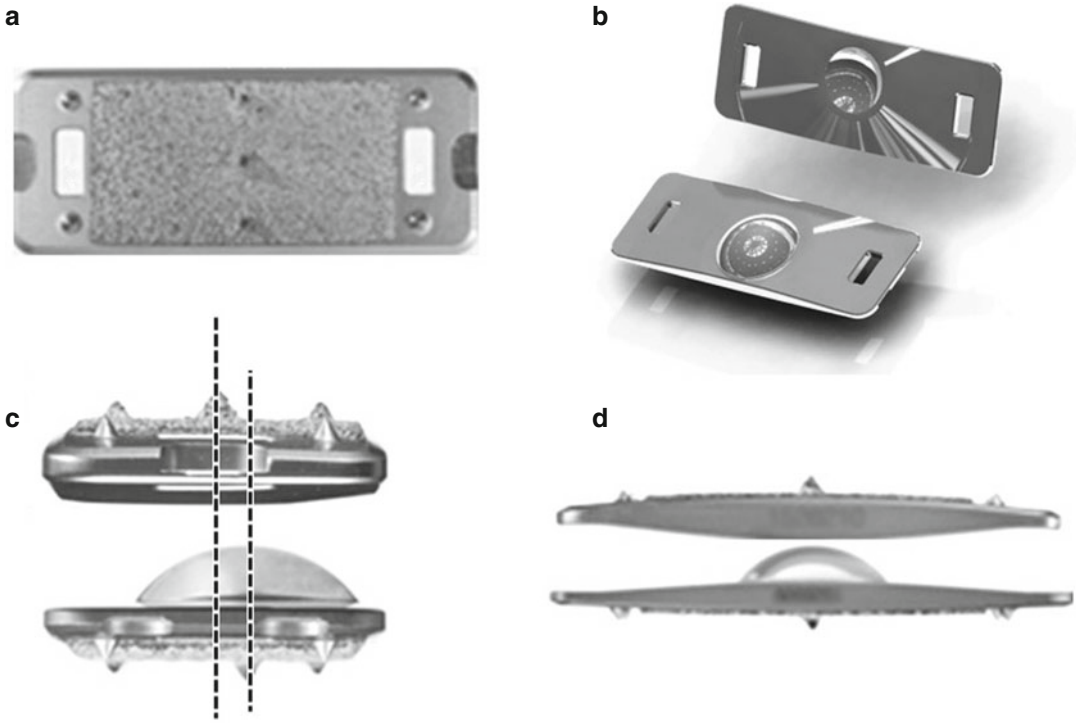

Fig. 42.5 (**a**–**d**) XL TDR (With permission and image provided by NuVasive, Inc.) (The NuVasive XL TDR® device is not approved in the United States. Caution – investigational device. Limited by US law to investigational use)

rotation and controlled anteroposterior translation of the polyethylene core, similar to the native IAR. The combination of rotation and translation may serve to unload the facets joints, thereby preventing implant-related facet arthrosis. An FDA trial started in 2007, enrollment was completed and currently it is in the final stages of data collection and submission [38].

There are also other devices that are currently on trials, such as the NuVasive XL TDR® (NuVasive – Fig. 42.5). It has metallic design that is implanted from the patient's side, with a similar approach to extreme lateral interbody fusion (XLIF) cages. An FDA trial started in 2009. The NuVasive XL TDR® device is not approved in the United States and limited by US law to investigational use.

The Freedom Lumbar Disk (AxioMed – Fig. 42.6) is made of a silicone polycarbonate-urethane polymer core that is bonded between the two metal end plates to allow controlled motion and enable shock absorption capability. The device has been used in Europe, and FDA trials began in 2008. The Triumph (Fig. 42.7) consists of two metallic end plates with a geom-

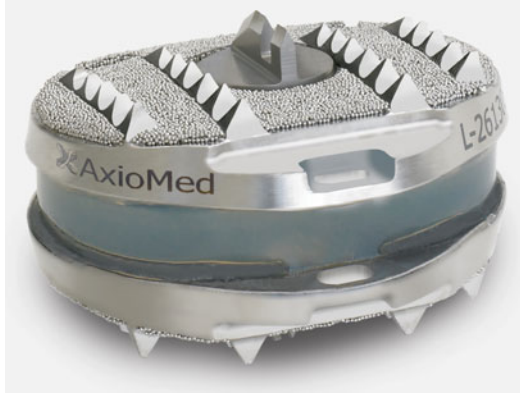

Fig. 42.6 Freedom TDR (With permission and image provided by AxioMed)

Fig. 42.7 Triumph TDR is an investigation device in the United States (With permission and image provided by Globus Medical, Inc.)

etry allowing it to be inserted through a posterolateral approach. An IDE study started in 2007; it is still ongoing but no longer recruiting.

42.5 Biomechanics of TDR Prostheses

42.5.1 Intervertebral Disk and Disk Replacement Center of Rotation

The center of rotation of the lumbar spinal motion segment does not move about a single fixed axis of rotation, but rather an elliptical locus of instantaneous axes of rotation, termed the centrode [39–42]. The centrode is located within the posterior half of the disk space in the normal intact spine. In early degenerative disk disease, the centrode lengthens, and in moderate disk degeneration, the centrode migrates caudally. Axial loading does not appear to influence the centrode dimensions or position.

Using an in vitro human cadaveric model, the multidirectional flexibility properties and COR of TDR (SB Charité) were determined and compared to conventional threaded fusion cages (e.g., BAK cages) and BAK cages augmented with transpedicular screw/rod fixation for single-level spinal instrumentation [43, 44]. The SB Charité prosthesis was associated with an increase in axial rotation by 44 % compared to the intact lumbar spine, whereas the BAK and anteroposterior reconstructions decreased range of motion by 29 % and 80 %, respectively. Flexion-extension range of motion was slightly increased for the SB Charité (3 %) versus the intact disk, whereas this was decreased in the BAK and anteroposterior stabilization groups (BAK = 57 %, anteroposterior = 93 %) when compared to the intact and SB Charité conditions. Based on flexion-extension radiographs, the intervertebral centers of rotation were in the posterior one-third of the operative intervertebral disk only for the SB Charité device and intact spine condition, with definitive evidence of physiologic intervertebral translation. Therefore, the TDR device preserved the kinematic properties and normal mapping of segmental motion at the operative and adjacent intervertebral disk levels, as compared to interbody instrumentation, with or without transpedicular screw/rod fixation.

42.5.2 Load Sharing After Lumbar Disk Arthroplasty

Using a finite element model, Dooris et al. [45] implanted a ball-and-cup-type artificial disk via an anterior approach and compared the data with in vitro data. Both small and large annulotomies were performed, and the implant was placed either anteriorly or posteriorly within the disk space. The restoration of an intact ALL

was also assessed. Models were subjected to either an axial compression force alone or a combination of flexion-extension moment with axial preload. In this model, the facet loads were found to be more sensitive to the anteroposterior location of the artificial disk than to the degree of annulotomy. Under pure axial compression, implanted models with an anteriorly placed artificial disk exhibited facet loads 2.5 times greater than loads observed with the intact model, whereas posteriorly implanted models demonstrated no facet loads in compression. Implanted models with a posteriorly placed disk also exhibited greater flexibility than the intact and implanted models with anteriorly placed disks. The restoration of the anterior longitudinal ligament resulted in reduced pedicle stresses, facet loads, and extension-rotation to near normal. This study suggested that by altering the placement of the artificial disk in the anteroposterior direction, the motion segment flexural stiffness and posterior load sharing may be modulated [45].

Biomechanical comparisons have also been performed between unconstrained and constrained lumbar artificial disk designs. These studies have revealed differences in facet loading and implant stresses (e.g., polyethylene core) [46]. An unconstrained artificial disk design is less sensitive to placement and unloads the facet joints, compared with a constrained design. The decreased core stress may result in a reduced potential for wear in an unconstrained prosthesis, which may potentially increase the functional longevity of the device.

42.5.3 Load-Displacement Curve and Motion Patterns of TDR Devices

The pattern of intervertebral load-displacement curves for Charité TDR-implanted motion segments has been studied by O'Leary et al. [47]. The prosthesis component motion patterns (PCMP) were divided into four types: PCMP1, angular motion predominantly between the upper end plate and core, with little or no visible core translation; PCMP2, lift-off of upper prosthesis end plate from core or of core from lower end plate; PCMP3, core entrapment, resulting in a locked core over a portion of the range of motion; and PCMP4, angular motion between both the upper and lower end plates and core, with visible core translation [47].

A gradually changing motion pattern was observed in normal lumbar segments, while the TDR-implanted segments displayed regions of both relatively small and large angular changes with gradual moment application. The disruption of the ALL and the anterior annulus during the insertion of the Charité TDR removes the biomechanical constraints imposed by these structures. As a result, a larger angular travel was observed in the absence of physiologic compressive preload for the same applied moment in TDR motion segments, compared with the intact motion segments. Under a compressive preload, entrapment and locking of the polyethylene core occurred over a portion of the sagittal plane motion – as reflected by the relatively flat portion of the load-displacement curves in the presence of a preload (Fig. 42.8). Once the core was released, a large angular change occurred, reflected by a sharp rise of the load-displacement curves (Fig. 42.8). The predominant angular motion within the prosthesis occurred between the upper end plate and the polyethylene core.

The effects that these TDR motion patterns may have on the long-term outcome, as well as on load sharing at the implanted level and polyethylene core wear, currently remain unknown. However, the nonuniform motion could potentially influence the wear of the implant. Other movement patterns, such as angular motion at one articulation with only a small amount of core translation, may also potentially influence load sharing within the implanted segment and at adjacent levels. Based on biomechanical studies, it may be concluded that several factors are likely to affect the function of the non- or semi-constrained TDR implants, including implant placement and orientation, intraoperative changes in lordosis, and the magnitude of physiologic compressive preload [47].

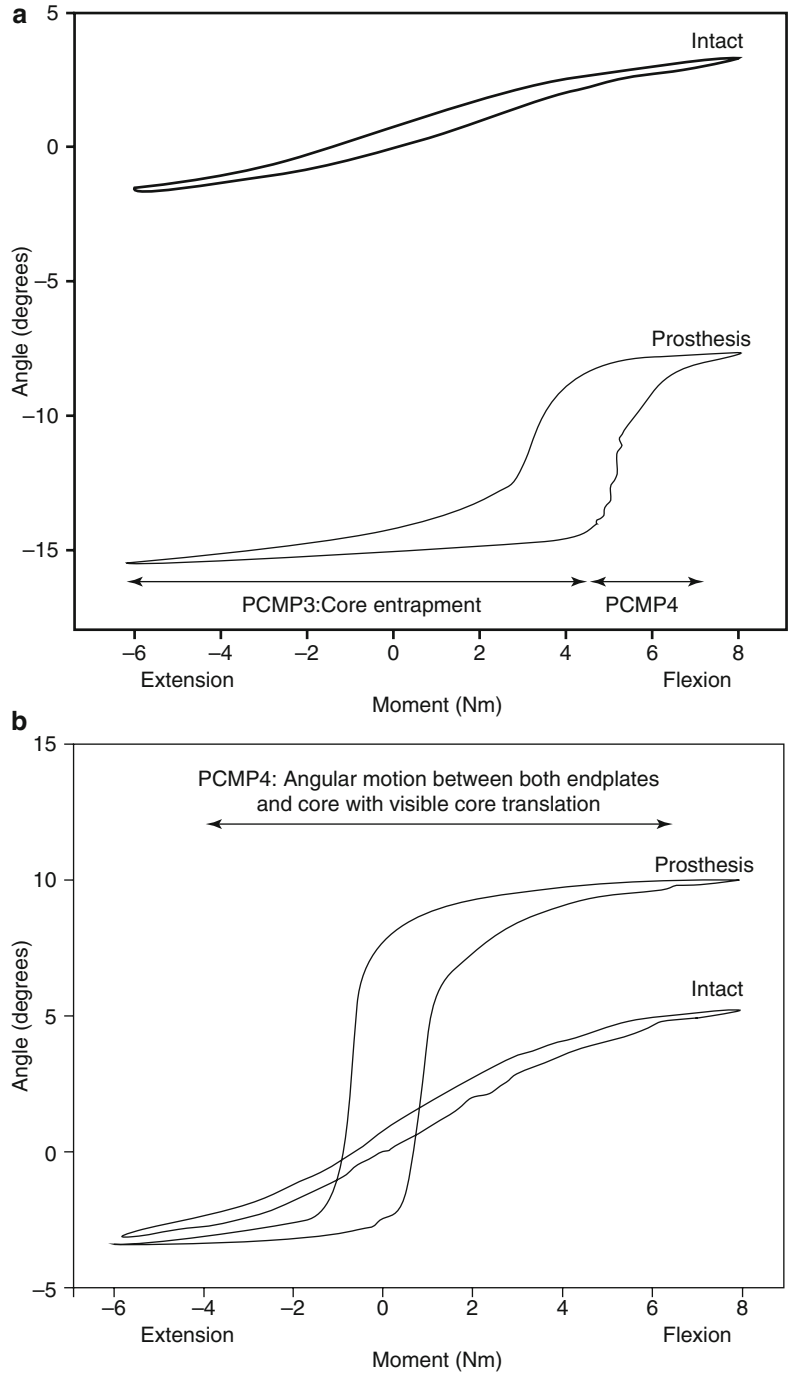

Fig. 42.8 Load angular displacement curves of intact lumbar spine and Charité TDR device implanted at the (**a**) L5–S1 and (**b**) L4–L5 levels in human lumbar spine. (**a**) Prosthesis motion pattern demonstrating core entrapment. A locked core is observed over a portion of the range of motion, with large angular change occurring with core release. (**b**) Prosthesis motion pattern with angular motion between both the *upper* and *lower* end plates and core, with visible core translation (Figure kindly provided by Dr. Avinash Patwardhan)

42.5.4 Adjacent-Segment Degeneration

Accelerated adjacent-segment degeneration is one of the most important morbidities associated with solid spinal fusion. It is for this reason that there is such a significant development of non-fusion motion preservation devices. Short-term results for the lumbar disk arthroplasty devices are encouraging. Long-term results, however, are not

yet available. Appropriately designed biomechanical studies of adjacent-level degeneration have provided insight into the potential success or failure of an implant with respect to motion preservation and adjacent-level degeneration. Although many biomechanical studies are available, the results have large variation and are conflicting, mostly due to the use of inappropriate and ill-defined methodologies. A relatively new testing method designed to study spinal adjacent-level effects, the hybrid test method, uses unconstrained pure moments to provide rotation input for multidirectional testing. The hybrid test method has four steps: (1) intact spine specimen with entire mobile region is used to measure various biomechanical parameters, e.g., disk pressures, ligament strains, and facet loads; (2) appropriate unconstrained pure moment is applied to the intact specimen and total range of motion is determined; (3) unconstrained pure moment is applied to the spinal construct (specimen with an implant) until the total range of motion of the construct equals that of the intact; and (4) statistical comparison of the biomechanical parameters between the construct and intact then allows for comparison of the adjacent-level effects [48–51]. Using a hybrid test method with a whole lumbar spine specimen (T12–S1), multidirectional adjacent-level effects due to implantation of one- and two-level ProDisc-L device were evaluated and compared to simulated one- and two-level arthrodesis. The single-level lumbar ProDisc-L preserved rotations at the non-operated levels but showed increased rotations at the operated level in both lateral bending and torsion. Conversely, two-level simulated fusion decreased the rotations at the fusion site and produced increased adjacent-level rotations in all directions, compared with lumbar arthroplasty devices. Therefore, it may be concluded that rotation lost/gained at the operated level is redistributed over the remainder levels. ProDisc-L implantation produced only small adjacent-level effects in comparison with significant effects produced by spinal fusion. Importantly, the study revealed that the adjacent-level effects were not confined to the adjacent levels alone but were seen throughout the entire specimen (i.e., whole lumbar spine specimen, T12–S1).

Adjacent-level biomechanics after multilevel disk arthroplasty in cadaveric lumbar spines have been evaluated by comparing operative- and adjacent-segment range of motion and intradiscal pressures [52]. The study compared two-level disk arthroplasty versus circumferential arthrodesis using anterior interbody cages and pedicle screws. A kinematics assessment revealed that segmental motion distributed over L2–S1 was preserved in the arthroplasty group but was significantly altered after circumferential fusion. After arthrodesis, adjacent-level range of motion and intradiscal pressures were increased proximally and distally under loading modalities of flexion-extension, axial rotation, and lateral bending. In contrast, there was no significant difference in either the range of motion or intradiscal pressures at adjacent levels between intact control and disk arthroplasty groups.

Harrop et al. [53] have performed a systematic review of the published incidence of radiographic adjacent-segment degeneration and symptomatic adjacent-segment disease after arthrodesis or total disk replacement. Their data supported the use of arthroplasty to reduce adjacent-level disk degeneration and disease, compared to arthrodesis. In the study, 34 % of patients undergoing arthrodesis and 9 % of patients in the total disk replacement group developed adjacent-level degeneration. Increased risk of adjacent-level degeneration was associated with older patients, arthrodesis, and longer follow-up [30, 53]. The risk of adjacent-segment failure appears to be higher for patients in whom lumbar fusion with rigid instrumentation is performed to treat degenerative instability, and the risk seem to be particularly high in postmenopausal women [54]. Adjacent-segment disease developed in 14 % arthrodesis patients compared to 1 % of arthroplasty patients. These results suggested a correlation between fusion and the development of adjacent-level degeneration, compared to arthroplasty. However, the association was dampened by the influence of patient age. Nevertheless, a strong correlation existed between spinal fusion and adjacent-level disease, compared to arthroplasty.

Another systematic review done by Wang et al. compared the incidence of adjacent-segment disease of two randomized controlled trials (Berg et al. and Guyer et al.), after a 2-year follow-up. The risk of clinical adjacent-segment disease (treated surgically) was 1.2 % (2/170) on the TDR group versus 7.0 % (8/115) on the fusion group. Another more recent study done by Zigler et al. published a randomized controlled trial with a 5-year follow-up, comparing the ProDisc-L versus circumferential fusion. Three (1.9 %) of 161 of the TDR group and 3 (4 %) of 75 fusion group required surgery at the adjacent level [38].

The aforementioned studies are challenged, however, by existing data that suggests that incidence of adjacent-segment disease is no greater in fused spines than in spines that did not undergo fusion. Furthermore, the maintenance of a lordotic posture appears to be critical for the prevention of adjacent-segment degeneration and disease [43, 55–68].

42.5.5 Motion Preservation

The preservation of segmental mobility represents a potential advantage of lumbar disk arthroplasty. One of the goals of lumbar arthroplasty is to restore and maintain mobility and to protect adjacent levels from abnormal motion, which may be a factor in transition syndrome following arthrodesis. The restoration of disk motion may preserve lumbar facet structure and function and prevent early degeneration. Results from clinical trials of disk replacement, however, do not yet have sufficient follow-up to determine whether the cascade of facet joint arthropathy is, in fact, halted or retarded. The mobility observed with TDR appears to be approximately 6° in flexion-extension at the L5–S1 level and 8° at L4–L5 [69]. Mobility in lateral inclination has also been analyzed and was found to be approximately 3–4°. Clinical and radiologic outcomes with a minimum follow-up of 10 years have been reported for the Charité artificial disk [69]. A total of 107 patients implanted with the Charité prosthesis through a standard anterior retroperitoneal approach (147 prostheses implanted, 54 one-level procedures, 45 two-level procedures, and 1 three-level procedure) were evaluated. Clinically, 62 % had an excellent outcome, 28 % had a good outcome, and 10 % had a poor outcome. Mean flexion-extension motion was 10.3° for all levels (12.0° at L3–L4, 9.6° at L4–L5, 9.2° at L5–S1). The mean lateral motion was 5.4°. In the sagittal plane, 6.1 % of the devices were anterior of geometric center, 34.0 % were centered, and 59.9 % were posterior of center. In the frontal plane, 75 % were centered, and 25 % were lateral of center. No subluxation of the prostheses and no cases of spontaneous arthrodesis were identified. Thus, with a minimum follow-up of 10 years, the Charité artificial disk demonstrated excellent flexion-extension and lateral range of motion with no significant complications [69].

The distribution of in vivo and in vitro range of motion (ROM) following single-level arthroplasty with the SB Charité III artificial disk has been compared with posterolateral fusion [70]. In this study, in vitro ROM in flexion-extension at the implanted and adjacent levels was measured, and the results were compared with in vivo, 2-year postoperative radiographic ROM evaluations. The results showed that single-level arthroplasty appeared to replicate the normal distribution of motion of the intact spine [17, 70].

A human cadaveric biomechanical study was performed to measure the facet forces and the IAR for different spinal positions under simulated weight-bearing conditions before and after total disk replacement at L5–S1 using semi-constrained (3° of freedom; ProDisc) and unconstrained (5° of freedom; Charité) articulated implants. With the ProDisc, the facets were partially unloaded, though the IAR did not match the fixed geometric center of the UHMWPE core, suggesting that joint surface incongruence is developed during movement. With the Charité, the IAR was less variable, yet the facet forces tended to increase particularly during lateral bending. These results highlight the important role that the facets play in guiding movement and that implant constraint influences facet-implant synergy. Rotational hypermobility and excessive torsional forces are potentially undesirable effects. Such hypermobility may induce exces-

sive loads on the posterior facets, promoting facet arthrosis and nerve root impingement. Moreover, the posterior elements in many patients with mechanical LBP are not fully intact, leading to further events of the degenerative cascade (e.g., disk degeneration, facet arthrosis) and subsequently producing pain.

The biomechanics of the lumbar spine treated either by fusion or total disk replacement (TDR) have been compared under severe loading conditions [71]. A three-dimensional model of a two-level ligamentous lumbar segment was created and simulated through static analyses with the finite element method. The analysis predicted that mobility after arthrodesis on the upper level was reduced in all rotational degrees of freedom by an average of approximately 44 %, relative to healthy normal disks. Conversely, the mobility after TDR on the upper level was increased in all rotational degrees of freedom by 52 %. The level implanted with the artificial disk showed excessive ligament tensions, high facet pressures, and a high risk of instability. The mobility and the stresses in the level adjacent to the arthroplasty were also increased. This model for an implanted artificial disk showed a greater risk of instability and further degeneration than predicted for the arthrodesis model [72].

42.5.6 Stability of the Implant-Bone Interface

The stability of an implanted lumbar arthroplasty device may be conceptualized into three categories: (1) short-term or immediate stability, (2) intermediate stability, and (3) long-term stability. The anchoring to the vertebral end plates via spikes or midline keel is considered important for immediate implant stability. The original SB Charité prosthesis was not solidly anchored, and this may have been associated with early expulsion of the device [32]. Several device end plates have been modified with a porous titanium and electrochemically bonded calcium hydroxyapatite coating, which allow for bony ingrowth into the end plate, providing intermediate or secondary stability with a potentially reduced risk of device expulsion [73]. Long-term stability may be defined as the cellular and microscopic changes of bony ingrowth and integration at the bone interfaces.

Following a 6-month survival period, the range of motion of the SB Charité and intact nonoperative controls were examined under axial compression, flexion-extension, and lateral bending. No statistical differences were observed between the groups [70, 71]. Plain film radiographic analysis showed no lucencies or loosening of any metallic prosthetic vertebral end plate, and gross histopathologic analysis of the SB Charité prosthesis demonstrated excellent bony ingrowth at the level of the implant-bone interface, without evidence of fibrous tissue or synovium. Furthermore, histochemical assays showed no local or systemic accumulation of particulate wear debris (titanium, ultrahigh molecular weight polyethylene, or cobalt-chrome) or cytokines, including TNF-α, PG_E2, IL-1, IL-2, or IL-6. The improved degree of porous ingrowth in total disk replacement prostheses, compared to other joint replacement devices, is likely due to ligamentotaxis, causing sustained compression forces across the metal-bone interface.

42.5.7 Wear Testing

An understanding of the wear potential of total disk replacements (TDRs) is critical as these new devices are increasingly introduced into clinical practice. In contrast to hip and knee wear, little is known about in vivo degradation or the contribution of wear debris to biologically mediated failure mechanisms of lumbar artificial disk devices. Ongoing retrieval studies have provided some evidence that clinically relevant wear and polyethylene degradation may occur in vivo with artificial disks. Implant subsidence, malpositioning, or migration may result in rim damage, plastic deformation, and component fracture. Chronic inflammatory reactions and wear debris in tissues have also been observed surrounding failed artificial disks. However, the clinical significance of wear in the spine remains poorly understood. Although it appears that wear particles may result

in a local inflammatory reaction, few cases of osteolysis around artificial disks have been reported. The wear potential of a ProDisc-L implant was determined using an adaptive finite element technique [1]. The testing scheme was validated using a model of a total hip replacement (THR) and was then used to model the ProDisc-L. The degree of flexion-extension, lateral bending, axial twist, and axial load were applied through ten million simulation cycles. The polyethylene wear rate of the ProDisc-L TDR was 9.8 mg/million cycles, whereas the comparable wear rate for the THR was 16.1 mg/million cycles. Thus, the wear potential of the TDR was better than the THR using joint-specific loading standards [1].

Metal-on-metal wear for the Maverick TDR (a semi-constrained, ball-and-socket implant) has been tested extensively, and there is essentially no metal wear at 31.5 years of simulated loading. The potential for toxicity of metallic wear debris to the surrounding neurologic structures has also been examined. The epidural toxicity of wear debris of the Maverick disk replacement was conducted in rabbits and there was no significant difference in epidural debris between control and Maverick-implanted animals [74]. Overall, the production of metal debris by the metal-metal TDR devices appears to be extremely low, which may enable metal-metal TDR devices to obtain an optimal longevity. In cases of THR, the polyethylene wear debris is responsible for prosthesis loosening over time, due to the macrophage reaction to wear debris particles. Similar studies have yet to be reported with TDR devices.

The extent of surface damage of the polyethylene core, including rim fracture and wear, after long-term implantation also remains poorly understood. Studies have been performed on Charité TDR components retrieved from patients undergoing revision TDR surgery and conversion to fusion [75]. All implants were removed due to pain, and the implants were associated with either subsidence, anterior migration, core dislocation, lateral subluxation, wear with wire marker fracture, end plate loosening, or osteolysis. Dimensional measurements and assessment of the extent and severity of polyethylene surface damage were assessed by micro-CT scanning, light microscopy, and white light interferometry. The dominant wear mechanism was adhesive/abrasive wear at both the dome and rim. End plate penetration (dome wear) was correlated with implantation time. There was also evidence of macroscopic rim damage, including radial and transverse cracking, fracture, plastic deformation, and third-body damage. Radiographic wire marker fracture was always associated with deformation, cracking, or fracture of the polyethylene rim. The TDRs displayed surface damage observed previously in both hip and knee replacements. Because of the evidence of increasing wear with implantation time, along with the demonstrated potential for osteolysis in the spine, regular long-term follow-up for patients undergoing TDRs is warranted.

42.5.8 Shock Absorption Capacity

The ProDisc-L (metal-polyethylene prosthesis) and the Maverick (metal-metal device) have been compared in terms of their shock absorption capacity and transmission of vibrations [74]. In this study, no significant differences were found between the implants regarding shock absorption or vibration transmission, with neither having any significant shock-absorbing effects. In pure axial loading, the axial stiffness of TDR devices is nearly infinite, demonstrating an absence of shock absorption capacity. This is strikingly different from the shock-absorbing properties seen in normal, and even severely degenerated, lumbar disks. However, the long-term consequences of these differences in shock absorption capacity are relatively uncharacterized. It is possible that an increase in posterior load transfer may occur after TDR, shifting a larger proportion of axial compressive load to the facet joints and potentially hastening the occurrence of facet joint arthropathy. Polymeric core disks address this problem. For example, the Freedom Lumbar Disk is made of a silicone polycarbonate-urethane polymer core that is bonded between the two metal end plates to allow controlled motion and enable shock absorption capability.

42.6 Complications of TDR Implants

Numerous types of complications have been documented with lumbar disk replacements. These include facet joint degeneration (facet compression or distraction), unexplained radiculopathy and/or back pain, extrusion of the implant, facet fracture, and acquired spondylolysis [31, 76]. These implant failures have been ascribed to surgical errors in either placement or sizing, surgical approach errors, inexperience, inappropriate indications, and patient noncompliance [77, 78]. Of note, the presence of anterior and posterior longitudinal ligaments, and the absence of collateral ligaments, facilitates side-to-side motion at the involved segment(s). Under normal conditions, the ALL may serve to limit excessive extension in the disk space. However, during disk replacement the ALL is incised, which may allow for a significant increase in lumbar extension. Since the ALL is focally absent, extrusion of the implant is a potential problem. It is also thought that abnormally high load sharing occurring posteriorly at the facet joints, along with a concurrent decrease in load sharing anteriorly, may further promote loosening and expulsion of the implant.

Potential complications of TDR include vertebral body fracture and implant subsidence, facet fracture, facet arthrosis, acquired spondylolysis, vascular injury, implant migration or dislodgement, and thecal sac/nerve root injury. A study of patients who presented with persistent or recurrent backache or leg pain after implantation of an artificial disk prosthesis (SB Charité III) revealed that migration of the prosthesis, subsidence into the vertebral body, adjacent-level disk degeneration at one or more neighboring levels, and facet arthrosis were the predominant complications [76]. In several cases, rupture of the metal wire around the polyethylene core occurred, as well as radiological signs of polyethylene wear. Subsidence of a metal end plate of the disk replacement into the vertebral body appears to be associated with fracture of the vertebral end plate. The artificial disk does not possess significant shock absorption capacity, and this may promote a more posterior transfer of load [74]. The excision of the ALL allows for an increased degree of lumbar extension, while the PLL remains intact. The above factors, along with an increase in disk space distraction by the TDR device, may potentially promote fracture of the adjacent end plates and, subsequently, subsidence of the implant.

Siepe et al. [79] published a prospective review on the ProDisc implant with a 5–10-year follow-up. The overall complication rate was 14.4 % (26/181): 11.9 % (18/151) for monosegmental TDRs and 27.6 % (8/29) for bisegmental interventions. The overall reoperation rate was 16.0 % (29/181 cases). Immediate device or technique-related complications occurred in 5 % (9/181), while general surgery-related complications occurred in 2.2 % (4/181). Reoperations for the treatment of persisting symptoms of LBP occurred in 5.5 % (10/181). A smaller subgroup in which reoperation was indicated for the treatment of adjacent-segment pathologies occurred in 2.2 % (4/181). Other published studies have reported widely diverging complication rates following TDR, the majority of which ranged between 10 % and 20 % [79].

42.7 Nucleus Replacement

There are no nucleus replacements or augmentation devices that are currently approved for use in the United States, but there are a number that are under clinical investigation. Hence, the following discussion revolves around devices in evolution.

42.7.1 Nucleus Replacement Devices

The treatment of chronic low back pain due to advanced disk degeneration requires restabilization of the lumbar column, mainly by restoring disk function. Disk restabilization involves restoration and stabilization of the ligaments and annulus. Such restabilization represents a new concept in treating lumbar disk pathology.

Clinically, indications for nucleus replacement may be separated into two general categories. First, nucleus replacement may be utilized in select post-diskectomy patients as a largely

prophylactic procedure to prevent recurrent disk herniations or progressive DDD. It is well documented that a small, but significant, proportion of patients (~3–15 %) undergoing standard microdiskectomy will develop recurrent herniations or progressive degenerative changes with symptomatic low back pain [11, 80, 81]. Iatrogenic changes seen post-diskectomy include loss of disk space height and desiccation [80, 82]. Partial disk replacement in the post-diskectomy setting offers the theoretical benefit of slowing future degenerative changes by maintaining disk space height and normal motion. Similar to TDR, nucleus replacement can also be utilized in patients with mechanical low back pain due to mild to moderate DDD. PDR allows for direct removal of the presumed pain generator (the diseased nucleus) and replacement with a device that maintains functional motion [19–24, 55]. Functionally, nucleus replacement devices can be divided into two broad classifications: elastomeric and mechanical [19–21, 44]. Elastomeric devices can be further subdivided into hydrogel and non-hydrogel replacements. These devices are either preformed or injectable. Injectable nucleus replacements are delivered in liquid form into the nucleotomy void and cure in situ, while preformed nucleus replacements are pre-cured polymers [19–24, 55, 83]. Mechanical devices can be subdivided into one- and two-piece designs [19–21].

42.7.2 Operative Technique

The surgical approach for nucleus replacement is variable depending on the specific device. Generally, devices can be placed via minimally invasive techniques, with multiple approach options available (e.g., anterior, lateral, posterior). The prosthetic disk nucleus (PDN; Raymedica) is implanted via a posterior hemilaminotomy or a transpsoatic approach [2].

42.7.2.1 Elastomeric Nucleus Replacement

The advantages of elastomeric nucleus replacement include the ability to recreate the natural function of the normal nucleus pulposus with uniform stress distribution and shock absorption capability. A central challenge involved in the utilization of preformed devices is implant extrusion due to their inherently deformable nature. For injectable devices, biocompatibility, long-term durability, as well as avoidance of leakage are of crucial importance. There are several elastomeric nucleus devices in active clinical trials [20, 21, 24, 25].

42.7.3 Prosthetic Disk Nucleus (PDN) (Centinel Spine)

PDN is composed of a preformed hydrogel core consisting of polyacrylonitrile and polyacrylamide with a polyethylene woven jacket. PDN was first implanted in humans in 1996. PDN remains the most widely studied nucleoplasty device worldwide [22, 48]. PDN is implanted dehydrated and subsequently hydrates and expands. It is designed to absorb up to 80 % of its own weight in water. Extrusion risk with the original design led to design and approach modification [17]. Subsequent designs include the PDN-Solo and, most recently, PDN HydraFlex [55, 77].

42.7.4 NeuDisc™ (Replication Medical)

NeuDisc is a compressible, preformed hydrogel consisting of an aquacryl polymer reinforced with Dacron mesh. It is implanted dehydrated and expands anisotropic to conform to the nucleotomy defect [20, 21, 25].

42.7.5 NuCore™ Injectable Disk Nucleus (IDN) (Spine Wave)

NuCore is an injectable non-hydrogel nucleus. It is an rDNA-based synthetic protein copolymer composed of silk and elastin. NuCore has been utilized in both the post-diskectomy and early DDD indication.

42.7.6 Dascor™ (Disk Dynamics): Prosthetic Intervertebral Nucleus

Dascor is a constrained, injectable, non-hydrogel nucleus. It is applied as a two-part in situ curable polyurethane and an expandable polyurethane balloon which is inserted into the disk space after the nucleus has been removed. The balloon is then injected under pressure with the flowable polymer that conforms to the shape and size of the disk space. The flowable polymer cures creating a firm but pliable implant.

42.7.6.1 Mechanical Nucleus Replacement

The advantages of mechanical nucleus replacement include strength and durability. Challenges include maintaining an even stress distribution and lack of shock absorption. The major weakness revolves around a lack of anchor to the end plates which predisposes to subsidence and expulsion. There are two mechanical nucleus devices in pilot feasibility study [19–21].

42.7.7 NuBac™ Disk Arthroplasty Device (Pioneer Surgical)

NuBac is a two-piece, mechanical nucleus. It is composed of poly-ether-ether-ketone (PEEK) and is the first PEEK-on-PEEK articulated intradiscal arthroplasty device. NuBac has a ball-and-socket design with a large surface contact area to distribute stress and theoretically lower the risk of subsidence. NuBac has been implanted through a lateral (XLIF) approach at L3–L4, L4–L5, as well as anterior retroperitoneal and posterior approaches at L5–S1 [19, 23, 49]. Currently the product is not available for distribution or use in the United States.

42.7.8 Regain™ (Biomet)

Regain is a solid, one-piece mechanical nucleus composed of a graphite substrate with a coating of pyrolytic carbon. It is applied at one-level L4–L5 or L5–S1 via an anterior retroperitoneal approach. Regain has a convex outer surface intended to conform to the natural convexity of the vertebral body end plates.

42.7.8.1 Percutaneous Nucleus Replacement (PNR: TranS1)

The percutaneous nucleus replacement (PNR) released by TranS1 consists of a titanium screw system anchoring itself onto the superior and inferior vertebrae, with a central membrane that is filled with curable material and acts as the nucleus. It is inserted in a caudal-rostral manner anterior to the sacrum axially through the vertebra to replace the damaged disk and restore the natural motion while also preserving the integrity of the annulus fibrosus and ligaments so as to reduce the risk of implant migration. Because of the approach, the system is limited to L5–S1. It has been in limited use since 2008, and its clinical performance has yet to be evaluated [38].

42.7.8.2 Perspectives on Lumbar Disk Arthroplasty

With the advent of new technology and techniques in lumbar disk arthroplasty, interest in preserving spinal motion at degenerated motion segments has increased. The goals of lumbar disk arthroplasty are to provide long-term pain relief at the degenerated disk level, to restore disk height to protect neural elements, and to preserve motion to prevent posterior facet arthropathy and adjacent-segment disease. Despite the relatively positive early clinical results of these devices, questions remain about the long-term efficacy in pain relief and maintenance of motion, the results of randomized comparative trials with fusion, and the life span of the devices. In addition, late sequelae and revision options are unknown. Further biomechanical clinical data involving TDR are needed before its large-scale adoption as a surgical procedure. Areas of potential future investigation may include the kinematics of TDR and hybrid constructs at different lumbar levels, effects of TDR on sagittal balance parameters, detailed in vivo retrieval and wear studies, anatomic press-fit designs for end plates, and long-term effects of TDR on adjacent segments and facet joints.

Conceptually, nucleus replacement offers the promise of a novel technology to add to the spectrum of surgical techniques to treat a variety of degenerative spine pathologies. Specifically, nucleus replacement has the potential to address degenerative pathologies more complex than simple disk herniation, but less advanced than severe DDD. Therefore, nucleus replacement may fill a surgical niche between simple diskectomy and TDR or spinal fusion. However, the potential success of nucleus replacement must also be tempered by the lack of long-term clinical results. Today, new technologies for spine surgery are judged on the basis of their safety and efficacy as well as cost-effectiveness. Several nucleus replacement devices are entering or completing pilot feasibility studies. Further clinical investigation with well-designed prospective, randomized pivotal trials is needed to ultimately determine the ideal indications and efficacy of nucleus replacement in the treatment of lumbar DDD.

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43 Pedicle Screw-Based Dynamic Stabilization Devices in the Lumbar Spine: Biomechanical Concepts, Technologies, Classification, and Clinical Results

Cédric Barrey, Eurico Freitas, and Gilles Perrin

43.1 Introduction

Spinal motion-sparing technologies were introduced to address the adverse effects of traditional spinal fusion: stiffness, pseudarthrosis, mechanical failure, and/or adjacent degenerative disease [1–8]. There are three different basic concepts involved with these technologies:

- Partial/total disk replacement
- Total facet replacement
- Posterior dynamic stabilization (PDS) devices

Compared to disk and facet replacement technologies, PDS systems are designed to stabilize the spinal segments without removing any part of the native disk and facet joints. They are classically divided into two categories [9–11]: interspinous process spacers and pedicle screw-based systems (Fig. 43.1).

Pedicle screw-based PDS systems have an advantage over total disk replacement in that they are based on techniques familiar to surgeons who have experience with posterior approach and traditional pedicular-based instrumented spinal fusions. The basic concept is to reduce the stiffness of the instrumentation to allow for load sharing between the instrumentation and the functional spine unit (FSU) at the instrumented levels [12]. Various implant designs have thus been developed to achieve this goal: reduction of diameter metallic rods, hinged pedicle screwheads that allow motion, damper components in the longitudinal elements, and more flexible rods made of non-metallic biomaterials.

Most PDS devices are approved for use as adjuncts to spinal fusion. However, inherent to their design, PDS systems are also utilized to address chronic low back pain by degenerative disk disease (DDD) and spinal stenosis. These devices may relieve symptoms of stenosis as well as discogenic pain by controlling motion, providing a certain degree of disk space distraction and indirect neurologic elements decompression, decreasing intervertebral disk stress, and unloading the facet joints. PDS devices may

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_43

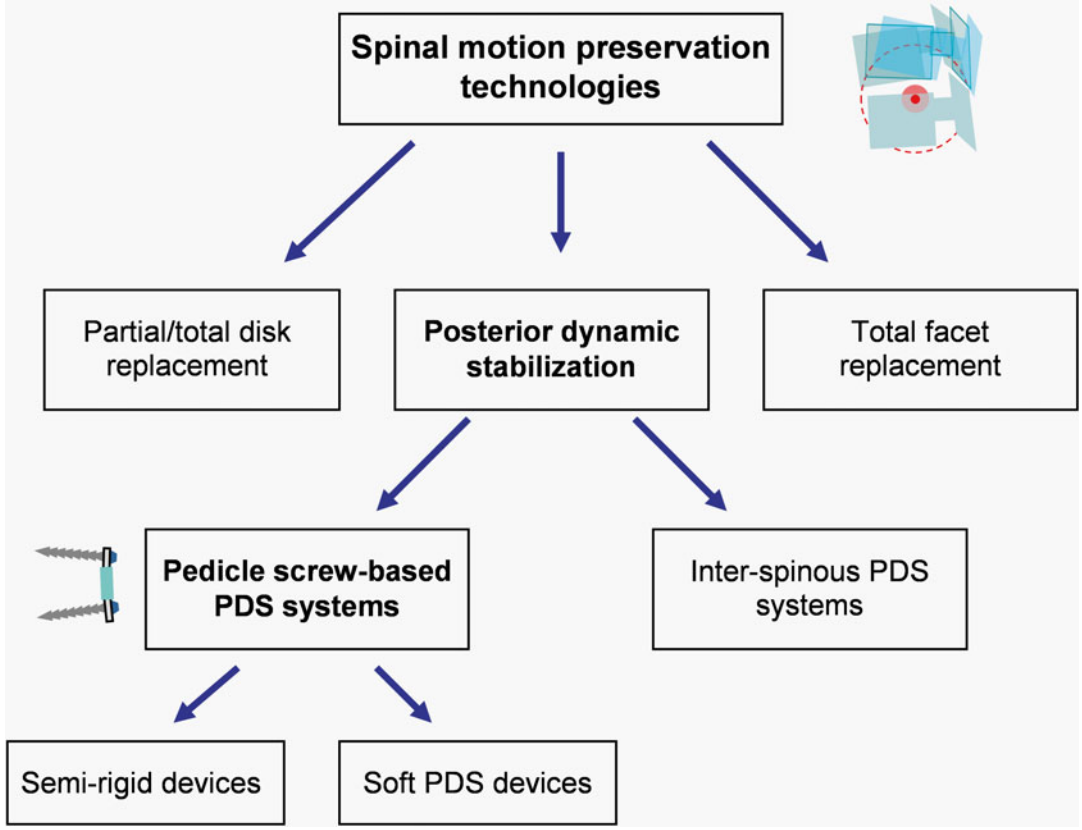


Fig. 43.1 Classification of spinal motion preservation technologies

also reduce transmission of stress to the adjacent levels and potentially decrease the incidence of adjacent segment disease [11, 13–16].

The authors recently performed an extensive review of biomechanical and clinical investigations involving pedicle screw-based PDS devices currently available for use clinically [17–22]. The current chapter presents the most significant results from this review in both the biomechanical and clinical fields.

43.2 Biomechanical Concepts

To analyze the biomechanical effects of pedicle screw-based PDS devices, we have to distinguish two different indications: non-fusion (i.e., posterior dynamic stabilization) and fusion (i.e., dynamic fusion).

43.2.1 Dynamic Stabilization

The three basic biomechanical requirements for an ideal posterior dynamic stabilization device are [23]:

- Unload the intervertebral disk evenly with a predictable load distribution
- Control physiologic 3D motion (range of motion, ROM, and location of mean axis of rotation, AR)
- Maintain/restore sagittal balance and anatomic alignment

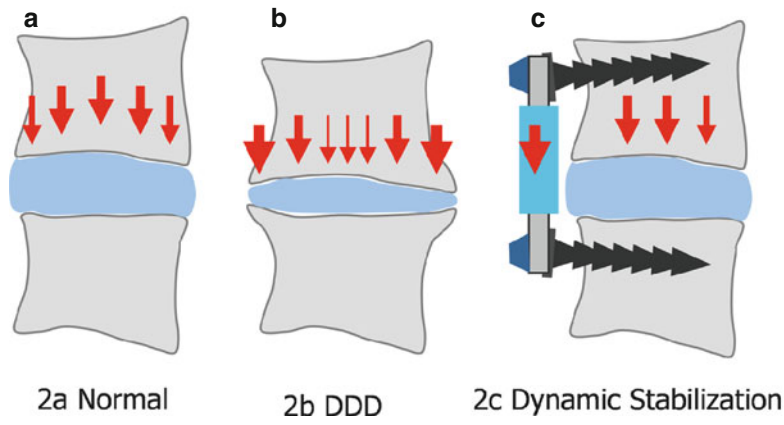


Fig. 43.2 Load distribution in the functional spine unit: in the normal (**a**), degenerative conditions (**b**), and following implantation of a posterior dynamic stabilization device (**c**)

43.2.1.1 Load Distribution

The intervertebral disk is composed of a homogeneous gel of collagen and proteoglycans and forms the main load-bearing structure in the FSU [24, 25]. Through experimental studies, the lumbar intervertebral disk demonstrated very high resistance to axial compression (ranging from 3,000 to 5,000 N) [24] with compressive loads on the nucleus redistributed evenly in a radial direction (Fig. 43.2a).

Degenerative disk disease affects the ability of nucleus to bear compressive loads, and consequently more load is transferred to the peripheral regions of the disk and annulus (Fig. 43.2b) [4, 5, 26]. Profilometry in vivo studies by McNally [13] confirmed this abnormal load distribution in degenerative disks. In addition, disk degeneration results in the loss of disk height and increase of axial compressive loads to the posterior elements, potentially accelerating facet arthrosis.

Sengupta recently proposed that asymmetrical load distribution rather than abnormal motion was the main cause of mechanical low back pain [16]. This concept is supported by correlations between abnormal stress distribution across the disk space and painful disks on discography. The presence of high load zones has been described as the "stone in the shoe" theory by Mulholland [12]. Although current surgical treatment has focused on restricting intervertebral motion, abnormal transmission of load across the disk space is likely a significant source of low back pain. Similar process has been observed for hip and knee joints with asymmetrical load distribution resulting in accelerating arthrosis. Correcting osteotomy in the lower limbs has been therefore proposed to obtain more even load distribution.

Pedicle screw-based PDS devices have been designed as load-bearing devices to unload the degenerated disk and minimize load transfer to the posterior facets (Fig. 43.2c). By reducing the pressure on the degenerated disk and facets, pedicle screw-based PDS devices may reduce mechanical pain associated with these structures [15, 16, 27].

Load transmission through the functional spinal unit (FSU) following implantation of PDS systems has been investigated by finite element analysis and by measuring intradiscal pressure in cadaveric studies using flexible pressure transducers [28] (Table 43.1). Through these biomechanical studies, significant unloading of the intervertebral disk was observed, especially in extension and after distraction, whereas in flexion, intradiscal loads were similar to the loads of the intact spine.

Table 43.1 Load transmission at the instrumented level following implantation of PDS device and compared to the intact condition

	Schmoelz et al. [29] experimental study		Zander et al. [30] FEA	Rohlmann et al. [31] FEA	
Loading condition	Dynamic	Rigid	Dynamic	Dynamic	Rigid
Standing	NT	NT	ns	↓	↓↓
Flexion	ns	ns	ns	ns	ns
Extension	↓↓	↓↓	ns	↓	↓↓
Lat bend	↓	↓	NT	NT	NT
Axial rot	↑	↓	ns	ns	ns

NT not tested, *NS* not significant, *FEA* finite element analysis, Dynamic: posterior dynamic stabilization, Rigid: rigid instrumentation

43.2.1.2 Kinematics

The intervertebral kinematics basically described the relative displacement of the upper vertebra with respect to the lower vertebra. The mean segmental flexion-extension range of motion (ROM) in the lumbar spine ranges from 10 to 18° depending on the vertebral level. In flexion-extension, the mean axis of rotation (AR) is located just below the surface of the upper endplate of the lower vertebra in the posterior one-third of the disk space (Fig. 43.3) [32]. The normal location of COR results from the natural tendency of the vertebra to move spontaneously in the path of least mechanical resistance.

In 1992 Panjabi defined "spinal instability" as an increase of the neutral zone on a load-displacement curve [33]. The neutral zone corresponds to the initial segment of the curve where there is low resistance offered by the FSU and subsequently great displacement occurs from minimal load application.

Although the relationship between low back pain and instability is not clearly defined yet, most authors accept that excessive non-physiologic motion may manifest as mechanical low back pain. According to the staged grading system of Kirkaldy-Willis, instability occurs in the early phase of disk degeneration, whereas the restabilization stage with reduction of motion and ankylosis of the FSU occurs in the late phase [34].

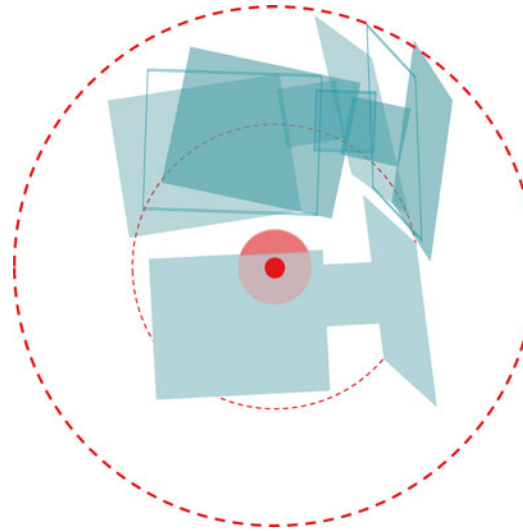


Fig. 43.3 Location of the mean AR in sagittal rotation (flexion-extension) in the lumbar spine [32]

Results from experimental studies involving pedicle screw-based PDS devices [11, 35–39] support the biomechanical concept of "controlled motion without instability." Scifert et al. has demonstrated in a calf model that PDS devices have the ability to provide significant stability with reduction of ROM compared to intact spines in flexion-extension and lateral bending [40].

By reducing excessive intervertebral motion, we can expect that implantation of such devices will result in relief of mechanical pain related to instability.

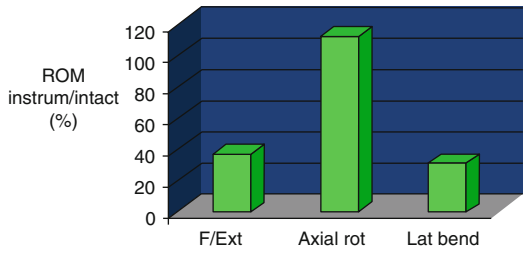


Fig. 43.4 ROM following implantation of the DYNESYS® implant (ROM Instrum) compared to ROM of the intact spines (ROM Intact) (averaged results from four different human cadaveric in vitro studies [35, 41–44])

However, the biomechanical studies have demonstrated that pedicle screw-based PDS systems were more efficient to control ROM in flexion-extension and lateral bending than in axial rotation. This is important clinically as these devices may not be beneficial in cases of rotational instabilities, laterolisthesis, or scoliosis deformities. As examples, ROM following implantation of the DYNESYS® device ranged from 20 to 45 % of intact ROM in flexion, from 33 to 94 % in extension, from 26 to 40 % in lateral bending, and from 76 to 181 % in axial rotation [35, 41–44]. The mean ratio that was measured from experimental studies between DYNESYS® ROM and intact ROM is presented in Fig. 43.4.

Compared to soft stabilization devices, especially DYNESYS® implant which was the most investigated pedicle screw-based PDS device through experimental studies, few data are available concerning the effects on ROM following insertion of semirigid devices. Compared to soft PDS systems like DYNESYS®, these devices may probably result in a greater control in 3D motion, especially in axial rotation. That could justify their use in cases of deformity or instability. In case of degenerative spondylolisthesis, although Freudiger et al. found that DYNESYS® implant could control partially horizontal translation [41], semirigid devices may also be more suitable than soft PDS.

Restoration of normal segmental kinematics requires the return of ROM in physiologic range as well as physiologic quality of motion with respect to the location of the mean AR. The posterior placement of PDS systems is relatively far away from the physiologic axis of rotation. Subsequently, the posterior shift of the mean AR induced by most of the pedicle screw-based PDS results in a compression effect of the whole disk in flexion (anterior and posterior annulus) and a distraction effect, i.e., the unloading of the whole disk, in extension (Fig. 43.5b). This is in contrast to the normal kinematic behavior of the FSU (Fig. 43.5a).

The non-physiologic kinematics following pedicle screw-based devices may result in overloading the intervertebral disk in some positions, especially when the spine is flexed (sitting position). Otherwise, some authors proposed the use of combination of PDS devices with total disk prosthesis anteriorly to deal with disk and facets degenerative changes [45]. According to us, there is a potential risk of conflict between the kinematic of the disk prosthesis and that of the PDS device. Although combination of the two types of motion preservation technology may be an attractive option, kinematic data suggest that such a combined construct may potentially result in overloading the disk prosthesis in flexion and complete unloading of the prosthesis in extension with the risk of dislocation.

More recently, using a nonlinear 3D finite element model of L4–L5, Jahng et al. [46] found that the center of rotation and stress distribution differed according to the design and materials used and also confirmed that the biomechanical effects induced by the implantation of dynamic stabilization systems produced non-physiological stress on the functional spine unit.

In 2014, using a 3D finite element model of the L4–L5 segment, Alapan et al. [47] confirmed that alterations in the location of the COR results in significant changes of load-sharing characteristics within the spine segment.

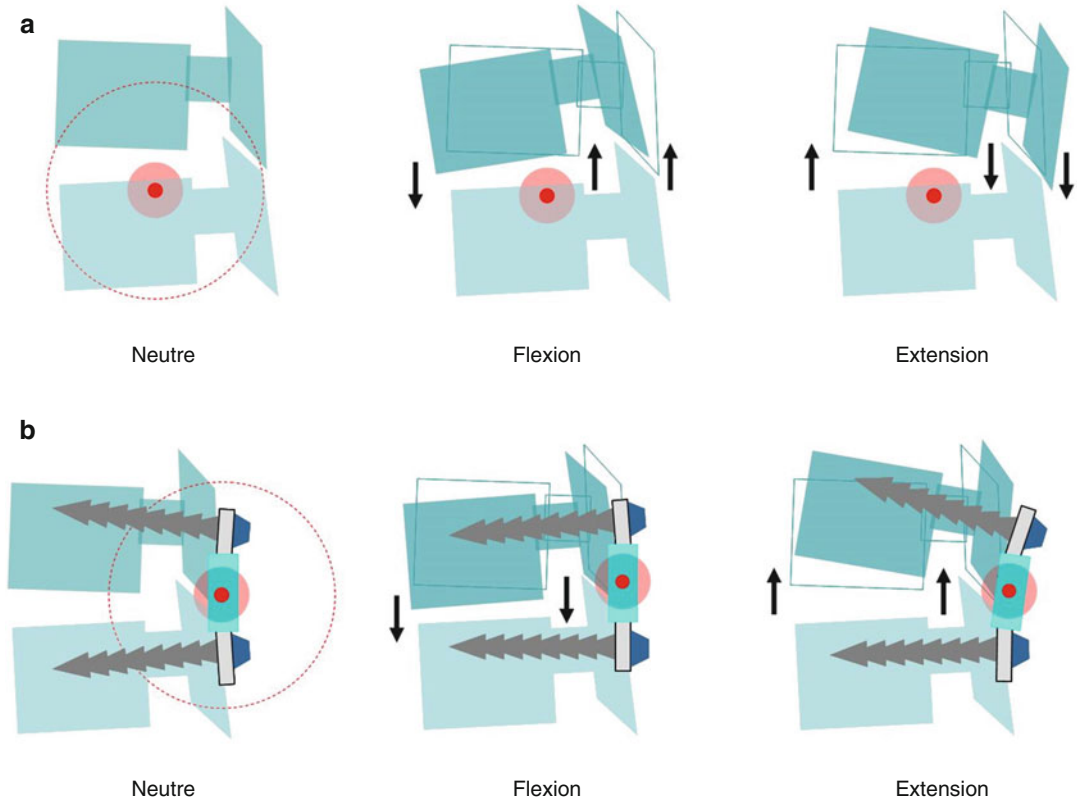


Fig. 43.5 Consequences of posterior shift of the axis of rotation on intervertebral kinematics [17]. (**a**) Normal kinematics of the FSU in flexion-extension. (**b**) Kinematics of the FSU after implantation of pedicle screw-based PDS system

43.2.1.3 Alignment/Posture

It is now well accepted that restoration of sagittal balance with respect to anatomic spino-pelvic parameters is paramount in optimizing outcomes after lumbar fusion surgery [48–50]. Referring to classes of pelvis incidence may be particularly helpful to evaluate the amount of lordosis required in a spinal fusion procedure [51]. In general, restoration of adequate lordosis during fusion surgery is achieved by contouring the rod and then realigning the spine along the bended rod.

The use of flexible rods may therefore pose difficulties when trying to manipulate, correct, and maintain spinal alignment in the setting of spinal deformity, making this technology less optimal in these settings. Restoration of a large amount of lordosis may also be challenging.

In addition, most PDS systems provide a certain degree of posterior distraction to unload facet joints and posterior annulus and widen neural foramina potentially resulting in radicular and discogenic pain relief. However, posterior distraction may also lead to focal kyphosis and subsequently increased adjacent level stresses (Fig. 43.6).

Legaye et al. reported a study on the unfavorable influence of pedicle screw-based PDS systems on the sagittal balance [52]. This author, who analyzed the impact of PDS implantation on sagittal alignment, noted that PDS devices were associated with loss of lumbar lordosis and pelvis backtilt, i.e., pelvis retroversion.

More recently, in 2011, Chen et al. [53] analyzed and compared the restoration of lordosis after implantation of hybrid versus purely dynamic instrumentation in the lumbar spine. Twenty-nine patients were included in the study. Local and global lordosis was measured using specific software. The authors concluded that hybrid construct could better preserve lordosis at

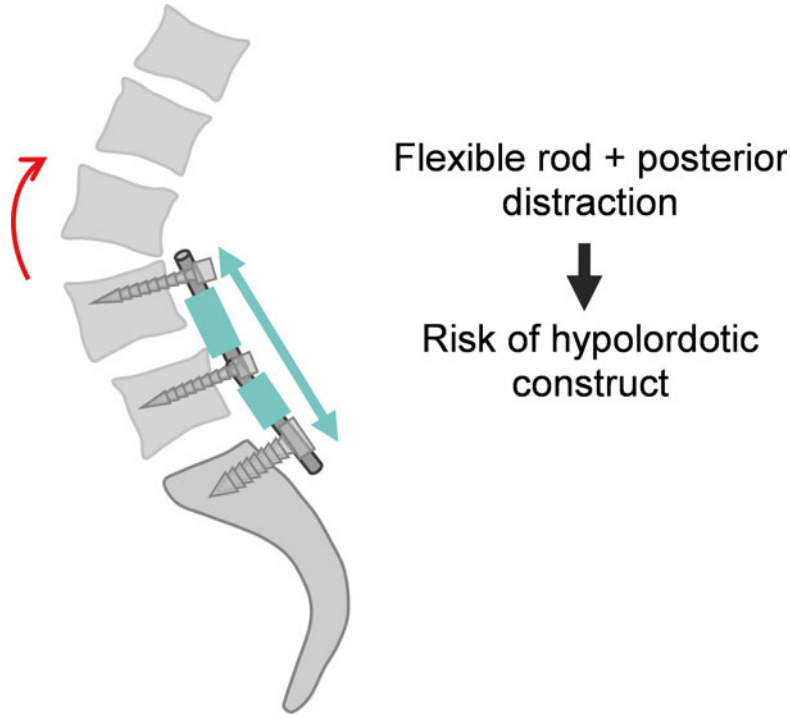


Fig. 43.6 Potential risk of sagittal imbalance and hypolordotic construct with dynamic instrumentation due to the design of the rod

the instrumented levels, therefore reducing the compensatory hyperextension of the adjacent spine above. Further study is needed to determine the efficacy of PDS devices in maintaining postoperative physiologic sagittal balance.

Otherwise, further clinical follow-up and correlation between pelvic morphometry (flat versus lordotic alignment) is necessary to better understand the consequences of such occurrences. The forces witnessed in the intervertebral disk depend partly on patient-specific spino-pelvic organization [50, 51] with predominant axial compressive forces noted in flat spines and predominantly shear forces in lordotic spines. Inherent to their design, pedicle screw-based devices are probably more suitable to control axial compression than shear forces, especially those with the presence of a spring/damper.

43.2.1.4 Implant Longevity and Adjacent Level

In contrast to traditional spinal fusion, dynamic devices must stay anchored to the bone in the setting of continued intervertebral motion. One of the complications that may therefore arise from instrumentation without fusion may be mechanical failure of the implant like loosening at the screw-bone interface or screw breakage [54]. Stoll et al. reported that rates of screw loosening, probably underestimated, were approximately 10 % in a series of 73 patients implanted with the DYNESYS® system (mean follow-up of 38 months) [55]. Benezech and Mitulescu recently reported the clinical and radiographical results of a series of 33 patients instrumented with the ISOLOCK® device without fusion [56]. After a mean follow-up of 45 months, they noted the presence of 5 mechanical complications (3 cases of screw breakage out of 148 screws implanted (2 %), 1 case of unscrewing of the screw nut, and 1 case of material loosening). However, there was no correlation between the presence of a mechanical complication and clinical results (the functional results were good or excellent in 76 % of patients with a return to previous work rate of 87 %).

Although mechanical failure of pedicle screw-based PDS devices may probably be unavoidable with time, such devices should have the advantage to delay the need of spinal fusion.

Otherwise, PDS offers a potential advantage over traditional rigid instrumentation in terms of adjacent segment load transmission [57]. However, to date, no clinical studies have reported their efficacy with regard to this objective. Additionally, some biomechanical studies did not find clear benefits of posterior dynamic stabilization in terms of minimizing adjacent level disease [29, 31, 44, 58]. As examples Schmoelz et al. [29] reported no difference in intradiscal pressure for both dynamic and rigid stabilization compared to intact spines, and Castellvi et al. [59] found only a 5.5 % reduction in maximal stresses provided by dynamic instrumentation versus rigid fixation at the adjacent level. These results suggest that the difference in the biomechanical effect between dynamic and rigid stabilization may not be as high as reported [58]. However, while the stress reduction may be small, it could be clinically significant because this effect is repeated over many loading cycles.

In 2012, Mageswaran et al. [60] reported results from a biomechanical experimental study involving seven human spine specimens and comparing three configurations: intact, one-level rigid instrumentation (L4–L5), and two-level hybrid construct (L3–L5) with dynamic stabilization at the level above (L3–L4). The idea was to evaluate the protective effect of the disk above (L3–L4) from excessive ROM and the creation of a transitional zone. The authors demonstrated that the biomechanical behavior of the dynamic instrumentation was very close to the rigid instrumentation. It reduced ROM at the above disk (L3–L4) but transformed one-level lumbar fusion into two-level lumbar fusion with augmentation of stresses and mobility at the supra-adjacent levels (L1–L2 and L2–L3).

Early clinical data suggests that results are as good as those reported using rigid instrumentation; however, further long-term follow-up studies comparing dynamic versus rigid stabilization are required to determine the efficacy of PDS on adjacent segment disease (Table 43.2).

Table 43.2 Biomechanics and pedicle screw-based PDS devices: key points

Capacity to unload the intervertebral disk in extension, lateral bending, and axial compression
Kinematics:
Control ROM in flexion-extension and lateral bending
Posterior shift of the mean axis of rotation
Only few data available concerning metallic semirigid devices
DYNESYS® implant has been the most investigated device
Risk of hypolordotic construct (inherent to their design)
Reduction of stresses at adjacent segments
Implant longevity as a limitation (high risk of screw loosening)

43.2.2 Dynamic Fusion

43.2.2.1 Introduction

Surgery for low back pain due to degenerative disk disease and/or facet arthritis can be divided into three main options (Fig. 43.7):

- Limitation of motion (i.e., dynamic stabilization using motion-preserving devices)
- Restoration of motion (i.e. involving disk/facets replacement implants)
- Intervertebral fusion (considered as the gold standard)

Each option requires specific and adequate instrumentation to achieve the aim of the surgery.

In almost all cases, intervertebral fusion is currently performed using traditional rigid instrumentation. However, some authors advocated using a less rigid instrumentation to enhance intervertebral fusion success, thus introducing the concept of dynamic fusion [61–63].

Historically, most pedicle screw-based posterior dynamic systems (PDS) were initially designed to improve interbody fusion success in combination with an interbody bone graft [17–21]. In fact, most PDS devices are currently approved in the USA and Europe for use as adjuncts to spinal fusion and not as dynamic

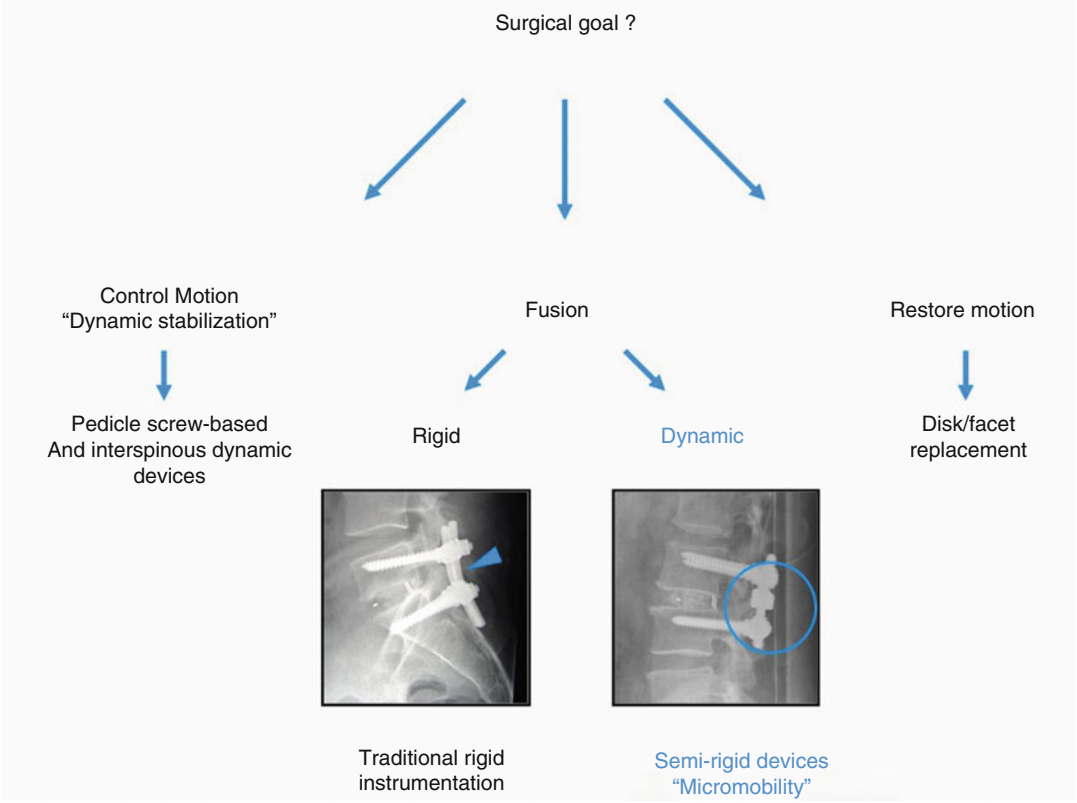


Fig. 43.7 Main strategies for low back pain surgery including the concept of dynamic fusion

stabilization system. What is confusing is that these technologies are most often used as non-fusion devices (dynamic stabilization). Most papers and clinical reports on pedicle screw-based PDS concerned the concept of dynamic stabilization without fusion. Using the following keywords in a PubMed search, "lumbar dynamic instrumentation and fusion" and "Dynamic fusion and lumbar spine," we found 47 papers on dynamic instrumentation, including 22 clinical reports, 14 biomechanical studies, and 5 reviews. All the papers involving pedicle screw-based PDS focused on the concept of dynamic stabilization but none on dynamic fusion.

43.2.2.2 Concept of Dynamic Instrumentation for Fusion

Dynamic instrumentation for fusion has been introduced in the 1990s to address the adverse effects of traditional spinal fusion observed with rigid instrumentation: pseudarthrosis, bone rarefaction, and mechanical failure.

Some authors suggested that eliminating mechanical loads on an interbody bone graft may result in negative bone remodeling, pseudarthroses, and osteoporosis [23, 64, 65]. This "stress-shielding" phenomenon at the disk space level may result from the excessive stiffness of traditional rigid instrumentation. Reducing the stiffness of the instrumentation, pedicle screw-based PDS allows for load sharing between the instrumentation and the functional spine unit (FSU) at the instrumented level(s). Using a finite element model of the lumbar spine, several authors demonstrated that posterior dynamic instrumentation, compared to rigid instrumentation, increases the amount of load transmission through the anterior column and the interbody bone graft, thus avoiding stress-shielding phenomenon. This may favor osteogenesis and enhance interbody fusion in

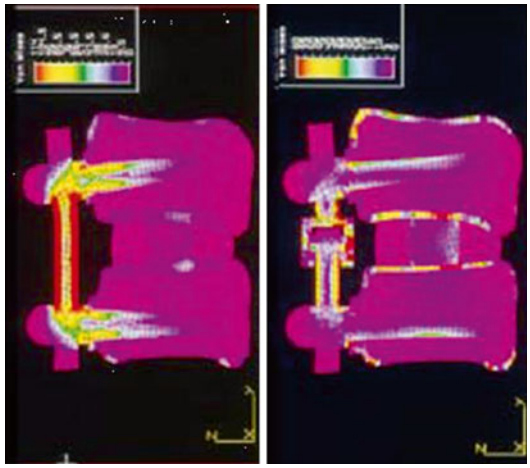


Fig. 43.8 Finite element analysis illustrating load-sharing phenomenon using posterior dynamic instrumentation (*right*) versus traditional rigid system (*left*) (From F Lavaste and G Perrin with permission, 1993, Laboratory of Biomechanics, ENSAM, Arts et Metiers Paristech, Paris, unpublished data)

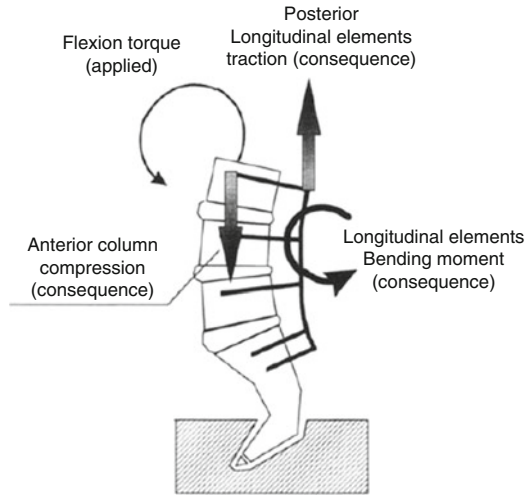


Fig. 43.9 In flexion, predominant load transfers through the system depend on instrumentation stiffness: a dynamic system results in anterior compression and posterior traction, while a rigid system results in axial pullout forces at the ends of the construct (Adapted from Templier et al. [65])

accordance with Wolff's law according to which the bone will adapt to the loads it is placed under, i.e., the structure and shape of bone permanently adapt to the loading conditions [66, 67]. Overload exposes to the risk of graft osteonecrosis, whereas underload may result in bone graft resorption. Thus, the basic concept of dynamic fusion is fewer loads through the instrumentation and more loads through the interbody bone graft without comprising stability, i.e., load sharing versus stress shielding.

In 1993, Lavaste and Perrin (unpublished data), using a finite element model of the lumbar spine, confirmed that dynamic posterior stabilization with *ISOBAR TTL*™, compared to rigid instrumentation, increases the amount of load transmission through the anterior column (Fig. 43.8).

Through a finite element analysis (FEA), Duffield et al. [64] compared the effects of three different longitudinal devices (4.8 and 6.3 mm rods and plate). They found that the axial load passing through the FSU was greater with 4.8 mm rod compared to 6.3 mm rod and/or plates (90 % versus 77 %, respectively). By using a canine model, Lim et al. [68] demonstrated that a less rigid stabilization device could reduce device-related osteopenia in the stabilized spinal segments and around the pedicle screws. In 1998, Templier et al. [65] using a 3D geometric FE model of the lumbar spine postulated that the TWINFLEX® semirigid device could offer a more favorable biomechanical environment for enhanced interbody fusion healing (Fig. 43.9). They evaluated the role of the longitudinal component in load transfer between the FSU and implant and noted that by reducing the stiffness of lumbar fixation, there was more homogeneous load transmission throughout the FSU without significantly reducing the rigidity of the instrumented spinal segment.

Finally, Goel et al. [61] developed a 3D finite element model to compare the load distribution of a hinged-dynamic posterior device versus a rigid construct and confirmed that the dynamic system

Table 43.3 Theoretical advantages of dynamic instrumentation for fusion: key points

Load sharing between the instrumentation and interbody bone graft
Avoid stress-shielding phenomenon in the anterior column
Stresses reduction at bone-to-screw interface
Less rigid fused segment

enabled more load to be transferred through the anterior column as compared with traditional rigid instrumentation without comprising stability.

Theoretical biomechanical advantages of dynamic instrumentation for fusion are summarized in Table 43.3. These advantages may result in increase fusion rates, limitation of bone rarefaction, and reduction of mechanical complications with the ultimate objective to reduce reoperations rates.

Presently, most pedicle screw-based PDS devices are FDA approved as an adjunct for spinal fusion. Although controversies remain regarding the support of such a classification, pedicle screw-based PDS systems are classically divided into semirigid rod systems and tension-band posterior-based systems used as a non-fusion technology [4–6, 10–12, 14, 16]. Only semirigid PDS systems could logically serve for dynamic fusion since excessive flexibility provided by soft stabilization PDS devices may allow for excessive motion and excessive anterior loading of the interbody graft, resulting in endplate failure, subsidence, decreased fusion rates, and sagittal plane deformity (flat back). Consequently, a classification of pedicle screw-based PDS devices based on motion restriction is needed to separate soft from semirigid rod systems with which a fusion is generally intended.

43.2.2.3 Biomechanical and Clinical Experience with ISOBAR TTL™ Technology for Fusion

Implant Design

The basic concept of posterior dynamic systems is to reduce the stiffness of the instrumentation to allow for more physiologic load transmission at the instrumented levels. Various technologies have been introduced to allow for partially controlled three-dimensional motion or micromotion: reduction of diameter metallic rods, hinged pedicle screwheads that allow motion, damper components in the longitudinal elements, and more flexible rods made of non-metallic biomaterials [19–21].

In the literature, pedicle screw-based PDS devices are divided as follows: metallic rod systems (considered as semirigid stabilization), tension-band posterior-based systems (considered as soft stabilization), and hybrid devices.

Fig. 43.10 ISOBAR TTL™, 1997, evolution of ISOLOCK® device 1993, Scient'x – Alphatec, France (Reprinted with permission)

ISOBAR TTL™ consists of a metallic semirigid pedicle screw-based PDS made of titanium (minimum artifacts on MRI and CT) (Fig. 43.10) [21].

It contains a damper element in its longitudinal element, a 5.5 mm titanium alloy rod. The damper, i.e., the dynamic component, allows reduced stiffness and limited amount of angular and axial micromotion (Figs. 43.11 and 43.12).

The damper provides ±2.25° angular ROM in flexion-extension and lateral bending, no limitation in axial rotation (unconstrained), and ±0.4 mm axial ROM (Fig. 43.12).

Concerning the surgical technique, this implant requires the same procedure as fusion performed with standard instrumentation using pedicle screws and rigid rod. Due to the familiarity of spine surgeons with pedicle screws placement, the learning curve for the implantation of the device is practically nonexistent.

In Vitro Testing

To support a classification of pedicle screw-based PDS systems, based on motion restriction, in vitro experimental investigations are needed. Concerning *ISOBAR TTL*™ device, the experimental evaluation was performed by N'dri in the laboratory of biomechanics, Arts et Metiers Paristech, Paris, France (unpublished data).

Six human L2–S1 spinal specimens were tested intact, injured (laminectomy at L4–L5), and instrumented at L4–L5 using *ISOBAR TTL*™ implant. Biomechanical tests were carried out using an optoelectronic system. Loads were applied to the upper vertebra (L2) with the lower vertebra (S1) fixed in a container. Pure moments were applied in flexion-exten-

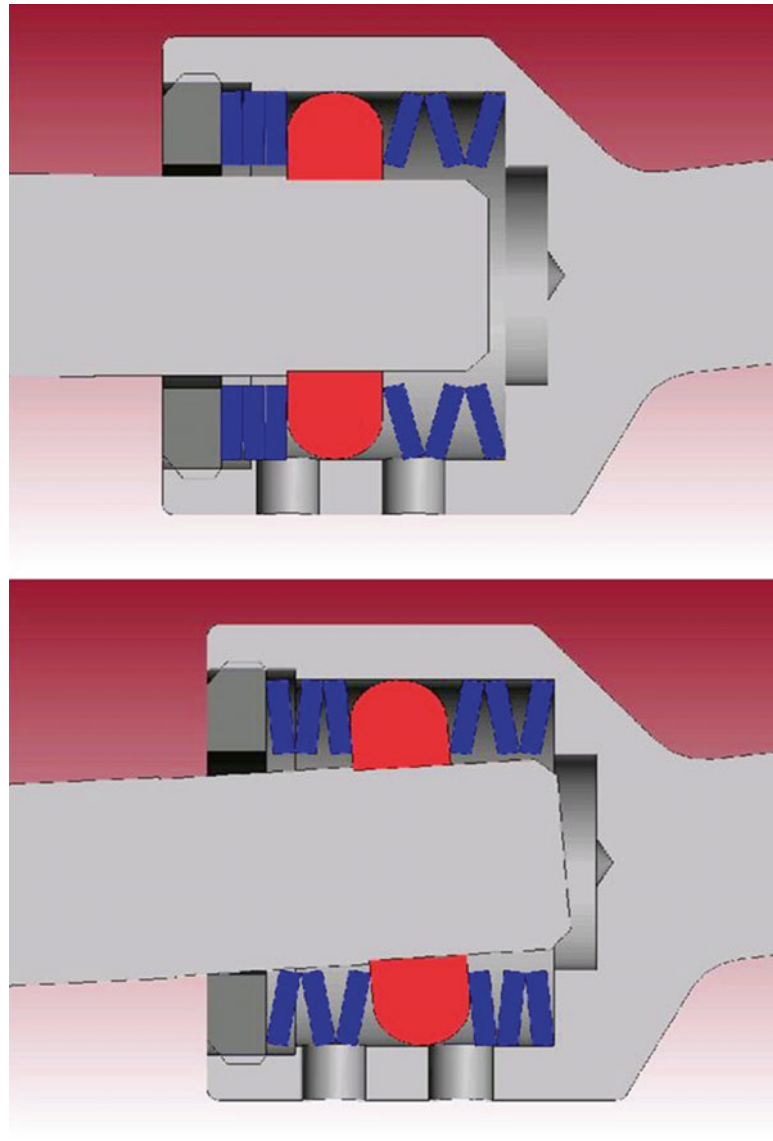


Fig. 43.11 Stacked washers within the dynamic component (From Scient'x – Alphatec, France, reprinted with permission)

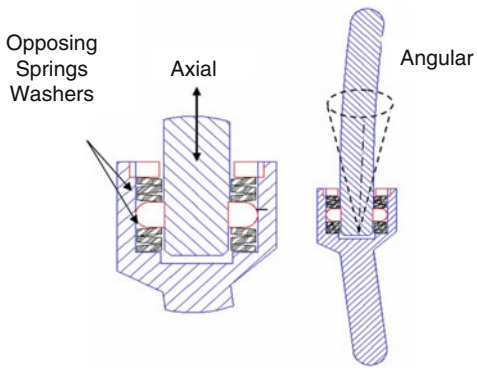


Fig. 43.12 Range of motion provided by ISOBAR TTL™ implant (Reprinted with permission)

sion, torsion, and lateral bending. Linear and angular displacements were measured using reflective markers rigidly fixed on L4 and L5 vertebrae (Fig. 43.13).

Results for instrumented spines in terms of range of motion, compared to intact spines, are presented in Fig. 43.14.

Through this experimental investigation, the authors found that ROM following implantation of the posterior dynamic implant *ranged from 20 to 50%*, depending on the loading condition. These results suggested that semirigid devices provide a greater control in 3D motion, especially

in axial rotation, in comparison with results reported for soft stabilization devices.

Clinical Experience

To the best of our knowledge, one of the first introduced semirigid rod is the ISOBAR TTL™ implant (1997, evolution of ISOLOCK® device 1993) which has been now used in Europe for over 15 years and was approved FDA clearance for use as an adjunct to spinal fusion in 1999.

Fig. 43.13 Testing device

The first clinical implantation of the ISOLOCK™ device was performed by G Perrin in June 1993. In 1996 he published a report on the usefulness of intervertebral titanium cages for PLIF and dynamic posterior fixation. Patients were treated with semirigid ISOLOCK® plates for lumbar degenerative disk disease and spondylolisthesis. The fusion rate was more than 95 % without any mechanical failure of the instrumentation (Figs. 43.15 and 43.16).

Unfortunately, there is no prospective study available comparing rigid versus dynamic instrumentation for fusion in the lumbar spine. Only case series have been reported in the literature [21, 63, 69]. The largest series has been reported by G Perrin (800 patients implanted with *ISOBAR TTL*™); however, this author unfortunately mixed in his series patients with dynamic stabilization (no fusion), dynamic fusion, and hybrid constructs (rigid + dynamic) making the results difficult to assess. He retrospectively reported an overall fusion rate of 98 % with no mechanical complications.

There is no data available in the literature concerning the fusion period and/or the bone graft volume comparing dynamic versus rigid instrumentation.

In fact we consider dynamic instrumentation as an option to treat degenerative disk disease for given indications and given lumbar levels. The use of metallic rods with dampers may pose difficulties when trying to maintain spinal alignment or to restore a large amount of lordosis. Because of these sagittal balance considerations [48, 49, 51, 52], we estimate that dynamic instrumentation should be avoided at L5–S1 level. The authors feel that the best indications correspond to one or two levels to

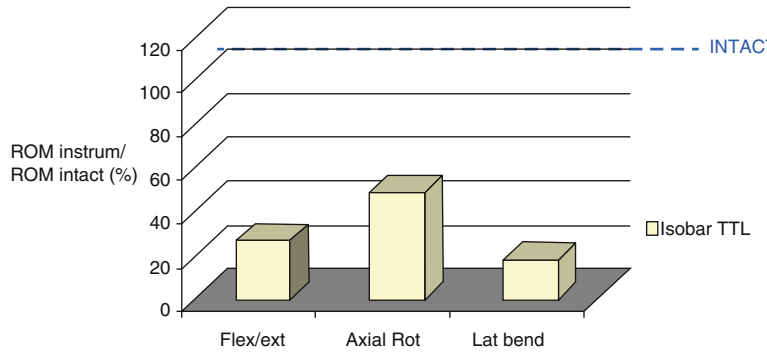


Fig. 43.14 In vitro evaluation of ISOBAR TTL™

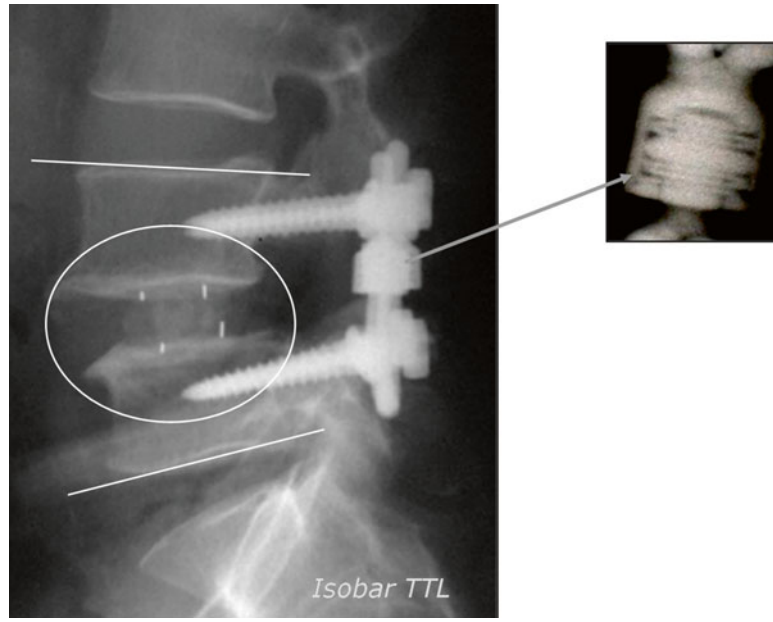


Fig. 43.15 Case 1: interbody fusion obtained at L4–L5 using semirigid posterior dynamic stabilization (*arrow*) in combination with interbody bone graft (PEEK cages, *oval* shape)

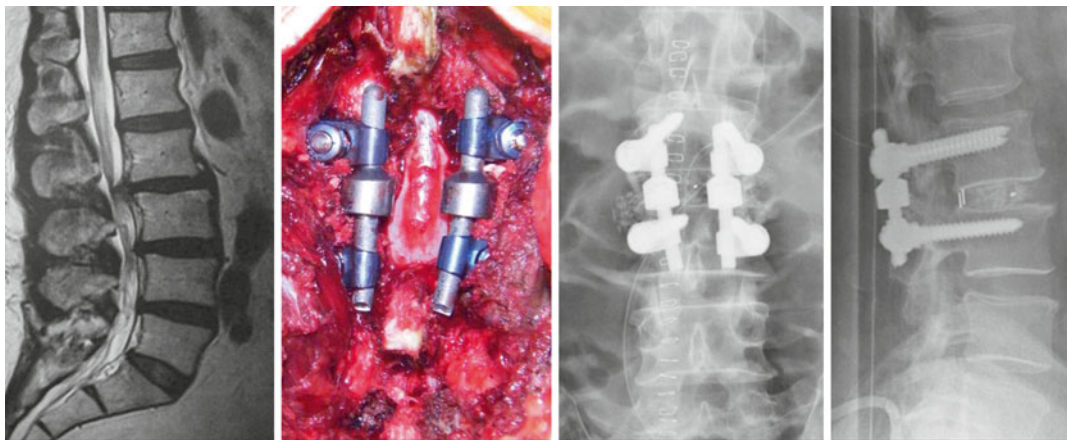


Fig. 43.16 Case 2: L2–L3 severe stenosis treated by L2–L3 interbody fusion using semirigid posterior dynamic stabilization in combination with interbody graft (PEEK cages). Simple interlaminar decompression without diskectomy was performed at L3–L4

be fused between L2–L3 and L4–L5 (Fig. 43.17). To restore sufficient segmental lordosis with ISOBAR TTL™, it is essential to apply compression between the screwheads along the rod.

Otherwise, when using dynamic instrumentation for fusion, the authors' preference is to place systematically the bone graft trough the intervertebral space (PEEK cages) rather than to realize an interlaminar and/or inter-transverse graft. Although some authors advocate the use of dynamic instrumentation in combination with posterolateral bone graft, we consider that dynamic instrumentation associated with interbody graft is more pertinent from a biomechanical point of view.

43.2.2.4 Conclusion

In comparison with the cervical spine, dynamic anterior cervical plates have been progressively

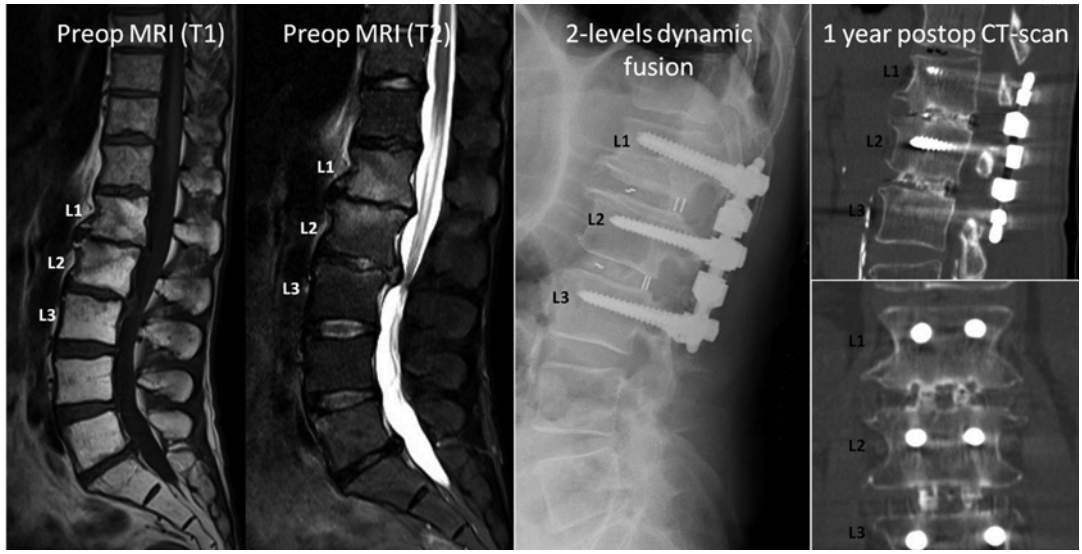


Fig. 43.17 A 55-year-old man presented with severe back and leg pain, not responding to conservative treatment. Imaging revealed a degenerative stenosis in L1–L2 and L2–L3 in relation with an L2–L3 disk hernia and inflammatory DDD at L1–L2. He was treated by decompression, followed by PLIF on two levels with cages and dynamic instrumentation. Surgical treatment provided a significant extent of immediate symptoms relief. One year after, a CT scan exam showed a solid fusion. Pain and disability levels decreased to 3/10 and 28/100, respectively

introduced to provide a better graft loading with the ultimate objectives to accelerate spinal fusion and lead to a lower incidence of postoperative mechanical complications [70]. The use of dynamic instrumentation for fusion in the lumbar spine applies the same biomechanical concept, i.e., favoring load sharing versus stress shielding.

Further prospective studies are now needed to confirm the efficacy of PDS devices in enhancing spinal fusion and especially determine the advantages of dynamic instrumentation in terms of fusion period, fusion rates, and fusion quality.

43.3 Technologies and Classification of Pedicle Screw-Based Dynamic Stabilization Devices

The basic concept of PDS systems is to reduce the stiffness of the instrumentation to allow for more physiologic load transmission at the instrumented levels. However, the design of these devices varies greatly. In the literature, pedicle screw-based PDS devices are divided as follows: metallic rod systems (considered as semirigid stabilization), tension-band posterior-based systems (considered as soft stabilization), and hybrid devices [71].

For these three categories, different implant designs have been introduced into the implant market:

- Implants that have introduced a small diameter rod to allow for greater motion: TWINFLEX® and BIOFLEX®
- An implant that utilizes a hinged pedicle screwhead to allow motion: COSMIC®
- Implants that contain a damper/coupler element in their longitudinal element: ISOBAR TTL®, ALADYN®, DYNAMO®, PERFX-2®, DSS®, and N-FLEX®
- Implants that replace the metallic longitudinal element by an elastic or solid polymer longitudinal element: GRAF ligament, CD HORIZON® PEEK rod, EXPEDIUM® PEEK rod, FLEXPLUS®, and DYNESYS®

Pedicle screw-based PDS systems are an attractive type of dynamic stabilization system due to the surgeon's familiarity with pedicle screw placement.

Tables 43.4, 43.5, and 43.6 show examples of currently available pedicle screw-based PDS systems.

Table 43.4 Soft PDS pedicular-based devices

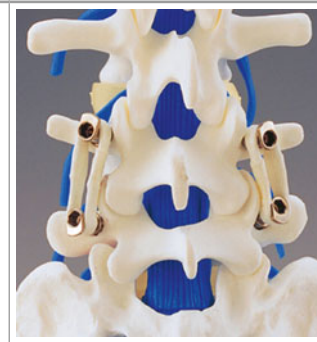
Device	Technology	Picture
Graf ligament Showa Ika Kohgyo, Japan (reprinted with permission)	8 mm braided polyester nonelastic tension bands	
DYNESYS® (DYnamic NEutralization SYStem) Zimmer Spine, USA (reprinted with permission)	Cylindrical polycarbonate-urethane (PCU) spacer Tensioned polyethylene terephthalate (PET) cord tunneled through the PCU spacer	
DYNESYS DTO® (DYnamic NEutralization SYStem) Zimmer Spine, USA (reprinted with permission)	Combined cord-rod construct and rigid rod offering the ability to transition from a rigid to dynamic system	
CD HORIZON® LEGACY™ PEEK rod Medtronic Sofamor Danek, USA (reprinted with permission)	PEEK rod (polyetheretherketone)	

Table 43.4 (continued)

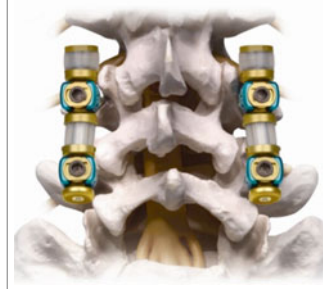
Device	Technology	Picture
CD HORIZON BalanC® Medtronic Sofamor Danek, USA (reprinted with permission)	Rod with a combination of silicone and PEEK materials	
TRANSITION® Globus Medical, USA (reprinted with permission)	Preassembled or intraoperatively assembled PET central cord, PCU flexible spacers, and compressible bumpers Titanium alloy spools	
EXPEDIUM® PEEK rod DePuy Synthes, USA (reprinted with permission)	Polyetheretherketone (PEEK) rod	
FLEXPLUS® Spine Vision, Paris, France	Multiple titanium fibers with a polycarbonate-urethane sheet	

Table 43.5 Metallic rod PDS pedicular-based devices

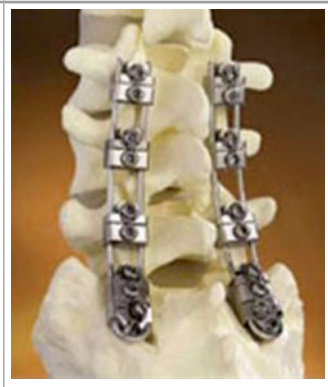
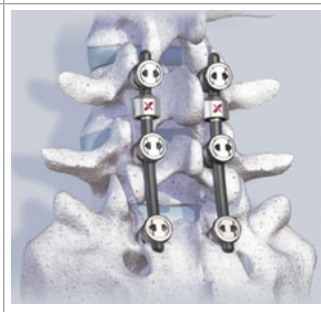
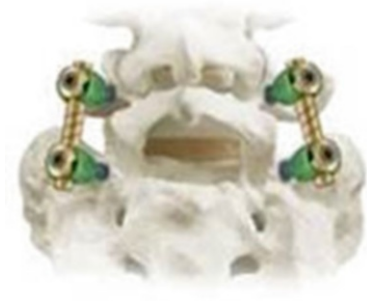
Device	Technology	Picture
TWINFLEX® (1992) Scient'X – Spine Network, France (reprinted with permission)	Twin rods 2 × 2.5 mm	
ISOLOCK® (1993) Scient'x – Alphatec, France (reprinted with permission)	Intrapedicular connection allowing micro-movements with the limits of 0.8 mm in axial compression and 4° in flexion-extension	
ISOBAR® TTL (1997, evolution of ISOLOCK® device 1993) Scient'x – Alphatec, France (reprinted with permission)	5.5 mm titanium alloy rod Damper allowing reduced stiffness and limited amount of angular and axial micromotion	
ALADYN® (2003) Scient'x – Alphatec, France (reprinted with permission)	S-shaped damper inside a rectangular box	

Table 43.5 (continued)

Device	Technology	Picture
ACCUFLEX®- Globus Medical, USA (reprinted with permission)	6.5 titanium rod Helical cuts	
BIOFLEX® BioSpine, Korea (reprinted with permission)	4 mm Nitinol spring rod (one or two loops) "Memory metal"	
DSS® Paradigm Spine, Germany (reprinted with permission)	Polyaxial screws with slotted and rigid couplers	
HPS® Paradigm Spine, Germany (reprinted with permission)	Rigid spinal fixation with a topping-off option (DSS® coupler)	

(continued)

Table 43.5 (continued)

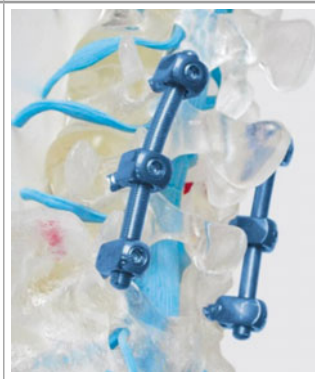
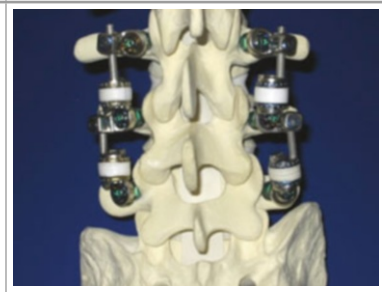
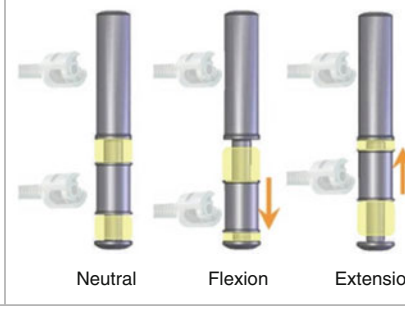
Device	Technology	Picture
COSMIC® Ulrich Medical, Ulm, Germany (reprinted with permission)	6.25 mm rod Integrated hinge in the pedicle screwheads	
DYNAMO® Scient'x – Alphatec, USA (reprinted with permission)	5.5 mm titanium alloy rod Damper allowing limited amount of angular and axial micromotion based on Scient'x ISOBAR®	
PERFX-2® Eden Spine, FL, USA	The dynamic rod damper provides ±5° in flexion-extension and ±2 mm of axial ROM	
WAVEFLEX® Medyssey, Seoul, Korea	Titanium alloy rod	

Table 43.6 Hybrid dynamic PDS pedicular-based devices

Device	Technology	Picture
STABILIMAX® Applied Spine Technologies, New Haven, CT, USA (reprinted with permission)	Dual spring combined with ball-and-socket joint mechanism Cobalt-chromium and titanium alloy	
N-FLEX® N Spine Inc., USA (reprinted with permission)	6 mm titanium rod with one end containing a composite titanium and PCU sleeve	

43.4 Clinical Investigations

43.4.1 Graf Ligament (Table 43.4)

Introduced in 1992, the Graf ligament was probably the first pedicle screw-based PDS device available for use clinically. It was initially proposed by his conceptor, Henri Graf, as an alternative treatment for spinal instability without fusion [72].

Summary of Biomechanical Investigations [73, 74]

- In vitro study: 2; FEA: 0
- Significant reduction of ROM in flexion-extension and lateral bending
- Failure to reduce intervertebral motion in axial rotation (107–132 % of intact ROM) and translation of the vertebral body
- Application of Graf ligament increases annulus and nucleus stresses
- Risk of exacerbating facet disease and neuroforamen stenosis due to increase of segmental lordosis

Henri Graf theorized that abnormal rotary motion might be the primary source of mechanical low back pain. The Graf ligament was therefore proposed to stabilize rotary motion and realign the segment in physiological lordosis. The "ligament" was also intended to compress the posterior annulus and allow healing of annular tears.

Initial outcomes following Graf ligament placement showed only modest improvement in functional ability with a high revision surgery rate.

Grevitt et al. [73] reported outcomes of 50 chronic lower back pain patients that were implanted with the Graf ligament device. They noted improvement in Oswestry Disability Index (ODI) scores from 59 preoperatively to 31. However, de novo postoperative radiculopathy was reported in 12 of 50 (24 %) patients, and 20 revisions or further procedures were performed in 13 patients. Only few mechanical failure of the construct were observed with one screw displacement and two screw breakages (1.2 % of screws used).

Hadlow et al. [75] published a retrospective case-control study comparing clinical and radiological outcomes at 1 and 2 years between soft stabilization with the Graf ligament and instrumented posterolateral fusion. They found significantly better outcomes in patients following a traditional spinal fusion compared to those treated with the Graf ligament, especially due to a higher revision rate in the Graf treatment group (55 and 73 % for Graf ligament group versus 37 and 43 % for the traditional fusion group at 1 and 2 years, respectively).

Rigby et al. [76] presented mid- and long-term results of a series of 51 patients treated with the Graf ligament. The mean follow-up of the study was approximately 4 years. Patients had only a six-point improvement in their ODI scores, and seven patients (14 %) required additional traditional fusion procedure. Finally, 41 % of patients reported that they wouldn't undergo a similar procedure again.

More recent prospective randomized evaluations reported better clinical outcomes in patients undergoing the Graf ligament placement compared to fusion.

In 2003 good to excellent results were reported by Madan et al. [77] in 93 % for patients operated with the Graf ligament group compared to 78 % for those treated by anterior lumbar interbody fusion. Their prospective randomized study compared the efficacy of Graf ligamentoplasty (28 patients) in comparison with rigid instrumented ALIF and insertion of the Hartshill horseshoe cage (27 patients) for similar severity of disk degeneration.

Kanayama et al. [78] reported a retrospective study aiming to assess midterm clinical and radiographic results of Graf artificial ligament stabilization in the treatment of degenerative spondylolisthesis. Sixty-four patients with degenerative spondylolisthesis were treated with the Graf ligament and the mean follow-up was approximately 5 years. Visual analogical scales of low back pain and radicular symptoms were significantly improved from 72 and 76 preoperatively to 14 and 15 postoperatively, respectively. The radiographic results demonstrated that Graf artificial ligament stabilization did not affect vertebral slip and disk height but maintained segmental lordosis (which was $9.8 \pm 5.9°$ before surgery, $12.8 \pm 6.7°$ immediately after surgery, and $12.2 \pm 8.9°$ at the final follow-up) and preserved segmental motion (ROM at the operative level was $11.2 \pm 5.6°$ before surgery and $4.7 \pm 4.6°$ at the final follow-up). Finally, the authors reported additional surgeries in only four cases (6.25 %) for adjacent degenerative disease.

The same authors recently published a retrospective long-term follow-up study with a mean 10-year follow-up [79]. Fifty-six patients who were treated with the Graf system were included in the study. Results showed that the construct maintained segmental lordosis and disability improved in patients with low-grade spondylolisthesis or flexion instability. A patient with scoliosis or lateral listhesis, however, had poor clinical improvement requiring reoperation.

43.4.2 TWINFLEX® (Table 43.5)

To the best of our knowledge, the TWINFLEX® implant was probably the first metallic semirigid PDS device available for use clinically.

Summary of Biomechanical Investigations [65]

- In vitro study: 0; FEA: 1
- Load sharing between the anterior column and the instrumentation
- Response to a flexion moment results rather in anterior compression and posterior traction than in axial pullout forces

Korovessis et al. [80] conducted a prospective comparative randomized study to compare the postoperative effects of a rigid versus TWINFLEX® instrumentation for degenerative spine disease and stenosis with a special focus on sagittal lumbar spine alignment. Thirty patients were included in the study with equal number of patients for each type of instrumentation. Evaluation of patients was mainly radiological analysis preoperatively and at 3 months postoperatively. The authors found that both rigid and dynamic instrumentations restored lumbar lordosis, sacral tilt, and distal lordosis and increased the foraminal diameter at the level L4–L5 resulting in an indirect decompression of the nerve roots at this level. They concluded that the dynamic system could be used with the same indications with the rigid in degenerative lumbar spine because it can offer equally good short-term results regarding sagittal spine alignment.

Champain et al. [69] performed a retrospective study to evaluate the interest of quantified radiographic analysis of lumbar spine in global outcome assessment of 49 patients treated by posterolateral lumbosacral fusion with iliac crest bone graft and TWINFLEX® dynamic instrumentation. The authors used Beaujon-Lassalle score to assess clinical outcome, and the mean follow-up of the study was 5 years. Sixty-one and 29 % of patients presented very satisfactory and satisfactory clinical outcomes, respectively. Complications were adjacent level degeneration in four cases (8 %), pseudarthrosis in two patients (4 %), and hardware failure in three cases (6 %), comparing favorably with literature data for rigid fusion.

43.4.3 ISOBAR TTL® (Table 43.5)

One of the first introduced semirigid rods is also the ISOBAR TTL® implant (evolution of ISOLOCK® device) which has been used in Europe for over 10 years and was approved FDA clearance for use as an adjunct to spinal fusion in 1999. Composed of a titanium alloy rod with a damper element made of stacked titanium alloy, the device allows a small amount of both axial and angular motion to the rigid rod.

Summary of Biomechanical Investigations [20, 21, 59, 81]

- In vitro study: 2; FEA: 1
- Axial (0.4 mm) and angular (2.25°) micromotion capacity
- Stabilization comparable to a rigid rod in terms of ROM
- Increase of anterior column loading
- Reduction of maximal stresses in the next adjacent level by approximately 5.5 % in flexion

The first clinical implantation of the ISOLOCK® device was performed by G Perrin in June 1993. In 1996 he published a report on the usefulness of intervertebral titanium cages for PLIF and dynamic posterior fixation. Patients were treated with semirigid ISOLOCK® plates for lumbar degenerative disk disease and spondylolisthesis [63]. The fusion rates was more than 95 % without any mechanical failure of the instrumentation.

Benezech and Mitulescu recently reported a retrospective study [56] to analyze clinical and radiographical long-term outcomes of

33 patients treated with the ISOLOCK® device. The surgical procedure was posterior dynamic stabilization without fusion, and the mean follow-up was 45 months. Seventy-five percent of patients had one-level stabilization and 25 % two levels. Good or excellent outcome was noted in 76 % with a return to previous work rate of 88 %. No spontaneous fusion was observed at the instrumented levels. The authors noted the preservation of preoperative disk height in more than 90 % of cases. Finally, they observed five mechanical complications: three screw breakages (out of 148 screws used), one unscrewing of the screw nut, and one material loosening.

In 2012, Li et al. [82] reported a 2-year follow-up study after insertion of the ISOBAR TTL® device. Thirty-seven patients were included consecutively with a minimal follow-up of 12 months. Both VAS and ODI decreased significantly postoperatively. New signs of degeneration at adjacent levels were observed on MRI in 14 patients (39 %), and revision surgery at adjacent segment was necessary for 3 patients (8 %). Finally, the authors observed screw loosening in four patients (11 %). They concluded that clinical improvement after implantation of ISOBAR TTL® was good but not really superior to traditional spinal fusion.

43.4.4 DYNESYS® (DYnamic NEutralization SYStem for the Spine) (Table 43.4)

The DYNESYS® device consists of two titanium pedicle screws connected by a cylindrical spacer (made of polycarbonate-urethane (PCU)) with a tensioned cord (made of polyethylene terephthalate (PET)) tunneled through the PCU spacer [83]. The spacer resists compression during extension and thereby maintains foraminal height while unloading the posterior annulus, and the tensioned PET cord resists tensile forces and provides resistance to spine flexion similar in concept to the Graf system. The device has been approved by the FDA as an adjunct for spinal fusion.

Using DYNESIS DTO® system allows surgeons to treat different stages of degeneration at contiguous levels.

Summary of Biomechanical Investigations [27, 31, 35, 38, 42–44, 58, 84–86]

- In vitro study: 8; FEA: 4
- DYNESYS® was probably the most pedicle screw-based PDS system investigated
- Limits ROM from 20 to 45 % in flexion compared to intact spines, from 33 to 94 % in extension, from 26 to 40 % in lateral bending, and from 76 to 181 % in axial rotation
- Impact of spacer length and posterior intervertebral distraction on kinematics and load transmission
- Unloads the intervertebral disk mainly in extension

Clinical studies on the DYNESYS® system used as a non-fusion device have shown heterogenous clinical outcomes compared to traditional rigid fusion [54, 55, 87–92].

The first clinical report was published in 2002 by Stoll et al. [55] who performed a prospective and multicenter study evaluating clinical and radiological outcomes of DYNESYS® in a series of 83 patients. Indications for the surgical procedure were segmental instability combined with spinal stenosis in 60 %, degenerative disk disease in 24 %, disk herniation in 8 %, and previous diskectomy in 6 %. The population of patients included 39 cases of degenerative spondylolisthesis as a secondary diagnosis. In most cases (56/83), dynamic instrumentation was combined with direct decompression and involved one level in 55 cases, two levels in 17 cases, three levels in 8 cases, and four levels in 3 cases. The mean follow-up was approximately 3 years. The mean low back pain score improved significantly from 7.4 to 3.1, mean leg pain scale from 6.9 to 2.4, and ODI from 55.4 to 22.9 %. There were ten

mechanical complications: two screw malplacements, one screw loosening requiring reoperation, and seven radiological signs of screw loosening. The authors concluded that the dynamic neutralization proved to be a safe and effective alternative in the treatment of unstable lumbar conditions.

In 2005, Grob et al. [88] published a retrospective study on 50 consecutive patients who were treated with the DYNESYS® system for symptomatic degenerative disk disease or stenosis with associated instability (listhesis). Results were analyzed from clinical and radiological data of 31 patients with a minimum follow-up of 2 years. The surgery involved one level in 32 % of cases, two levels in 52 %, three levels in 13 %, and four levels in 4 %. The authors found that back and leg pain improved in 67 % and 64 % of patients, respectively; however, functional capacity only improved in 40 %, and within the 2-year follow-up period, 19 % of patients required an additional surgical procedure. They conclude that the results of the study provided no support for the notion that dynamic stabilization of the lumbar spine results in better patient-oriented outcomes than those of traditional fusion.

A prospective study published by Schnake et al. in 2006 especially focused on the use of DYNESYS® implant in cases of instability [91]. A total of 26 patients with lumbar spinal stenosis and degenerative spondylolisthesis were included in the study. The dynamic stabilization was combined with interlaminar decompression. Twenty-four patients were evaluated after 2 years with a mean follow-up of 26 months. The authors observed that mean leg pain, evaluated with VAS scale, decreased significantly from 80 preoperatively to 23 postoperatively and that mean walking distance improved significantly from 250 m to more than 1,000 m. 87.5 % of patients would undergo the same procedure again. Radiographically, overall progression of spondylolisthesis was not significant and evaluated at only 2.1 %. The authors noted asymptomatic implant failure in four patients: three screw loosening and one screw breakage. They concluded that in patients with spinal stenosis and degenerative spondylolisthesis, dynamic stabilization with the DYNESYS® device combined with decompression leads to similar clinical results than those reported in established protocols using decompression and fusion with pedicle screws.

Welch et al. [92] recently reported the results of a multicenter, randomized study (FDA and IDE clinical trial) examining the non-fusion application of the DYNESYS® device in a population of 101 patients. Indications for the surgical procedure were grade I degenerative retrolisthesis ($n=3$), grade I degenerative spondylolisthesis ($n=20$), and spinal stenosis ($n=66$). At 12 months follow-up, the mean VAS scale for back and leg pain and ODI improved significantly from 54 to 29, from 80 to 25, and from 56 % to 26 %, respectively. Fifteen of 101 patients (15 %) required 18 reoperations by the time of the 1-year follow-up evaluation. Ten of these 18 additional surgeries were performed at the same level due to low back pain, radiculopathy, or increased instability. The authors concluded that the early clinical outcomes of treatment with DYNESYS® were promising; however, long-term follow-up care was still needed.

Finally, in 2010, Kocak et al. [90] reported a review of the literature to determine the occurrence of screw loosening after DYNESYS® implantation. These authors found that revision surgery due to screw loosening was not necessary in the majority of cases and concluded that it is not clear if screw loosening influences the clinical results.

In 2010, the FDA recommended against approval for DYNESYS® as a spinal non-fusion technology because of the risk of unfavorable outcomes (such as screw loosening) and an unclearly defined patient population.

Fay et al. [86] reported in 2013 a retrospective comparative study involving patients with ($n=24$) and without degenerative spondylolisthesis ($n=14$) and operated with DYNESYS® at one or two levels. Mean follow-up was 41 months. Postoperative ROM at the index level in FE decreased from 10 to 2.7°. The authors observed screw loosening in 4.6 % of screws and 21.1 % of patients. There was no difference between the

two groups in terms of VAS, ODI, screw loosening, and reduction of ROM at the index level. They concluded that results were similar regardless of the presence of preoperative degenerative spondylolisthesis.

Another clinical study was reported in 2013 by Haddad et al. [93] with 4-year follow-up. The authors retrospectively compared outcomes of patients operated with DYNESYS® system ($n=32$) versus traditional rigid fusion ($n=32$). Improvement of VAS (back and leg pain) and ODI was greater for the fusion group, and more patients were satisfied after fusion compared to after DYNESYS.

43.4.5 ACCUFLEX® (Table 43.5)

The ACCUFLEX® rod has been developed with a double helical cut within a standard 6.5 mm rod to reduce rod stiffness and is presently FDA approved as an adjunct for one-level fusion when used in conjunction with an interbody graft.

Summary of Biomechanical Investigations

- In vitro study: 0; FEA: 0
- Only fatigue tests were performed
- Intended to limit axial rotation and lateral bending while permitting flexion-extension
- Amount of flexibility depends on the number of circumferential cuts

Mandigo et al. [94] reported a prospective and randomized study of 170 patients in which 54 received the ACCUFLEX® rod system. Results at 1-year follow-up were comparable between the dynamic ($n=54$) and the rigid ($n=116$) group with similar fusion rates (92 % and 95 %, respectively) and clinical outcomes (evaluated by VAS and short form-16 scales). No instrumentation failure was reported in this series.

43.4.6 CD HORIZON® LEGACY™ PEEK Rod (Table 43.4)

The implant consists of non-metallic rods made of polyetheretherketone (PEEK) with a modulus of elasticity close to that of natural bone. It has been FDA approved as an adjunct for fusion when used in conjunction with an interbody graft (one-level interbody fusion). In addition, the rod is radiolucent allowing the surgeon to assess the quality of spinal fusion using X-rays.

Summary of Biomechanical Investigations [95]

- In vitro study: 2; FEA: 1
- Intended to allow some motion
- More flexible than titanium but comparable flexion-extension rigidity when PEEK rod is combined with an interbody spacer
- Unloads the bone-screw interface and increases anterior column load (approximately 75 % anterior and 25 % posterior)
- Control 3D motion better in FE and LB compared to AR (80 % of ROM reduction in FE, 70 % in LB, and 54 % in AR)

In 2007, Highsmith et al. reported their preliminary clinical experience with the LEGACY™ PEEK rod implant [96]. They described three cases in which the PEEK rod was implanted. Indications for surgery were adjacent segment disease, degenerative disk disease, and grade I degenerative spondylolisthesis. In all three cases, the dynamic implant was used as an adjunct for fusion. No data are available concerning clinical and radiological methods used for evaluation.

In 2012, Medtronic introduced the CD HORIZON BalanC™ spinal system which uses a unique combination of PEEK and silicone

materials and geometry. The rod is made of silicone and PEEK in its dynamic portion, while the fusion portion is entirely made of PEEK, thus creating a transitional zone between the fused and the mobile segments. The device is indicated to treat multilevel spinal surgeries requiring fusion at one or more levels and neutral stabilization (non-fusion) at adjacent level (only for use outside the USA).

In 2013, Athanasakopoulos et al. [97] reported a series of 52 patients who underwent posterior spinal fusion with CD HORIZON PEEK rod with a mean follow-up of 3 years. Mean Oswestry index improved from 76 % preoperatively to 30 % at 1 year. Bone fusion evaluated on standard and dynamic radiographs was observed in 96 % of patients ($n = 50/52$). Two complications were recorded in the series: one infection and one hardware breakage necessitating revision surgery.

43.4.7 STABILIMAX® (Table 43.6)

The device is FDA approved since 2007. During normal spine kinematics, the neutral zone (NZ) is a region of intervertebral motion around the neutral posture where little resistance is offered by the passive spinal column. This NZ is increased at the early phase of the disk degeneration process resulting in instability, excessive motion, and mechanical pain. The STABILIMAX® uses a rod with concentric springs to maintain the spinal segment in a neutral position during spinal motion.

Summary of Biomechanical Investigations [98]

- In vitro study: 1; FEA: 0
- Reduction of the NZ by increasing resistance of the passive spinal system around the NZ while preserving maximal ROM
- No precise data available concerning effects on NZ and ROM

Clinical trials are planned under an investigational device exemption from the US Food and Drug Administration.

43.4.8 BIOFLEX® (Table 43.5)

The BIOFLEX® system is a pedicle screw-based system COMBINING a Nitinol rod shaped with one or two loops confering stability in flexion, extension, and lateral bending. Nitinol is an alloy of nickel and titanium, commonly referred to as "memory metal" for its ability to return back to its original shape after deformation.

Summary of Biomechanical Investigations

- In vitro study: 0; FEA: 0
- No data available

Kim et al. reported outcomes on 103 patients who underwent implantation of the BIOFLEX® device [99]. Patients were divided into two groups: dynamic stabilization without fusion ($n = 46$) and dynamic fusion in which the dynamic device was combined with an interbody cage and graft ($n = 57$). In the dynamic stabilization group, mean VAS score decreased from 7.3 preoperatively to 1.4 postoperatively, ODI from 35 % to 12 %, and ROM from 4 to 10°, respectively. In the dynamic fusion group, mean VAS score decreased from 7.4 preoperatively to 2.1 postoperatively and ODI from 38 to 14 %, and the fusion rates of segments treated by BIOFLEX® and PLIF were approximately 90 %. Complications observed in the two groups were one cage retropulsion, presence of a halo in three cases, one screw breakage, unstable levels in eight cases, and one screw loosening. The authors concluded that the BIOFLEX® device was safe and efficient and could serve as a dynamic stabilization device and as an adjunct for dynamic fusion.

43.4.9 DSS® and DSS® HPS (Table 43.5)

The DSS® hybrid performance system (HPS) is designed to combine rigid spinal fixation with a topping-off option including the DSS® coupler. The system was developed in collaboration with the Biomechanical Laboratory of Ulm University (Germany). The system allows for mono- and multilevel constructs. It has been implanted in several thousand of cases all over the world with good outcomes.

43.4.10 EXPEDIUM® PEEK Rod (Table 43.4)

The EXPEDIUM® PEEK rod more closely mimics the material characteristics of cancellous or cortical bone with a lower modulus of elasticity compared to titanium. It therefore allows for load sharing between the posterior elements and the interbody bone graft. In addition, PEEK rod is associated with imaging compatibility with reduction of artifacts and better visualization of fusion mass.

Summary of Biomechanical Investigations

- In vitro study: 0; FEA: 2
- Reduction of ROM: flexion motion the most limited and axial rotation the least limited

Conclusion

To conclude this chapter, we would like to underline the point that pedicle screw-based posterior dynamic systems could serve as *fusion technology* and also as *non-fusion technology*.

Historically, pedicle screw-based posterior dynamic systems (PDS) were initially designed to improve interbody fusion success in combination with an interbody bone graft; however, these technologies are most often used as non-fusion devices (dynamic stabilization) resulting in confusion through the literature.

Dynamic fusion using semirigid devices to improve rates of interbody fusion success is now well documented through fundamental investigations; however, further clinical prospective studies are now needed to confirm the efficacy of PDS devices in enhancing spinal fusion and especially determine the advantages of dynamic instrumentation in terms of fusion period, fusion rates, and fusion quality.

Pedicle screw-based PDS devices have also been progressively introduced to serve as *dynamic stabilization* devices. In this last setting, they intend to address the adverse effects of traditional spinal fusion, especially to minimize the incidence of adjacent segment degeneration by restoring some native motion at the instrumented level. Biomechanical investigations have widely demonstrated that such devices could control intervertebral motion without instability while unloading the intervertebral disk. These systems can therefore be considered as an alternative to fusion to treat degenerative disk disease.

Early clinical results suggest that results are as good as those reported using rigid instrumentation. In fact, *no clear significant differences were identified between traditional spinal fusion and dynamic stabilization regarding VAS, functional scales, and postoperative complications. Therefore, no clinical data from comparative studies really support the use of dynamic stabilization over standard spinal fusion*.

Otherwise, further long-term follow-up studies comparing dynamic versus rigid stabilization are required to determine the efficacy of PDS on adjacent segment disease.

Finally, the question of implant longevity in the setting of continued intervertebral motion is still controversial, and it might be possible that posterior dynamic stabilization systems could serve to delay the need of spinal fusion but not avoid its requirement at long term.

Until now, no dynamic stabilization devices received FDA approval for use other than as an adjunct to spinal fusion. The FDA specified that separate approval would be required for "off-label" marketing of these devices, including but not limited to use as stand-alone device (spinal stabilization in the absence of fusion).

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A Word from the Inventor of Intervertebral Dynamic Fixation: On Interspinous Devices

44

Jacques Sénégas

44.1 Introduction

The idea of developing a system of dynamic lumbar fixation came to me in the early 1980s. At that time, the only thing everyone talked about was fusion and pedicle screw systems represented the ultimate technique. I began working in the cadaver laboratory testing various constructs in 1982 with R. Bréard, whose company SEM (Science et Médecine) primarily developed hip prostheses. His engineer, J. Frismand, suggested that I should begin with a system adapted to pedicle screws, which they were starting to manufacture. After several in vitro biomechanical tests, it became apparent to me that the constraints of a dynamic system would go beyond the long-term capacities of pedicle screw fixation, at least at that period of its development, and that the risks of screw loosening were too high. Consequently, I proposed the alternative of a "floating" interspinous device without intraosseous fixation. The first patient was operated in 1986, and the patent was obtained in 1987 by Bréard. The intent was to find an alternative to lumbar arthrodesis, which appeared to accelerate degenerative changes at adjacent levels. This initial device consisted of one metal interspinous spacer to which was attached a long polyester cord. The cord was passed around one of the spinous processes limiting that interspinous space, back through a tunnel in the spacer, around the other spinous process, and back through a second tunnel in the spacer where it was prevented from backing out by a Morse taper. This interspinous spacer was made of metal to avoid being split by the Morse taper. The metal spacer could be completed at up to four other interspinous levels with plastic spacers, each containing two tunnels for passage of the cord (the same attached to the primary spacer) in opposing directions. After passage around the spinous processes and through the various spacers, the extremity of the cord was blocked in the steel spacer by the Morse taper [1, 2]. The device was intended to restore, in degenerate intervertebral segments, the high-flexibility zone flexion-extension stiffness, which is diminished in symptomatic degenerative disk disease and worsened by posterior decompressive surgery [3, 4].

My spine team colleagues agreed with me to test the concept. Previously, in many patients with unstable degenerative lumbar disorders that

In this chapter, Professor Sénégas provides a unique perspective regarding a field of spine surgery that he pioneered. His account in conversation form, is unique from both a historical and clinical perspective.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_44

called for decompressive surgery, we performed an arthrodesis when we believed their preoperative instability had contributed to low back pain resistant to conservative treatment for several months. These degenerative disorders requiring decompression included lumbar canal stenosis at one or, more often, more than one level and certain types of disk herniation (recurrent herniated disks, herniated disk of L4–L5 when there was sacralization of L5, and unusually massive herniated disks). These were the criteria of selection of indications for this first study. In patients fulfilling these conditions who gave enlightened consent, we would complete decompressive procedures with interspinous stabilization instead of arthrodesis. The patients were informed that, if their low back pain remained unresolved, they could have the arthrodesis that they initially chose not to undergo. We cautiously proceeded in this manner without commercialization of the device, waiting to judge the results over time.

The trial was very successful for these indications. Actuarial survivorship analysis of the patients operated between 1987 and 1995 demonstrated that only 17 % needed either replacement of the device by arthrodesis or any other lumbar surgical procedure within the first 10 years of the operation with a 95 % confidence interval of plus or minus 6 % [5]. We believed that interspinous dynamic stabilization does indeed delay adjacent segment syndrome given that, even when lumbar osteosynthesis is correctly performed and achieves fusion, additional surgery at adjacent levels has been reported in 36 % of patients within the first 10 years with a confidence interval of plus or minus 10 % [6]. Furthermore, our patients who were not reoperated had quality-of-life scores that were almost the same as those of the age- and sex-matched general population, while the patients in whom arthrodesis was later performed had poorer quality-of-life scores [7]. These differences with the general age-matched quality-of-life scores were similar to those reported elsewhere in a similar group of patients 10 years after osteosynthesis [8].

Positive clinical feedback from this cohort led to the development and widespread diffusion in 2002 (20 years after the first version) of the Wallis system, an improved version of the initial device [9] (Figs. 44.1 and 44.2). We later devel-

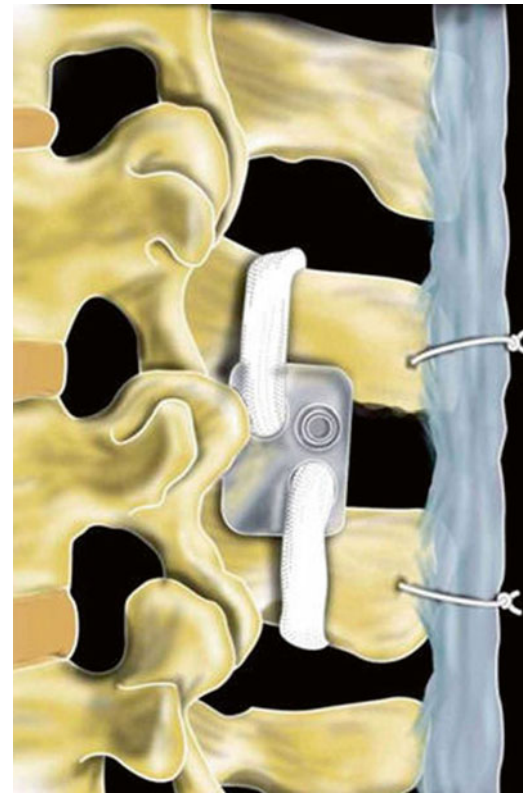

Fig. 44.1 First-generation Wallis device

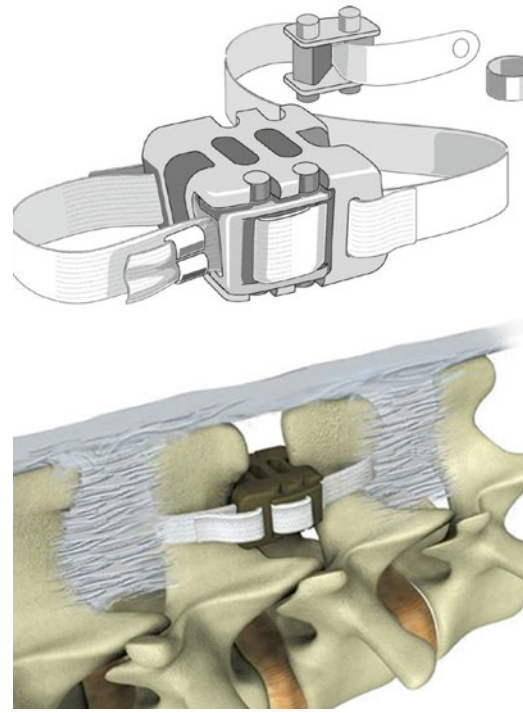

Fig. 44.2 Wallis implant

Fig. 44.3 UniWallis implant

Table 44.1 Interspinous dynamic stabilization is indicated for degenerative lesions with potential or reducible instability (less than 2 mm on dynamic films)

1.	After disk surgery, especially massive disk herniation, transitional L4–L5 disk if sacralization of L5 is present, and recurrent herniated disk
2.	Chronic low back pain with degenerated disk and/or facet joint arthritis, or Modic I changes refractory to conservative treatment
3.	After decompressive laminotomy for central stenosis
4.	For dynamic foraminal stenosis with retrolisthesis on dynamic X-rays due to posterior disk collapse
5.	Stabilization of one or two symptomatic apical levels in lumbar degenerative scoliosis in elderly patients (alternative to deformity corrections with extensive fusion constructs)
6.	Instability adjacent to a prior lumbar fusion
7.	"Topping off" for a degenerated adjacent segment above lumbar fusion or total disk replacement

Table 44.2 Contraindications for interspinous dynamic stabilization include

1.	Spondylolisthesis of any grade and nonreducible retrolisthesis
2.	Spinal deformities of children and young adults
3.	Psychological, social, and professional issues

oped a third generation of the Wallis system (UniWallis) in 2008 to permit unilateral insertion and simplify placement, tightening, and locking of the tension band (Fig. 44.3).

Our indications for our system have evolved over the years. The current principal indications and contraindications of the Wallis and UniWallis devices are summarized in Tables 44.1 and 44.2.

At the same time as our second-generation interspinous dynamic stabilization implant was being launched, the interspinous implant X-Stop was developed *for an entirely different reason*, *to distract the interspinous space in order to relieve neurogenic claudication without using laminectomy or laminotomy in patients with lumbar canal stenosis* [10, 11].

The interspinous dynamic stabilization devices we developed were followed by other interspinous devices that were also intended for dynamic stabilization, not distraction. Among the first of these were the Interspinous U (which later became the Coflex) [12] and the DIAM [13], but many others have appeared over the years: LimiFlex [3], In-Space [14], Ligament Vertebral de Renfort [15, 16], BacJak and Viking [17], Dallos [18], InSWing [19, 20], and Locker [21, 22]. Likewise, there was a proliferation of devices intended for interspinous distraction rather than dynamic stabilization that were marketed after the appearance of X-Stop: Aperius [23, 24], an unnamed device from Kinoshita Giken Corporation, Japan [25], In-Space [26, 27], Superion [28, 29], SMID [30, 31], and ExtenSure [32]. This fundamental difference in indications (dynamic stabilization vs. distraction) is not always perceived by authors reporting on interspinous devices in the literature [32–39]. Moreover, devices like In-Space are used for dynamic stabilization by some authors [14], for distraction by some [26], and for both by others [40]. One study even compared the clinical efficacy of distraction alone for canal stenosis with Wallis, Coflex, and X-Stop, with no associated surgical decompression: as would be expected, VAS pain score improvements were poor for all

three devices used in this indication [41]. Although the distraction principle improves symptoms of lumbar canal stenosis more than conservative treatment [26, 42], distraction is well documented to be less effective than surgical decompression [23, 27, 37, 43–48], except in one meta-analysis, which was based upon indirect comparison of these techniques [49]. Furthermore, other disadvantages have been reported in patients treated for canal stenosis with interspinous distraction instead of surgical decompression [50–53]. Reviewers who believe that all interspinous devices are used for distraction have concluded that "interspinous technology" is unproven and unreliable or that the risks outweigh the benefits [54, 55]. Tamburrelli et al. put it well, concluding that "as generally occurs with any new technique, the early contagious enthusiasm—resulting in an excessive and sometimes incorrect use of the device—has resulted in a rising number of failures and in a critical consideration about the indications and the true advantages of the technique [17]." This situation is further complicated by reviewers who consider that the only posterior dynamic stabilization systems are pedicle screw-based devices, appearing to ignore entirely the existence of interspinous dynamic stabilization [56, 57].

Keeping in mind this confusion of interspinous dynamic stabilization with interspinous distraction, a review of available evidence on interspinous implants intended solely for dynamic stabilization indications is very enlightening, albeit still a complex undertaking. First, the biomechanical experimentation varies with the different conceptions of how dynamic stabilization should function. As for clinical results, there are also a variety of hypotheses and explanations for the therapeutic action of the devices and generally good patient outcomes. Lastly, among the available interspinous dynamic stabilization devices, there are fundamental differences that further complicate the picture, primarily whether or not there is a flexion-limiting tension band system coupled with an extension-limiting spacer, which move loads away from painful areas of the lumbar motion segment in flexion and in extension, respectively [58]. Over the past few years, there has been an explosion of evidence in the literature on interspinous dynamic stabilization, particularly from Asia. This chapter represents, to the best of my knowledge, an exhaustive review of all peer-reviewed articles pertaining to interspinous dynamic stabilization that have appeared over the last 5 years.

44.2 Results of In Vitro Biomechanical Investigations

- *Stabilization in terms of reduced range of motion and increased stiffness*,
- *Unloading of the disk*

The available sizes of interspinous spacers correspond to measurements of the interspinous spaces published in two studies [59, 60]. These studies suggest that the spacers should be placed anteriorly in the interspinous space, where the cortex is thicker and the interspinous process distance is greatest [60]. An in vivo radiographic study found smaller interspinous spaces, suggesting that bone trimming is typically necessary to avoid creating undesired kyphotic changes in segments treated by interspinous dynamic stabilization [61], confirming our own experience.

Maintaining segmental lordosis is capital and merits a short digression regarding several important operative and postoperative aspects: first, in order to select a spacer size that will not induce kyphosis, the patient must be operated in the prone position, not in the genu pectoral position. To insert the Wallis or the UniWallis when the patient is in the prone position, one may use a distractor. If the device fits tightly when the patient is in the genu pectoral position, the bands will loosen whenever the patient is upright. This will certainly not contribute to restoring segmental stiffness! The spacer should be pushed in against friction, but not be large enough to induce kyphosis. It is also important to use a spacer that is not too small. If it is too small, there is a risk of excessive movement that might scratch the spinous processes. Another operative point concerns the supraspinous ligament, the distal end of

which is L4 in the majority of subjects. I always thought it important to disinsert the fascia of the paraspinal muscles from the spinous processes after the initial incision, then, at the end of the Wallis implant procedure, to reattach them with a suture through a small hole at the tip of the spinous process. It is also important to insist that the patient must wear a lumbar corset for 1 month following the operation to optimize development of scar tissue around the implant. Finally, just as one should do in selecting patients for fusion, surgeons should take into account psychological, social, or workers compensation-related issues when deciding which patients would best benefit from dynamic stabilization (end of digression).

In interspinous dynamic stabilization implants that do not have flexion-limiting bands, there is conflicting biomechanical evidence. In one study with axial preloading applied to cadaver specimens of the lumbar spine, Coflex, In-Space, and Aperius reduced range of motion (ROM) of the implanted segment in both extension and flexion even though the supraspinous ligament was removed for placement of the Coflex [62]. In a similar study with preloading, In-Space reduced ROM in extension, but not in flexion, lateral bending, or axial rotation; reduced disk pressure of the operated segment, with little effects on ROM or disk pressure in the adjacent segments [63]; and unloaded the facet joints when loaded in extension [64]. In contrast, cadaver studies of spacers alone (without tension bands) without axial preloading show significant limitation of ROM in extension, but not in flexion, as well as no influence on axial rotation or lateral bending [65–67]. This would apply less if the stabilization devices could be implanted without injury to the thoracolumbar fascia, fascia of the longissimus thoracis muscles, or fascia of the multifidus muscles, although avoiding these injuries is difficult when decompressing the lumbar canal [68]. Regarding the segments adjacent to implantation by a spacer alone, Hartmann et al. reported that flexion-extension ROM above and below was increased in most of their cadaver specimens with and without a follower load of 400 N [69]. Mao et al. reported increased ROM only in extension at L2–L3 with a Coflex at L3–L4, which limited flexion-extension ROM there with little effect on axial rotation or lateral bending, adjacent to L4–L5 with rigid pedicle screw fixation [70]. An in vivo radiographic study has reported that limitation of flexion by the Coflex device is possible in case of bone overgrowth into the device, but generally not expected [71]. Coflex can be used to strongly limit flexion, but the solution calls for rivets through the spinous processes, with high risk of spinous process fracture especially in L5 and in patients with poor bone quality [72].

In an ovine model, Gunzburg et al. showed that an interspinous spacer reduced total segmental ROM in flexion-extension by only 17 % and that the combination of a spacer plus a tension band around the spinous processes reduced the ROM by 46 % [19]. Contrary to some interspinous dynamic stabilization devices, all three generations of our interspinous stabilization devices have a strong cord or band that limits flexion. A recent cadaver study with application of compressive preloads mimicking the stabilizing action of axial musculature demonstrated that anatomical alterations corresponding to degenerative and iatrogenic lesions result in decreased segmental stiffness. This loss of stiffness was less amenable to compensation by axial muscular activity in flexion than in extension, suggesting to the authors the potential usefulness of surgical implants that specifically increase flexion stiffness and limit flexion ROM to counteract the iatrogenic instability resulting from surgical decompression [4]. Without preloading, other cadaver studies have shown that the Wallis system restored ROM to that of the intact specimen in both flexion and extension, while Coflex and DIAM restored ROM only in extension, but not in flexion; all three systems reduced lateral bending by 10 % and axial rotation by 20 % [66, 67]. In a randomized trial of patients operated at L4–L5 for herniated disks or canal stenosis by either PLIF or Wallis dynamic stabilization, Li et al. measured the stiffness of degenerated L4–L5 segment. L4–L5 stiffness before decompression was 37 Nm; after decompression, it fell to 26 Nm, and after Wallis stabilization, it was restored to 46 Nm. The stiffness of the intact overlying

adjacent segment (L3–L4) was significantly higher above the Wallis than above the pedicle screw-augmented PLIF (46 Nm vs. 35 Nm; $p<0.05$), confirming their own experimental cadaver studies [73, 74]. Other cadaver studies of the second-generation Wallis have shown a 14 % reduction in flexion-extension ROM of the stabilized L3–L4 segment, with small increases in ROM at the uninstrumented L2–L3 and L4–L5 segments of 7 % and 3.5 %, respectively, and little influence on lateral bending and axial rotation [75]. Similar biomechanical results in cadavers have been found with another device that has a spacer and a tension band, which device also was shown to reduce pressures in the posterior annulus and central nucleus [22]. Comparing Wallis to a pedicle screw-based dynamic stabilization system, Schulte et al. reported that the Wallis implant reduced extension by 69 % and flexion by 62 %, with almost no action on lateral bending or axial rotation [76].

A study of distance between spinous processes showed that the variations in interspinous process distance (ISPD) are greater in patients with degenerative disk disease than in healthy subjects, demonstrating the risk of implant dislocation for interspinous devices that do not limit ISPD during flexion [77]. Indeed, among dynamic stabilization devices that do not strongly limit flexion, dislocation has been reported for Coflex in several studies [12, 78–80]. In this respect, the DIAM device appears to be an exception. Even though cadaver studies show that it fails to limit flexion [66, 67], the tethering laces probably explain the lack of reported postoperative dislocations [81]. Next to the Wallis system, other interspinous stabilization devices with strong flexion-limiting bands have been developed to restore segmental stiffness more consistently, including the Ligament Vertebral de Renfort [16], Dallos [18], InSWing [20], and Locker [21]. In a porcine study, the supraspinous ligament (SSL) and the laces of DIAM were both observed to have a mechanical role, leading the authors to recommend preservation of the SSL and use of the laces, which also were thought to prevent postoperative dislocation [82]. The LimiFlex device has flexion-limiting bands, but not an interspinous spacer [3].

44.3 Review of Clinical and Radiological Findings

In contrast to the poor efficacy associated with interspinous distraction (see above), over the last 5 years, 29 clinical studies of interspinous devices used for dynamic stabilization have reported improved clinical status and persistence of the improvement regardless of the device: Wallis [83–92], Coflex [78, 80, 86, 89, 90, 93–101], DIAM [102–107], In-Space [14, 108], Ligament Vertebral de Renfort [15, 109], or Dallos [18].

Using interspinous dynamic stabilization devices to decompress nerve roots and to off-load disks and facet joints, many authors report radiological data that shows increased foraminal dimensions, disk height, or both [14, 91, 92, 99, 101, 110, 111], with the exception of DIAM, which has a spacer made of silicone [103]. Even though these mechanisms of action undoubtedly contribute to the efficacy of dynamic stabilization devices [112], we developed the Wallis line of implants primarily to relieve chronic low back pain associated with loss of intersegmental stiffness. Other authors agree that the clinical action of interspinous dynamic stabilization devices is theoretically due to unloading of the facet joints, restoration of foraminal height, and/or increased intervertebral stability [108, 113–116]. As stated above, experimental in vivo proof in patients demonstrates that the Wallis device does indeed restore physiological stiffness of the treated segment without adversely affecting the stiffness of the adjacent segments [73]. However, because direct measurement of stiffness in patients is impractical, to measure stabilization authors report instead radiological flexion-extension ROM restrictions achieved and maintained by dynamic stabilization devices compared to the preoperative ROM. The overall flexion-extension ROM, which is increased by intervertebral degenerative disease and further increased by decompressive procedures, is consistently improved by the placement of an interspinous spacer, even if the spacer has no flexion-limiting attachments. When the implant has nothing that limits flexion, postoperative adherences between the spinous processes and the medial fascia of the paraspinal muscles may limit flexion of the

implanted segment after several weeks. In any case, because spacers do reduce extension, this automatically reduces overall flexion-extension ROM. Most authors who have compared preoperative to follow-up flexion-extension ROM in their patients have reported improved (reduced) ROM of the treated segments at follow-up [18, 84, 95, 97, 99, 104, 107, 113]. Others have reported almost no change between preoperative ROM and ROM at final follow-up [95, 96, 110]. Sun et al. reported more restriction of flexion-extension ROM achieved with Wallis (10°) with its flexion-limiting band than with Coflex (13°) ($p=0.019$) [90], and Chao et al. showed that the ROM in extension decreased, but that the ROM in flexion increased in lumbar segments implanted with Coflex [95].

The ROM of the intervertebral segments adjacent to the treated segments is equally important. Above a fused lumbar segment, ROM of the adjacent segment increases, which is thought to accelerate adjacent segment disease [113]. We developed dynamic stabilization devices that would stiffen the treated segment without completely eliminating flexion and extension there in order to preserve physiological functioning in the adjacent segments. Ideally, the flexion-extension ROM in adjacent, healthy segments should not be affected by placement of an interspinous dynamic stabilizer. All authors who have measured adjacent segment ROM report no undesired increase in that ROM during follow-up of the interspinous dynamic stabilization devices that they use [84, 95, 99, 111, 113]. In a study of 60 patients who underwent decompression of L4/L5 for degenerative canal stenosis, Liu et al. reported that the follow-up ROM of L3/L4 was increased and the disk height of L3/L4 was decreased significantly more in the 31 patients who had 360° fusion of L4/L5 compared to the 29 patients stabilized at L4/L5 by an interspinous dynamic stabilization device ($p<0.05$), leading those authors to conclude that dynamic stabilization would delay degeneration of L3/L4 [97].

In one study, Kaplan-Meier analysis of survival from failure showed that decompression by laminotomy and flavectomy stabilized by fusion was 76 % at 5 years, with all failures caused by additional surgery for adjacent level syndrome. In that study, among the patients who had the same operation without fusion, 5-year survival from failure was 92 %, with both failures at the index level [43]. In patients who had lumbar decompressive surgery, Hong et al. compared 18 patients who had no stabilization to 23 who had dynamic interspinous stabilization, resorting to revision by fusion for symptomatic instability in 1 of the 23 patients (4 %) in the stabilized group and in 5 of the 18 patients (28 %) in the unstabilized group [109]. In a matched retrospective comparative study, Liu et al. reported that, compared with isolated PLIF of L5–S1, PLIF at L5–S1 combined with Wallis or Coflex dynamic stabilization at L4–L5 restricts the ROM of L4–L5 in extension and prevents excessive olisthesis of L4 in both extension and flexion. Based upon these findings and convincing MRI evidence of differences in L4–L5 disk degeneration and Modic changes, they concluded that follow-up of their patients longer than 24 months would potentially show that interspinous dynamic stabilization reduces degenerative changes adjacent to fusion [113, 117]. Even the DIAM device, which limits flexion and extension less than the Wallis system [66, 67], has been reported to slow the development of radiological adjacent segment degeneration above a PLIF ($p=0.03$), although no significant difference in additional surgery at the segment rostral to PLIF was observed in that cohort [81]. In a randomized controlled study of Wallis dynamic stabilization above lumbar osteosynthesis procedures, Korovessis et al. have provided the best evidence that these devices can delay symptomatic adjacent segment disease: the ROM in flexion and extension of the adjacent segments protected by a Wallis implant remained stable after the operation, while there was progressive significant increase ($p<0.02$) in the adjacent segment ROM of the control patients who had no protection above the fusion; this was associated with better ODI scores in the Wallis group ($p<0.05$) and more adjacent segment revision operations in the control group (14 % vs. none) [85].

In a study of patients who underwent revision surgery for degenerative disease of the segment

adjacent to prior fusion, Cho et al. recommended treatment by decompression and an interspinous dynamic stabilization device instead of extending fusion, because clinical results were equally good and dynamic stabilization preserves posterior complex integrity [118].

As we have recommended for our system, authors using other systems also preserve the supraspinous ligament [14, 78, 79], which contributes to segmental stability [119, 120], sends proprioceptive information to the paraspinal musculature [121, 122], and prevents increased ROM in flexion and extension in the adjacent segments [123].

Some authors have reported less favorable results for interspinous dynamic stabilization devices or results not superior to control groups. In each of these reports, the less favorable results can be attributed to either use of the devices in controversial indications or insufficient length of follow-up. Because dynamic stabilization devices are intended to relieve instability-related pain, many months may be necessary before differences in low back pain appear between decompressed patients with and without stabilization. In a study with 24 months of follow-up, no difference was found in clinical outcome, which was good, between patients with or without Coflex stabilization after decompression of canal stenosis (with spondylolisthesis in half of the patients) [115]. In an as yet unpublished randomized controlled trial presented by Mahir and Marsh at the British Orthopaedic Association 2012 Annual Congress in 2012, both groups (30 patients treated by decompression alone compared to 30 patients treated by decompression and Wallis dynamic stabilization), postoperative clinical results were good, practically identical and stable in the two groups at 1 year and 2 years, but the unstabilized group worsened after 3 years while the same good results persisted in the group stabilized by Wallis [124]. Clinical results regarding symptomatic adjacent segment disease are also time dependent, more than 2 years of follow-up being necessary to demonstrate superiority of interspinous dynamic stabilization over arthrodesis in terms of revision surgery for adjacent-level syndrome [5, 6].

In two examples of less favorable results involving controversial indications, Mayer et al. reported revision surgery within 34 months in 8 of 32 patients in whom they used In-Space for arthrogenic low back pain [40], and, using the Coflex device for distraction in 20 patients who also had isolated facet joint pain, Cabraja et al. reported reduction of 50 % in VAS pain score in only 7 patients (35 %) after 2 years [125]. This suggests that unloading the facet joints with an interspinous spacer for isolated facet joint pain may be a poor indication. These poor results might be attributable, however, to the use of too much distraction of the treated segments (L4–L5), with a radiographically demonstrated loss of lordosis there, ($p<0.001$) and increased lordosis at L3–L4 ($p<0.032$). These changes induced in the sagittal profile may have contributed to further facet joint degeneration possibly explaining why the clinical outcome of these patients was better at 1-year follow-up than at final follow-up [125].

In patients with grade I degenerative spondylolisthesis, which, in my opinion, is certainly a contraindication, interspinous dynamic stabilization devices have failed to prevent further slippage [16, 21, 126] and, in one study, good clinical results were achieved in only two thirds of the patients [16]. A 6-year study of 23 patients stabilized with an interspinous dynamic device for grade I degenerative spondylolisthesis compared to 22 patients treated for the same indication with pedicle screw-augmented PLIF provides even more convincing confirmation that interspinous dynamic stabilization should not be used for spondylolisthesis [127].

44.4 Complications of Interspinous Dynamic Stabilization Devices

The reported complication rates are generally lower in interspinous dynamic stabilization studies than in reports on patients with degenerative disease treated by fusion. In 131 patients treated with Coflex, Xu et al. reported only three implant-related complications (loosening, wing breakage,

and spinous process fracture), along with five other complications requiring additional surgery (recurrent disk herniation at the treated level in two, a residual herniated disk in one, spinal canal hematoma in a patient taking anticoagulants, and incomplete decompression in one) [78]. Zang et al. reported a total of only 13 complications among 133 patients [79]. Nachakian et al. reported one revision procedure (for recurrence of neurologic symptoms) among 134 patients [98]. In a single-unit study of complications in 168 patients who had either Wallis or Coflex dynamic stabilization, the overall complication rate was 10.7 % (18/168), 6.2 % (8/130) in the Wallis group and 26.3 % (10/38) in the Coflex group ($p<0.01$) [128]. Xu et al. reported that none of their 96 patients had complications related to Wallis dynamic stabilization [91]. In 48 Wallis patients, Liu et al. observed no intraoperative complications [87]. Other studies have also recorded no implant-related complications with Wallis ($n=0/20$) [84], ($n=0/15$) [88], ($n=0/25$) [85], Coflex ($n=0/20$) [94], ($n=0/29$) [97], ($n=0/21$) [96], DIAM ($n=0/8$) [107],($n=0/16$) [106] ($n=0/68$) [105], and Locker ($n=0/23$) [21].

Among complications of interspinous stabilization devices, unresolved low back pain is not a serious issue, because these systems spare vertebral anatomy; they do not preclude or significantly complicate later treatment with a more definitive procedure (i.e., fusion). Some reports of interspinous dynamic stabilization include a few cases of straightforward removal and replacement by fusion [78, 79, 81, 98, 100]. The complication that naturally occurs at the index level more often after any kind of dynamic stabilization than after fusion is disk herniation, because dynamic stabilization preserves disk function, posterolateral fusion reduces disk function, and lumbar interbody fusion eliminates the disk. As shown by Floman et al. the frequency of recurrent disk depends upon the diskectomy procedure more than upon the dynamic stabilization technique [83]. After a Wallis procedure, Liu et al. reported a recurrent disk in 6 of 48 patients, 3 of whom were treated conservatively and 3 simply by removal and fusion [87]. In a study comparing Wallis in 25 patients to Coflex in 27 patients, Sun et al. reported 4 recurrent disks in the Coflex patients and none with Wallis [90]. In another series of 68 patients treated by interspinous dynamic stabilization, Li et al. reported 2 cases of recurrent disk [129]. Hrabálek et al. reported no recurrent disks among 68 patients [105].

The rate of intraoperative and postoperative spinous process fractures complicating interspinous dynamic stabilization devices is quite low in my experience with the technique, but I always used small spacer sizes to avoid distraction and preserve segmental lordosis. This contrasts with the high incidence of spinous process fractures when interspinous spacers are used for distraction to treat canal stenosis without undercutting [24, 44, 55], because larger spacers are used to obtain segmental kyphosis instead of preserving segmental lordosis as we recommend in dynamic stabilization to avoid facet joint pain. A report by Fabrizi et al. illustrates the indication-dependent aspect of this complication of interspinous devices. Among 1315 patients in whom they used an interspinous device for dynamic stabilization after decompression, they observed 7 spinous process fractures (0.5 %), whereas among 260 patients in whom the same surgeons used an interspinous device for distraction in elderly patients to avoid surgical decompression and general anesthesia, they reported 3 spinous process fractures (1.2 %) [102]. The interspinous spacers and soft polyester bands of our system may be less aggressive to the spinous process than metallic interspinous dynamic stabilization systems. Spinous process fractures have been reported with the use of Coflex [78, 79, 100, 115]. In a series of 133 patients who had Coflex dynamic stabilization, 3 had an intraoperative spinous process fracture and 2 had postoperative spinous process fracture [80]. However, in a study by Sun et al. of interspinous dynamic stabilization complications in 168 patients with either Wallis or Coflex, no spinous process fracture was reported [128]. Using a soft interspinous spacer in 65 patients, Lee et al. reported that none of the patients had a spinous process fracture [16]. In vivo radiographic analysis in 176 patients shows that the average loads exerted by an interspinous dynamic stabilization spacer on the spinous pro-

cess and lamina are estimated to be only 11 % and 7 % of their respective static failure load, which would help explain the observed low rates of postoperative fractures [71].

There have been reports of heterotopic ossification leading to fusion between the spinous processes in patients with the Coflex system [130]. After a fortuitous discovery of interspinous fusion around a Coflex device in one patient [131], Tian et al. found this complication in 81 % of their Coflex patients [132]. To the best of my knowledge, this complication has not been reported in other interspinous devices used for dynamic stabilization. Compared to other interspinous stabilization devices, one difference Coflex has is the presence of retaining teeth on the metal wings that are squeezed against the spinous processes. This may result in freshening of the lateral aspects of the spinous processes with bleeding that might mediate the observed heterotopic ossification. Tian et al. hypothesized that the resulting consistent stress at the interface between the bone and implant might stimulate growth of heterotopic bone [132].

There have been reports of osteolysis with interspinous devices [133]. Park et al. reported radiolucent gaps between the Coflex implant and the spinous processes in 17 of 30 patients (57 %), the gaps being most prominent around the spikes on the spacer [126]. In our experience with the first-generation interspinous stabilization device, some osteolysis was observed at long-term, systematic follow-up in some patients. Further investigation with CT scans revealed remodeling of the spinous process in contact with spacers or polyester cords. The cortical bone was preserved, but took on the shape of the cord or the spacers, suggesting a slow process of bone remodeling in response to surface stress. Because the distance between interspinous processes diminishes with age [134], the observed remodeling might be due to spinous processes growing around the spacer and cords rather than spacers and cords cutting into the spinous processes. In any event, our discovery of this remodeling process was rare and fortuitous in asymptomatic patients. When the process occurs, it appears to be self-limiting, because no patients have presented with spinous process fractures associated with these macroscopic features.

In the largest series of interspinous dynamic stabilization (1315 patients in whom the 1832 devices were made with polyester), deep infection was observed in only 10 patients (0.8 % of patients; 0.5 % of devices) [102]. Another group using the same implant in 22 patients reported deep infection in 1 (4.5 %) [104]. Using another polyester interspinous stabilization device, Hong et al. reported 1 infection among 23 patients [109]. In 68 patients treated with the latter polyester device, Hrabálek et al. reported no wound seroma or deep infection [105].

Among rare complications of interspinous dynamic stabilization devices are blockage of drainage of an epidural hematoma by the implant with resulting cauda equina syndrome [135], an inflammatory reaction to a polyester device [16], a foreign-body reaction to a polyester and silicone device [17, 136], irritation and fluid around a spacer made of PEEK and titanium [40], and bilateral stress fracture of the inferior spinous process [137].

Conclusions

In vivo proof has been published showing that an interspinous spacer *combined with tension bands around the spinous processes* actually does restore physiological stiffness of the treated degenerative segment, even after decompressive procedures that further reduce segmental stiffness more than the degenerative process itself. In segments adjacent to interspinous dynamic stabilization, stiffness is not lost and ROM is not increased, contrary to what is observed in segments adjacent to fused lumbar levels.

The rate of implant-related complications is much lower with interspinous dynamic stabilization than with intervertebral fusion procedures. Fewer implant-related complications are reported regarding implants that have an interspinous spacer combined with tension bands than in those that have an interspinous spacer without tension bands. Interspinous dynamic stabilization preserves patient anatomy, facilitating more invasive surgical alternatives if chronic low back pain is not resolved.

In patients with chronic low back pain related to degenerative instability who undergo diskectomy or decompression for canal stenosis, there is very strong published evidence that

outcome is better in patients who have interspinous dynamic stabilization than in those who are not stabilized. There is strong evidence that, in these two indications, patients who have interspinous dynamic stabilization have lower rates of revision surgery in general and lower rates of revision for adjacent level disease in particular than patients stabilized by arthrodesis. In patients who undergo lumbar or lumbosacral fusion for degenerative conditions such as spondylolisthesis, there is also strong evidence showing that fewer revision surgeries are necessary for symptomatic adjacent-level disease if an overlying degenerate adjacent segment is stabilized with an interspinous implant than if no stabilization is used. Among patients who have symptomatic adjacent segment disease, those treated by interspinous dynamic stabilization have better outcome than those treated by extension of fusion.

Provided that interspinous dynamic stabilization devices are not used for distraction, i.e., provided that lordosis of the treated segments is preserved, that these devices are not used for spondylolisthesis, and that they are not used to prevent recurrence of disk herniation, no one has observed poor results with this technique. On the contrary, all 29 of the clinical studies regarding interspinous dynamic stabilization for appropriate indications published over the last 5 years have demonstrated good clinical results.

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Interspinous Process Fixation for Motion Preservation

45

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45.1 Introduction

Neurogenic claudication from lumbar stenosis was first reported by Verbiest in 1954 [1]. It is a debilitating condition that affects 1.7–8 % of the US population and is particularly common in the elderly. Patients often find relief in flexion and exacerbation of symptoms in extension. Causes range from hypertrophy of the facet complexes or ligamentum flavum, disk herniation, and spondylolisthesis [2–4].

When 3–6 months of conservative therapy fails, operative intervention is typically indicated. The "gold standard" treatment for lumbar stenosis includes laminectomy, removal of hypertrophied ligament, and partial facetectomy, with or without diskectomy [5]. Fusions are commonly indicated in those patients with concomitant translational instability, coronal plane deformity, or need to remove a significant amount of the joint in order to achieve adequate neurologic decompression. Minimally invasive options for lumbar decompression are also available with the use of tubular intramuscular dilators [6].

Interspinous devices (ID) are an alternative minimally invasive option in the lumbar spine for treatment of neurogenic claudication and back pain from lumbar stenosis. First described by Minns and Walsh, there are now multiple devices on the market. They are applied through a percutaneous or mini-open approach, with or without laminotomy, laminectomy, or diskectomy [7]. The basic premise behind their design is to create a state that prevents extension, thereby offloading the facet complexes and straightening out a "buckled" ligamentum flavum (e.g., for IDs without laminotomy), theoretically preventing a state of persistent nerve compression thereby decreasing the chances of restenosis. Some also provide an alternative to rigid arthrodesis for mild instability.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_45

45.2 Current Devices

Examples of current IDs available in either the United States or outside US markets are ones that do not require laminectomy and are positioned in between the spinous processes: (1) *X-Stop* (Medtronic, Minneapolis, MN)—rigid titanium, second-generation PEEK body, through midline mini-open incision (Fig. 45.1); (2) *Aperius* (Medtronic, Tolochenaz, Switzerland)—rigid titanium through para-midline percutaneous incision and those IDs that are deployed following laminectomy/laminotomy/or diskectomy ; (3) *DIAM* (Medtronic, Tolochenaz, Switzerland)—nonrigid polyester coated silicone with cord to anchor around spinous processes; (4) *Wallis* (Abbott Spine, Bordeaux, France)—second-generation nonrigid polyether ether ketone (PEEK) with ribbon to anchor around spinous processes; and (5) *Coflex* (Paradigm Spine, New York, NY)—titanium "U"-shaped device that clamps on superior and inferior spinous process (Fig. 45.2). X-Stop and Coflex are FDA approved for use in the United States. In this chapter we provide current evidence supporting or refuting the use of ID for motion preservation in the setting of stenosis without or without spondylolisthesis. Table 45.1 *provides descriptions of various IDs*.

Fig. 45.1 X-Stop device

Fig. 45.2 Coflex device

45.3 General Indications for ID Placement

Patients should have relief of buttock, leg, and even back pain in a partially flexed forward position in order to be candidates for some of the devices. Following placement, in the early postoperative period, radiographic and clinical parameters are often significantly improved including foraminal height/width and intervertebral disk height [8, 9]. General contraindications include severe osteoporosis (due to the increased risk of spinous process fracture post placement), radiologic ankylosis/fusion at proposed treatment level, grade 2 or greater spondylolisthesis, severe scoliosis, and greater than two lumbar levels of stenosis (some articles

Table 45.1 Descriptions of IDs

Device	Manufacturer	Design	Indications	Potential complications
X-Stop[a]	Medtronic (Minneapolis, MN)	Interspinous spacer providing indirect decompression	Lumbar spinal stenosis	Implant dislodgement
				Improper placement
				Spinous process fracture
				Implant mechanical failure
Aperius	Medtronic (Tolochenaz, Switzerland)	Percutaneous lumbar interspinous decompression system	Lumbar spinal stenosis	Same as above
DIAM	Medtronic (Tolochenaz, Switzerland)	Silicon device secured to spinous processes to provide flexible support	Lumbar spinal stenosis	Same as above
Wallis	Abbott Spine (Bordeaux, France)	PEEK spacer providing indirect decompression and providing resistance against flexion	Lumbar spinal stenosis	Same as above
Coflex[a]	Paradigm (New York, NY)	Interlaminar stabilizer and motion preservation after decompression	Lumbar spinal stenosis	Same as above

[a]FDA approved for use in the United States

implant IDs over three levels however), the presence of motor deficits, and the presence of flat back with a lumbar lordosis-pelvic incidence (LL-PI) mismatch over 10°.

45.4 Gold Standard Treatment for Neurogenic Claudication Is Laminectomy

Recent studies have supported laminectomy over continued conservative management for neurogenic claudication from lumbar stenosis. The Spine Patient Outcomes Research Trial (SPORT) demonstrated the superiority of laminectomy versus conservative management for lumbar spinal stenosis at both 2- and 4-year time points [10, 11]. In a European prospective study of 159 patients who underwent laminectomy and partial facetectomy for neurogenic claudication, at 5 years 79 % of those patient's reported a "good" global outcome [12].

A certain percentage of patients, however, fail laminectomy due to recurrent stenosis and ultimately require a fusion operation. For example, in the SPORT trial at 2 years, reoperations occurred in 8 % of patients ($n = 289$), half of those reoperations were due to recurrent stenosis (i.e., a failure of the initial operation), and most of those patients received a fusion operation [10]. One explanation for why patients fail laminectomy is due to the presence of worsening deformity from iatrogenic instability [13]. Additionally, the utility of laminectomy alone in the setting of significant back pain or spondylolisthesis is questionable [14, 15]. Fusion may be indicated in these settings, and those patients tend to maintain greater pain relief and improvement in function over time [16, 17].

Proponents of IDs state that lumbar fusions carry nascent risks in both the perioperative and late postoperative periods including pseudoarthrosis and painful hardware. Intraoperative risks are also encountered with the placement of pedicle screws and interbody devices [18]. Adjacent segment degeneration (ASD) is a controversial topic and likely has contributory factors from both the patients' own progressive arthritic disease state and the shear forces on non-fused segments from prior fused vertebrae [19]. Consequently this may lead to further surgery for extensions of fusion.

45.5 Do IDs Provide the "Intended" Bridge Between Laminectomy and Laminectomy/Fusion?

The implementation of alternative stabilizing devices (i.e., ID) that preserve motion with or without laminectomy provides a minimally invasive alternative to either laminectomy alone or laminectomy with fusion in certain situations [20]. In a large retrospective cohort analysis ($n=99,084$) of patients who received an ID, ID + laminectomy, decompression alone, or lumbar fusion (one to two level), the authors found that patients receiving an ID were generally older, yet did not have a higher degree of comorbid conditions preoperatively compared to the other groups.

Patients undergoing ID placement encountered a lower percentage of procedural morbidity (i.e., faster operative times, less blood loss, less CSF leaks, ability to utilize non-general anesthesia) but had higher rates of further inpatient surgery in the future for revision operations. This is the major drawback of the implantation of IDs [21]. *Is a small gain in upfront risk associated with the initial procedure worth a higher long-term risk of reoperation compared to other therapies*?

Common complications reported in various studies with IDs include spinous process fractures (most are asymptomatic), device malposition over time, failure of the device to provide continued stabilization of the motion segment and decompression of the neural elements, and creation of flat back. Kim and colleagues reported that a higher incidence of spinous process fractures occurred when a particular ID was used in patients with spondylolisthesis [22].

45.6 Biomechanical Data

45.6.1 Cadaveric

Wilke et al. analyzed 4 IDs (Coflex, DIAM, WILLIS, and X-STOP) in a set of 24 cadavers. In summary all devices similarly limited motion by 50 % in extension compared to the state of the intact spine without the device. Intradiscal pressure was also reduced in extension compared to the intact spine. Flexion, lateral bending, and axial rotation were affected very little by either of the devices [23]. Lafage et al. noted similar results in a cadaveric study examining only the Wallis implant [24].

An alternate biomechanical study by Tsai et al. of the Coflex ID reported different results, however. They found that Coflex did not allow significantly more or less motion than an intact cadaveric specimen following partial destabilization (removal of supra-/interspinous ligaments, ligamentum flavum, medial facetectomy) in flexion/extension or axial rotation. In this study Coflex restored a spine segment to preoperative levels of stability following decompression [25]. Phillips in a similar study using the DIAM device noted that the ID restored pre-diskectomy stability in flexion/extension and reduced but did not restore in lateral bending. There was little to no effect on axial rotation [26].

Multiple cadaveric biomechanical studies examining the X-Stop device have been performed. Wiseman et al. observed that specimens with an ID had significantly lower forces on the facets, while Swanson noted decreased intradiscal pressures at the instrumented level [27, 28]. No effect of the device was observed at the adjacent-level segments in either of the studies. Richards et al. noted that following placement of an X-Stop ID in a cadaveric specimen, during extension the ID significantly increased the canal diameter and foraminal size [9].

45.6.2 In Vivo

Zucherman et al. noted no differences in radiographic parameters (spinous process distance, A/P disk height, foraminal height) when the surgical group was compared to the control nonoperative arm at both 12 and 24 months with the X-Stop device [29]. These findings are in contrast to a study by Lee et al. who noted a 23 % increase in canal diameter in preoperative versus postoperative MRI following X-Stop placement for primarily single-level stenosis [30]. In a retrospective

study by Sobottke et al. of 129 patients who received either the DIAM, Wallis, or X-Stop ID, they observed significant changes in foraminal measurements and disk height compared to pre-op [8]. There was no strong correlation between the magnitude of correction and symptom relief. During the follow-up period, the radiographic findings tended to revert back to pre-op without a return of symptoms.

Holinka et al. noted decreased instability in flexion and extension postoperatively following interlaminar decompression and DIAM implantation in 22 patients with low-grade <5 mm spondylolisthesis [31]. Kong et al. in a case series of 42 patients comparing Coflex to PLIF noted increased motion at the adjacent segment in the PLIF cohort and no increased motion in the Coflex at 1 year [32]. Following lumbar decompression and DIAM placement, Kim noted no change in disk height or sagittal alignment at the mean 12-month follow-up [33]. Korovessis conducted a prospective case-control study examining adjacent segment degeneration (ASD) in patients with fusion alone versus fusion plus the Wallis implant at the adjacent superior segment in an average follow-up of 60 months [34]. Disk height significantly increased and range of motion decreased in all planes in the Wallis group. Over time ASD was noted in a greater number of non-Wallis-treated spines.

45.7 Devices: Clinical Literature and Surgical Technique

45.7.1 Interspinous Devices Placed Without Removal of Ligament/Laminectomy or Laminotomy

45.7.1.1 X-Stop (Titanium or PEEK Mini-Open Midline Approach): Clinical Literature

The X-Stop device exists as a minimally invasive alternative to open laminectomy in patients with lumbar spinal stenosis and neurogenic claudication. This device is also intended to indirectly open the foramen. It has been on the market for more than 10 years and involves placement of the device in the interspinous space and maintains the segment in some degree of flexion and limits extension, thereby enlarging the spinal canal and neuroforamina and off-loads the facets and disk space at the instrumented level.

It is best utilized in patients with stenosis from ligamentum flavum buckling and not favored in patients with boney stenosis or rigid spinal segments. Biomechanically the X-Stop device has no effect on axial rotation or lateral bending at the instrumented level and has no effect on any parameter at adjacent levels [27, 28, 35]. Although not reported extensively in the literature, there is a second-generation X-Stop titanium outer ring and PEEK-bone interface device available and approved by the FDA that provides greater contact area with bone when compared to the first-generation all titanium [36].

A multicenter randomized controlled trial (RCT) showed that ID (X-STOP) had improved outcomes compared to conservative therapies and epidural injections in both short- and long-term follow-up (4 years) [29, 37]. Anderson et al. also conducted an RCT in patients with spondylolisthesis and showed that patients who received ID had improved measures in all parameters compared to conservative therapy [38]. Verhoof noted that patients with spondylolisthesis and ID placement had a high return rate for revision decompression and fusion within 2 years (7/12, 58.3 %) [39]. A cost-effective analysis of the treatment of the lumbar stenosis population found laminectomy was the lowest cost followed by X-Stop and then conservative management [40].

Patil et al. examined reoperation rates, complications, and costs in patients who had received an ID (X-STOP) in a retrospective study of 498 patients over a mean of 1.2 years. They found that reoperation rates were significantly high (22 %) with the most common reoperation being laminectomy ($n=60$) versus new ID placement ($n=52$), mean hospital stay was approximately 1.5 days, and mean hospital cost was close to 20,000 dollars. When compared to a match cohort for laminectomy ($n=348$), the group found that persons who received an ID had incurred an increased cost at the index hospitalization that

had leveled out by the 12- and 18-month mark and the laminectomy patients had more complications at the 30- and 90-day mark [41].

Other groups have shown cost-effectiveness when it can be performed as an outpatient procedure [42]. Stromqvist et al. conducted a prospective randomized controlled trial of 100 patients comparing this particular ID done under local anesthesia to decompressive laminectomy for one- to two-level stenosis without spondylolisthesis [43]. Mean surgery time and EBL were significantly less in the ID group. Zurich Claudication Questionnaire (ZCQ), visual analog scale (VAS), and SF-36 improved similarly between the groups at 6, 12, and 24 months. Three (6 %) patients in the laminectomy group received a reoperation, while 13 (26 %) received one in the ID group. Eleven of those 13 patients who received an ID had no symptom alleviation throughout the course following the procedure. Although the reoperation rates in that study were particularly high, and the reason for reoperation was ineffective treatment of symptoms by the device, in an alternate prospective series of 175 patients, Kutchta et al. found a much lower reoperation rate at 24 months ($n=8$, 4.6 %) [44]. Barbagallo reported in a retrospective review of 69 patients who received the X-Stop device seven postoperative complications (10.1 %) (three spinous process fractures and three device dislodgements) all requiring revision surgery [45].

Only one trial has compared the "gold standard" treatment for neurogenic claudication (i.e., laminectomy) versus an ID without laminectomy. Moojen et al. conducted a randomized controlled trial of 159 participants [46]. ZCQ analysis revealed no significant differences in long-term follow-up at 2 years, yet reoperations were significantly higher in the ID ($n=21$, 29 %) group versus the laminectomy ($n=6$, 8 %).

45.7.1.2 Aperius (Titanium Percutaneous Posterolateral Minimally Invasive): Clinical Literature

Multiple studies without control groups have shown clinical benefit compared to preoperative symptoms following placement of the Aperius device. It is not approved by the FDA for general use in the United States as of 2014. Two retrospective studies using Aperius ID (1 in 40 patients and the other in 152 patients) with a follow-up over a period of 9–12 months reported improvement in measured outcomes (VAS, ZCQ, and Macnab criteria) [47, 48]. In a safety study, Van Meirhaeghe et al. reported on 156 patients who received the device at one to three levels all with 12-month follow-up [49]. The mean duration for one-level procedures was 15.5 min. They noted improvements in walking distances, VAS and ZCQ scores at both 6-week and 12-month time points. Mean lordosis (L1–S1) decreased from 54.1 to 52.4° at 12 months. During the 12-month follow-up, 12 patients (7.7 %) had their ID removed due to persistent symptoms (most common), spinous process fracture, or malposition.

Two more powerful studies have compared the Aperius ID with open laminectomy with less than satisfactory results supporting ID placement. Postacchini compared $n=36$ receiving the ID and $n=35$ with laminectomy. The long-term follow-up was over a period of 2 years [50]. They separated the patients into subgroups of moderate versus severe stenosis. Approximately a one-third of patients in each group had grade 1 spondylolisthesis in addition to stenosis. Mean postoperative ODI and ZCQ scores for the laminectomy group were significantly better than the ID at all time points. For the ID, the rate of "good" results was significantly better in patients who had moderate (<40 % constriction of the canal diameter on MRI) and not severe stenosis. Additionally, 6/36 (16.7 %) had their device removed between 2 and 16 months because of no improvement in symptoms or initial improvement with return of symptoms, while only one patient in the open decompression group had revision surgery.

Beyer et al. reported on 2-year outcomes of 45 patients with neurogenic intermittent claudication comparing standard lumbar laminectomy to ID placement in a prospective nonrandomized observational study. Group 1 patients ($n=12$) received the Aperius ID. 5/12 patients required implant removal due to return of preoperative symptoms. No device dislodgments were noted.

All five patients had devices removed with a standard decompression at a mean of 13 months. The remaining patients in Group 1 showed no significant decrease in back and leg pain or outcome measures ODI/SF-36 over 2 years, but did have significant improvements in walking assessment. Group 2 patients on the contrary who received laminectomy had significant decreases in their back and leg pain at both 12 and 24 months as well as significant improvement in outcome measures and walking assessment [51].

45.7.1.3 Surgical Technique: X-STOP and Aperius

The patient is placed in the prone position over a Wilson frame. Monitored anesthesia care (MAC) with local anesthesia or local alone is used. Some groups have advocated the use of spinal epidural anesthesia as well.

A midline (X-STOP—Medtronic, Minneapolis, MN) or posterolateral (1.5 cm from midline—Aperius—(Medtronic, Switzerland) is performed over the respective level in the lumbar spine. The fascia is opened and trocars or spacers are sized through the interspinous ligament for the successive preparation of the interspinous space. Preservation of the supraspinous ligament is achieved.

An initial trial of 8 mm is used, and dilation through the interspinous ligament can continue in increments of 2 mm. The most common size of implant in one study was 12 mm. Maximum trocar size and implant is 14 mm [49]. X-Stop PEEK is sized up to 16 mm. Intraoperative fluoroscopy is utilized to check midline position of the implant before the wings are deployed.

45.7.2 Interspinous Device Mini-Open with Microsurgical Decompression (Laminotomy/Laminectomy With/Without Diskectomy)

45.7.2.1 Coflex

Coflex (Paradigm Spine, New York, NY) is a novel metallic "U"-shaped interspinous device utilized in one- or two-level stenosis of the lumbar region L1–L5. It is designed to impart a stabilizing effect on the operative levels. In preoperative assessment similar to other IDs listed above, the patient should experience relief of symptoms in flexion. Unlike the X-Stop or Aperius, the Coflex is placed after decompression (laminectomy/bilateral laminotomy) of the affected segments. The wings have serrated bone gripping surfaces and are attached to the superior and inferior spinous processes. The device is MRI compatible and is contraindicated in spondylolisthesis equal to or greater than grade 2, prior fusion, total removal of hypertrophic facets that would destabilize the spine, and degenerative scoliosis >25°.

45.7.2.2 Coflex: Clinical Literature

Davis et al. conducted a prospective, randomized, multicenter trial evaluating the safety and efficacy of Coflex compared with posterior spinal fusion in treating one- to two-level stenosis (with neurogenic claudication and back pain) with or without spondylolisthesis grade 1 ($n=322$ patients (215 Coflex, 107 fusions) [20]. Patients were randomized to receive laminectomy with Coflex interlaminar stabilization or laminectomy with posterolateral fusion and pedicle screws (*without BMP or interbody*). This was an investigational device exemption (IDE) study. Very few of these types of studies exist in the spine literature.

Coflex was designed to maintain some motion, yet provides stability following laminectomy. The Coflex cohort exhibited increased ZCQ and SF-12 scores versus control, a trend toward better ODI at 24 months, no difference in VAS scores (except early post-op period trend for Coflex with back and leg pain), shorter hospital stays, lower blood loss, and shorter operative times.

At 2 years the Coflex group maintained normal operative and adjacent-level motion versus fusion. The study did not address whether this resulted in lower reoperation rates at the adjacent levels. Adverse events were comparable in both groups. Surgical adverse events were 23.7 % in Coflex group versus 30.8 % in the fusion.

Spinous process fracture incidence (most were asymptomatic) in the Coflex group was 14 %; however, approximately half of those had

healed at 2 years. Reoperation rate was higher in the Coflex group. 10.7 % (23/215) and 13/23 were converted to a fusion versus 7.5 % (8/107) reoperation rate in the fusion group. The authors stated those that were converted to fusion (some > than 12 months) from receiving Coflex that this device may serve as a "bridge" between conservative therapy and fusion. *This study did not compare Coflex to the "gold standard" treatment for lumbar stenosis* (*lumbar laminectomy*). In summary Coflex provided equivalent in some and superior in other outcome measures when compared to fusion for lumbar stenosis with neurogenic claudication, with or without low back pain and spondylolisthesis; however, reoperation rates for the device were higher.

Davis et al. also performed a subgroup analysis in the study above of only those patients treated with either Coflex ($n=99$) or fusion ($n=51$) for spondylolisthesis [18]. ODIs, SF-12, VAS, and ZCQ were similar among the two groups at 2 years. Preoperative spondylolisthesis in both groups averaged 1.12 mm in the Coflex group versus 0.98 mm in the fusion controls *which could be argued as nominal or physiologic in some cases*.

As expected, at 2 years in the operative level, the Coflex group had more angulation versus the fusion (4.32° vs. 1.64°), but less at the adjacent above level (3.49° versus 5.42°), and similar at the adjacent below level. No worsened spondylolisthesis was noted in the Coflex group at the operative level at 2 years. At the superior adjacent level, Coflex group experienced a reduction in translation (0.87 → 0.74 mm) versus an average increase in the fusion group (0.64 → 0.97 mm).

Spinous process fractures were noted in 18 % of Coflex patients (18/99), while 6.4 % of patients had movement of their Coflex device. The rate of radiographic fusion was 71 % (36/51) (*no BMP or interbody was utilized in this study*), yet no difference in outcome was noted in patients with a solid fusion versus pseudoarthrosis. Fusion rates for local autograft versus iliac crest were similar as well.

In summary both groups met the study's criteria for success; however, this subgroup analysis Coflex patients returned to the operating room a higher number of times versus the fusion group (14.1 % 14/99 vs. 5.9 % 3/51) and 8/14 patients were converted to a fusion.

Richter et al. conducted a 2-year prospective controlled study comparing laminectomy with Coflex device ($n=31$) versus laminectomy alone ($n=31$) [52]. No significant differences were noted in all outcome parameters. One implant dislocation occurred, and three patients in the ID group were converted to fusion. Two patients in the laminectomy group required a later fusion.

45.7.2.3 Surgical Technique: Coflex

A midline incision is made exposing and removing the ligamentum flavum, and a bilateral hemilaminotomy is carried out with a high-speed burr along with a partial facetectomy. The supraspinous and interspinous ligament is taken last. Shaping of the two spinous processes with the burr may be necessary for an appropriate fit. Care must be taken to keep at least 14 mm of spinous process present as less increases the risk of spinous process fracture [18]. Trials (smaller first) are then deployed to choose a proper end sized implant. They come in five different sizes and range from 8 to 16 mm in 2 mm increments. The goal is to provide 1–2 mm of facet distraction. Following trial deployment, an appropriately sized Coflex device is inserted into the interspinous space. The wings of the Coflex device can be opened with a bender to facilitate positioning. The device is seated 1–2 mm above the dura or the apex of the "U" at the midline of the facet joint. The wings are then crimped. If necessary removal is achieved with bending of the wings open with chisel and forceps. Postoperative x-rays are demonstrated for a multilevel procedure (Fig. 45.3).

45.7.2.4 "Soft Devices": Wallis, Second-Generation (PEEK), and DIAM, Second-Generation (Silicone)

Clinical Literature and Surgical Technique

The Wallis and DIAM devices are referred to as "soft" IDs due to their non-titanium composition. These IDs are not FDA approved for use in the United States as of 2014. They have cords

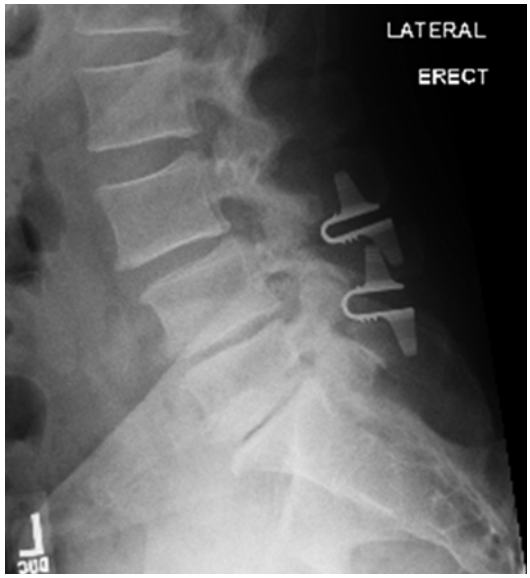

Fig. 45.3 Postoperative lateral x-ray demonstrating two-level decompression and placement of Coflex L3/L4, L4/L5 (Complements of Gary Gropper, MD)

that are fixated around the respective spinous processes of the level treated. In some of the reported literature, patients have had a prior lumbar operation (i.e., diskectomy or laminotomy) and placement of the device is intended to stabilize the segment following a revision, or in some cases, a diskectomy is performed along with the implant placement. A portion of the superior and inferior spinous processes must be preserved similar to the Coflex device. These IDs may be placed like the X-Stop without a decompression where the intention is intended to unbuckle the ligamentum flavum or indirectly open the foramen.

They are placed through a midline mini-open incision similar to the X-Stop and Aperius. The Wallis implant is 30 times less rigid than its first-generation titanium counterpart [34]. It consists of an interspinous PEEK block that is appropriately sized (10–16 mm) to the interspinous space. The DIAM on the other hand is an "X"-shaped silicone wedge covered in polyester knit. The Wallis requires removal of the interspinous ligament, while the DIAM preserves the supraspinous ligament and fits through the interspinous ligament in procedures that do not require a decompression. Trials are utilized to determine the appropriate final size of the implant. The implant is then inserted and seated with a tamp and mallet. The cords are then wrapped around the superior and inferior spinous process, tightened, and then crimped.

Mariottini et al. performed a study on the DIAM device on 43 patients. They reported 97 % satisfying results over the study period where this device was placed following laminotomy and microsurgical nerve root decompression [53]. Taylor and colleagues also reported satisfactory results with very few device-related revisions in a retrospective study of 104 patients who received the DIAM ID [54].

Senegas et al. examined 107 patients with the Wallis implant retrospectively over a period of 13 years and noted a good outcome (ODI, SF-36, VAS) in 80 % while 20 % had to be reoperated on where the implant was removed and a fusion performed [55]. Kim et al. compared 31 patients ($n=8$ with recurrent disk herniation with equal back and leg pain, $n=15$ with disk herniation with equal back and leg pain, $n=8$ with lumbar stenosis with mild instability) who received a DIAM following lumbar surgery with 31 patients receiving lumbar surgery without ID in a case-control safety study with mean of 12-month follow-up. They noted no differences in outcomes between the two groups and a higher complication rate of the DIAM group mainly due to resultant spinous process fractures or recurrent disk herniations (authors did not elaborate on a cause) [33]. Floman et al. did not find a reduced incidence in recurrent disk herniations in Wallis ID versus non-ID diskectomies over a 16-month period, and Korovessis et al. noted increased ASD in patients who had instrumented lumbar fusions without Wallis at the superior adjacent segment [34].

Conclusions

The premise behind IDs is to provide stabilization at the operative level and create an environment of restricted extension. A distinction should be made between those devices that provide indirect decompression following deployment (X-Stop/Aperius/

DIAM/Wallis) versus those that can be placed in conjunction with a laminotomy (Coflex, DIAM) or diskectomy (Wallis). The ideal candidate has yet to be conclusively determined for ID placement. *While some patients have long-term benefit following ID, a high percentage of patients with IDs need revision operations* (*this is the biggest disadvantage of this particular therapy*). They may be indicated for a limited number of patients (i.e., those who would encounter morbidity with general anesthesia), but the surgeon may be trading off early risk with the initial operation for a higher rate of return to the operating room for revision.

Key Points

1. The "gold standard" treatment for neurogenic claudication from lumbar stenosis without translational or coronal instability is LAMINECTOMY.
2. The X-Stop and Aperius ID are placed without a bony decompression, while the Wallis, DIAM, and Coflex are placed following a bony decompression.
3. Patients who undergo ID placement generally have a lower procedural morbidity but have higher percentages of return to the operating room for revisions compared to the gold standard laminectomy.
4. ID complications include spinous process fractures, device malposition, and failure of the device to provide continued stabilization of the motion segment and decompression of the neural elements.
5. IDs tend to limit the spine in extension, reduce intradiscal pressure, and offload facets at the instrumented level, but have little effect on the adjacent levels.
6. Avoid ID in patients with flat backs who have LL-PI mismatch over 10° as the devices increase kyphosis.

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Part VIII

DDD and Spine Deformity and Sagittal Balance

Degenerative Scoliosis: Surgical Treatment

46

Jeffrey L. Gum and Jacob M. Buchowski

46.1 Demographics and Natural History

Adult scoliosis can typically be divided into two types: idiopathic and degenerative (de novo) scoliosis. The former is usually a patient with a history of adolescent idiopathic scoliosis (AIS) that progresses into adulthood [1], whereas adult degenerative scoliosis (ADS) patients have no history of scoliosis and most commonly present in the sixth decade with spinal stenosis symptoms [2, 3]. Other symptoms often include worsening mechanical pain or radiculopathy. Structurally, the lumbar curves typically have an L2 or L3 apex and are associated with a distal fractional curve (L4–sacrum) but not a structural thoracic curve, although a compensatory thoracic curve can be present. ADS curves are thought to develop as the result of asymmetric disk degeneration, osteoporosis, and vertebral compression fractures [4]. Similar to AIS, curve prevalence in ADS is inversely proportional to curve magnitude with an overall prevalence ranging from 1 to 10 % [5–8].

46.2 Preoperative Evaluation

A thorough clinical evaluation should start with a detailed history and physical examination. Inquiries regarding a previous history of scoliosis are helpful to exclude the possibility of a degenerative idiopathic deformity. Although pain is the most common presenting symptom (>90 %), other aspects of the chief complaint can be very helpful when formulating a workup and operative plan [9, 10]. Pain is evaluated in regard to onset, location, duration, characteristics, and aggravating/relieving factors. Mechanical or axial pain is more likely associated with radiographic parameters such as lateral or rotatory subluxation often in the setting of severe spondylitic changes (Fig. 46.1) or sagittal imbalance and therefore should be addressed in the operative plan. Delineation of radicular pain or leg pain is important because lateral recess stenosis requires a more generous decompression compared to that of central stenosis. Although the literature suggests that radicular symptoms typically originate from the apex of the major curve, our experience suggests that the concavity of the fractional curve is the more common location for symptomatic foraminal stenosis [11]. Neurogenic claudication

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_46

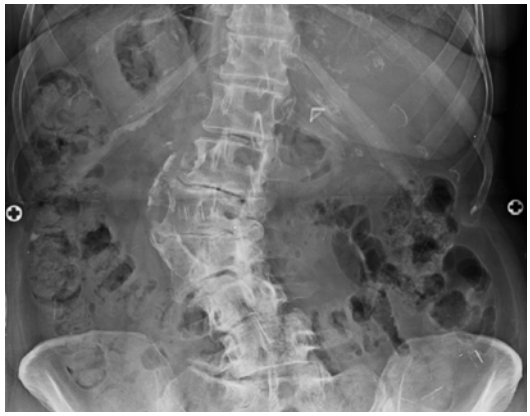

Fig. 46.1 PA view of patient with degenerative scoliosis showing severe spondylitic changes from L1 to the sacrum with L2–L3 and L3–L4 being the worst. There is significant lateral listhesis at L4–L5 and obliquity at the L5–S1 disk space typical of the fractional curve. The patient complained of left lower extremity pain extending to the dorsum of her foot. Radicular symptoms from the concavity of either the major curve or fractional curve is typical with this type of deformity

pain from central spinal stenosis in ASD (vs purely degenerative lumbar spinal stenosis) is typically not relieved by forward posture, unless the patient sits with his/her trunk supported by the arms [2]. Again, this validation would alter the construct to make sure areas requiring significant decompression were included in the instrumented fusion levels, whereas it may be possible to avoid instrumented fusion on levels with minimal decompression.

It is important to inquire about increasing clinical deformity. Rapidly progressing deformity can be a sign of neurogenic scoliosis, although rare in this adult population. This type of scoliosis results from a central nervous system condition with altered signaling to the spinal musculature and merits complete neural axis imaging [11]. Besides timing of deformity, patients often relate increasing deformity as an increasing rib or paraspinal hump, decreased height, or even the feeling of falling forward as the day progresses. The rotational deformity should be evaluated and documented with a scoliometer at each visit along with height recording. Any shoulder or pelvic asymmetry should be noted. Several subtleties on physical exam can help illuminate increasing sagittal or coronal imbalance. As the day progresses, these patients have to utilize more and more compensatory mechanisms to keep them upright with minimal energy expenditure and may complain of spinal extensor fatigue. The pelvis retroverts and hips extend while the knees flex. Hyperextension of the neck along with shoulder extension can all be seen in patients with a sagittal imbalance, as they are trying to center their head over their pelvis. These exam findings are reflected on long-cassette 36″ standing radiographs as well. Overall, it is very important to pay attention to the sagittal profile when deciding which surgery and instrumentation construct as extending the upper instrumented vertebra (UIV) more proximally is likely necessary for significant sagittal imbalance.

Adult deformity patients pose a more challenging medical scenario compared to adolescent patients. And the role of comorbidities has been well documented as an important determinant of postoperative clinical outcome improvement [12]. Surgical interventions, especially long instrumented fusions, tend to be lengthy and maximally invasive and require diligent presurgical screening. Cardiopulmonary status and general medical condition should be evaluated and approved by the patients' general medical physician and/or cardiologist. Nutritional status assessment and bone quality analysis are important for the treatment algorithm as well [13]. A preoperative dual-energy x-ray absorptiometry (DEXA) scan is helpful. If patients are osteoporotic and have yet to be treated, one should consider provisional treatment.

Full-length (36-in.) standing anterior-posterior and lateral radiographs are required for preoperative planning. The addition of "spot" films (lumbosacral or thoracolumbar junction) in the correct profile, as rotation can be significant, can be useful for pedicle assessment. Supine long-cassette radiographs (gravity removed) are utilized to assess flexibility. Push-prone or bending radiographs can aid in the assessment of flexibility although these are typically rigid deformities. Cobb angle measurements, coronal and sagittal balance (sagittal- and coronal-vertical axis), and

spinopelvic parameters (lumbar lordosis, pelvic incidence, pelvic tilt) are all determined. Advanced imaging with computed tomography (CT) scan (± myelogram) and/or MRI can be useful to help evaluate the degree of central, lateral recess, or foraminal stenosis. CT myelograms in this population are particularly useful as a significant percentage of these patients will have a contraindication (pacemaker, stent, coil, implanted stimulator) to an MRI. Additionally, a CT myelogram allows for the best appraisal of the bony architecture.

46.3 Surgical Options and Navigating a Surgical Algorithm

Patients that fail nonoperative modalities and have symptoms that correlate with radiographic findings should be considered for operative treatment.Specific radiographic parameters that tend to correlate with postoperative clinical improvement include lumbar curves >30–40, ≥6 mm of lateral listhesis, >3 mm increase in listhesis with flexion/extension, L3 and L4 endplate angulations, thoracolumbar kyphosis, and progressive curves (>10°) [1, 2, 8]. Lenke and Silva et al. describe six levels of operative treatment: I, decompression alone; II, decompression and limited instrumented posterior spinal fusion; III, decompression and lumbar curve instrumented fusion; IV, decompression with anterior and posterior spinal instrumented fusion; V, thoracic instrumentation and fusion extension; and VI, utilization of osteotomies for deformity correction [2].

Level I treatment includes decompression alone. This treatment is typically utilized best in the setting of neurogenic claudication secondary to central stenosis requiring only a limited decompression. The potential for deformity progression has been well documented and must be considered. To minimize this risk, patients with radiographic evidence of deformity stability should be selected. The presence of anterior osteophytes, collapsed disk space, and no more than 2 mm of subluxation can be helpful signs of inherent stability. Additionally, the curve should be <30° without hyperkyphosis and/or sagittal or coronal imbalance. Lastly, these patients should have minimal to no mechanical back pain or deformity complaints as these symptoms will not improve and likely worsen [2].

Level II treatment is level I + limited instrumentation involving only the area of decompression. Patients requiring a more extensive decompression (lateral recess) or evidence of instability prior to decompression are good candidates for this option. Radiographic clues are similar to above, and patients without anterior osteophytes, a well-preserved disk space, and/or more than 2 mm of subluxation may be better served with the addition of instrumented fusion. The curve should still be <30° without hyperkyphosis and/or sagittal or coronal imbalance as only a limited fusion outside of these parameters could promote deformity progression or accelerated adjacent segment breakdown [2, 11]. Daubs et al. present a series of 55 consecutive patients with ADS treated either with decompression alone (level I, 16 patients) or decompression with limited instrumented fusion (level II, 39 patients). Although the level II patients were younger and had larger curves, at a minimum 2-year follow-up, 62 % of the level I versus 82 % of the level II patients reported a good-excellent result ($p<0.05$). At 5-year follow-up, 75 % of the decompression-only patients had recurrent stenosis, while 36 % of the decompression/limited fusion patients had adjacent level stenosis ($p=0.008$) [14].

Level III treatment encompasses fusion of the entire lumbar curve and any necessary decompressions. As to not stop the upper instrumented vertebra (UIV) at a physiologic apex, this level of treatment typically involves T10 or T11 instrumentation down to the sacrum/pelvis. Clinically, these patients commonly complain of axial or mechanical pain associated with their deformity. The curves are typically >45°, having >2 mm of subluxation, lack anterior osteophytes, but still have reasonable balance in both coronal and sagittal planes (Fig. 46.1) [2]. Although there is no clear literature that ascertains a critical construct length that pelvis fixation should definitely be included (versus just sacrum), it is common

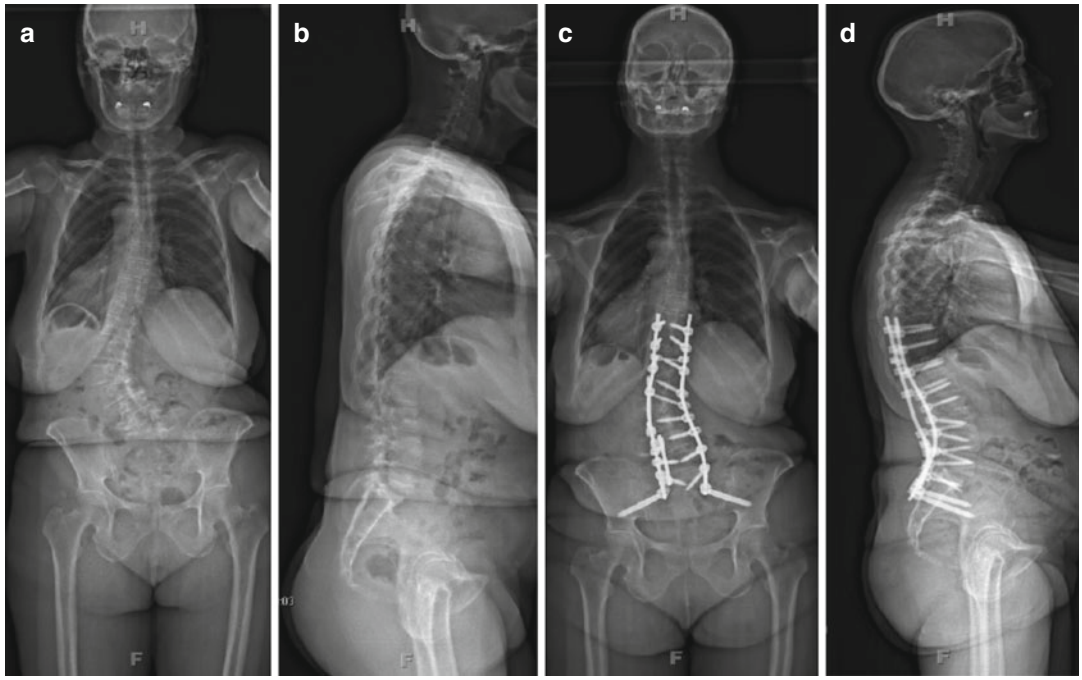

Fig. 46.2 Level III treatment example. PA (**a**) and lateral (**b**) of patient with lumbar degenerative scoliosis with acceptable coronal and sagittal balance. The patient underwent a posterior spinal fusion from T10 to the sacrum/pelvis with S2 alar-iliac screws placed (**c**, **d**). Decompression was performed from L4 to L5 and L5 to S1 for central stenosis

practice to consider pelvic fixation at our center when the UIV is L2 or proximal [15–19]. Additionally, anterior column support with interbody fixation (via TLIF) should be considered with this surgical option. The combination of anterior column support and sacropelvic fixation may reduce pseudarthrosis rates, screw pullout, and instrumentation failure [20].

Level IV treatment includes both anterior and posterior fusion of the lumbar spine. Traditionally, anterior spinal fusion has played a significant role in the correction of lumbar hyperkyphosis and sagittal imbalance. The load sharing and increased fusion surface area are obvious biomechanical advantages that will help decrease pseudarthrosis rates and instrumentation failure [2]. Additionally, this adds indirect decompression via foraminal distraction. At our center, the refinement of posterior-only techniques has significantly decreased the need for formal anterior exposures and fusions. The current trend and increased utilization of lateral-based procedures will likely further decrease the use of formal anterior lumbar fusion procedures.

Level V treatment includes the extension of the instrumented fusion into the upper thoracic region. This is needed in patients with thoracic hyperkyphosis, thoracic decompensation, thoracolumbar junctional kyphosis, and/or sagittal or coronal imbalance (Fig. 46.2) [2]. O'Shaughnessy et al. evaluated a series of 58 patients from a single center with an average 3-year follow-up and compared outcomes of patients with lower thoracic (LT) versus upper thoracic (UT) primary instrumented fusions in patients with adult scoliosis. The UT group had a greater preoperative thoracic kyphosis and coronal Cobb and increased blood loss. The UT group experienced more perioperative complications (30 % vs 16 %), a higher pseudarthrosis rate (20 % vs 5 %), and a higher prevalence of revision surgery (20 % vs 11 %). The LT cohort developed more proximal junctional kyphosis (18 % vs 10 %) but rarely requiring revision surgery [21].

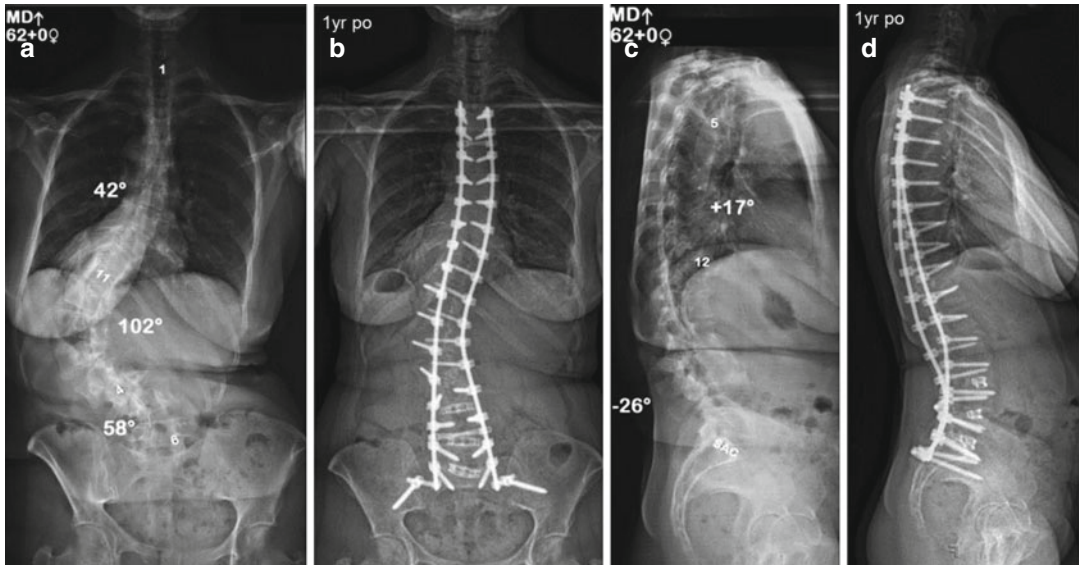

Fig. 46.3 Level V treatment example. A 62-year-old female with complaints of increasing deformity and left lower extremity pain. PA (**a**) shows a large, 102°, lumbar curve with a 58° fractional curve. Preoperative coronal and sagittal balance (**c**) are acceptable, which is different than most patients requiring level VI treatment. The patient underwent T2–sacrum/ilium with conventional iliac fixation and three-level TLIFs and five posterior column osteotomies (PCOs) with significant coronal and sagittal plane correction as seen in both the postoperative coronal (**b**) and sagittal (**d**) radiographs

Level VI treatment involves the use of an osteotomy. Patients whose deformity corrects >30 % with supine, push-prone, or bending films do not require osteotomies as these are considered flexible deformities [2]. Not all rigid deformities require an osteotomy as well, especially if well balanced. Again, the preoperative evaluation is critical in this group of patients as long instrumented fusions with 3-column osteotomies are a great physiologic stress on the patients. The majority of patients that require level VI treatment do so secondary to sagittal imbalance (Fig. 46.3) [2]. Again, attention to the sagittal profile is critical. Global balance, segmental or regional balance, and spinopelvic parameters such as pelvic incidence (PI), pelvic tilt (PT), and lumbar lordosis (LL) are all components that contribute to the overall sagittal profile. Smith-Peterson or posterior column osteotomies (PCO) can be utilized at sequential levels for segmental imbalance and potentially avoid a larger, more complex osteotomy. To maximize the corrective affect of a PCO, it is important for the disk space to still have some mobility allowing extension. The pedicle subtraction osteotomy is the next most corrective osteotomy option. Typically, it provides ~30° of lordotic correction without the need for anterior releases or structural grafting making it desirable for global imbalance. It is useful in osteoporotic patients and patients with suboptimal bone healing potential such as diabetics or smokers [2]. The bone-to-bone contact created during osteotomy closure provides relatively high fusion rates. For concurrent coronal imbalance, an asymmetric PSO can be utilized to achieve biplanar correction. The most corrective potential is achieved via a vertebral column resection (VCR) but is rarely needed for this patient population.

46.4 Fusion Level Selection

Upper instrumented vertebra (UIV) or proximal fusion level should begin at a neutral and stable vertebra, established to be the center sacral vertical line (CSVL) [22, 23]. The thoracic physiologic apex should be avoided as well [24]. Additionally, the fusion should not stop at a level with signs of

radiographic instability such as rotatory subluxation or listhesis. One should consider all the above for determining the lower instrumented vertebra (LIV) as well. There is debate about the sparing of only one motion segment by stopping at L5. This is possible but the integrity of the L5–S1 disk should be considered, and if there is any obliquity, which is typical of the fractional curves >15°, the sacrum and/or pelvis should be included [2].

As mentioned several times previously in the chapter, there are numerous factors, from spondylosis to medical comorbidities, to consider when evaluating health-related quality-of-life outcomes of patients who have surgery for ADS. The largest study comparing level I, level II, and level III treatment options was reported by Transfeldt et al. and included 85 patients retrospectively studied with a minimum 2-year follow-up [25]. They found that the complication rate was highest in level III treatment (56 %) and lowest in level I treatment (10 %) with Oswestry Disability Index only reaching a significant improvement in these two cohorts as well. Overall, the SF-36 scores had significant improvement for all cohorts and the satisfaction questionnaire showed the highest success to be in the level III treatment group with an average radiographic improvement in Cobb from 39 to 19°. Their regression analysis echoed other concepts in deformity surgery, revealing that sacrum to curve apex fusions and positive postoperative sagittal imbalance were associated with poor outcomes. Their conclusion was that both good and poor results were seen with each of the three procedures confirming the variability in this patient population and the difficulty in stratifying treatment [25]. A systematic review by Liang et al. included 16 studies and 553 patients that had operative treatment for degenerative scoliosis. Obviously, a very wide spectrum regarding level of treatment but overall a mean improvment in ODI from 36.0 to 23.3 with a mean reduction in curve magnitude of 48.5 %. The overall incidence of complications was 49.0 % with a rate of revision surgery of 15.3 %. They concluded that despite a relatively high rate of complications, surgery is an effective and reasonable treatment providing significant functional improvement and deformity correction [26].

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47 The Importance of Sagittal Balance for the Treatment of Lumbar Degenerative Disk Disease

João Luiz Pinheiro-Franco and Pierre Roussouly

47.1 Introduction

Low back pain (LBP) has a lifetime prevalence of approximately 80 % [1]. A primary source of LBP, lumbar degenerative disk disease (DDD), is related to aging and may not be symptomatic. Disk degeneration is a natural phenomenon of the aging spine and the distinction between physiological and pathological DDD is not obvious. Lumbar pain in the setting of DDD may be the result of complex and intricate underlying processes with multiple variables involved. DDD is deemed to be induced mechanically and mediated by biochemical responses, often concurrent with aging and probably influenced by genetic particularities [2].

Beyond the disk, important sources of LBP are the vertebral posterior elements (facet joints) and the musculoligamentary system. According to Roussouly et al., global lumbar hyperlordosis and focal lumbar hyperextension (two adjacent functional segments in hyperextension) may result in increased stress on facet joints and may cause lumbar facet pain [3]. Moreover, failure of both discal and facet joint structure may determine segmental instability and this may play a role in LBP.

More recently, iatrogenic sagittal unbalance of the spine has been credited as one of the principal reasons for chronic LBP after spinal fusion surgery. The balance of spine and pelvis in the sagittal plane may be involved in lumbar pain when lordosis requirements are not respected.

Sagittal balance and bipedalism are mutually linked. The verticality of human bipedalism is obtained by a specific combination of shape and orientation of both spine and pelvis. Bipedalism specificities, as pelvis verticality, lumbar lordosis, and C7 plumb line alignment, are encountered in human population only. Spinopelvic sagittal alignment may be analyzed by a combination of spinopelvic and lumbar lordosis parameters and the global spinal balance may be evaluated by C7 plumb line.

Studies on asymptomatic volunteers have drawn the conclusion that there are conditions for an ideal sagittal balance. The first one is the maintenance of the C7 plumb line over the sacral plateau [4]. This is obtained by adaptation of the spinal curvatures, mainly lumbar lordosis, to the different shapes of pelvis. There is an interaction between shape and position of the pelvis with

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_47

shape and position of the spine curvatures in order to maintain global balance (C7 plumb line over the sacral plateau).

Four types of spinal curvature settings were described according to the pelvic shape parameter named pelvic incidence [5, 6]. The four different shapes of lordosis may comprehend and represent the overall distribution of mechanical stresses of loading on the spine according to the pelvic spatial orientation. With aging, mechanical stresses may induce specific degenerative patterns regarding each spinopelvic organization. The degeneration of the spine in one or several functional segment units may change the global spinal alignment and even induce sagittal plane compensatory mechanisms in spine or pelvis in order to maintain C7 plumb line in a balanced position. When these compensations are overpassed, C7 plumb line is displaced forward, first forward the sacral plateau and then forward the femoral heads. Even if these compensatory mechanisms allow the patient to maintain a standing position, the situation may be uncomfortable and difficult to maintain for a long time. The principal aim of a surgical treatment for that condition is the restoration of sagittal balance. This implies the repositioning of C7 over the sacral plateau, by adjustment of the spinal curvatures, with decreasing of the pelvis compensation. In surgery, it is mandatory to respect the spinal alignment, according to the pelvic shape given by the pelvic incidence.

The sagittal spinopelvic alignment in spinal disorders has been studied in developmental spondylolisthesis [7, 8], degenerative spondylolisthesis [9], adolescent idiopathic scoliosis [10], and adult spinal deformity [11] and in the asymptomatic population [5, 12]. Some authors also analyzed spinopelvic balance in LBP and lumbar DDD [13–16]. However, the relationship between sagittal alignment and pathology is not well understood.

There is no ideal sagittal balance but a unique physiological sagittal balance for a given individual. In asymptomatic individuals, there is a great variability in sagittal spinopelvic alignment with large standard deviations. Therefore, although statistically significant differences may be found, differences in sagittal spinopelvic alignment in chronic LBP are only small, and clinically, multiple factors other than spinopelvic alignment contribute to LBP and/or lumbar disk degeneration. However, there seems to be trends to specific patterns of degeneration according to specific spinopelvic morphotypes.

For decades, the surgical treatment of spinal pathologies has focused on focal problems (e.g., the neurodecompression in a lumbar disk herniation) with no concern to regional lumbar or global spine sagittal balance. In the last 20 years, however, there has been a marked interest in the spinal sagittal balance. The maintenance of the balance should be one of the pillars of the surgical treatment for spinal diseases.

47.2 Bipedalism and Lumbar Lordosis

Over hundreds of thousands of years, man has been transformed. Not just we have been, we are in transformation. The combination of multiple factors made the primitive ancestor to evolve from a quadruped position to a standing one, the bipedalism. For this to elapse over millennia, there were obviously important anatomical modifications in the structure. From the skull base to the lumbar spine, striking changes occurred. The pelvis, previously a linking organ between trunk and lower members, became the pedestal over which the spine must equilibrate. Anatomical and physiological adjustments in the musculoligamentary system occurred to adapt to a new posture.

Human pelvis changed: it is the only one that is retroverted, the sacral plateau being backward the bifemoral heads' axis (balanced spine). In mammals, the sacral plateau is always anterior to the femoral heads' axis. This human disposition is the only mechanical possibility to allow the erect position, with the trunk over the pelvis. Therefore, evolution made possible the *extension of the lumbar spine*, *named lumbar lordosis*, unique among mammals and all the vertebrates. Bipedalism allows static and dynamic stability. The sacrum, defined by Doubousset "pelvic

vertebra," is the keystone in the pelvic-spine structural joint, joining the mobile spine and the hip. Its position in the space is essential to the local (lumbar) and global balance of the spine. If all primates can move in a bipedal way, man is the only primate capable of doing it for a long time and long distances [17]. This is possible due to the sagittal balance of the spine over the hips. Apes have a column marked by a global kyphosis that prevents them from maintaining a stable, steady upright stance. Their hip is high and narrow in the anterior-posterior plane. Using the upper limbs supported in pronation, they can somehow stand for a certain period and even walk. However, their march without support is difficult and limited. Studies have shown that the orangutan is very often bipedal, with his knee in extension (a feature associated with human bipedalism). The kangaroo, like the extinct Tyrannosaurus, walks (or walked) on two legs but have (or had) a stabilizing tail. The bipedalism of birds, as well, in no way resembles the human bipedalism. Hence, human verticalization, lumbar lordosis acquisition, and the obtention of spinal sagittal balance are intrinsically linked.

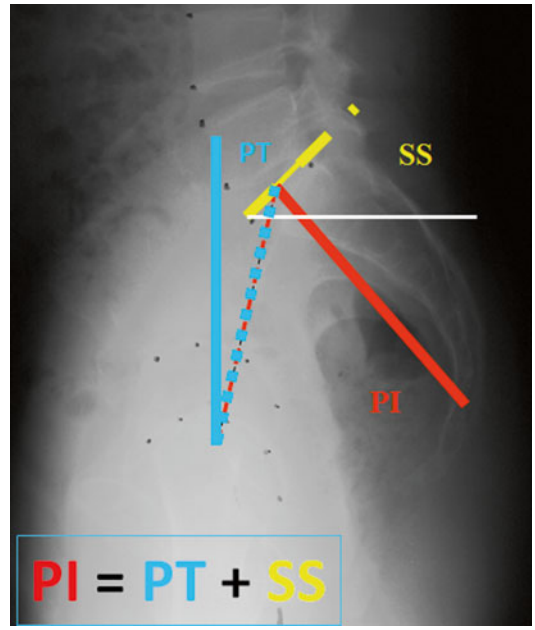

Fig. 47.1 Pelvic parameters: pelvic incidence (*PI*), sacral slope (*SS*), and pelvic tilt (*PT*) (From Barrey [18]; with permission)

47.3 Sagittal Balance and the Pelvic Parameters of the Spine

The sagittal balance of the spine can be defined as the harmonious balance of the trunk over the pelvis with a minimum expenditure of muscular energy in order to place the weight-bearing axis in a physiological position [18]. The spinopelvic alignment may be assessed by three groups of parameters: pelvic parameters, spinal curvatures, and C7 plumb line positioning.

47.3.1 Pelvic Parameters

The most commonly used pelvic parameters were described by Duval-Beaupère [19]. *Pelvic incidence* (PI) is a shape parameter that relates the sacral plateau with the bifemoral axis. Pelvis tilt (PT) is a positional parameter that gives the rotational position of the pelvis around the femoral heads. Sacral slope (SS) is a positional parameter that gives the angle between the sacral plateau direction and the horizontal.

PI angle consists of the angle between two lines, namely, the line drawn between the midpoint of bicoxofemoral axis (midpoint of the line joining the center of both femoral heads) and the middle of the sacral plateau and the line perpendicular to the middle of the sacral plateau (Fig. 47.1). PI is a morphological immutable angle in adulthood, being specific to each individual [18]. PI is anatomically determined by the shape of the sacrum: pelves with high PI have generally a short sacrum tending to horizontalization (sacral plate is far below and behind the top of iliac wings in lateral view) while those pelves with low PI have a long vertical sacrum in lateral view (sacral plate close to the top of iliac wings) (Fig.47.9). Definitive value of PI is acquired when final skeletal growth is achieved. There is some controversy concerning a possible variation of PI (increase) with aging by sacroiliac joint degeneration.

The second pelvic parameter is the *sacral slope* angle (*SS*), which is the angle formed by two lines: a horizontal line and the line passing through the sacral endplate (Fig. 47.1). The steeper the sacral plateau, the greater the SS. Thus, the more inclined anteriorly the sacrum (anteverted pelvis), the greater the SS; the more verticalized the sacrum (retroverted pelvis), the lower the SS. The longitudinal analysis of the flattening or the slope of the sacral plateau in a same patient may reflect a compensatory mechanism for an imbalanced spine. When there is a compensatory retroversion, the sacral plateau flattens and SS decreases. The horizontalization of SS may affect the forces acting on disks and facets.

The third pelvic parameter is the *pelvic tilt* angle (*PT*) (Fig. 47.1), the angle between two lines, namely, a vertical straight line and the line drawn from the midpoint between the two femoral heads' centers to the midpoint of the sacral endplate. The PT sets the oscillating motion of the hips around the bicoxofemoral axis, the femoral heads. This is possible due to the spherical shape of coxofemorals. When the pelvis swings forward, anteversion, the PT is lower; when it swings backward, pelvis retroversion, the PT is higher. The retroversion of the pelvis, the first compensatory mechanism of sagittal imbalance, aims to bring back the spine to the balanced situation, with C7 plumb line behind the posterior part of the sacrum. Thus, PT and SS are positional parameters, variables [12].

Legaye et al. [20, 21] and Duval-Beaupère et al. [19] noted important correlations between pelvic parameters, linked by the geometrical relation PI = PT+ SS [19, 20, 21]. The algebraic equation is: $A = x + y$, where A is constant and x and y are variable. Even if many studies have described a strong correlation between PI and SS (R: 0.8, $P < 0.001$) and PI and PT (R: 0.65 $p < 0.001$), it is mathematically impossible to write a linear relation between PI and SS or PI and PT.

If $A = x + y$, then $x = kA + b$ or $y = k'A + c$; but this is not totally true to PI = PT + SS. A direct extraction of PT or SS from PI is a statistical approximation but cannot be written under a mathematical equation.

Interpretation of PI = PT + SS could be done in two means:

- For a same person, PI is constant: when PT increases, SS decreases (retroverted pelvis=smaller SS); when PT decreases, SS increases (anteverted pelvis=higher SS).
- For different people, a marked pelvis retroversion (high PT) is possible with higher PI only. Even with a small PI, a high SS is possible when the pelvis is very anteverted (small PT or negative PT).

An increase of the PT is the earliest compensatory mechanism resulting from the loss of lordosis of natural aging or may be the result of lack of lordosis obtention after fusion surgery (flat back syndrome).

47.4 Spinal Parameters

47.4.1 Spinal Segmentation and Length of Lumbar Lordosis (LL)

To assess the sagittal balance, the authors took into account the part of the spine between C7 and T1 and the sacral plateau, excluding the cervical spine. While in animals the thoracic and lumbar spine have only one kyphotic curvature, in humans, two successive curves are described: thoracic kyphosis and lumbar lordosis. Anatomically, the first, corresponding to the thoracic vertebrae, is limited by C7–T1 disk above and T12–L1 disk below, and the second by T12–L1 proximally and S1 plateau distally (Fig. 47.2a) [12, 19, 22]. However, *if we consider that lordosis is composed by vertebrae in the part of the spine where the curve is in extension, the length of extension in lumbar area may be variable* (Fig. 47.2b). This concept has brought Berthonnaud et al. to describe a segmentation model of the spine with two curves between vertebrae T1 and S1: thoracic kyphosis and lumbar lordosis, limited by an inflection point where kyphosis turns into lordosis [5]. Thus, lordosis may be defined as the segment of the spine

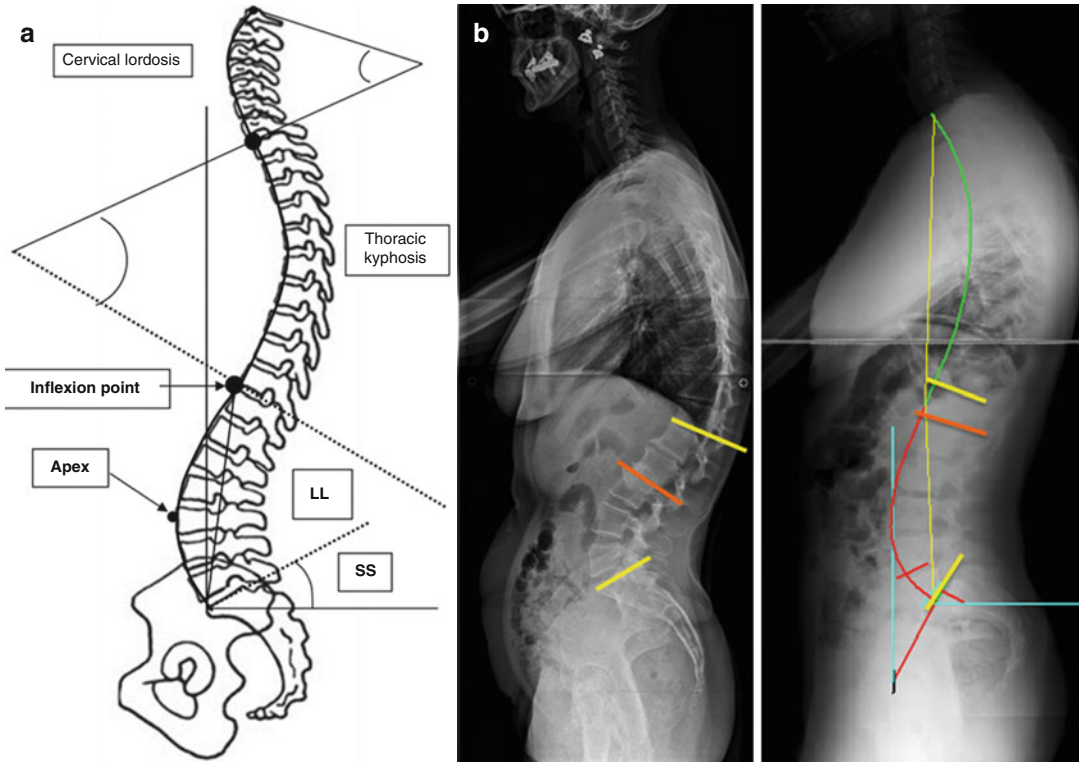

Fig. 47.2 (**a**) Subdivision of the sagittal spinal curvatures. Cervical spine goes from C1 to C7. Thoracolumbar spine is limited by C7–T1 and the sacral plateau. Inflection point is the place where the lordosis curve turns into kyphosis. This is a variable limit between lordosis and kyphosis (From Roussouly and Pinheiro-Franco [17]; with permission). (**b**) There is a great variability of the length of lordosis. Note shorter and marked lordosis on the *left* (lower pelvic incidence) and long and more harmonious lordosis on the *right* (higher pelvic incidence)

between the sacral endplate and the inflection point, without any reference to a specific anatomical landmark. The inflection point may be at the level of T12–L1 disk, a little bit higher or a little bit lower. In Roussouly type 1 lordosis, a thoracic vertebra, T12, may be at least in part in the lordotic spine, as it has been demonstrated in previous studies [12, 23]. Thus, this concept may affect the planning of an arthrodesis. The same remark may be done when using Cobb measurement. As for frontal scoliosis measurements, sagittal Cobb method has to address the most tilted vertebrae to measure a curve angle.

Stagnara pointed out the relation between LL and SS [24], with a description of static and dynamic spinal curvatures. Statistically, a strong correlation between LL and SS was well established [20] and Duval-Beaupère has extracted a statistical equation: $LL = -5,4 - 1,06SS$. More recently, Roussouly et al. [6] proposed a classification of LL according to SS (Fig. 47.3). This classification was fundamented by the lordosis concept from the aforementioned segmentation model [5], being lordosis defined from the inflection point to the sacral endplate. LL curvature is divided into two arcs of circle tangent on the horizontal line passing on the apex of LL.

47.5 Lumbar Lordosis Geometrical Analysis [17]: Basis for Roussouly Classification

Lumbar lordosis is not homogeneous throughout its extension. The angle of lordosis is not evenly distributed from the sacrum endplate to the proximal limit in the inflection point where the spine

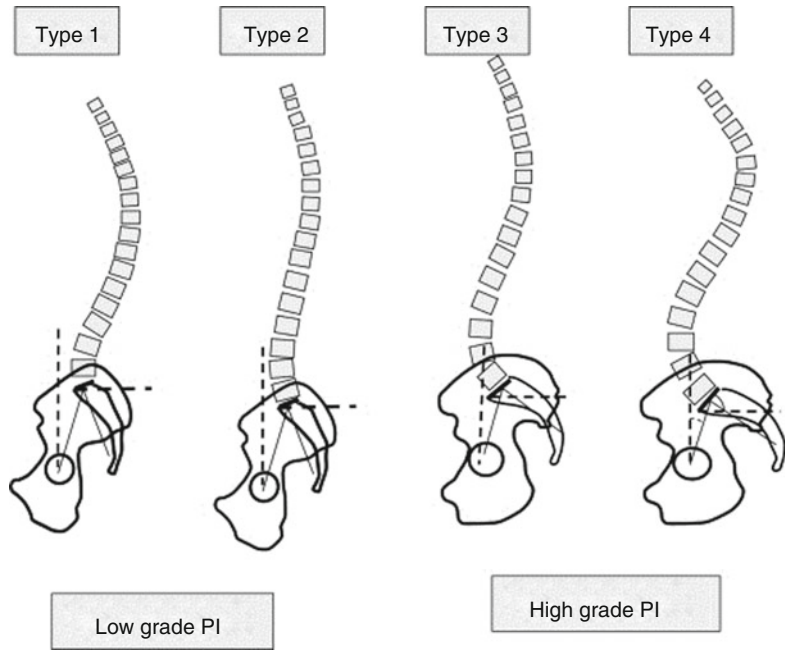

Fig. 47.3 The shape of lumbar lordosis depends on SS orientation. Types 1 and 2 have SS <35°; type 3 has 35° < SS <45°; and type 4 has SS >45° (From Roussouly and Pinheiro-Franco [3]; with permission)

bends into kyphosis. The contribution of each functional segment unit to the lordosis increases progressively from L1 to L5. Two-thirds of the total lordosis is depicted in the lower lumbar spine L4–S1 [18]. A meta-analysis demonstrated that 66 % of LL concentrates in L4–L5 and L5–S1 ($n=552$) [25]. Geometrical constructions of the spine have been proposed to describe LL: arc of circle [5] and quadrant of an ellipse [26]. The ellipsoid design is very realistic but difficult to use in everyday clinical practice [18]. Berthonnaud et al. [5] described a mathematical construction of lumbar lordosis. These authors proposed that *lumbar lordosis* could be measured using the Cobb method between the *upper plateau of the sacrum* and the *inflection point where lordosis turns into kyphosis*. The point of tangency of a vertical line with the anteriormost part of the convex side of lordosis with the vertical is the *apex of lordosis*. A horizontal line is traced from the apex of lordosis and defines two arches (Fig. 47.4): a lower arch (from the apex horizontal line to the sacral plate line) and an *upper arch* (from the apex horizontal line to the inflection point into kyphosis). The angle of the *lower arch* and the SS are equal and vary together by definition [6] (Fig. 47.4). Roussouly et al. demonstrated that the mean value of the upper arch angle was 20° and was stable whatever the value of SS was [6]. This explains why the lordosis is linked to the value of the lower arch (and therefore to SS). This has important implications in lumbar spine fusions.

47.6 The Roussouly Classification

Based on the geometrical model aforementioned, Roussouly et al. developed a classification of spinopelvic morphotypes translated by four types of lumbar lordosis according to the angle of SS and PI. The variation of lordosis was defined by the extent of the lower arch, and thus the SS. The separation of the values of the SS, according to Gauss curve, allowed the SS values to be classified into three groups depending on their values: SS <35°, 35° < SS <45°, SS >45° (Fig. 47.3). The values 35° and 45° were previously established [6, 18].

When the SS is small (<35°), two spinopelvic morphotypes of lordosis could be demonstrated:

- Type 1: short acute lordosis (concentrated in L4–L5 and L5–S1). The thoracic kyphosis extends slightly into the lumbar spine and

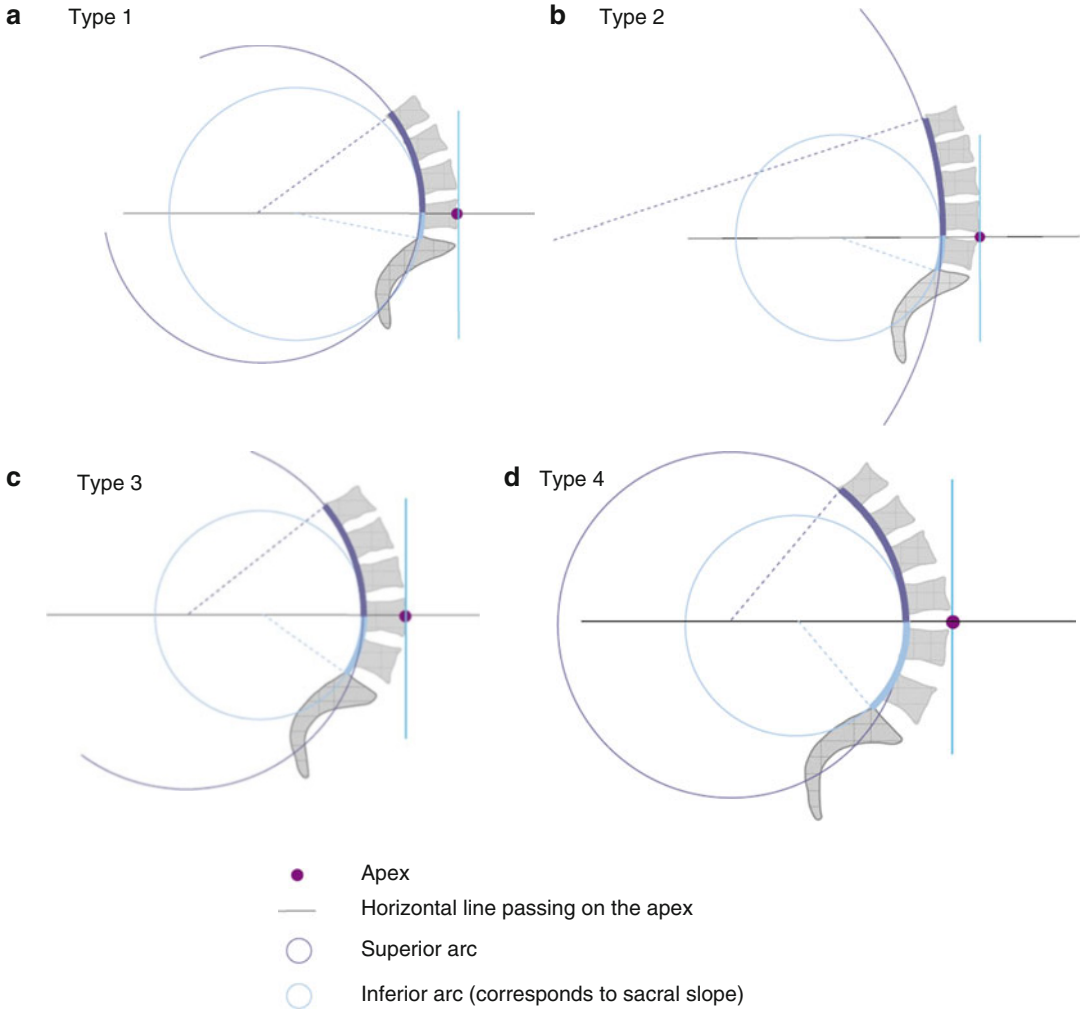

Fig. 47.4 (**a**) Schematic representation of arc of a circle model for type 1 lordosis. Note that the lower arch of the lumbar lordosis (=SS) is too small and the apex of lordosis is very low. There is a backward displacement of the top of lordosis and a very positive weighbridge angle. (**b**) Schematic representation of arc of a circle model for type 2 lordosis. The lower arch (SS) is slightly larger than in type 1, and the lordosis is still very small. The angle of weighbridge is from positive to zero. (**c**) Schematic representation of arc of a circle model for type 3 lordosis. Lordosis is divided between the two arches and the apex is at the center of L4. (**d**) Schematic representation of arc of a circle model for type 4 lordosis. The inflection point may be at the lower thoracic region. The lordosis angle increases as the number of vertebrae increases in the lordosis. The apex rises above L4 (From Barrey [18]; with permission)

therefore, the thoracolumbar (TL) junction is under the classic T12–L1 disk. The lower arch of the lumbar lordosis (=SS) is too small, and the apex of lordosis is very low. There is a backward displacement of the top of lordosis and a very positive weighbridge angle. As lordosis is short, the kyphosis is long and extends a little beyond the thoracolumbar spine (Fig. 47.4a);

- Type 2: corresponds to "flat back." The lumbar spine is usually quite flat. The lower arch (SS) is slightly larger than in type 1, and the lordosis is still very small. The angle of weighbridge is from positive to zero (Fig. 47.4b).

When SS has an average value (between 35 and 45°):

- Type 3: the best balanced spine. The inflection point is at the thoracolumbar junction. Lordosis is divided between the two arches and the apex is at the center of L4. There are usually four to five vertebrae in the curvature. The angle of weighbridge is from positive to zero (Fig. 47.4c).

When the SS is high (>45°):

- Type 4: The inflection point may be at the lower thoracic region. The lordosis angle increases as the number of vertebrae increases in the lordosis. The apex rises above L4. The toggle angle is generally from zero to negative. As lordosis is extended, the thoracic kyphosis is shortened (Fig. 47.4d).

47.6.1 LL and PI Relations

In asymptomatic volunteers, there is a strong correlation between LL and PI but less than between LL and SS. The authors have seen that due to the relation PI = PT + SS, there is a strong correlation between PI and SS but without concluding to a linear relation. Generally for a small PI, SS is smaller and this situation is represented mainly by types 1 or 2 lordosis. On contrary, for high-grade PI, SS is generally higher, with more type 3 or 4 lordosis. Occasionally, the authors have seen that PT may be small (<10°) or even negative in very anteverted pelvis. This situation may allow SS >40° even with a small PI and conducts to type 3 or 4 lordosis with a small PI. The value of PI may bring to a tendency of LL morphotypes, but to extract LL value from PI is an inexact extrapolation.

47.6.2 LL and Thoracic Kyphosis Angle (TK)

LL and TK are linked by their length and angles. Spinal parameters LL and TK are interdependent (Fig. 47.2). Jackson and McManus [13] found a significant correlation between LL and TK [27]. One change in one segment induces a change in the reciprocal segment according to the flexibility of the spine. If the TK increases, LL increases in order to maintain C7 in the balanced position. Reversely, when LL decreases, TK decreases, flattening the back.

- Following the inflection point, the distribution of both LL and TK is variable. In case of short LL, TK may reach the thoracolumbar area. With long LL, TK may be shortened in the more proximal thoracic area. *Sometimes, both LL and TK curves are separated by a straight segment of a variable number of vertebrae* (Fig. 47.2). The importance of this disposition is not well validated but requires further study.
- If we consider the tangent arcs of circle segmentation, there is a direct relation between the upper arc of LL and the lower arc of TK. An increased TK may induce an increased LL. This is more relevant in type 1 (too small lower arch of LL) where the total LL depends mostly on the upper arch of LL that has to compensate the higher lower arc of TK in the thoracolumbar area.

47.7 Global Balance of the Spine

47.7.1 The Global Balance [17]

To the analysis of the global balance of the spine, several points have been proposed. One of them, the external ear conducts, is useful to indicate the head positioning. The T9 tilt was described by Duval-Beaupère et al. as an indicator of the spine balance at the body mass center level [19, 27]. Historically, a vertical [4] plumb line originating in the center of the C7 vertebral body was deemed to be in approximately the same place in the sagittal plane as a vertical line passing through the patient's center of gravity (Fig. 47.5). Easy to be read on sagittal X-rays, C7 plumb line is the most commonly used index of the global balance. Kuntz et al. [28] noted in a review of the literature that global parameter as C7 plumb line was a stable, reliable index of the sagittal balance,

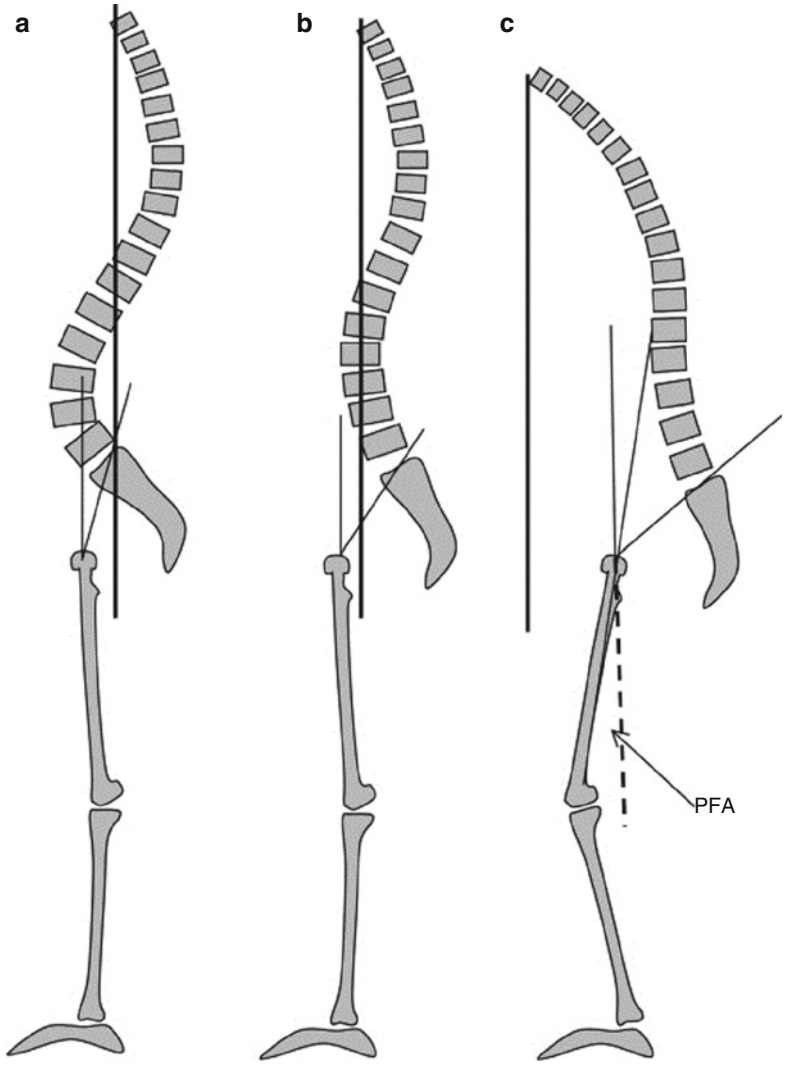

Fig. 47.5 Mechanism of compensation of a progressive kyphosis. (**a**) Balanced spine – C7 PL over the sacral endplate. (**b**) With progressive loss of lordosis, pelvis retroversion permits maintaining C7 PL behind the femoral heads. (**c**) Severe unbalance, retroversion reaches its limits, knees flexed in attempt to "put backwards C7 PL"; note the Pelvifemoral angle (PFA) (From Roussouly and Pinheiro-Franco [3]; with permission)

being maintained in narrow ranges for alignment of the spine over the pelvis and femoral heads. This parameter has been historically quantified by measuring the position of a vertical line originating in the center of the C7 vertebral body with respect to the posterior superior corner of S1.

The center of the vertebral body of C7 may be considered as the upper limit of the thoracic spine and, indeed, of the whole spine below the cervical area. Before recent radiograph quality advances, C7 was considered easier to be identified rather than T1 that was hidden by the shoulder superposition.

The *positioning of C7* has been widely studied and its implication in sagittal balance well established. *Three ways of evaluation* are possible:

- *Distance measurement*: sagittal vertical axis (SVA) is the distance between the posterior edge of the sacral plateau and the C7 plumb line projection. Schwab et al. [29] considered that a value superior to 5 cm is an evidence of

imbalance. Radiograph distance measurement is controversial. It is necessary to have a precise calibration of the radiographies as comparison between the radiographies may lead to potential errors. On another way, if SVA >5 cm is certainly an imbalanced situation, SVA <5 cm does not depict obvious balance.

- The authors prefer to use angles or distance ratio, as these are not subject to calibration variations typical of radiographs.
- *Angles measurement*: using the line from the center of C7 to the center of the sacral plateau, two angles are designed:
  - *C7 tilt* is a positional parameter with the vertical direction. This angle is very stable in a normal population around 3–5° backward.
  - *Spinosacral angle, SSA,* is a shape parameter drawn with the sacral plateau line (angle between the line from the center of C7 to the center of the sacral plate and the sacral plate line itself). It is representative of the total kyphosis of the whole thoracolumbar spine (cervical spine excluded). Its very high correlation ($R>0.9$) with SS in an asymptomatic population demonstrates the stability of positioning C7 plumb line over the sacrum in normal conditions.
- *Distance ratio*: described by Barrey [18], the ratio between the distance of the C7 plumb line and the posterior edge of the sacrum, and the distance of the C7 plumb line and center of femoral heads, allows the positioning of C7 plumb line relative to these two anatomical landmarks.

C7 plumb line must be related to an anatomical pelvic landmark as the center of the femoral heads (CFH) or the posterior point of the sacral plate (PP-S1). Usually, the horizontal distance between C7 PL and an anatomical landmark is calculated. It is not recommended to use distance to characterize this position. Barrey proposed a ratio between the horizontal distances from C7 PL to CFH and between CFH and PP-S1 (Fig. 47.6). This ratio provides an adimensional value concerning the position of C7 PL in relation to the vertical lines passing through CFH and through PP-S1 (Fig. 47.6):

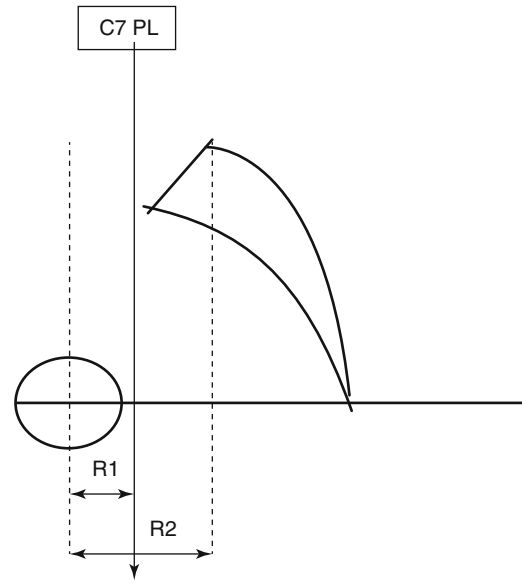

Fig. 47.6 In order to avoid errors with distance magnification C. Barrey proposed a ratio between horizontal distances from the center of the femoral heads (FH) and C7PL (R1) and the distance from FH and the posterior edge of the sacral plate (R2). R1/R2 is negative when C7 PL is forward FH, $0<R1/R2<1$ when C7PL is between FH and the sacrum, and $R1/R2>1$ when C7PL is behind the sacrum (From Roussouly and Pinheiro-Franco [17]; with permission)

- When C7 PL is behind the PP-S1 (ideal, balanced situation), the ratio value is superior to 1.
- When C7 PL is between CFH and PP-S1, the ratio is between 0 and 1 (balance is compromised).
- When C7 PL is forward CFH, the ratio value is negative (noncompensated severe imbalance).

47.7.2 Method of Measurement [27]

The analysis of the sagittal balance of the spine requires radiographs in a standardized fashion. The Cobb method may be used. A lateral radiograph of the spine must be made with vertical 30- to 90-cm film with a constant distance from the radiographic source. The knees must be fully extended and the arms flexed forward to 45° and resting on supports. According to Vedantam et al. [30], positioning the arms at

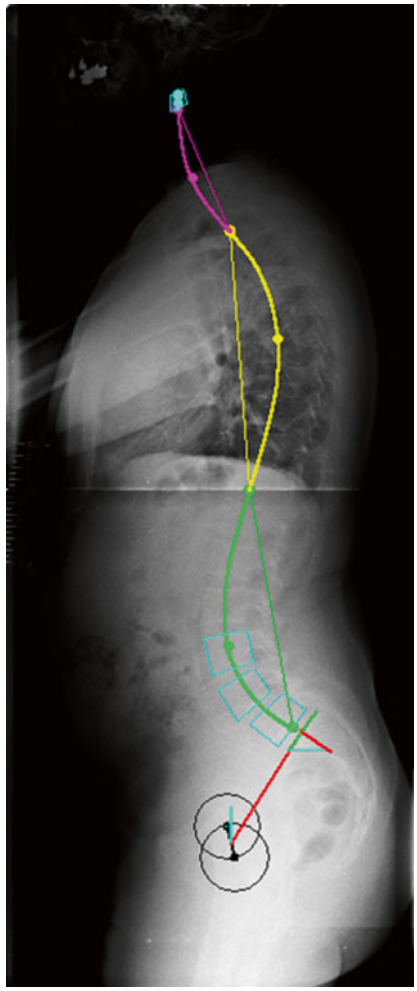

Fig. 47.7 Analysis of the sagittal balance using digitized imaging and software KEOPS (SMAIO, Lyon, France)

90° rather than 30° resulted in a negative shift of the sagittal vertical axis. Marks et al. [31] affirmed that shoulder flexion of 45° is the best position to use when a lateral radiograph is made, in order to repeatedly measure the sagittal vertical axis.

The radiograph must show the femoral heads caudally and C7 cranially. Radiographs should be digitized, and all measurements may be performed by specialized softwares. The present authors use KEOPS (SMAIO, Lyon, France) (Fig. 47.7). The software permits rapid and precise measurement of all angular parameters on digitized radiographs. Other authors [32] demonstrated in a similar software that the intraobserver and interobserver reliability is very high and that the results obtained by the numerical process are similar to those obtained by manual measurement. Recently, the EOS system was developed allowing full-spine standing imaging with minimal irradiation.

- The KEOPS sagittal balance analyzer is a Web-based software aimed to measure key spinopelvic parameters on long-standing sagittal X-rays from femoral heads to center of ears; compare measured parameters to those of asymptomatic populations using specific cursors and simulate surgical correction on sagittal spinopelvic reconstruction. Accuracy and repeatability were validated with multiple users performing two times 30 measurements [33]. It was observed that the measurements were more reliable than manual measurements performed by the same users. The software proposes a global acquisition mode in which femoral heads, S1 plate, center of C7, and a b-spleen line passing through the middle of each vertebral body are acquired in less than 2 min. A synthesis allows users to compare patient spinopelvic morphology and positioning parameters with those of an asymptomatic population (709 asymptomatic volunteers were assessed). The simulation modules allows to measure effect of pelvic tilt decompensation on C7 balance and simulate PSO as well as Smith-Petersen osteotomies depending on the level and the amount of correction.

47.8 Distribution Values of Lumbar Lordosis and Pelvic Parameters

LL, PI, and SS vary considerably in the asymptomatic population. Lordosis is characterized by a relatively large variability in the population with physiological values ranging from 20° to 85° [18]. The variability of SS according to the great range of PI may explain the different spinopelvic morphologies of lordosis that Roussouly et al. classified in four main types.

There are studies in the literature providing physiological standards for pelvic and spinal parameters that describe spinal balance [22, 27]. A study in a cohort of 300 asymptomatic adult volunteers [27] had mean 60° for LL (30–89), mean 41° for SS (17–63), mean 13° for PT, and mean 55° for PI (33–82). A strong correlation was found between SS and PI, LL and SS, LL and PI, and PI and PT. Similar results were found by Boulay et al. [22] in a population of 149 asymptomatic individuals from their medical staff: mean PI = 53 (33–77), mean SS = 41 (0,5–19), and mean PT = 11,9(−2–30) [22]. The more SS is pronounced and the more important is lordosis, plus the weight-bearing axis is transferred to the posterior structures of the lumbar spine, the facet joints [3].

There is no ideal mean lordosis, as it may vary [13, 24, 25, 34, 35]. *Length of LL* is an important issue: for a given angle of LL, a short LL on three segments has not the same stress on the posterior structure than a long one. Another parameter to take into account is *the proper flexibility of the spine in extension*. Some spines are less extensible and the maximum of LL angle they may provide may be insufficient according to a high PI value. This limited maximal extension is reached when there is a contact between spinous processes on standing x-ray. There exists optimal lordosis for each individual. It is not possible to define values of the ideal sagittal balance, but indeed a physiological sagittal balance for a given person.

47.9 Sagittal Imbalance and Clinical Symptoms

There is a wide range in spinopelvic parameters and spinopelvic alignment in an asymptomatic population. Some authors demonstrated trends to patterns of degenerative changes for each spinopelvic morphotype [3]. LBP is strongly associated with lumbar DDD, a multifaceted problem, and for what will probably never be possible to describe one single factor that causes it.

Glassman [36] et al. reported a correlation between poor clinical outcome and positive sagittal balance. The same finding was verified by other studies. It was suggested that pelvis retroversion correlates with decreased health status scores [7, 24]. Schwab et al. affirmed that pelvic tilt is highly correlated with patient self-reported function (ODI, SF-12, and SRS) [37]. Patients with suboptimal sagittal balance have significantly lower total and self-image subscale SRS-24 outcome scores compared to patients with optimal sagittal balance. Appropriate sagittal plane alignment is an important factor (and sometimes the most important) in clinical outcomes and patient satisfaction [36, 38, 39]. Sagittal balance has been pointed as a quality-of-life indicator [40]. Patients with fixed sagittal imbalance tend to expend more energy in gait and standing leading to chronic pain after surgery. Grobler et al. [41] described the sagittal imbalance with forward thrusting of the trunk as a source of pain and fatigue. Gautier et al. found no correlation between the type of LL (assessed by proximal vs. distal LL) and LBP [42]. These authors did not find any difference in segmental and total LL nor PI when comparing 74 subjects with a history of LBP to 152 asymptomatic subjects.

Chaléat-Valayer et al. reported the largest database in the literature on the evaluation of sagittal spinopelvic alignment in chronic LBP in comparison with the asymptomatic adult population [43]. Prospective adult cohorts of 198 subjects with chronic LBP (LBP cohort) and 709 controls without spinal disorder (control cohort) were compared. Significant but small differences are found for various parameters of pelvic, lumbar, and thoracic segments in subjects with LBP. The type of LL is also distributed differently among subjects with LBP. A significantly increased proportion of subjects with LBP stand with abnormally small SS (<35) and PI associated with a long but small LL, when compared to controls. There was a greater proportion of chronic LBP in patients with low SS, low LL, and small PI, suggesting the relationship between this specific pattern and the presence of chronic LBP.

Jackson and McManus [13] observed decreased total LL associated with decreased distal and increased proximal LL as well as a more vertical sacrum in 100 patients with LBP compared to 100 matched controls. Similarly, Barrey et al. [14] showed similar PI, but decreased SS, LL, and thoracic kyphosis (TK), as well as increased PT in 57 patients with DDD or hernia-

tion prior to lumbosacral arthrodesis, compared to 154 controls. Rajnics et al. [15] also observed significant differences for SS, PT, and LL—but not PI or TK—in 50 patients presenting with LBP and disk herniation compared to 30 healthy subjects. Other studies also reported conflicting results concerning [16] LL in patients with LBP.

Type 1 LL is the least common type of LL found in asymptomatic adults and in patients with chronic low back pain [18, 43]. Roussouly stated that type 2 LL has a trend to develop LBP greater than other types of LL. Other authors obtained a significantly greater proportion of subjects with LBP presenting type 2 LL (37.4 %), as compared to controls (23.3 %). At contrary, the proportion with type 3 LL was significantly decreased in the LBP cohort when compared to controls (38.9 % vs. 47.7 %) [43]. The proportion of subjects with either type 1 or type 4 LL was similar between the two cohorts. Therefore, the distribution of the types of LL was shifted from type 3 LL (and to a lesser extent type 4 LL) toward type 2 LL in subjects with LBP [43]. This finding confirmed that a greater proportion of subjects with chronic LBP tended to present a small SS (<35) associated with a long but small LL (flat back). Consequently in the LBP cohort, there was also a shift toward a greater proportion of subjects with abnormally small PI (usually associated with type 1 or type 2 LL). Because PI is a morphological parameter and is linked to the type of LL, it is possible that individuals with an abnormally small PI are at increased risk of LBP because of increased disk pressure/degeneration secondary to decreased LL and/or of suboptimal muscular/postural biomechanics needed to maintain adequate balance.

47.10 Sagittal Balance and Pathology

47.10.1 Mechanical Mechanisms of Compensation in Sagittal Balance Disturbance

In degenerative spine, with aging, the main pathological effect is a decrease of SSA that may be an expression of a true kyphosis or a loss of lordosis and sometimes both. Two main compensatory mechanisms are automatically involved in the restoration of the global balance (C7 plumb line over the sacrum):

- *Hyperextension of the adjacent vertebral functional segment unit* above or below the area of balance defect. This mechanism occurs when the spine is flexible. This local hyperextension may be painful by facet joints hyperpressure.
- *Posterior tilt of the pelvis*: increased PT and small PI or retroverted pelvis. This mechanism is possible when the spine is rigid either by degeneration or by iatrogenic unbalanced operated spine. Considering that PI and PT are linked by the relation PI = PT + SS, the theoretical maximum of PT compensatory increase for a very small SS (close to zero) has the same value of PI. It is easy to understand that the bigger is PI, the higher are the possibilities of pelvis retroversion. PT is limited by hip extension. The more the pelvis is retroverted, the more the hips are in extension. When hips extension possibilities are overpassed, the patient has to tilt the femoral shafts by flexing the knees. Even if this mechanism of compensation is efficient, it remains very uncomfortable for the patient, limiting ability of walking and even standing. On another hand, limitation of PT compensation in small PI pelvis (type 1 or 2 lordosis) may bring to an important global imbalance, with C7 plumb line forward the femoral heads even for a small loss of SSA. With aging and likely loss of lordosis, the hip may undergo retroversion, with increase of PT. Mac-Thiong et al. suggested that the nonpathological upper limit of PT would ideally be less than 50 % of PI [44]. A PT approaching the value of SS denotes imbalance. Likewise, the ideal values for SS should exceed 50 % of PI. In pathology, SS never reaches a negative position, less than 0. The minimal value of SS is 0, which is the horizontal sacral plate. This situation corresponds to the maximal retroversion possible.

If the PT is high (active compensation of imbalance), it is the PI that allows differentiating

a degenerated type 2 from a degenerated type 3 or 4. If PI and PT are high, the lordosis is a type 3 or 4 that has lost original lordosis. If PT is high but PI is low, this is a degenerated type 2 lordosis. A lumbosacral arthrodesis for type 3 or 4 should seek to restore lordosis, sometimes via an osteotomy, with the risk of perpetuating the important hip retroversion if the amount of lordosis is not sufficiently assured. If the PI is small, the need of restoring great lordosis has not the same importance. A lumbar fusion should restore the original type of lordosis, be it type 1, 2, 3, or 4.

Concerning normal or optimal value of PT, as PI = PT + SS, it would be reasonable to think that PT increases with PI and that the more the PI is high, the more the PT is high. This would be right without considering hips extension limits. It seems that the maximum of 25° for PT is the acceptable limit of hips extension. Over this limit, knees have to play a role, displacing the center of rotation of the set "pelvis-femur" on the femorotibial joint. This was first described by Mangione et al. [45] who described the pelvifemoral angle (PFA) (Fig. 47.5). PT is becoming an addition of PFA plus hips extension. More recently, Le Huec et al. [46] described the FBI angle considering that the true PT is the visible PT plus PFA and that the LL correction has to follow this hidden PT. In our opinion, the global positioning of the spine is following the true PT and when the LL reduction is obtained, the true PT is decreasing. If the PFA value is reached, hips extension limit is reached and the femur vertical position is now possible.

47.10.2 Gravity Stress on the Spine

To maintain the human body in erect position, the system has to "fight" against gravity. Of course, this stress increases in weight-bearing situation. To simplify, the authors take into account only the standing position. Different studies have shown that the gravity line in standing position is passing a little bit behind the center of the femoral heads and just forward the sacral plateau. The normal tendency of gravity is to flex the spine forward. To control the gravity force, the spinal system is built as a crane with the spine as a pylon and the spinal lumbar muscles acting as a counterforce against gravity [3]. As for a crane, the contact force (CF) applied on the basis of the pylon is the addition of both forces of gravity and lumbar muscles. To balance the crane, the moment of the gravity has to be equal to the lumbar muscles moment. Therefore, the more the gravity displaces forward, the more the muscle force increases and the more the CF increases. This is the situation in case of weight bearing where the charge's weight is coming in addition to the body gravity. In pathology, when the spine flexes forward with degenerative changes, the gravity moves forward increasing CF tremendously. The counteraction of the lumbar muscles may be quickly overpassed explaining the painful difficulties of standing position and the progressive flexion of the body during the day.

47.11 Spinopelvic Morphology and MR Imaging

Roussouly et al. noted a relationship between the four lumbar spinopelvic morphotypes and the degenerative findings depicted in CT scans and MRIs [47]. In an unbalanced spine, the forward momentum of gravitational force moves forward and the compensatory forces in the paravertebral musculature increase, which increases the contact force. The contact force distribution into the joints of the functional spine unit (into the disk or into facet joints) is made according to the global sagittal orientation of the column. If the spine is in flexion, the contact forces are forward, over the vertebral bodies and disks. If the spine is in extension, contact forces pass backward over the articular facets (Fig. 47.3). Roussouly hypothesized that each of the four spinopelvic morphotypes would have a different tendency to degenerate according to how the forces would interact in the disk or in the facet joints.

Moreover, depending on the orientation of vertebral plates and disk, the contact force may be divided into two as a result, parallel and perpendicular to the lower plateau. A strong slope of

the plate increases resultant parallel, shear/slipping forces. When the plateau is slightly inclined, it is the force of pressure that is increased (Fig.).

In "flat back" or in lumbar kyphosis, the resultant contact forces are ahead and the forces of disk pressure are increased. In a lumbar spine with much lordosis or in lumbar hyperextension, the contact forces are exerted on the posterior parts and over the facet joints. The sloping plateau favors slipping and may constitute the olisthesis. The overpressure on posterior articular facet may determine facet arthrosis and degenerative spondylolisthesis.

Beginning with four spinopelvic morphotypes of lordosis and their specific organizations, Roussouly et al. sought to deduct the hypothesis of types of lordosis' degenerative evolution [6].

Type 1 lordosis (Fig. 47.8a): defined by a small SS (<35°). The PI is often small (<45°), with a very short but marked distal lordosis and a thoracolumbar kyphosis. This geometry may promote a short distal (L4–L5–S1) lumbar hyperextension and a zone of disk overpressure at the level of the thoracolumbar kyphosis. The likely degenerative evolution can combine discopathies by overpressure in the thoracolumbar kyphosis and retrolisthesis in the junctional zone. In the region of short distal lordosis (L4–L5 and mainly L5–S1), disks often have normal appearance on magnetic resonance imaging (MRI). However, mechanical stress is felt posteriorly in the very distal acute lordosis, being observed by interspinous contact when the individual is upright and also with the densification of the joints in the CT scan. This local hyperextension may explain root pain in standing position by narrowing the foramens when extension is at its maximum. The distal lumbar hyperextension is proportional to the amplitude of thoracolumbar kyphosis. Lumbar distal hyperextension (marked distal short acute lordosis) can lead to lysis of L5 isthmus by fatigue fracture due to impaction of the inferior articular facet joints. This explains the L5-S1 "nutcracker" mechanism associated with isthmic spondylolisthesis in patients with low PI [6] (Fig. 47.5). Pain may occur. As PI is small, the possibility of compensation to a sagittal imbalance is small.

Type 2 lordosis (Fig. 47.8b): defined by a small SS (<35°) and PI generally small (<45°). The division between lordosis and kyphosis is smooth, but the overall lumbar lordosis angle is small, featuring a flat back. The small lordosis displaces the contact forces forward. The intervertebral plates are horizontalized. The most important forces affect the distal lumbar plates L4–L5 and L5–S1. The disk overpressure may be responsible for early disk degeneration manifested by a central disk herniation or early disk degeneration at multiple levels. This may be the case of many lumbar disk herniations in individuals in the third or fourth decades of life. Barrey stated that disk herniations in subjects under 45 years old have a trend to develop in type 2 (flat back) lordosis [18]. However, after 45 years old, there is a homogeneous distribution of disk herniations between all four types of lumbar lordosis. A type 2 lordosis is identified through the small PI and there are small retroversion possibilities. When conducting an arthrodesis, there is no need to obtain significant lordosis. However, care must be taken not to further reduce the small amount of lordosis. The patient must be aware of this, understanding that his/her spine has lower possibilities of compensation for loss of lordosis due to aging and that more spinal troubles are a real possibility due to his/her spinopelvic anatomy.

Type 3 lordosis (Fig. 47.8c): harmonious and theoretically is not prone to a particular type of degeneration.

Type 4 lordosis (Fig. 47.8d): has a large SS (>35°) and large PI (>55°). It features smooth curvature with large lordosis. The lordosis angle and the number of vertebrae in lordosis are high. The contact forces are moved backward, and in front, the disks are protected from early degeneration. The slope of the distal disks L4–L5 and L5–S1 may predispose to spondylolisthesis by isthmic lysis by shearing forces. 80 % of the L5 isthmic lyses have a large PI (>60°). The type 4 without isthmic lysis can degenerate by two modes, early or late:

Early: the mechanical loads on the posterior facet joints may cause a later interapophysary osteoarthritis (Fig.), and eventually a degenerative

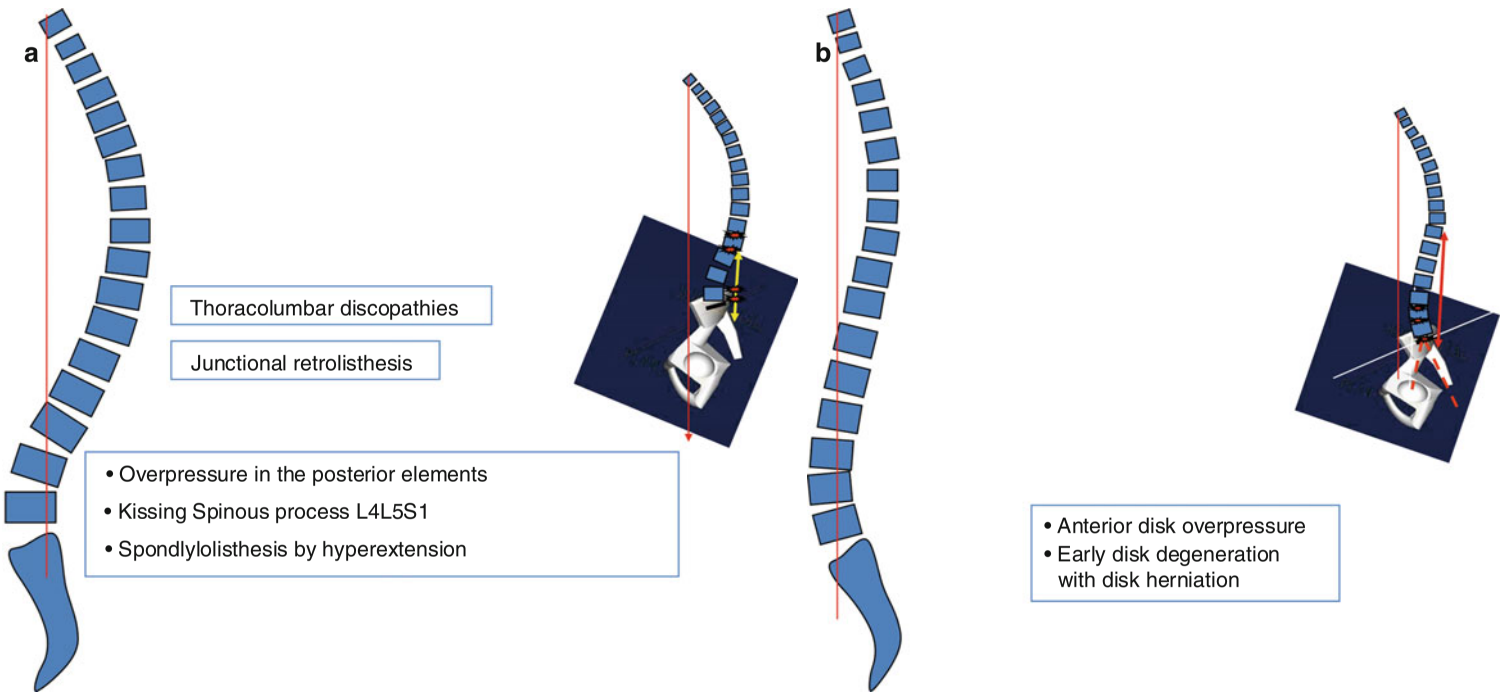

Fig. 47.8 (**a**) Mechanical consequences of a type 1 lordosis. Note a short distal (L4–L5–S1) lumbar hyperextension and a zone of disk overpressure at the level of the thoracolumbar kyphosis. The likely degenerative evolution can combine discopathies by overpressure in the thoracolumbar kyphosis and retrolisthesis in the junctional zone. (**b**) Mechanical consequences of a type 2 lordosis (harmonious flat back). Note a short distal (L4–L5–S1) lumbar hyperextension and a zone of disk overpressure at the level of the thoracolumbar kyphosis. The likely degenerative evolution can combine discopathies by overpressure in the thoracolumbar kyphosis and retrolisthesis in the junctional zone. (**c**) Type 3 lordosis. (**d**) Type 4 lordosis, Harmonious but long and intense curvature

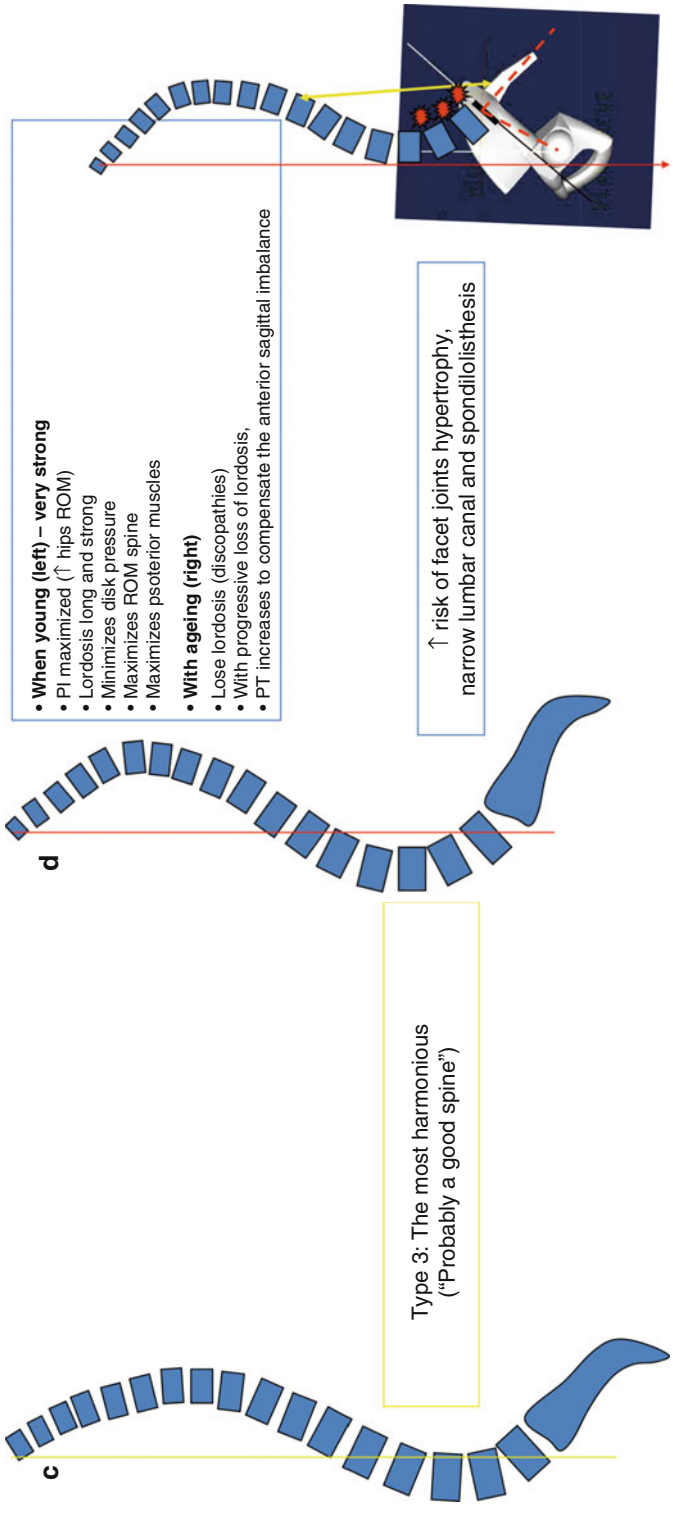

Fig. 47.8 (continued)

spondylolisthesis especially in L4–L5, by functional derangement of the joint and disk.

Late: it is frequent in older individuals, where disk degeneration is linked to aging. The loss of disk height causes a lumbar hypolordosis and, as a result, retroversion of the pelvis. This situation of flat back with retroverted pelvis must be distinguished from a true type 2 where it is a native flat back without pelvis retroversion

The type of lordosis, be it type 2 or type 4, may affect the morphology of posterior vertebral elements (facet joints/interspinous processes). According to the arc of a circle mathematical model, in type 2 lordosis, as the lordosis is smooth and flat, the anterior body line exhibits a huge radius for the circle of the inferior arc and almost the same for the facet joint line. This is not the case in type 4 lordosis where the radiuses of the arcs are smaller, with inconsequence of a smaller length of the posterior facet line (Fig. 47.9a). Consequently, we may expect larger spaces for facets and spinous processes in type 2 than in type 4 lordosis and maybe more contact between facet joints in type 4 lordosis, what would be a predisposing factor for facet joint arthritis and arthrosis (Fig. 47.9b). Facet joints and spinous processes are probably bigger in type 2 than in type 4. Anatomical or radiological studies relating to the size of the facet joints to the spinopelvic morphotype of lordosis are required to confirm this hypothesis.

In an asymptomatic population, types 1 and 2 represent only 30–35 % of subjects [18]. They are significantly more frequent in the group of herniated disks and disk disease. In contrast, there are few types 1 and 2 in the group of degenerative spondylolisthesis. Types 3 and 4 were found in the group of discopathies and herniated disks while they constitute nearly 85 % of lordosis found in the group of degenerative spondylolisthesis. These results show the influence of the very probable spinal statics in the determination of spinopelvic type.

- In the asymptomatic population ($n = 160$), Barrey found 21,2 % as type 1, 11,2 % as type 2, 37,5 % as type 3, and 30 % as type 4. In total, it seems that there are disk herniation, DDD, spondylolisthesis, and lumbar

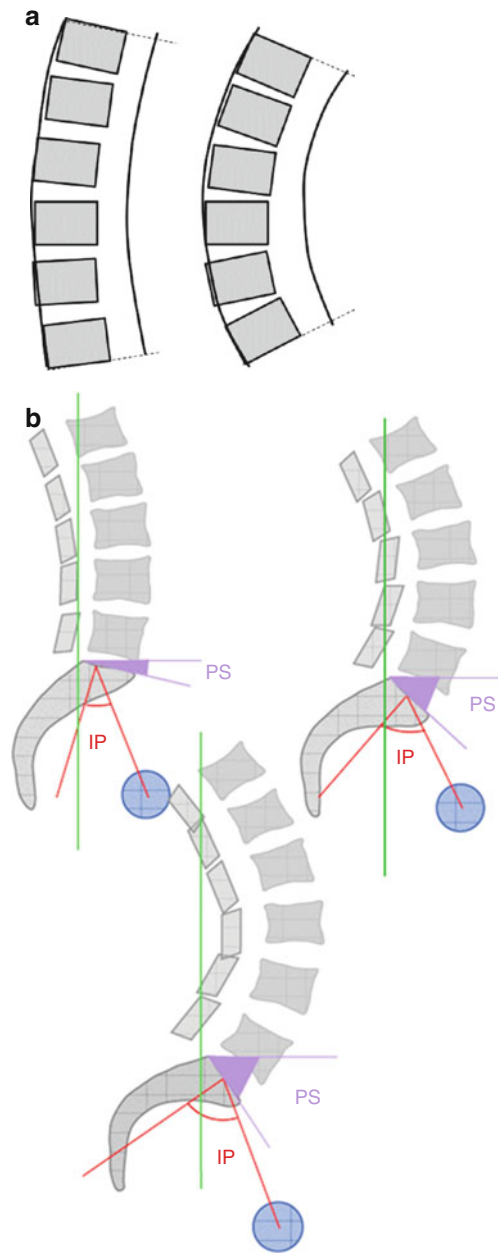

Fig. 47.9 (**a**) In a type 2 lordosis (*left*), the area occupied by posterior elements is longer for a same number of vertebrae than in a type 4 lordosis (*right*). By this way, posterior elements (facets and spinous processes) are smaller in type 4 than in type 2 (From Roussouly and Pinheiro-Franco [17]; with permission). (**b**) Vertical forces and different spinopelvic morphotypes. Note how these forces may affect posterior vertebral elements, depending on types of lumbar lordosis. Type 4 lordosis (*bottom*) should be more prone to facet joint disease. Less concentrated lordosis (*top left*) should be less prone to facet problems (more facet "impaction" when marked lordosis exists) (From Barrey [18]; with permission)

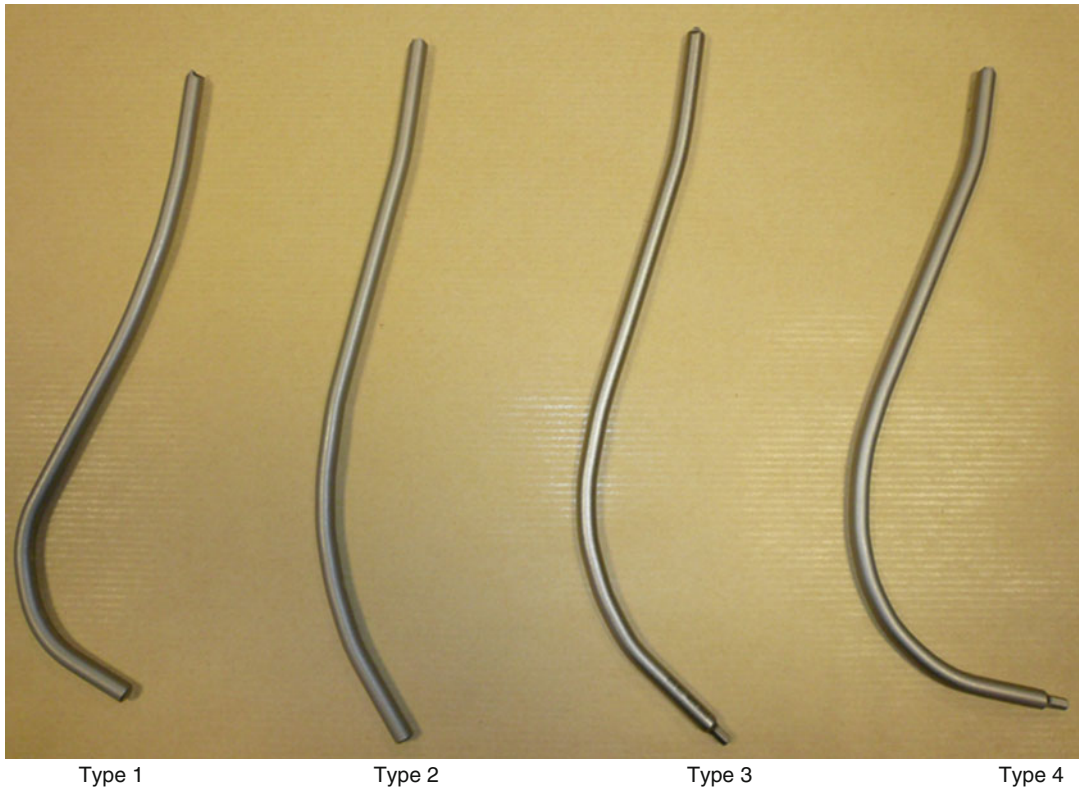

Fig. 47.10 When performing a spine fusion, it is mandatory to give the proper lordosis to the fused part of the spine according to the global shape of the spine and pelvis

narrow canal for each type of lordosis but there are fairly clear trends. The less lordotic curvatures are rather prone to disk problems while lordosis with strong curvatures is more susceptible to degenerative slippages. In the group of disk pathology, the spinal profile varies significantly with age. In young subjects with disk problems (lumbar disk herniation or discopathies), the morphotype is formed in nearly two-thirds of cases of lower PI. On the contrary, with aging, the prevalence of disk problems tends to join the normal population. In other words, the subjects presenting discopathies or herniated disk disease early in life have a tendency to present a particular spinal profile (type 1 or 2). With aging, the findings of disk problems including lumbar disk herniations have a much more homogeneous distribution in the range of the four spinopelvic morphotypes.

47.12 How to Organize a Spinal Arthrodesis

When performing a spine fusion, it is mandatory to give the proper lordosis to the fused part of the spine according to the global shape of the spine and pelvis (Fig. 47.10).

47.12.1 Strategy of Fusion in Case of Small PI

Lumbar lordosis may have an aspect of type 1 or type 2.

Type 1 evolution: Degenerative effect may induce TL kyphosis and promote a short hyperlordosis by compensation. In young patients, the surgical strategy has to focus on TL kyphosis reduction in order to obtain a compensative reduction of lumbar hyperlordosis.

In older patients, the TL kyphosis reduction may be more demanding and may pose risk for pseudarthrosis. The authors propose to maintain the TL kyphosis with a partial reduction and to maintain the type 1 shape by fusing lower lumbar spine with a short hyperlordosis until the sacrum.

Type 2 lordosis: the lumbar spine has a global aspect of a flat back, and in the worse degenerative evolution, a lumbar kyphosis may occur. Restoration of a small angle of lordosis is sufficient. Sometimes, in case of lumbar kyphosis, a PSO may be necessary to restore an adequate lordosis. A small-angle PSO is sufficient enough to rebalance the spine. As there is a poor impact of lumbar reduction on the thoracic kyphosis, the risk of adjacent kyphosis is small, and it is not necessary to address the thoracic spine in long lumbar fusions.

Type 4 evolution: Two situations are possible—the spine has still a big amount of lordosis or the spine has lost the lumbar lordosis and the pelvis is in retroversion (high PT).

- When the lumbar spine remains hyperlordotic, it is mandatory to maintain this long and curved lordosis. As we have seen that the lower arch of LL is equal to SS, the more SS is tilted, the more the lower arch is curved. This is the reason why it is mandatory to restore the maximum of curvature between L4, L5, and S1. A short L4–L5 fusion for a degenerative L4–L5 spondylolisthesis without enough extension will bring painful compensatory hyperextension to the adjacent level L3–L4.
- When the lumbar lordosis is lost, the authors have observed that the balance compensation is obtained by pelvis retroversion and, sometimes, by a flat thoracic spine due to the extension of the thoracic area reducing the normal kyphosis. This situation is very challenging. Restoration of a big amount of lordosis necessitates osteotomies either by Smith-Petersen or PSO. Problems of junctional kyphosis may occur because of the spontaneous changes of thoracic spine in relation with the new lumbar shape. This relation between thoracic and lumbar spine lordosis has to be analyzed further to better understand the problem of junctional kyphosis.

Conclusion

To obtain the sagittal balance of the human body in upright posture is not only to put C7 over the sacrum. The various spinopelvic shapes, determined by PI ranges of values, induce different spinal morphologies. The mechanical arrangements of each morphotype permit to explain the physical properties of one spine and the degenerative changes in the elderly. Treatment strategies for spinal pathologies have to take into account this strong relation between spine and pelvis, mainly when planning surgical arthrodesis where mistakes in balance obtention may bring to unsuccessful situations.

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48 Compensatory Mechanisms Contributing to the Maintenance of Sagittal Balance in Degenerative Diseases of the Lumbar Spine

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Abbreviations

LL	Lumbar lordosis
PI	Pelvic incidence
PT	Pelvic tilt
SS	Sacral slope
SSA	Spinosacral angle
SVA	Sagittal vertical axis
SVA/SFD	Ratio SVA/sacro-femoral distance
TK	Thoracic kyphosis

48.1 Introduction

The aging spine is characterized by degenerative disk disease, hypertrophic facet joints, arthritis, bone remodeling, and atrophy of extensor muscles. This may result in a progressive kyphosis of the lumbar spine with the risk of developing progressive sagittal imbalance [1, 2]. It has been extensively reported in the literature that patients with multi-segmental lumbar degenerative disk

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_48

diseases often present with significant modifications of the sagittal balance and may, in fact, present with anterior sagittal imbalance, loss of lumbar lordosis, and increased pelvic tilt [3–6]. In these patients the anterior imbalance results mainly from the loss of lumbar lordosis due to the degeneration of lumbar disks, but in some cases, the respective part of structural and postural loss of lordosis is difficult to determine. These changes in spinopelvic alignment result in deterioration of clinical status and functional scores [7].

Except for the loss of lordosis, which is related to the degenerative process, the other spinopelvic parameter changes (i.e., decrease of sacral slope, reduction of thoracic kyphosis, increase of upper lumbar lordosis) generally correspond to compensatory mechanisms. These compensations represent a compromise for the patient in order to maintain an erect posture in a physiological position with minimal muscular effort. To optimize the management of lumbar degenerative disorders and to avoid underestimating the severity of degenerative disease, it is important to recognize and take into consideration these compensatory mechanisms.

In the asymptomatic population, correlations between the shape of the pelvis (reflected by the pelvic incidence), the sacral slope, and the sagittal curves of the spine (especially lumbar lordosis) have been well documented in the literature [1, 6, 8–13]. The pelvic incidence represents the only parameter not modified by degenerative changes, thus providing useful information on the original morphology of the spinopelvic complex. Consequently, using these correlations from the normal population, it is relatively easy to understand the changes of spinopelvic parameters for patients with degenerative disorders in the lumbar spine. The compensatory mechanisms contribute to maintaining normal overall sagittal balance of the spine above the pelvis in an economic position, limiting the consequences of lumbar kyphosis in terms of sagittal anterior imbalance, and minimizing muscles efforts. They may involve the spine adjacent to the kyphotic segment, the pelvis, and/or the lower limbs. These mechanisms may present isolated or combined (in case of severe deformity), depending on the intensity of the sagittal imbalance [14].

The objective of this chapter is to describe in details all of these different compensatory mechanisms in patients with severe degenerative lumbar spine disorders.

48.2 Assessment of Global Balance

It is essential to have an optimal congruence between pelvic and spinal parameters in order to achieve an economic posture placing the axis of gravity in a physiological position with minimal muscle efforts [8, 10, 15, 16]. When analyzing the spinopelvic alignment of patients with spinal deformities, the first step should be to evaluate the global balance of the patient. This can be done optimally by using strength plate and measuring positioning of the gravity axis in the sagittal plane [13]. However, in clinical practice, global balance is appreciated more simply by describing the relative positioning of the spine in reference with the pelvis on standing full spine radiographs. Global sagittal alignment is typically determined by calculating the position of the vertebra C7 related to the sacral plate. The offset (distance in mm) is measured between the posterior corner of the sacrum and the vertical line passing through the vertebral body of C7 (i.e., sagittal vertical axis, SVA). Instead of measuring a linear distance, we recommend using angular measurements and/or ratios to characterize the positioning of C7 in relation to the sacrum. Angular parameters are assessed via the spinosacral angle (SSA), and the ratio corresponds to the SVA/sacro-femoral distance ratio (SVA/SFD). These two parameters have already been reported and validated [3, 17].

The SSA was defined as the angle between the sacral plate and the line connecting the centroid of C7 vertebral body and the midpoint of the sacral plate (Fig. 48.1a). In the normal population, the mean value of this angle is 135° ± 8 [17].

The method to measure SVA/SFD ratio is presented in Fig. 48.1b. This ratio is equal to zero, when C7 plumb line projects exactly on

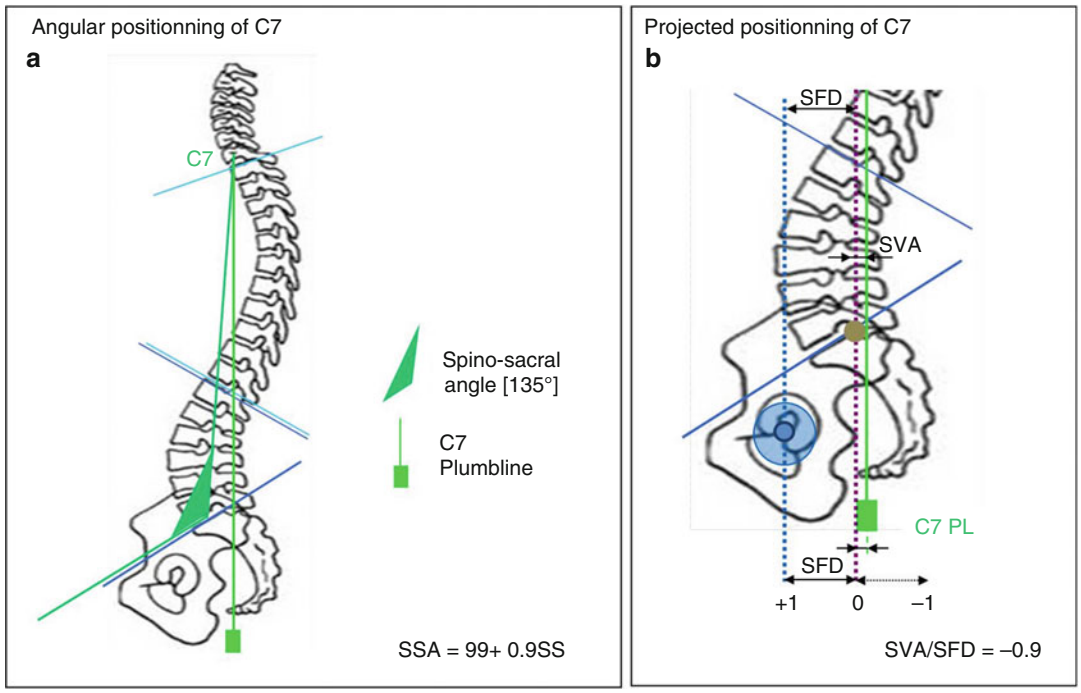

Fig. 48.1 Evaluation of global sagittal alignment using the spinosacral angle (**a**) and the SVA/SFD ratio (**b**). The SSA is defined as the angle between the sacral plate and the line connecting the centroid of C7 vertebral body and the midpoint of the sacral plate [17]. Sacro-femoral distance (*SFD*) is the horizontal distance between the *vertical* bicoxofemoral axis and the vertical line passing through the posterior corner of the sacrum. The horizontal distance between C7 PL and the posterior corner of the sacrum (i.e., SVA) was also measured. Then we calculated the SVA/SFD ratio corresponding to the ratio between SVA distance and SF distance [3]. This ratio is equal to zero, when C7 plumb line projects exactly on the posterior corner of the sacrum, and to one, when C7 plumb line projects exactly on the bicoxofemoral axis. It is negative when C7 plumb line projects posteriorly to the sacrum and more than one when C7 plumb line projects from anterior to the femoral heads [3] (From Barrey et al. [3])

the posterior corner of the sacrum, and to one, when C7 plumb line projects exactly on the bicoxofemoral axis. It is negative when C7 plumb line projects posteriorly to the sacrum and more than one when C7 plumb line projects from anterior to the femoral heads. In the normal population, the value of this ratio is -0.9 ± 1 [3].

The spinosacral angle and the C7/SFD ratio facilitate the evaluation of the global sagittal alignment of the spine above the pelvis. According to the severity of the imbalance, we propose the identification of four different stages (from I to IV): balanced, compensated, partially compensated, and imbalanced (Fig. 48.2). In the last stage, the compensatory mechanisms are not efficient enough to maintain the sagittal balance and C7 plumb-line falls in front of the femoral heads (SVA/SFD ratio >1). An illustration of each situation is presented in Fig. 48.3.

48.3 Compensatory Mechanisms

Compensatory mechanisms can be observed in the spine, the pelvis, and/or the lower limb areas and are summarized in Fig. 48.4. Although these mechanisms are rarely observed all together in the same patient, they are usually associated at different degrees, depending mainly on the stiffness of the spine, the musculature status, painful phenomenon, and the severity of the imbalance.

Their basic concept is to extend adjacent segments of the kyphotic spine, facilitating the acquisition of compensated spine. Most of these

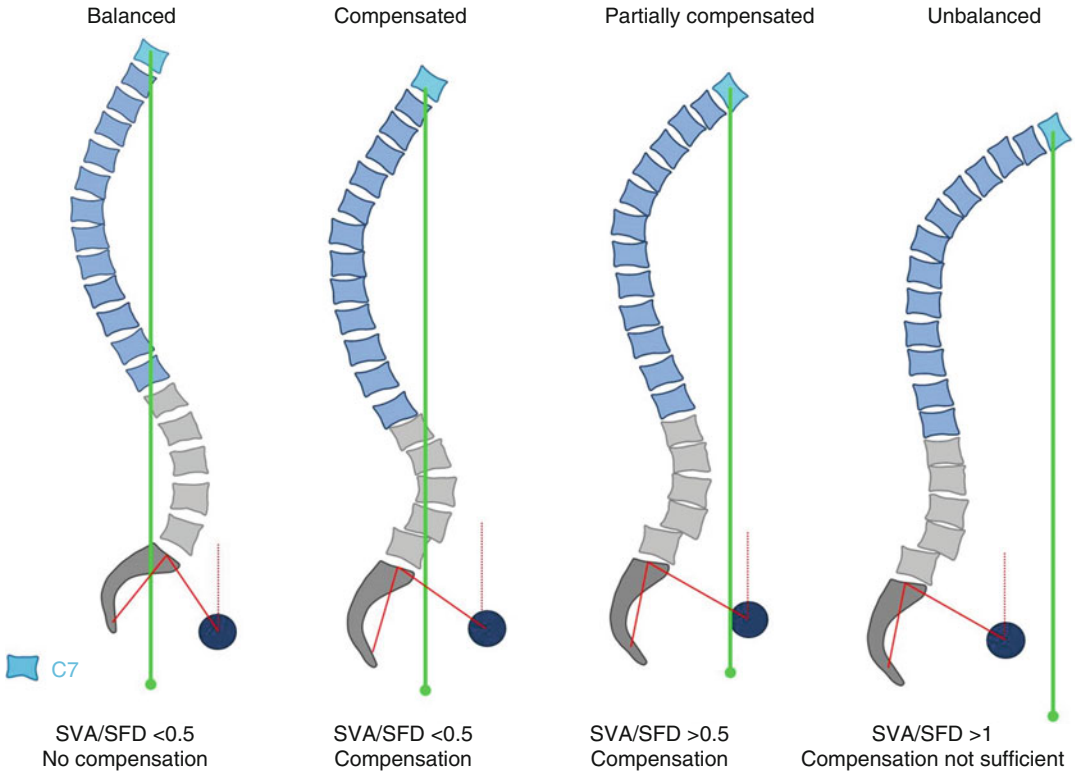

Fig. 48.2 Classification of global sagittal alignment in 4 stages with respect to the severity of the imbalance. *Balanced*: C7 plumb line falls close to the posterior corner of the sacrum, SVA/SFD ratio is close to 0, there is no compensation. *Compensated*: C7 plumb line is closer to the posterior corner of the sacrum than to the femoral heads, SVA/SFD ratio is <0.5, compensation is present. *Partially compensated*: C7 plumb line is closer to the femoral heads than to the posterior corner of the sacrum, SVA/SFD ratio is >0.5, compensation is present. *Imbalanced*: C7 plumb line is placed in front of the femoral heads, SVA/SFD ratio is >1, compensation is present but not sufficient to keep the balance

mechanisms result from muscle action, thus exposing the subject to chronic pain and muscle fatigue.

To understand the variations of positional parameters such as sacral slope (SS), pelvic tilt (PT), LL, and TK in the patients' population, we previously published values of six different classes of pelvic incidence in a normal control group of 154 subjects [4]. Values of positional parameters for each class of PI (from I to VI corresponding to a progressively increase of the PI value) are summarized in Table 48.1. Theoretical normal values for spinopelvic parameters (i.e., theoretical PT and theoretical LL) may also be estimated from mathematical relations (Table 48.2). Otherwise, to analyze segmental changes, we have to keep in mind that the L4–S1 segment provides the two third of the total lumbar lordosis [6, 11, 19].

48.3.1 Spine

48.3.1.1 Cervical Hyperlordosis

Although in most cases the cervical spine is not well evaluated on full spine radiographs, it should be included in the sagittal balance assessment since compensatory curvature can be observed at this level. Hyperextension of the cervical spine is a typical compensatory mechanism above a thoracic hyperkyphosis in order to maintain the horizontality of the gaze. Inconvenience related to

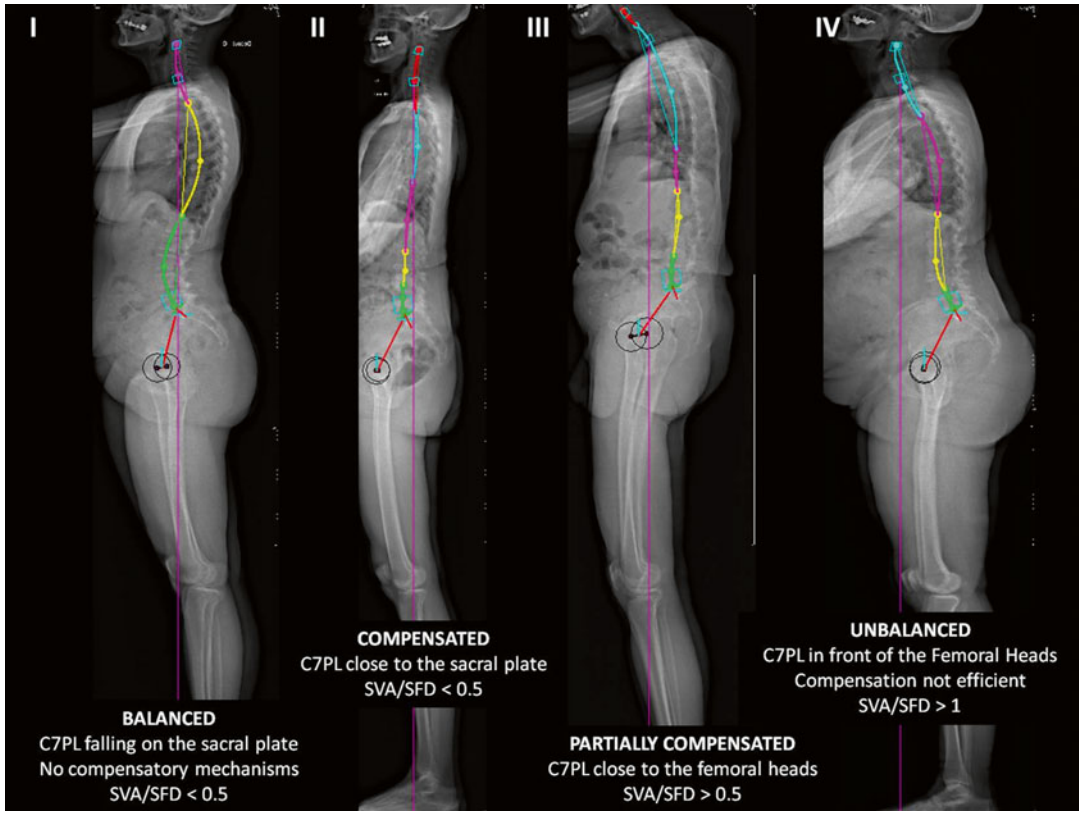

Fig. 48.3 Illustrations showing the four situations of sagittal balance

this hyperlordosis is not negligible – resulting in acceleration of degenerative changes in the cervical spine (i.e., hypertrophic facet joints arthritis and kissing spinous processes), presence of axial neck pain, foraminal stenosis, and the risk to develop spondylotic myelopathy.

48.3.1.2 Reduction of Thoracic Kyphosis

Reduction of thoracic kyphosis permits the limitation of anterior translation of the axis of gravity and is typically observed in young patients with a flexible spine (Fig. 48.5). It is the consequence of active muscle actions and therefore implies a good quality of erectors muscles of the spine. Takemitsu et al. described this mechanism for patients with lumbar kyphosis [20]. In a previous work, we also found that patients with degenerative disk disease and disk herniation were characterized by flat spine with significant reduction of both lumbar lordosis and thoracic kyphosis. This profile was more marked for patients with disk diseases below 45 years old [4]. Our findings were concordant with those reported by Rajnics et al. through a similar study [21]. When the spine is rigid (aging of the spine is kyphosis and ankylosis) or in case of atrophy of spinal erectors, it is not possible for the patient to reduce the magnitude of the thoracic curve.

In severe cases of sagittal imbalance, reduction of thoracic curve is not sufficient (Fig. 48.6). Considering that the compensatory thoracic hypokyphosis is potentially reversible after restoration of sagittal balance, it is thus possible to limit the extent of the fusion and preserve the thoracic spine mobility. Reappearance of physiological thoracic kyphosis may be observed postoperatively after correction of the lumbar spinal deformity (Fig. 48.5).

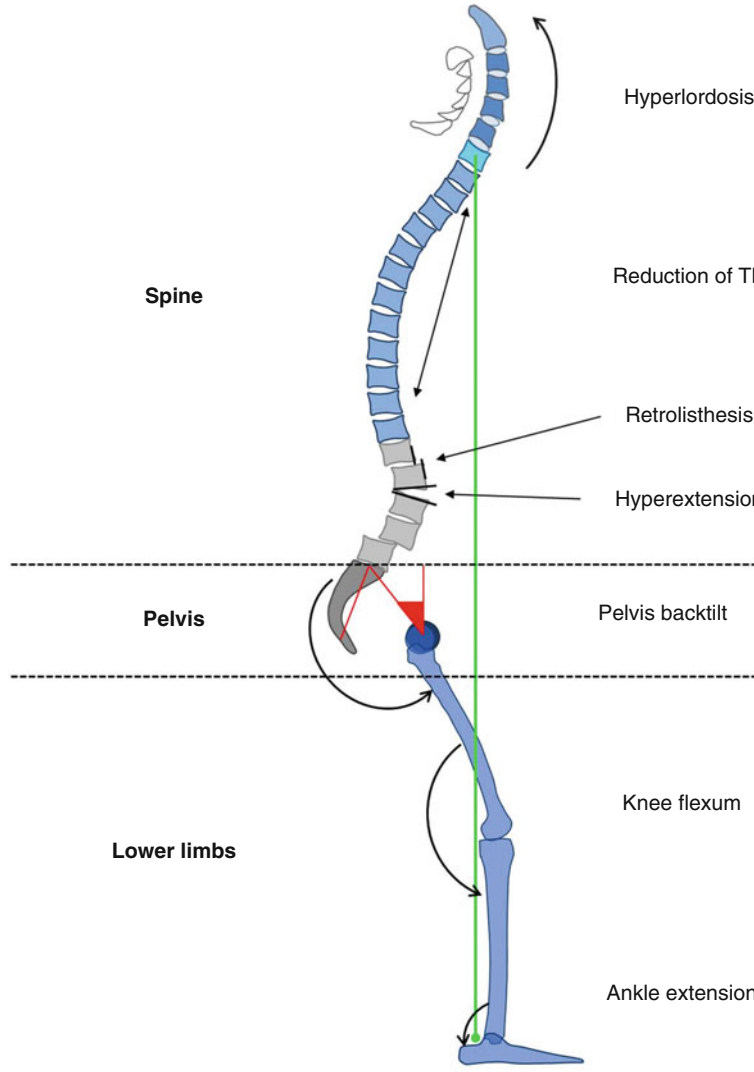

Fig. 48.4 Sagittal imbalance and the different compensatory mechanisms in the spine, pelvis, and lower limb areas (From Barrey et al. [18])

Table 48.1 Classes of pelvic incidence and corresponding values of spinopelvic positional parameters from a group control of 154 subjects [4]

	n	PI	PT	SS	LL	TK
I 28° < PI < 37.9°	12	35.4 ± 1.3 [33.7–37.9]	3.9 ± 4.5 [−1.5–13.3]	31.5 ± 5.2 [21.2–38.5]	53.3 ± 6.6 [41.2–62]	43.8 ± 9.1 [22.5–51.5]
II 38° < PI < 47.9°	44	42.7 ± 2.8 [37.9–47.6]	8.9 ± 4.8 [–5.1–18.2]	33.8 ± 4.8 [23.1–48.4]	55.5 ± 8 [41.5–76.5]	48 ± 8.8 [24–64.7]
III 48° < PI < 57.9°	59	52.6 ± 2.8 [48.2–57.4]	12.5 ± 5.6 [−1.2–23.2]	40.1 ± 5.5 [28.2–52.9]	61.5 ± 8.4 [43.1–81.9]	47.4 ± 10.7 [24–70.3]
IV 58° < PI < 67.9°	26	62.6 ± 2.8 [58.2–67.6]	15.8 ± 4.3 [7.1–26.8]	46.8 ± 4.2 [37.9–58.5]	68.3 ± 5.1 [60.9–76.3]	47.6 ± 7.8 [34.7–64.7]
V 68° < PI < 77.9°	11	72.6 ± 2.8 [69.6–77.4]	19.7 ± 5.5 [12.6–27.9]	52.9 ± 5.2 [46.2–59.6]	74.9 ± 6.8 [62.2–81.6]	46 ± 10.2 [29.7–62]
VI 78° < PI < 87.9°	2	81.4 ± 3.3 [79.1–81.4]	21.9 ± 12.3 [13.2–30.6]	59.5 ± 9 [53.1–65.9]	76 ± 8.3 [70.1–81.9]	44.6 ± 12.2 [36–53.3]

Table 48.2 Theoretical pelvic tilt and lumbar lordosis according to the pelvic incidence [4]

PI class	PI (°)	Theoretical PT (°)	Theoretical LL (°)
I	<38	4	PI + 18
II	38–47	8	PI + 13
III	48–57	12	PI + 9
IV	58–67	16	PI + 6
V	68–77	20	PI + 2
VI	>78	24	PI – 5

As examples, for PI measured to 40°, expected PT should be 8° and LL should be 53°; for PI measured to 52°, expected PT should be 12° and LL should be 61°; and for PI measured to 64°, expected PT should be 16° and LL should be 70°

48.3.1.3 Hyperextension of Adjacent Segments

Hyperextension of adjacent segments is a very common local compensatory mechanism to limit the consequences of lumbar kyphosis on the shift of axis gravity (Fig. 48.7). Previous studies demonstrated that low back pain subjects were characterized by less caudal lordosis, a more vertical sacrum, and greater rostral lumbar lordosis [5, 23]. Higher values of proximal lumbar lordosis signify more extension in the upper lumbar spine. Recently, Schuller et al. found that upper lumbar spine (L1–L2

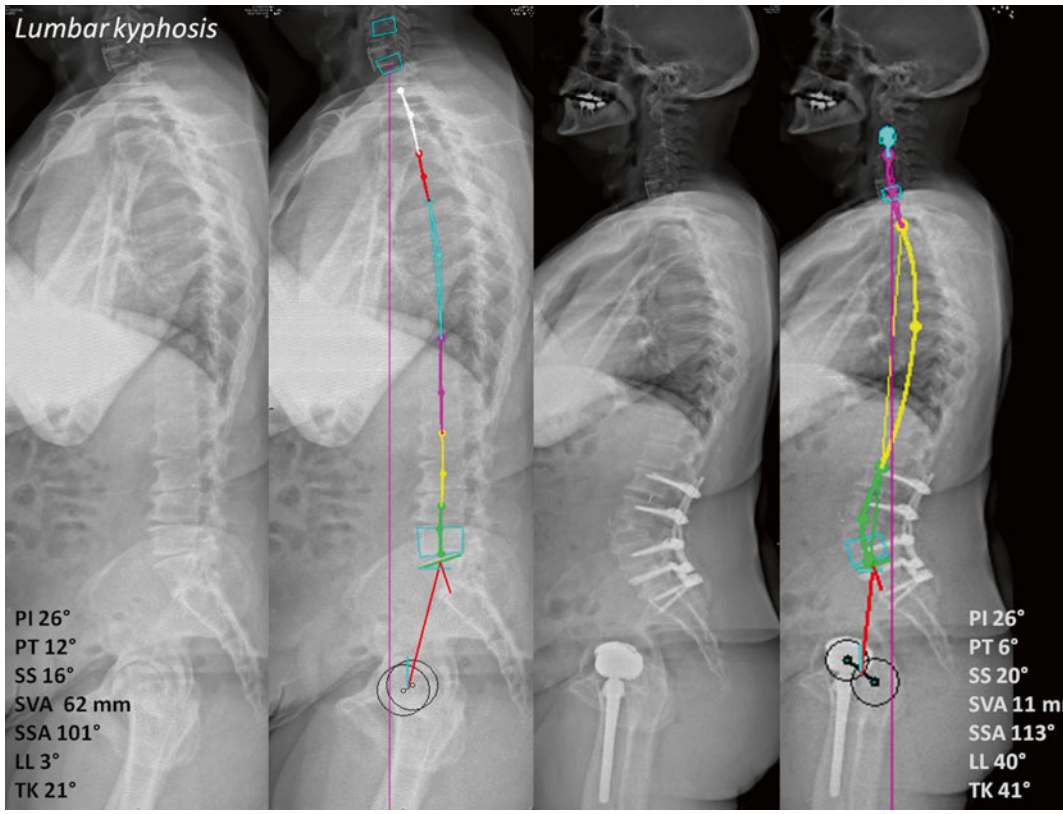

Fig. 48.5 Patient with lumbar kyphosis due to severe multilevel degenerative disease stenosis from L2 to S1. The patient is unbalanced (C7PL/SFD >1). Thoracic spine is clearly flattened (thoracic curve measured to only 21°). PI was measured to 26°, PT was 12°, and SS was 16°. Compared to group control from normal and asymptomatic population, we should expect value of PT around 4°. After corrective surgery in the lumbar spine and restoration of good sagittal balance (C7PL/SFD <0.5), we noted the reappearance of the thoracic kyphosis and reduction of PT (from 12 to 6°)

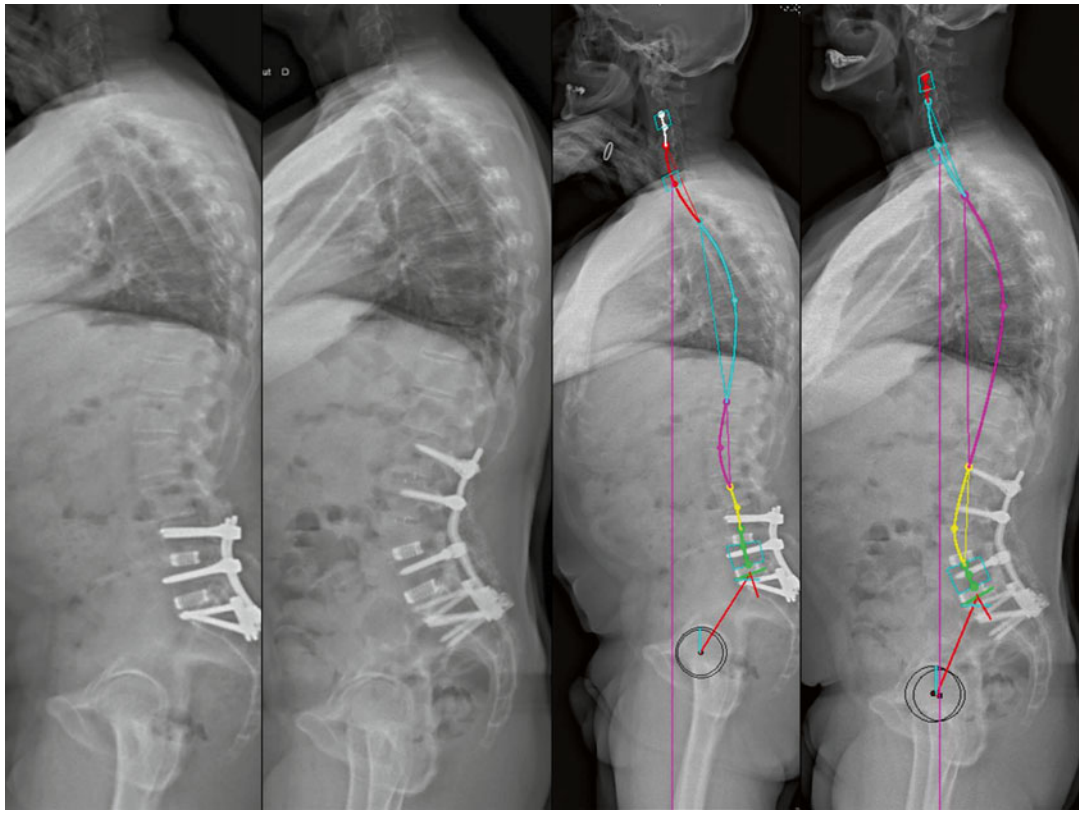

Fig 48.6 Illustration of patient presenting with thoracolumbar lordosis above a hypolordotic construct from L4 to S1

and L2–L3 segments) was more extended for patients with L4–L5 degenerative spondylolisthesis [24]. On the other hand, in cases of thoracolumbar kyphosis, hyperlordosis in the lower lumbar spine (L4–S1) is very common (Fig. 48.7) [25].

Hyperextension can be regional (multisegmental) or local (mono/bi-segmental). Regional hyperextension may affect the thoracic spine, the thoracolumbar junction, and a part of the lumbar spine (the upper or the lower part). For example, lower lumbar hyperlordosis is typically observed in patients with thoracolumbar kyphosis, regardless of the kyphosis (congenital, degenerative, posttraumatic, etc.).

Local hyperextension in this situation is sufficient to position the upper spine posteriorly; however, this generates increase of stresses on posterior structures (Fig. 48.7), exposes to the risk of retrolisthesis, and may result in accelerated facet joint arthritis, interspinous hyperpressure (Baastrup disease), and sometimes isthmic lysis.

From a biomechanical point of view, we consider that compensatory discopathy must be differentiated from classical aging discopathy (Fig. 48.8). Compensatory discopathy is characterized by a discal hyperextension (more than 15°) compensating for a loss of lordosis. It is associated with increased stresses on the posterior elements with facet arthritis and hyperpressure contact between the spinous processes. On the contrary, aging discopathy (the most frequent type) is characterized by a disk narrowing with parallel end plates resulting in loss of lordosis. The spinal segment is kyphotic in aging DDD but hyperextended in compensatory DDD, with increase of stresses on the posterior elements. The sagittal orientation of disk space (extended, neutral, kyphotic) is therefore very important to consider when analyzing consequences of degenerative discopathy on global balance.

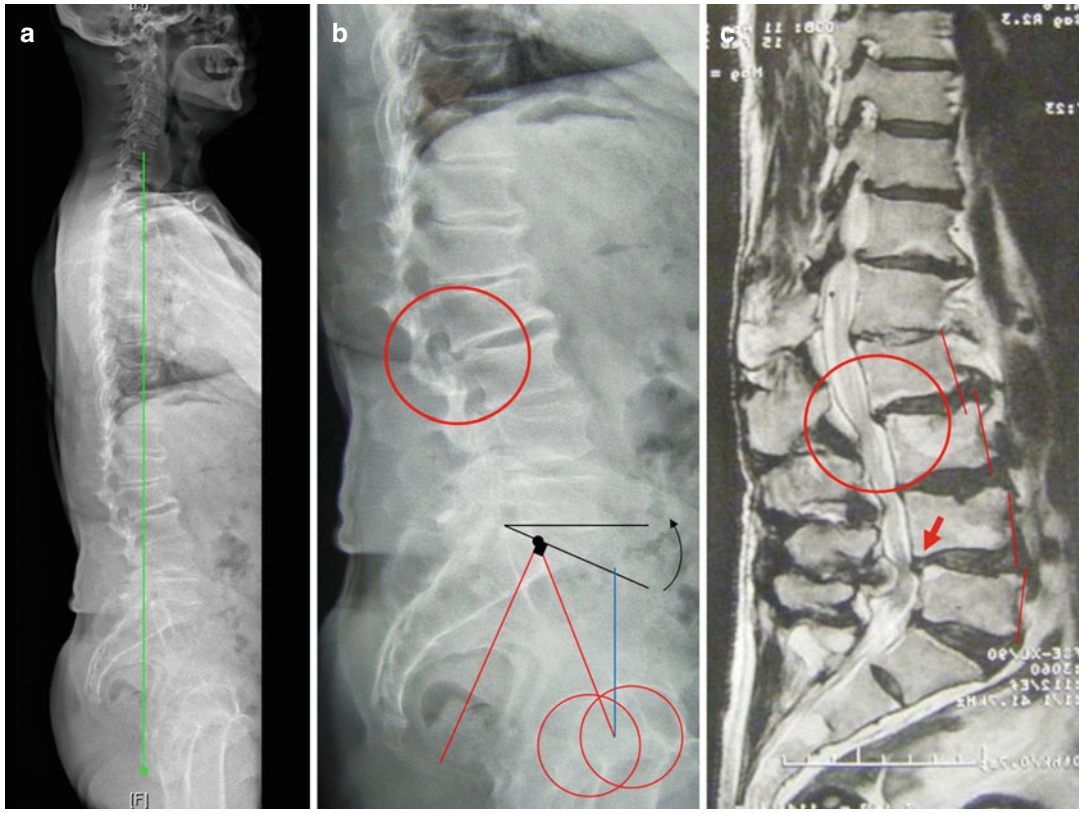

Fig. 48.7 Patient with lumbar stenosis from L2–L3 to L4–L5 and thoracolumbar kyphosis: full spine radiographs (**a**), X-rays focused on lumbo-pelvic zone (**b**) and sagittal T2-weighted MRI sequence (**c**). The patient is well balanced (C7PL/SFD is −0.3); however, some compensatory mechanisms are present in the lumbar area. Hyperextension is observed at L5–S1 (*curved black arrow*) (local lordosis was measured to 24°), and there is multilevel retrolisthesis at L2–L3 (*red circle*) and L4–L5 (*large arrow*). The pelvic tilt was quite normal as it was calculated to 22° and the PI to 46° (From Barrey et al. [22])

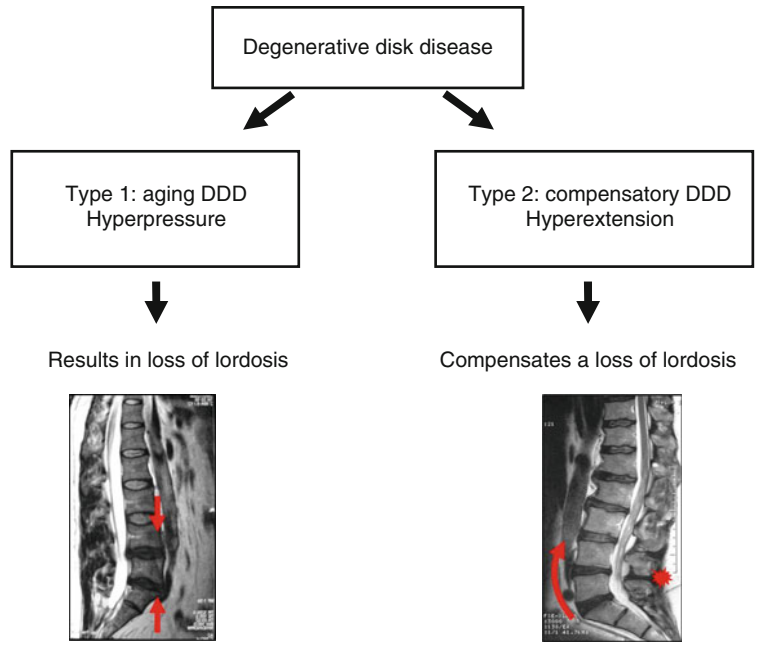

Fig. 48.8 Classification of degenerative disk diseases into aging discopathy and compensatory discopathy. Compressive forces (*arrow*), spine working in extension (*curved arrow*) and stresses on posterior elements (*star*)

48.3.1.4 Retrolisthesis

Retrolisthesis, defined as the posterior slippage of the upper vertebra in reference to the lower vertebra, is typically limited to 2–3 mm slippage in the lumbar spine. It often results in severe foraminal stenosis and more rarely in central stenosis (Fig. 48.7). Retrolisthesis is usually observed at the immediate adjacent lower or upper segments of the lumbar spine that had some kyphotic changes: L5–S1 and upper lumbar spine L1–L2 and L2–L3) are common sites. Retrolisthesis is typically underestimated on supine radiological imaging techniques (CT scan and MRI); however, they can be suspected on MRI imaging in the presence of subluxation of facet joints with fluid collection.

48.3.2 Pelvis

The only compensatory mechanism in the pelvic area is pelvic back tilt (also called pelvic retroversion), defined by the increase of the pelvic tilt and corresponding to the posterior rotation of the pelvis around the femoral heads, similar to that occurring during hip extension (Fig. 48.9). This motion is permitted by contraction of the hip extensor muscles and results in posterior positioning of the sacrum related to the coxofemoral heads. Bringing backwards the sacral plate related to the coxofemoral heads (and increasing the sacro-femoral distance), this mechanism permits the subject to compensate for the anterior translation of the axis of gravity. The pelvic incidence determines the global capacity of pelvic retroversion which is easily achieved for patients with a great pelvic incidence. In fact, considering that PI = SS + PT and that SS cannot be a negative number, one can tilt more with a high PI than with a low PI, since there is a much wider range through which adaptation can occur. Numerous studies reported that patients with chronic low back pain and lumbar degenerative disease were characterized

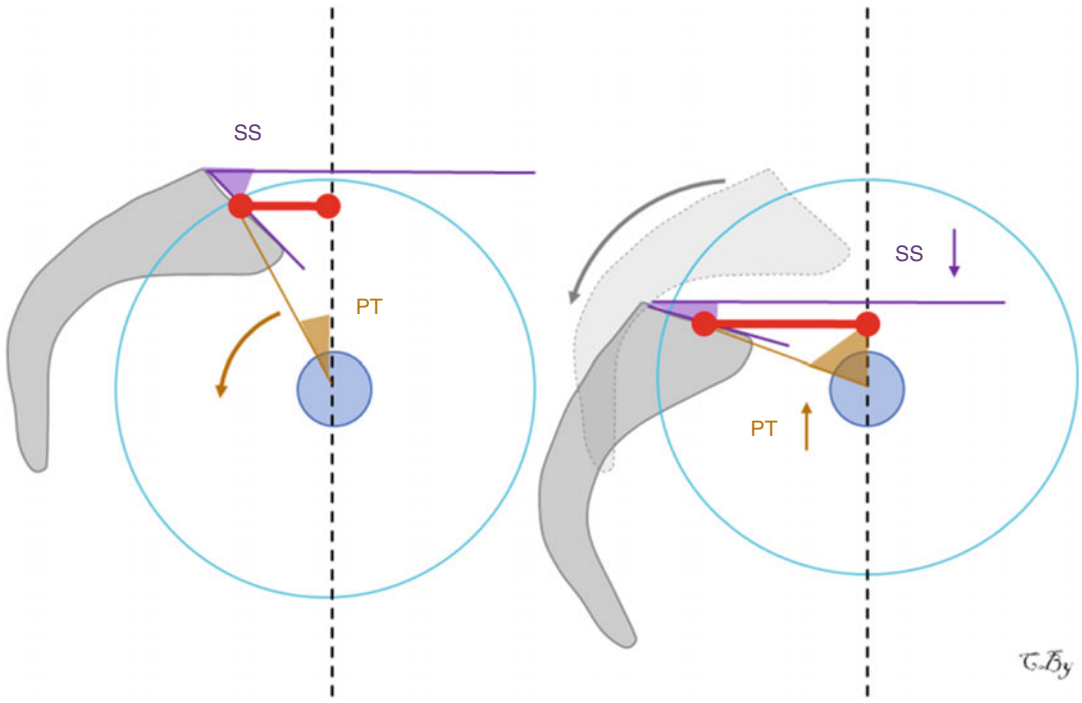

Fig. 48.9 Pelvic backtilt mechanism. Increase of pelvic tilt results in posterior placement of sacrum related to the coxofemoral heads, thus increasing the sacro-femoral distance (*red line*) and bringing back the axis of gravity (From Barrey et al. [26]; with permission)

by decrease of sacral slope and increase of pelvic tilt [4, 5, 23] as demonstrated in our illustrated cases in Fig. 48.3.

48.3.3 Lower Limbs

48.3.3.1 Knee Flexion

Knee flexion can be evaluated by the pelvifemoral angle described by Mangione et al. [27]. This is a well-known compensatory mechanism for patients with severe degenerative spine and has already been widely reported [2], Fig. 48.10. It permits to translate posteriorly the axis of gravity with respect to the feet. More recently, Obeid and Vital demonstrated the strong correlation between knee flexum angle and the lack of lordosis (which was estimated from the theoretical lordosis) [28]. Knee flexum is usually observed in severe sagittal imbalance at late stage of the degenerative process with global kyphosis of the lumbar and thoracic spine. The posture with knee flexed is very uncomfortable for the patient with limited walking distance.

48.3.3.2 Ankle Extension

Through a prospective study, Lafage et al. recently underlined that the pelvic translation was a parameter as important as the pelvic rotation (measured by the pelvis tilt) and probably induced by extension in ankle joint [15]. Therefore, they suggested that the patients should be analyzed from head to feet.

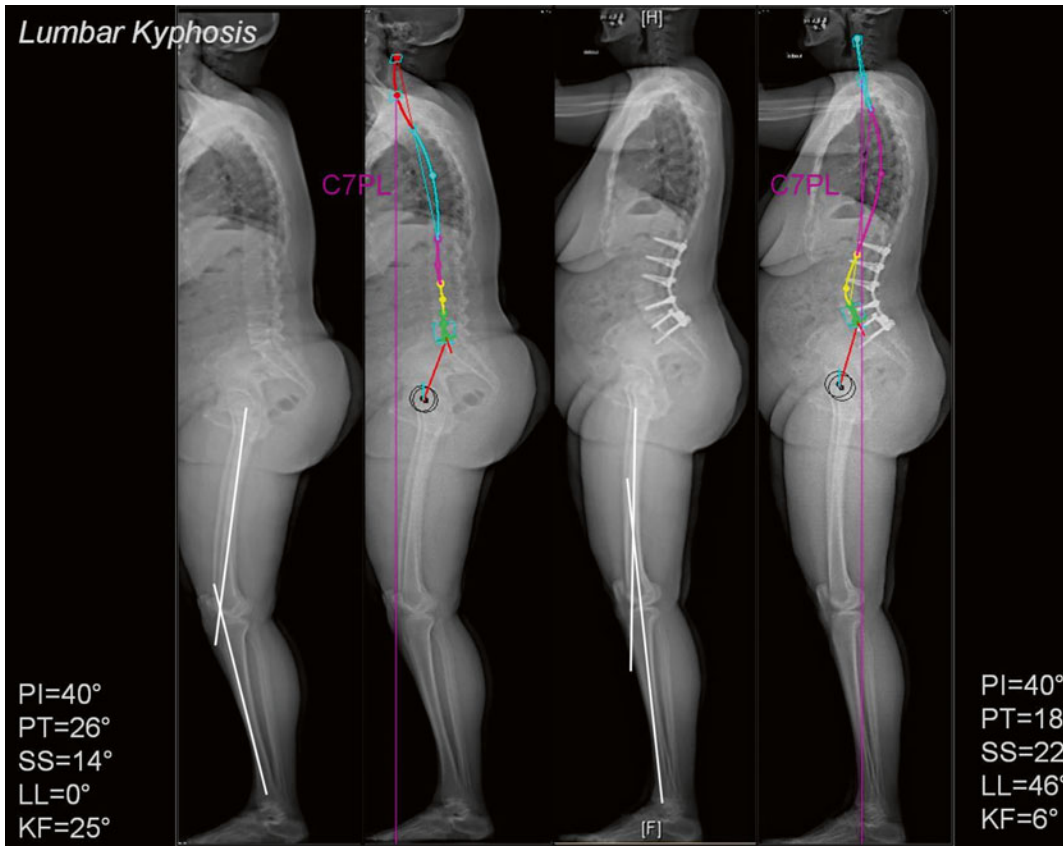

Fig. 48.10 Illustrative case with lumbar kyphosis and compensatory knee flexum. After surgical correction of the kyphosis (TPO procedure at L4), the knee flexum significantly reduced postoperatively suggesting the improvement of the global sagittal balance

48.4 Algorithm

Finally we propose a three-step algorithm to achieve the analysis of sagittal balance and determine the presence or not of compensatory mechanisms:

First step What is the value of the pelvic incidence? The knowledge of the pelvic incidence permits to determine the expected theoretical values of the spinopelvic positional parameters (Tables 48.1 and 48.2).

Second step Is the patient globally balanced? Global sagittal alignment is evaluated by analyzing the positioning of C7, related to the sacrum, using measurement of SSA and/or SVA/SFD ratio.

Third step Are there some compensatory mechanisms?

- In spinal area: analysis of this zone consists of measurement of lumbar lordosis and thoracic kyphosis and looking for the presence of compensatory discopathy(ies) and retrolisthesis and/or abnormal regional curves (i.e., thoracolumbar lordosis). Cervical curvature analysis should also be included.
- In pelvic area: is the pelvic tilt (PT) adequate with respect to the pelvis incidence? The presence of horizontal sacral plate is highly suspected of pelvic backtilt mechanism. The use of PI classes is useful to determine the theoretical PT (Table 48.2).
- In lower limb area: are the knee flexed? One must care to this point considering that knee flexum minimizes the importance of sagittal imbalance on full spine radiographs. Measurement of knee flexum angle is mandatory but implies full body radiograph (as provided by EOS™ system).

Conclusion

Meticulous and exhaustive analysis of spinopelvic parameters allows for identification of the main compensatory mechanisms observed in patients with sagittal balance disorders. These mechanisms have to be considered prior to therapeutic options. This may probably optimize the management of patients with severe degenerative spine especially when surgical treatment with instrumentation of the spine is planned.

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49 Posterior Impaction Osteotomy for Correction of Sagittal Imbalance in Iatrogenic Flat Back: Surgical Technique

Christian Mazel, Laurent Balabaud, and Alexandre Cogan

49.1 Introduction

Sagittal imbalance can be defined as the inability to stand erect without compensatory flexion of hips and knees. Loss of lumbar lordosis, often associated to increased thoracic kyphosis, is the most characteristic presentation of this biomechanical disorder, which is often named "flat back." Muscle degeneration is usually present [1]. Several degenerative, inflammatory, and infectious pathologies have been recognized to lead to this clinical picture. Flatback posture is also the common result of distractive instrumentation used in the lumbar spine for a myriad of spinal disorders. Lumbar fusion for scoliosis or other degenerative disorders is a well-established iatrogenic cause of flatback deformity [2] and failed spine surgery. The first line of management is nonoperative treatment that, unfortunately, is often not effective [3]. Most patients with this disabling condition often require an osteotomy to restore a satisfying lumbar lordosis. Two osteotomy techniques are currently performed: Smith-Petersen osteotomy [4] and the transpedicular closing wedge osteotomy frequently attributed to Thomassen [5, 6].

49.2 Clinical and Radiological Assessment of Sagittal Imbalance

The most common symptoms reported by patients with flatback syndrome are buttock pain, calmed down by a sitting position, back pain, radicular pain or neurogenic claudication, and neck pain.

Neck pain is largely due to cervical spine extension to maintain horizontal gaze. Radiculopathy and neurogenic claudication could be explained by disk and facet joint complex degeneration causing hypermobility at involved levels. The appearance of a forward pitching position, with insufficient knees flexion to compensate for sagittal imbalance, is a typical finding on clinical assessment (Fig. 49.1). A thorough neurological assessment is required, along with various functional outcome measures such as ODI, SRS, and possibly JOA scores. Hips and knees joint range of motion should be carefully measured.

Radiological assessment of sagittal balance (Fig. 49.2a, b) is performed using full-length lateral radiography, measuring spinal parameters

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_49

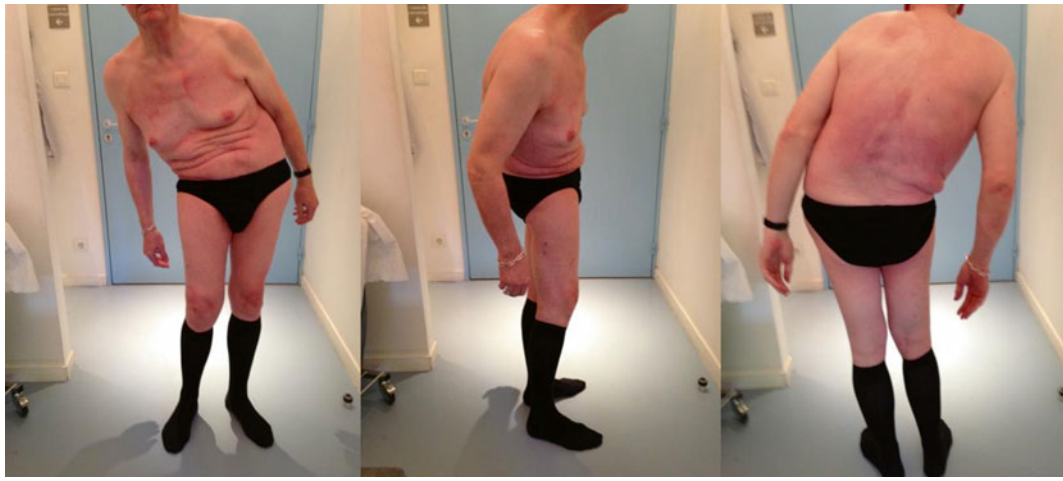

Fig. 49.1 Clinical presentation of a sagittal and coronal imbalance

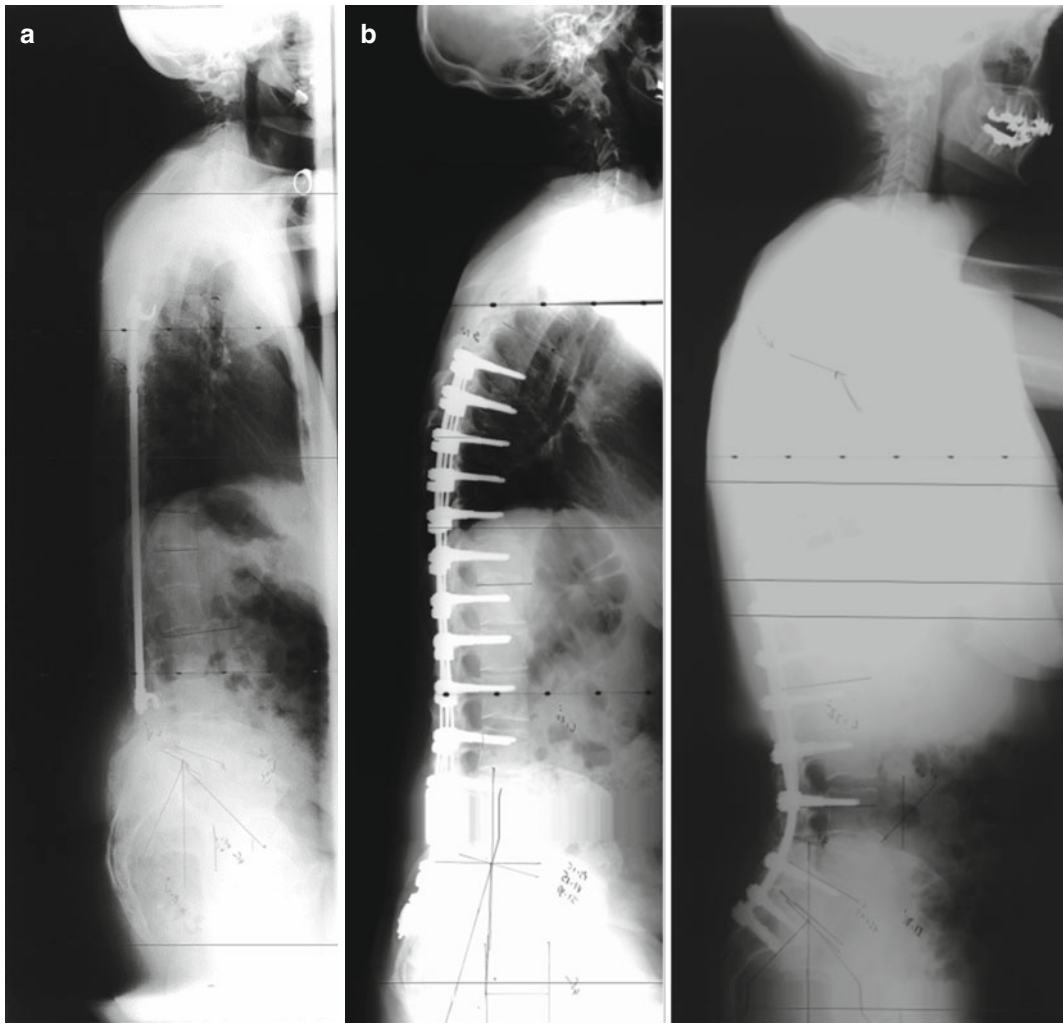

Fig. 49.2 (**a**) Full-length radiography demonstrating a flatback posture post a Harrington procedure. (**b**) Full-length radiography demonstrating a flatback posture following a multi-segmental scoliosis procedure Pr and post-op

such as lordosis, kyphosis (Cobb's angle), sagittal tilting, and pelvic parameters such as incidence, sacral slope, sacrofemoral tilting, and overhang [7]. Two additional parameters to those previously defined also include regional kyphosis (angle between the superior end plate of the vertebra above the planned osteotomy and inferior end plate of the vertebra below) and the sagittal vertical axis also referred to as the plumb line (distance between a projected vertical line drawn from the center of C7 and the anterosuperior end plate of the sacrum). If the projection passes in front of the anterior aspect of the sacrum, the measure is positive. Van Royen et al. used the posterosuperior end plate of the sacrum as a second anatomical landmark to evaluate sagittal vertical axis [8].

The use of various methods to assess lumbar lordosis makes comparing radiological outcomes between series difficult. The large variability of sacral inclination, for example, makes the superior end plate of S1 an unreliable landmark [9, 10]. In our series, we measured lumbar lordosis from the superior end plate of L1 to inferior end plate of L5.

49.3 The Different Surgical Techniques

49.3.1 Smith-Petersen Osteotomy (SPO)

The first cases of osteotomy reported by Smith-Petersen et al. in 1945 were for post-ankylosing spondylitis deformity. This technique (Fig. 49.3) consists of posterior element subtraction, taking away the spinous process, lamina, and facet joints on one or more levels. Correction is obtained through external manipulations resulting in compression of the posterior elements, opening of the disk space, and tearing of anterior longitudinal ligament. The major drawback of this technique is that it lengthens the anterior column, potentially injuring the spinal cord and tearing the great vessels. Lengthening of the anterior column has been measured by Scudese and Calabro who noted 1.7 cm of lengthening for a 40° correction [11]. Moreover, closure of the posterior elements may compress the foramen, causing radiculopathy. The average correction that can be expected is 5–10° per osteotomy level [12].

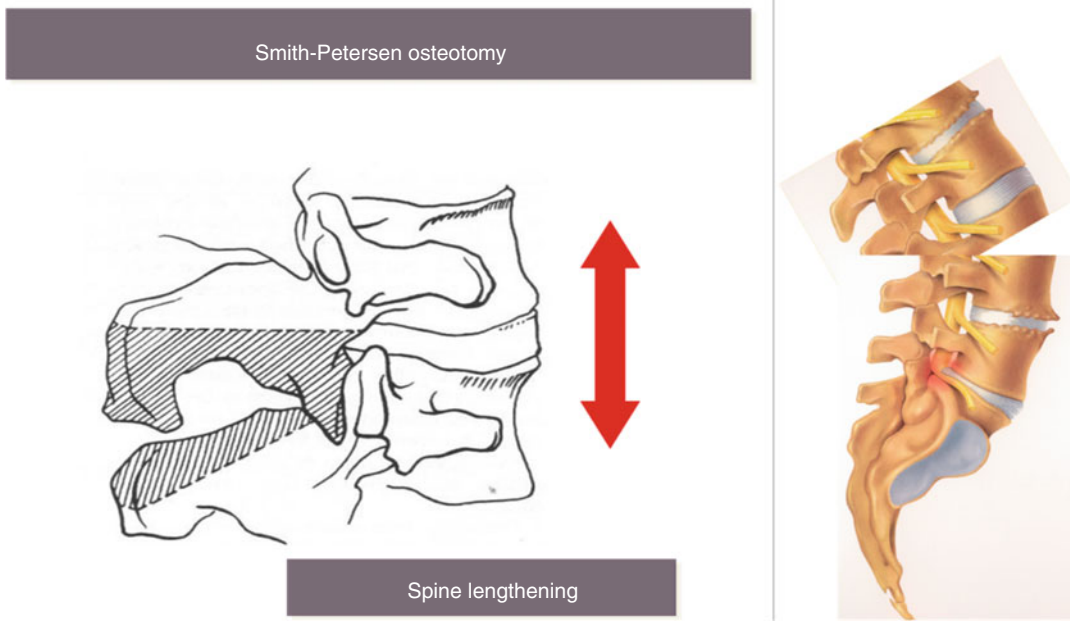

Fig. 49.3 Smith-Petersen osteotomy (SPO) is lengthening the anterior column of the spine

49.3.2 Ponte Osteotomy

The *Ponte-type osteotomy* was first described by Ponte et al. in 1984 for Scheuermann kyphosis although the terminology only entered the US literature in 2007 [13]. The Ponte osteotomy was described as wide segmental osteotomies followed by posterior compression along unfused regions of the deformity in Scheuermann patients.

The authors are mostly speaking of multilevel facet and lamina local osteotomy that by their multilevel situation corrects the sagittal deformity. The surgical technique is a multilevel reshaping of the canal associate to an inferior and medial facetectomy, with ligamentum flavum resection (Fig. 49.4).

Although today the terms Smith-Petersen and Ponte are often used interchangeably, the technique currently used is Alberto Ponte's. In addition, SPOs have become a mainstay in the correction of coronal deformities, such as adolescent idiopathic scoliosis; however, they were not originally described for this indication.

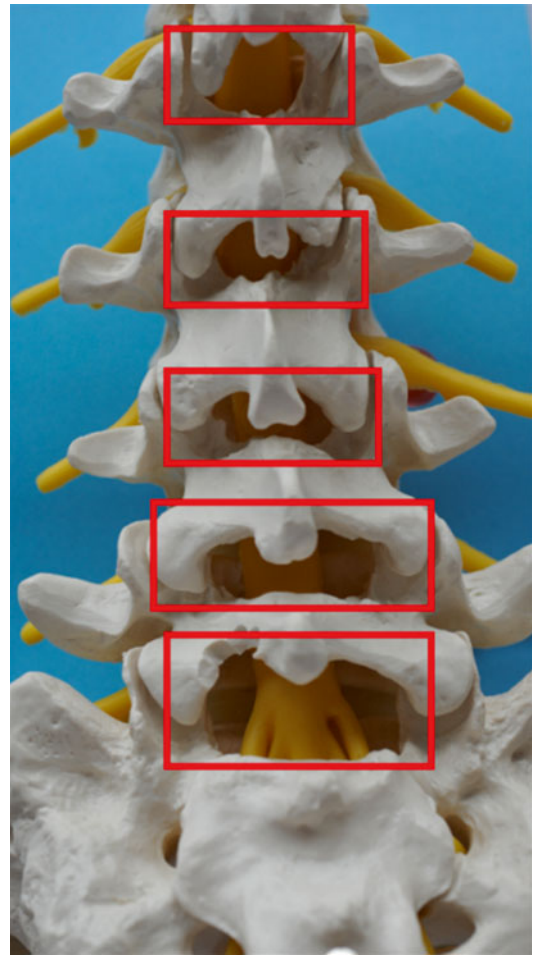

Fig. 49.4 Ponte osteotomy. Multilevel resection of the medial part of the *upper* and *lower* facets. Correction is spread on the different adjacent levels

49.3.3 Posterior Subtraction Osteotomy (PSO)

Corporeal subtraction osteotomy consists of a wedge osteotomy of the vertebral body performed through a posterior approach (Fig. 49.5). It allows shortening of the posterior column without lengthening of its anterior aspect, thus sparing the neural elements. Moreover, it gives a larger surface of compressive bone contact than the Smith-Petersen technique, thereby enhancing stability and fusion.

Comparison between Smith-Petersen osteotomy (SPO) and pedicle subtraction osteotomy (PSO) underscores major differences. The SPO group tends to produce more coronal decompensation and requires multiple levels of osteotomy for substantial correction [13]. There is a higher risk of vascular injury as well as a higher rate of nonunion because the opening is through the disk space. The bulk of axial loads in the standing position passes through the anterior column, so opening of the disk space predisposes to

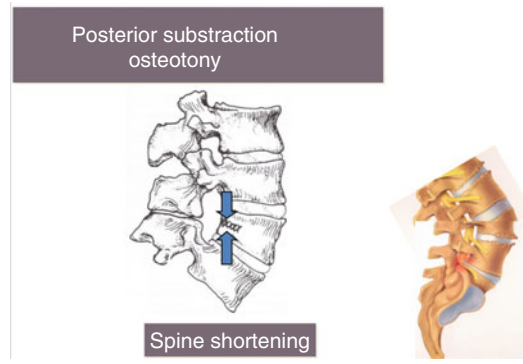

Fig. 49.5 Posterior subtraction osteotomy (PSO) shortens the spinal column

nonunion [14]. A PSO on the other hand is associated with a significantly higher blood loss and a higher union rate [15, 16].

49.3.4 Posterior Impaction Osteotomy (PIO)

These results and complications explain our surgical evolution and desire to minimize bleeding and to simplify the osteotomy procedure. The development of the posterior wedge intracorporeal impaction osteotomy is to us a good way to obtain such results.

The main principles of this technique are to accomplish the posterior closing osteotomy by intracorporeally impacting the cancellous bone of the posterior vertebral body wedge. The apex of the osteotomy must be as close as possible to the anterior cortex while preserving a hinge.

The patient is placed in the prone position on an Allen® radiolucent carbon surgical table (Fig. 49.6a, b). The chest is supported by two thoracic mobile stands (up and down) while the iliac crest and pelvis are positioned on a fixed one; the fixed lower limbs are positioned along the body's axis. This setup leaves the abdomen free from compression, thereby decreasing bleeding, and favors the natural restoration of the lumbar lordosis by hyperextending the lumbar spine.

A posterior incision is made. Muscle must be handled with care because of its importance in spinal stability and injuries caused by previous surgery. Dissection is gently done with a knife. Knife dissection is preferred because it decreases the risk of dural tears, especially if a laminectomy was performed on previous procedures, and of muscle necrosis in multi-operated cases. Monopolar cautery may be used to dissect soft tissue off any spinal instrumentation. The surface anatomy is thoroughly cleaned of all soft tissue in order to identify essential anatomical landmarks before starting the osteotomy. Intraoperative radiographic control is used to verify the level of the selected vertebra. Anatomical limits of bone resection, depending on the amount of correction, are represented by two lines drawn with monopolar cautery on either side, perpendicular to the spinal axis of pedicles screw holes easily visible after instrumentation removal. Instrumentation length is tailored to each individual case, taking various factors into account (quality of bone, adjacent pathologies, topping of syndrome, nonunion, etc.). A minimum of two levels over and under the osteotomy level is recommended. Bone resection consists of a laminectomy at the selected level and cephalad vertebral level including the target level pedicles, facet joints, and transverse processes. The neural elements, i.e., the nerve roots above and below the pedicle of interest, are protected by cotton pads. The pedicle subtraction is performed using a high-speed diamond drill. This results in a large foramen whose contents include the two exiting nerve roots, maintained in distraction using a distraction clamp (Fig. 49.6a, b). Bleeding from epidural veins can be controlled by haemostatic agents (Surgicel®, Surgiflo®, or others) or bipolar cautery if necessary. Corporeal osteotomy starts on the posterior wall, using two osteotomes. The

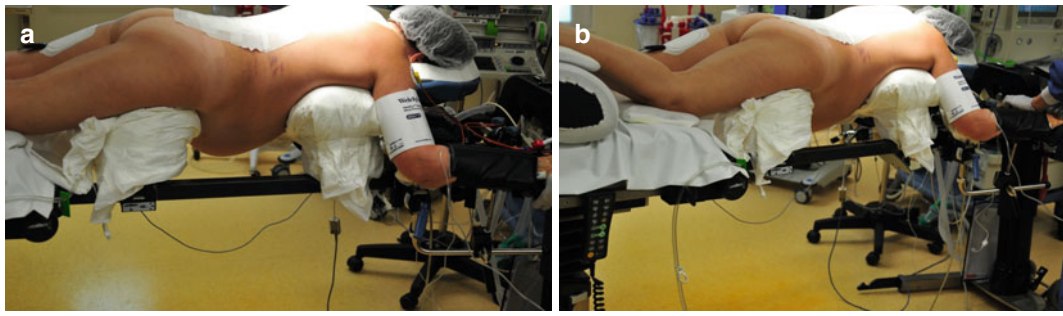

Fig. 49.6 (**a**) Radiolucent table: Belly is entirely free of all anterior compression. (**b**) Radiolucent table giving a lower limb hyperextension capacity

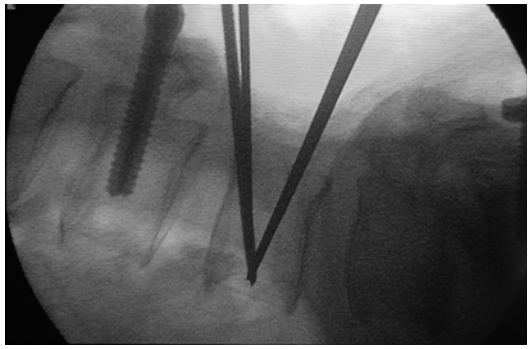

Fig. 49.7 Peroperative view of the bone scissors before impaction of the wedge-shaped part of the vertebral body (By courtesy of JM Vital)

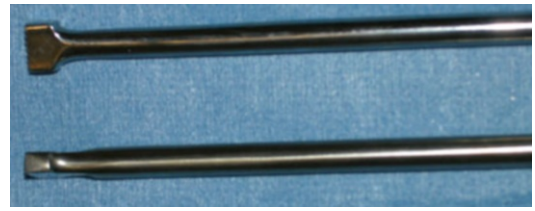

Fig. 49.8 Bone impactors of different sizes enable to compact the bone inside the vertebral body, impaction posterior osteotomy (IPO)

extent of posterior body resection is determined by the obliquity required to affix the osteotomy margins just behind the anterior vertebral cortex, leaving an anterior bony hinge that prevents forward translation. Osteotome progression inside the vertebral body is controlled by fluoroscopy (Fig. 49.7).

There are two major differences between the PIO and PSO techniques at this step of the procedure. With the PSO technique, it is recommended to progressively remove the cancellous bone from the vertebral body, creating a wedge-shaped void giving place for future closure and correction. With the PIO technique, the cancellous bone, as well as the posterior wall of the vertebral body, is impacted inside the vertebral body. Impacting the bone instead of removing it decreases intraoperative bleeding. It also simplifies the procedure. Bone impactors have been designed specifically for this purpose. They are long enough to deal with obese patients and narrow enough to be easily handled up to the anterior extent of the osteotomy (Fig. 49.8). The cancellous vertebral body bone is progressively impacted out of the osteotomy site, alternating on both sides. This is the first step of the osteotomy procedure.

The second step of wedge creation is the cutting of the lateral vertebral body wall. In the PSO technique, you elevate the lateral soft tissues and then cut the lateral wall with an osteotome. Control of the lumbar segmental vessels is difficult and local bleeding can be voluminous. In PIO you weaken the lateral edges of the vertebral body with the bone impactor. The tip of the impactor is manipulated from inside the vertebral body, weakening the lateral wall without injuring the lumbar vessels.

The last step of the decancellation is the resection of the vertebral median posterior wall just in front of the dural sac. It is the last hurdle to closing the wedge. The resistance of this median posterior cortical wall depends on the patient's bone quality. In most cases the same weakening technique used to deal with the lateral wall is employed. A smaller bone impactor is used. The instrument is inserted obliquely from both sides in front of the dural sac and a progressive impaction maneuver will break it down.

The wedge is now complete, bleeding is controlled by cancellous bone impaction, and posterior closure is obtained by progressively releasing the distraction clamp (Fig. 49.9a, b). Satisfying lumbar lordosis is obtained in most cases at this point. In stiffer patients, in order to complete the posterior wedge closure, it is necessary to perform an upward translation of the thoracic platform and a hyperextension at the site of the osteotomy by raising the lower limbs until the upper and lower osteotomy limits contact bone on bone. A thorough evaluation of the posterior decompression is assessed to make sure there is no dural impingement or foraminal compression. Careful inspection of each foramina and nerve root is mandatory all along the closure. Root entrapment or impingement is the most frequent possible complication. The procedure is completed by local decortication and posterolateral graft application using locally harvested morsellized bone chips. Mechanical

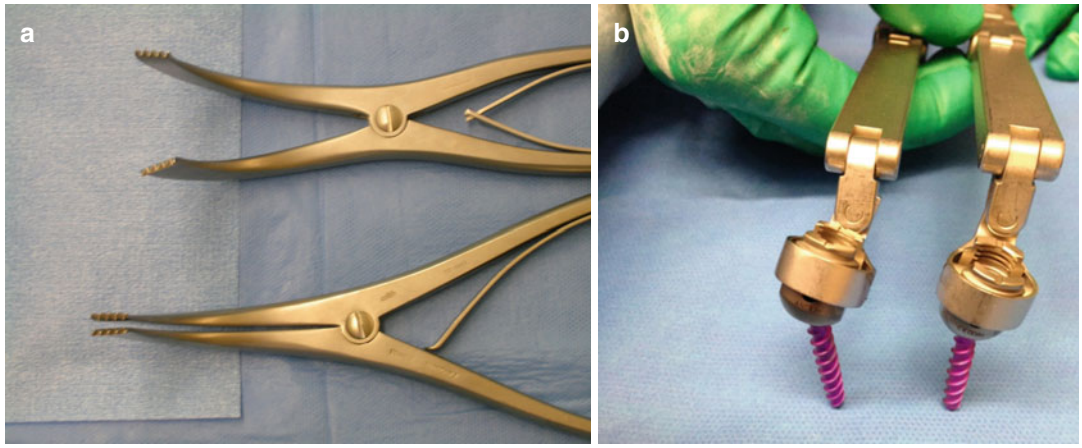

Fig. 49.9 (**a**) Spreading Meary-type clamp. Mostly applied directly on the bone margins, they avoid pedicle screw mobilization of other types of distracting clamp. (**b**) Pedicle-type distracting clamp

stability is obtained by strict patient fixation to the operative table, thus avoiding instrumentation at this time of the procedure. Spinal fixation is then performed spanning at least two levels above and two levels below the osteotomy. This is possible due to the stability of the patient on the operative table. We use rigid instrumentation, favoring highly rigid chromium cobalt alloy rods to titanium ones. Finally, lumbar lordosis is obtained using the operative table. The desired posture is maintained by placing screws in previous pedicle trajectories and using precontoured adapted rods (Fig. 49.9a, b). There is no need to perform in situ bending. Two suction drains are placed into the epidural space and the wound is closed in layers. The patient is kept supine for the first day postoperatively and then mobilized on the second post-op day with a rigid Boehler-type brace which is used for walking and standing for the first 3 months. Sitting is not allowed for the first 45 days for osteotomies lower than L3.

49.3.5 PIO with Partial Pedicle Resection

The complete resection of the pedicle is the standpoint of PSO or IPO techniques; in some cases where the needed correction is lower than 20°, it is possible to only remove the lower two-third of the pedicle. It avoids violating the upper foramina, thus decreasing morbidity, and shortens the surgical time (Fig. 49.10).

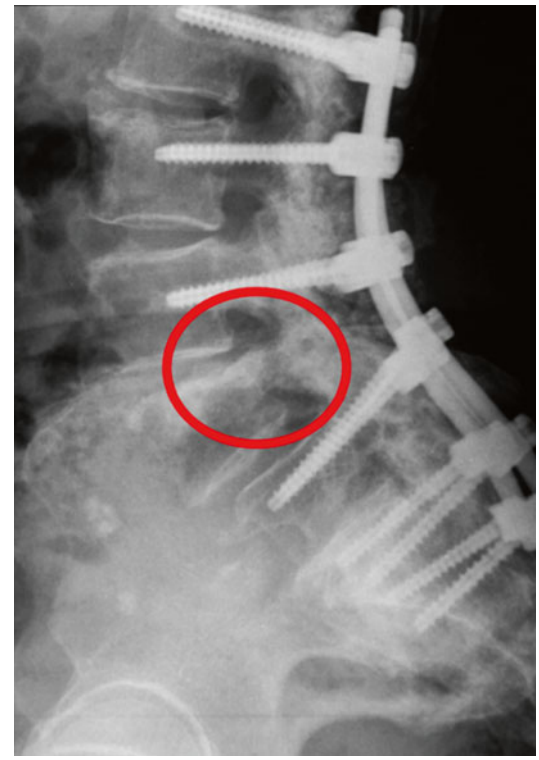

Fig. 49.10 Partial IPO with preservation of the upper part of the pedicle (*Circle*). Only one foramina is open preserving the adjacent one and decreasing morbidity related to root impingement

49.3.6 Choice of Technique

The choice Ponte osteotomy and PSO/PIO mostly depends on deformity reducibility. Correction of the sagittal imbalance is assessed on lateral full spine X-rays (EOS® system if possible) and flexion-extension films (Fig. 49.11a, b).

Multilevel deformities are more often addressed by a Ponte osteotomy. Stiff deformities will need PSO or PIO; reducible ones will be addressed with Ponte osteotomy.

The axial extension of the deformity is also considered. A localized deformity is more efficiently dealt with by a PSO or PIO (Fig. 49.12).

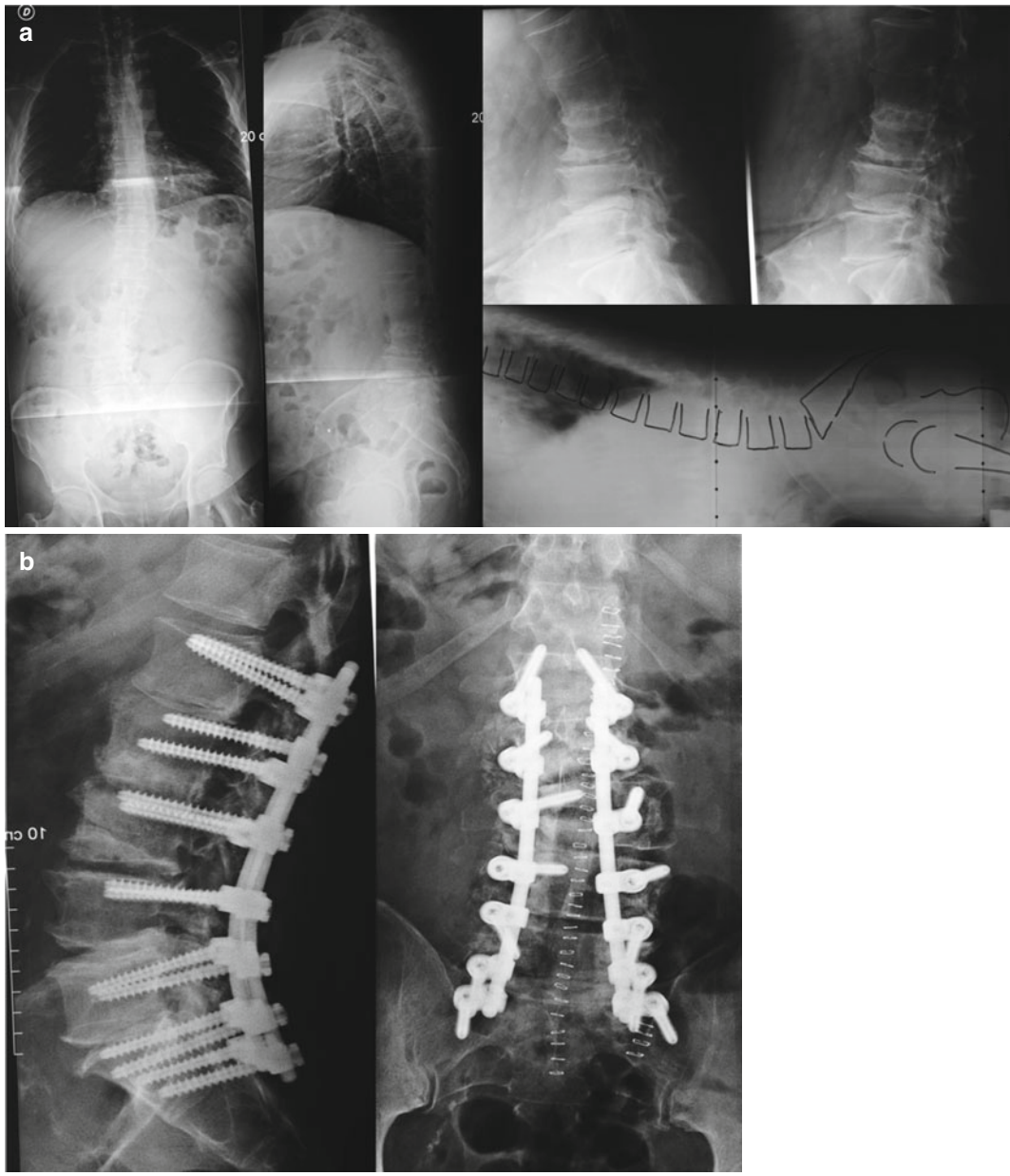

Fig. 49.11 (**a**) Reducible kyphotic deformity shown on the lateral film in supine position more than on flexion-extension lateral films. (**b**) Post-op films after Ponte multilevel osteotomy

49.3.7 Choice of Level in PSO and PIO

Multiple factors (type and level of pathology, local modifications) weigh on the choice of the osteotomy level. The indication is tailored to each pathology and deformity.

Lower levels carry less neurological risk (cauda equina versus cord), and the lower the level from L1 to L5, the higher the correction angle, but the more challenging a stable fixation. With an L5 osteotomy, both transiliac and sacral screws are needed for stability.

The best compromise is L4: low enough to give a good correction, high enough to spare enough levels under the osteotomy to maintain mechanical stability.

In previously operated cases, local conditions can modify this strategy. Priority can be given to a level free of dural scar with no previous vertebral canal exploration or to a nonunion.

49.4 Case Series: Results and Discussion

This retrospective series includes 49 patients who underwent corrective surgery for functional sagittal imbalance using a closing wedge osteotomy by intracorporeal impaction over an 8-year period from July 1999 to December 2011.

The mean age was 54 years (range 21–84 years). There were 40 women and 9 men.

All but one patient had previously undergone spinal fusion. The average number of prior spine interventions was 2, with a maximum of 7. The initial spine surgery was a fusion for thoracic or thoracolumbar scoliosis (with sacral fusion) for 23 patients, an instrumented fusion for degenerative indications for 25 patients, and a laminectomy for 1 patient. The average period separating the last spinal procedure and the osteotomy was 47 months (ranging from 12 to 132 months).

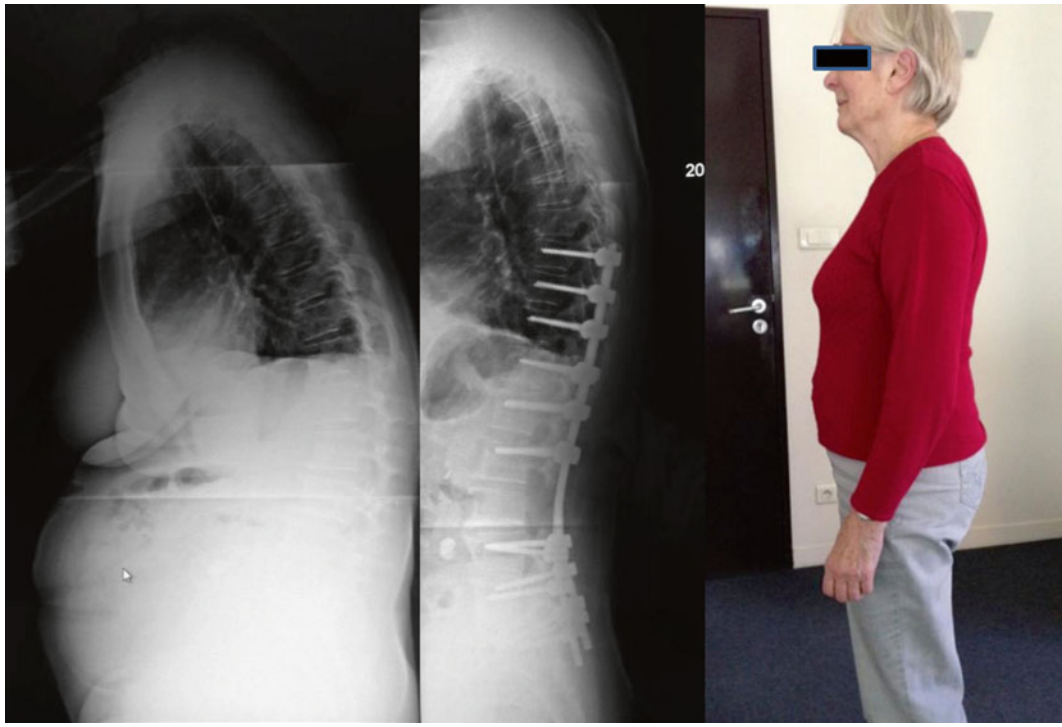

Fig. 49.12 Pre-op kyphotic deformity of L3 corrected by a PSO. Radiological and clinical outcome

Preoperative X-ray finding is presented in Table 49.1.

In our series of osteotomy for iatrogenic flat-back deformity (Fig. 49.10), follow-up shows clinical improvement in 90 % of patients. Intraoperative data revealed a mean operative time of 208 min (range 120–360) and a mean blood loss of 1856 ml (range 650–4000). The mean hospital stay was 12 days (range 6–34). We used Cell Saver® autologous transfusions to compensate for the vast majority of the peroperative blood loss (Table 49.2). Seventeen patients required additional postoperative heterologous transfusion.

Intraoperative incidents included a dural tear in 11 patients. All were stitched and hermetically closed. Patients with a dural tear were kept in bed the first postoperative day, and non-aspirate drainage was left in place 24 h. There was no cerebrospinal fluid leakage or meningocele. There was no nerve root injury.

Postoperative complications (Table 49.3) included six transient motor nerve root deficits (12.2 %), five painful transient nerve root irritations (10.2 %), and one superficial wound infections (2 %). There was one tragical case of higher level postoperative paraplegia, without any direct relation with the osteotomy site. It is not included in these data. Instrumentation extended up to T3 level in this patient, and early revision of a malpositioned screw in the upper part of the osteosynthesis did not bring neurological improvement.

There was one case of perioperative collapse of the anterior hinge, resulting in a small translation without any neurological consequences.

Table 49.1 Preoperative radiological data

	Normal values	Average	Minimum	Maximum
Thoracic kyphosis	45°	27.1°	0°	62°
Lumbar lordosis	61°	12.2°	−13°	24°
Incidence angle	53°	62.9°	39°	90°
Pelvic tilt	12°	37.8°	13°	60°
Sacral slope	41°	25.1°	13°	40°
Regional kyphosis	NA	12.6°	−8°	28°
Sagittal alignment	11°	7.1°	−4°	15°
Overhang	23 mm	64.5 mm	25 mm	100 mm
Sagittal vertical axis	0 mm	96.5 mm	20 mm	180 mm

Table 49.2 Operative time and blood loss

Items	Mazel et al.	Bridwell et al. [19]	Chiffolot et al. [20]	Boachie-Adjej et al. [21]	Ikenaga et al. [17]
Operative time(min)	208	750	260	304	277
Blood loss(ml)	1856[a]	2400	1400	2700	1988

[a]Cell saver autotransfusion is not included

Table 49.3 Operative complications of lumbar osteotomy

Complications	Mazel et al.	Bridwell et al. [19]	Chiffolot et al. [20]	Boachie-Adjej et al. [21]	Ikenaga et al. [17]	Kim et al. [22]
Nbre of patients	49	33	34	24	67	45
Dural tears	11	2	5	4	1	–
Infection	1	–	2	2	2	–
Neurol. deficit	6	6	–	0	2	5
Radicular pain	5	–	4	1	1	4
Pseudoarthrosis	2	8	8	3	7	–
Addit. ant. surg	2	14	–	7	7	–

Instrumentation corrected the displacement and resulted in fusion.

An anterior approach was deemed necessary in one case. This patient had an instrumented T5–L3 fusion using Harrington rods for thoracolumbar scoliosis associated with an L5 isthmic spondylolisthesis. Due to decompensation of the adjacent levels, the fusion was elected to be extended to the sacrum. An L4 osteotomy was necessary in order to compensate for the associated previous thoracolumbar flatback deformity. Resection of the L5 posterior arch as part of the procedure (Gill procedure), resulting in local instability, indicated a complementary anterior approach in order to fuse the L4–L5 and L5–S1 interspaces.

A complementary anterior approach should be associated with a transpedicular osteotomy every time posterior instrumentation alone appears insufficient for optimal stability. This complementary approach may be indicated in cases of severe osteoporosis, correction through the disk space, or insufficient correction. In two patients, the correction was mostly at the level of the intervertebral disk and not in the vertebral body itself, but the osteosynthesis was stable enough. In these cases we neither have to harvest additional bone graft nor use an anterior cage.

Two cases of nonunion were observed.

The first patient had Forestier disease with a kyphotic lumbar deformity and lumbar stenosis. He had previously undergone a laminectomy and instrumented fusion from T11 to S1. His postoperative flat back was corrected by an L4 posterior transpedicular wedge impaction osteotomy. Rod failure due to nonunion occurred 6 months after surgery. The revision consisted of posterior decortication, bone grafting, and new fixation with an anterior L3–L4 fusion during the same procedure.

The second patient had previously undergone a laminectomy and instrumented fusion from L3 to L5 for a lumbar stenosis. Her postoperative flat back was corrected by an L3 posterior transpedicular wedge impaction osteotomy with a T9 to sacrum fusion. She was revised 33 months later for a union at the lumbosacral junction, with an anterior L5–S1 fusion.

Impaction bone grafting preserves cancellous bone and in our opinion reduces blood loss and nonunion. Preservation of the anterior cortical bony hinge decreases the risk of anterior translation with nerve entrapment and probably enhances local stability and fusion rates. The Allen® operative table with its thoracic and pubic platform configuration allows minimal abdominal compression and decreases intraoperative bleeding. Moreover, it assists in osteotomy closure following the osteotomy [17, 18].

Postoperative radiological outcomes are presented in Table 49.4.

Many heterogeneous case series of flatback deformity have been reported with PSO. Globally, the average correction for a one-level PSO is approximately 30° [17, 19–22]. In our series, the average improvement in regional kyphosis was 19.6°. The average improvement in lumbar lordosis was 23.5°, less than quoted in

Table 49.4 Summary of mean correction obtained in different series

Items/mean correction	Mazel et al.	Bridwell et al. [19]	Chiffolot et al. [20]	Boachie-Adjej et al. [21]	Ikenaga et al. [17]	Kim et al. [22]
Number of patients	49	33	34	24	67	45
Thoracic kyphosis	8.2°	12.2°	–	10°	6.3°	4
Lumbar lordosis	23.5°	33°	31.5°	41°	35.2°	34
Regional lordosis	19.6°	28°	28.9°	–	34.2°	–
Sacrofemor. tilting	−7.8°	–	−16°	–	–	–
Sacral slope	7.5°	–	8	–	–	16°
Sagittal alignment	3.5°	–	–	–	–	–
Overhang (mm)	12.2	–	–	–	–	–
Vertical sagittal Axis (mm)	−70.9	−14.9	−50	−108	−17	−86

the literature. This difference may be due to the cause of the deformity. As far as we know, our series is the largest one reported regarding iatrogenic flat back. Furthermore, we did not try to maximize correction but rather to recreate a harmonious balance of the spine [17, 23]. The wide range of normal values of lumbar lordosis implies that each person has its own means of self-balance. We therefore believe that the most reliable criteria to assess correction of sagittal alignment are the vertical sagittal axis [24]. Choosing the osteotomy level is still a matter of debate among authors. Some [24–26] recommend that it should be performed in the lower lumbar spine in order to maximize spinal sagittal correction and avoid spinal cord injury. Others [17] do not hesitate to make osteotomies at the thoracic level.

In addition to the potential for direct trauma during an osteotomy procedure, the procedure itself may lead to loss of blood flow to the spinal cord if performed at the spinal cord level [27]. Bridwell et al. [19] prefer to avoid performing a PSO in close proximity to conus medullaris [19, 21], while Booth et al. [28] perform their osteotomies above L1 at the apex of the deformity. Lagrone et al. [29] prefer to perform the osteotomy at a nonunion level. As a preexisting nonunion may predispose to recurrent postoperative deformity at the same site, it may be the optimal level to improve bone fusion by compression and instrumentation.

In our series, the osteotomies were always performed in the lower lumbar spine, mostly at L4 (Fig. 49.11). We also believe that there is less risk of neurological injury at that level, especially in multi-operated cases. Moreover, an osteotomy at this level allows for the greatest correction of alignment; with the same angular correction, the translational effect on the upper body and head is greater if the rotational arc is longer and thus if the vertebral osteotomy is at a lower level. Such a distal level raises the issue of stable fixation: we routinely use four points of fixation in the sacrum, two screws in S1 and two laterally directed screws in S2. The choice of osteotomy level is also influenced by the presence of an underlying nonunion.

When using a Smith-Petersen osteotomy, it is taught that for every 1 mm of bone resection, the deformity may be corrected by 1° [30]. Wang and Berven [31] recommend preoperative planning by taking a long cassette lateral X-ray and cutting a wedge out on tracing paper, aiming for a final lumbar lordosis of 30° along with moving the plumb line to the posterior sacrum. Pigge et al. [32] reported the results of an eight patient series where they used preoperative surgical planning assessing all pelvic parameters aiming for an optimal sagittal vertical axis as defined by Van Royen et al. [8]. To accomplish this they used the assistance of a computer program called ASKyphoplan to choose the level of osteotomy and degree of correction, correlated to the parameters mentioned above.

We suggest a preoperative planning method using a standing full spine sagittal X-ray. We draw the anterior hinge on the chosen vertebra and then a first osteotomy cut line. Then we cut the X-ray along this line but keep the part of the anterior hinge intact. By rotating the upper part of the X-ray around this hinge, we reposition the spine in the desired position through the use of the vertical sagittal axis. Once the sagittal imbalance is corrected, we just measure the required angle of osteotomy necessary for obtaining this correction. We also measure the angle between the superior and inferior end plates of the osteotomized vertebra which we then compare with the peroperative X-rays. Once the osteotomy closure is finished, the radiographic measurement of the angle between the upper and lower end plates of the osteotomized vertebra indicates if there is enough correction.

Conclusion

Taking into account the various parameters of sagittal spinal imbalance is paramount to treat a symptomatic deformity and restore balance.

Pedicle posterior wedge osteotomy is a technically demanding procedure. There are significant potential complications. Pedicle impaction osteotomy may alleviate those complications. Late complications such as nonunion often lead to further challenging surgery.

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Part IX

Lessons from a Life

Rational Evaluation and Management of the Patient with Spinal Pain

50

Donlin M. Long

50.1 Introduction

My views on the management of patients with spinal pain have been formed by a group of diverse influences. These began by training in the traditional neurosurgical approaches to the spine concentrating upon the truly herniated lumbar or cervical disk. My mentor and long-time friend Dr. Shelley Chou began collaborating with orthopedic surgery for spinal decompression in complex repairs of the spine in scoliosis. I learned a team approach with neurosurgical skills with the nervous system and orthopedic emphasis upon bone and cartilage combined. I chaired the committee which oversaw the introduction of spinal stimulation for pain into medical practice [1, 2]. Thus, I began a lifelong interest in salvage for the so-called failed back syndrome patients. My current experience with these patients is more than 8000, and nearly 2500 patients have come to surgery or other treatment. With my colleagues Warren Torgerson and Mohammed BenDebba I organized and directed the National Low Back Pain Study [3, 4]. This examination of nearly 4000 patients with first-time or first recurrent lumbar disk disease examined the opposite end of the spinal surgery spectrum from the surgical failures. These data on nearly 12,000 patients either personally seen or studied have formulated my general approach to the patient with spinal pain [5].

There is one other influence that has been important. In 1974, I founded a Chronic Pain and Evaluation Treatment Center at Johns Hopkins and was responsible for the clinical operations until 1982. The center functioned in close collaboration with psychiatry. The behavioral and psychological issues identified and treated remain an important part of my patient evaluations [6].

My current evaluation and management of new patients are based upon the 5-year examination of new-onset low back pain with or without sciatica from the National Low Back Pain Study. From that study, I was able to learn natural history, the lack of effect of any of the currently available nonoperative therapies, and the value of surgery for the small number of patients who actually required an operation [7, 8]. From the experience with thousands of patients with failed back syndrome, I was able to understand the causes of the ongoing complaints and thus design better treatments. From the Pain Treatment Center experience, I appreciate the psychosocial factors that can play such an important role in the generation and maintenance of pain complaints as well as the value of cognitive therapies for these patients [5, 9].

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_50

There is one other important influence in my practice. Dr. Nikolai Bogduk came to my laboratory as a medical student and convinced me of the lack of accurate anatomical understanding of the innervation of the spine. He began his studies in my anatomical laboratory and has continued the anatomical studies and dissections which allow us to understand the innervation of all of the spinal structures and thus have a much better understanding of the origins of spinal pain. I apply these anatomical lessons to practice regularly [10, 11].

50.2 Causes of Spinal Pain

One of the major difficulties with dealing with the problem of spinal pain is that there is little definitive evidence for what causes pain in the majority of patients [12]. Low back pain is ubiquitous and virtually the normal human condition. Over a lifetime, three fourths of adults have at least one episode of low back pain. The overall incidence of consistent complaints of low back pain is above 30 %, and at least 10 % of adults are complaining at any one time. Low back pain is one of the most common reasons why anyone sees a physician and one of the most common reasons for referral from one physician to another [13].

Many different groups of therapists treat patients. Generalists usually tell patients the problem is musculoskeletal in origin. This is repeated by all those involved with the utilization of passive physical measures and manipulation of the spine. These therapists usually believe in the musculoskeletal therapy and add correctable malalignment as a cause. Neurosurgeons have focused upon the intervertebral disk as the cause of pain and only in the recent past have begun to emphasize the biomechanical causes of spinal pain. Orthopedic surgeons have emphasized instability and disrupted biomechanics which they try to correct. Spinal surgeons today are more likely to have both skills and therefore treat both the disk and biomechanical issues together [14].

Since the majority of the acute spinal pain syndromes relent spontaneously without treatment, it is virtually impossible to ever determine the cause. Once we go beyond a point that spontaneous improvement is likely to occur, then it becomes much more feasible to actually determine a cause of pain and thus develop the most rational solution for that pain. Unfortunately, many physicians still maintain a stereotyped approach based upon a simplistic assessment of symptoms and without any of the diagnostic adjuncts which are currently available. My goal in this presentation is outline my own highly personal approach to spinal problems causing pain in hopes that this will lead others to develop similar protocols which can be expanded as new information becomes available. The emphasis will be upon pain. This is because the majority of spinal surgery is done for pain, not neurological deficit. When neurological deficits are important, they can be emphasized, but my fundamental premise is that most surgery is carried out for pain and in the absence of pain would not be required no matter what the imaging abnormalities. The few exceptions can be emphasized [3, 13, 15].

50.3 The Evaluation of the Patient with Spinal Pain

The first issue is always history. The importance of an accurate history cannot be overemphasized. In the National Low Back Pain Study, the 16 experts who were the investigators in the eight nationally recognized centers of the study made a correct diagnosis and predicted therapy in virtually every patient after the history was complete and before a physical examination was done or imaging studies were reviewed. The correct diagnosis and eventual treatment were chosen in over 90 % of patients, and the changes made after physical examination and imaging studies usually were related to levels rather than fundamental diagnosis. Key issues are the severity of pain, the presence of neurological complaints, the spatial and temporal characteristics of the pain as related to known anatomical radicular patterns, a history of intercurrent disease, and an assessment of the impact of the problem on the patient's life.

The physical examination is textbook and needs no reiteration here. The only important point is the lack of specificity in the physical

examination for the majority of patients. We have all learned in training the triads of reflex, sensory, and motor change which specify the root involved or spinal level. In the National Low Back Study, the textbook triads occurred in less than 1 % of patients subsequently shown to have one or more lumbar roots compressed requiring surgery. The nonspecific findings of back tenderness, lack of range of motion, and focal pain to palpation had no value in diagnosis or decision making. Thus, the physical examination is rarely an important issue unless it demonstrates a significant neurological deficient which requires urgent care [7].

A history of bladder or bowel difficulty or findings of significant perineal sensory loss, sphincter disturbance, or a lower extremity neurological loss one would not want to be permanent may all be indications for urgent care.

Remember the history of intercurrent disease should focus upon the possibility of infection, trauma, or cancer as particular causes of pain and deficits.

50.4 Management of Acute Back Pain With or Without Sciatica

Some years ago, the Health Policy Institute formulated back pain guidelines through the consensus process with a large number of experts in the management of spinal pain contributing. The conclusions were that in the presence of acute low back pain with or without sciatica, and the absence of a history of trauma or a significant neurological deficit, no imaging of the back pain problem was required. Expectant management with symptomatic relief could be instituted for at least 1 month and if symptoms persisted, then imaging was recommended. With a history of trauma plane spine films immediately could be obtained but were not required. This is more a legal issue in the United States than a medical consideration. Early mobilization was recommended [3, 15].

Intractable pain not easily relieved, a history of trauma, a concern for intercurrent disease, or a significant neurological deficit may all be reasons for proceeding with immediate evaluation depending upon severity.

From the National Back Pain Study, we learned that even patients with classic herniated disk syndromes virtually all improved spontaneously without any therapy [3]. Thus, my approach to the patient with the herniated disk is to treat the pain and mobilize the patient quickly, and the majority will recover without intervention. If the patient has severe radicular pain which is limiting function, a local steroid injection around the root will nearly always give relief. If the patient has severe pain without such a specific radicular component, then oral steroids for 4 or 5 days will usually provide relief. From the National Low Back Pain data, it appears that nearly all patients will be improving at 1 month and most will be fully functional at that time. Nearly all will recover over 3 months. Indications for surgery become intractable pain that cannot be relieved, a significant or progressive neurological deficient, or a social situation that does not tolerate 1–3 months of incapacitation. Some patients are simply unwilling to wait and want a solution.

Another important issue is mobilization following an acute back syndrome. There is excellent data indicating that patients are benefited by early mobilization. When true disk herniation has occurred, I limit vigorous activity such as strenuous sports and heavy lifting for a minimum of 3 months and typically for 6 months until I have MRI evidence of disk resolution.

Over the years, I have operated upon 7–10 % of those patients referred to me with known acute disk herniations. The remainder recovered spontaneously [7].

50.5 The Value of the So-Called Conservative Therapy Measures

It is common for patients with acute and chronic low back pain to be offered physical therapy, analgesics, manipulation therapy, or employ a wide variety of nonoperative treatments which they choose for themselves. In the National Low Back Pain Study, we were able to examine the outcome of these therapies for over 2000 patients. We could not determine that any therapy including physical therapy and exercise, manipulation

therapy, and acupuncture had any statistically verifiable influence upon the rate of recovery or the eventual outcome for the patient. Therefore, I use none of them in the management of patients [3, 16].

A major issue for American neurosurgeons is the virtual requirement by the majority of insurance carriers that surgery be preceded by a prolonged course of physical therapy. All the evidence we have suggest that this is a waste of time and money. On the other hand, simply waiting or providing the best symptomatic control possible will allow a substantial number of patients to recover spontaneously. Lack of understanding of this natural history has led many practitioners in the field of spinal pain to believe their specific therapies were responsible for recovery when they are simply observing the natural history of the disease [13].

50.6 What Do We Do with the Patient Who Fails to Recover?

Even though the majority of patients with acute spinal pain recover, there are a significant number who do not. Because of the enormous numbers of patients with spinal pain worldwide, the small percentage who do not recover remain a very large public health problem. These are the patients typically referred to spinal surgeons for evaluation. When confronted with a patient who has not made the expected spontaneous recovery, it is important to have a rational understanding of spinal pain as a problem and an equally rational evaluation system to try to determine the specific pain generators in an individual patient. It is equally important to identify present or impending neurological issues as well and to understand psychosocial factors.

50.7 Clinical Features of Spinal Pain

It is not my purpose in this chapter to try to define every spinal syndrome [12]. Rather it is to emphasize that the history is key in determining whether the patient requires treatment or not and usually will lead to diagnosis and guide that treatment. However, diagnoses made are frequently not specific and need to be verified and supplemented from other sources.

There are some generalities that are helpful. Local spinal pain without radiation suggests an axial problem. This may be muscle/ligament disease, it may be degenerative disk disease, and it may be from vertebrogenic sources. Radicular pain obviously implies root compression. Pseudoradicular pain cannot be differentiated clinically, and referred radicular pain is slowly being recognized as a real clinical phenomenon. It is poorly understood and cannot be completely defined at present. Nevertheless, there is good evidence that irritation of joint capsules, annulus, and posterior longitudinal ligament may produce an apparent radicular pain syndrome without obvious nerve root compression.

The history will usually localize the region of the spine where the pain originates. The severity is a key issue because treatment typically is dependent upon the influence of the pain upon the life of the patient. There is no reason to contemplate a major interventional procedure for a patient whose pain is relatively minor and easily tolerated. The history suggests the possibility of an underlying serious disease. Significant neurological loss emphasizes the need for prompt action. Once the problem is severe enough for referral to a spinal surgeon, then imaging is appropriate if it has not already been accomplished.

50.8 Imaging Correlations

The standard examinations are well known. Plane spinal films with oblique and dynamic views are still important. They help appreciate motion and anomalies of the spine which may be important in surgery.

The CT scan is now available with two- and three-dimensional reconstructions. These studies are important for assessment of bony anatomy.

The MRI with and without contrast is important because it gives the best views of soft tissues. The nerve roots and spinal cord with all surrounding structures can be well evaluated [8].

It is important to remember that a rare patient has low lumbar and sacral pain associated with sciatica on the basis of sacral and/or pelvic pathology. So when imaging studies are not definitive for a typical clinical syndrome, then examinations of these areas may be required with the same modalities.

The problem with imaging studies is that nonspecific degenerative changes are present in the majority of the adult population. They do not correlate well with clinical complaints. Simply finding severe degenerative changes in the lumbar spine does not suggest the patient with those changes will even have any symptoms. Minor changes can rarely be associated with specific clinical syndromes.

There are a few obvious diagnoses which correlate very well with the clinical syndrome. Such things as spinal tumor, infection, and spinal stenosis are adequately defined by imaging. The truly herniated disk and/or spinal stenosis is typically well defined also. Severe scoliosis and spondylolisthesis are satisfactorily diagnosed as well. Corrective procedures can be planned for all of such specific syndromes. However, the patient with nonspecific back pain with or without leg pain and degenerative disease without obvious canal or foraminal stenosis may need more definitive evaluation. There has been a great tendency in the past to dismiss these patients without complete exploration of the possible causes of spinal pain and the things which might be done to alleviate it.

Myelography with associated postinjection CT is still occasionally required for specialized situations. For the usual patient with back pain, the myelogram is rarely needed.

50.9 Diagnostic Blocks as an Adjunct in Diagnosis

The majority of patients who present with spinal pain will not have a definitive diagnosis made on the basis of history, physical examination, and imaging [17]. These measures will be adequate to diagnose almost all patients needing urgent care since progressive neurological deficit is typically related to a specific imaging finding. The large number of patients without these specific abnormalities are usually dismissed by the surgeon and relegated to ineffective modalities of treatment. I personally think that it is important they be investigated for potential interventions by going further to try to identify the causes of spinal pain. These additional steps require the use of diagnostic blockade [10, 11, 13].

The theory and utility of these blocks require some explanation. They are poorly understood by the majority of physicians even those expert in spinal problems. The theoretical basis for their application is straightforward. The first concept indicates that irritating the painful part may reproduce the pain which the patient experiences. Thus, placing a needle onto a painful joint may cause the same pain the patient suggests. Placing the needle close to an irritated nerve root will have the same effect. Thus the first phase of the procedure is to determine if placing the needle may reproduce the patient's pain. The second concept is that the anesthetization of the structure or its innervation with a local anesthetic will provide temporary respite from the pain. The relief of pain should be related to the duration of action of the anesthetic used or controlled by placebo.

It has been demonstrated that placebo blocks interposed with real blocks will provide the best selectivity and specificity. An alternative proposed by Bogduk is single blinding of the block so the patient does not know the actual structure being blocked and utilization of anesthetic agents of differing durations to assess the veracity of patient responses [13].

Thus, in a typical block situation, the patient does not know what structure is being blocked and does not know the duration of relief expected from the anesthetic. The individual performing the block should be skilled in questioning patients concerning outcome. The patient is queried concerning the production of concordant pain. That is, does the procedure reproduce the patient's usual pain? Then ideally, a third individual not directly related to the procedure or the patient's care should query the patient concerning the outcome for pain relief over the relevant time period. Bogduk and several collaborators have studied selectivity and specificity of these blocks and have demonstrated acceptable values which make

them useful adjuncts for the determination of the origins of spinal pain. Placebo control blocks approach 90 % accuracy. Those without placebo control fall more in the 70 % range. A positive block (one following which pain is relieved) has greater value than a negative block (one in which pain is not relieved). Accepting the limitations, these blocks can be helpful in determining origins of pain in patients with indeterminate imaging studies and form an important part of the diagnostic capabilities of the spinal surgeon. There is another important point, however. The decision for surgery is not based upon the outcome of these blocks. The purpose of the block is to determine origins of pain to guide a reparative surgical procedure to be the most specific possible. The decision for surgery is based upon the full patient evaluation and the totality of the examinations.

50.9.1 Root Blocks

Individual roots may be blocked using fluoroscopic or CT control. The needle is simply placed in immediate proximity to the root, usually at a foramen, and a small amount of the local anesthetic injected. The block should be characterized by appropriate motor and sensory loss to be verifiable. The blocks are indicated when the specific roots involved in the pathological process cannot be defined or when some uncertain process such as Tarlov cyst involves the root, and the question is whether the involvement is symptomatic.

50.9.2 Facet Blocks

The zygapophyseal joints may be blocked by placing the local anesthetic in the periarticular region or by blocking the innervation of the joint by anesthetizing the medial branch of the posterior primary ramus.

Pain relief following blockade can lead to periarticular steroid injection, radiofrequency destruction of the medial branch, and help select levels for fusion.

50.9.3 Diskography and Disk Blockade

Diskography has been in use for a half century and has major value in determining painful disk levels particularly with regard to interbody fusion. The technique was originally used to identify degenerated disks, and the decision for surgery was based upon the presence of degeneration alone. That approach was discredited years ago. Now the so-called provocative diskography is much more specific. Needles are carefully placed into the nucleus with image guidance. Injections into any other structures around the spine will be painful and negate the value of the test. Once the needles are in place and position verified the disk is distended by the injection of saline. The most important part of the test is provocation of the patient's usual pain. The patient must be awake enough to respond, and the questioner must be skilled in not leading the patient to an answer. Some diskographers then determine the degree of disruption of disk anatomy by the injection of a contrast agent. When the annulus is intact, a local anesthetic can be injected, and the relief of pain is an added proof of the importance of that particular disk in the painful process. When the annulus is disrupted, injection of local anesthesia has no localizing value. Again it is important to emphasize that the decision to operate is not based upon the provocative diskogram. The purpose of the diskogram is to specify levels for a proposed procedure and sometimes to emphasize the necessity for interbody fusion.

50.9.4 Sinuvertebral Block

The sinuvertebral nerve enters the posterior vertebral body at the exit point of the large draining vein which empties posteriorly. This nerve innervates the posterior third of the vertebral body, the posterior longitudinal ligament, some of the dura locally, and periosteum out into the foramina. The possibility that some back pain is purely vertebrogenic in origin is being explored now. The clinical value of these blocks is

uncertain, but they are done with a technique similar to vertebroplasty, and this is a new area for exploration.

50.10 The Decision for Surgery

When these diagnostic techniques are employed together in totality, they will eventually provide the information required to make a decision for or against a surgical procedure [18]. Surgery is proven to benefit nerve root compression and instability. Most spine surgeons believe that pain can be generated from abnormal facets in the same way that pain is generated from any other abnormal joint. Loss of resiliency, annular degeneration and tears, and abnormal stress distribution from degenerated disks are generally less widely accepted as the causes of spinal pain. Procedures specific to the disk such as interbody fusion have been based upon diskography. It has also been used to help identify the number of levels to be fused. Facet blocks have the same value and may lead to simple percutaneous treatments but may also lead to incorporation of specific joints into posterior fusion. However, the choice for surgery is never based simply upon imaging studies, except in very unusual circumstances, and is never based upon diagnostic blocks alone. The patient's complaint incapacity must first be judged seriously enough to warrant treatment, and then adequate localization of the probable pain generators by imaging and/or diagnostic blockade is required. When all these factors are concordant, then surgery is a reasonable choice [16, 19, 20].

50.11 Surgery on the Spine

The decision for surgery with herniated lumbar disk is usually straightforward. Patients with intractable pain unrelieved by the usual measures can go directly to surgery without the interposition of any physical therapy in my opinion. I know of no evidence of that physical therapy presents the need for surgery in these patients. For those who tolerate the pain and can afford the period of disability, spontaneous recovery is the rule and surgery is not required.

Spinal stenosis nearly always requires surgery for correction, so the only question is, are the symptoms serious enough to warrant treatment? Simple decompression is adequate in the majority of patients without demonstrated instability. In my own series, approximately 1 in 20 requires fusion from that category. Of course evidence of instability means fusion is likely indicated [21].

Patients with canal and foraminal stenosis fair just as well with surgery as those with disk herniation though the operation is somewhat more complex [21].

Fusion is required for demonstrated instability or the correction of spinal deformity when that deformity is symptomatic or threatens neurological function. Pain is not an indication for fusion unless the origins of that pain can be defined and shown to be related instability. A patient's complaint without supporting evidence is never an indication for surgery [21].

50.12 The Failed Back Syndrome

This term is imprecise and has no diagnostic value but is widely used. The diagnosis vaguely indicates that the patient has had previous procedures upon the spine and has failed to be improved by surgery. There are few specific diagnoses and the term is usually based upon a nebulous spectrum of therapies. The use of such a meaningless diagnosis also affects the behavior of those involved with these patients. It leads to the inaccurate perception that nothing can be done and implies psychiatric disease [16, 19, 20].

The goal in dealing with the patient who has failed previous treatments should be the same as the goal for those to be diagnosed and treated. That is, the surgeon must define the causes of the ongoing complaints and recommend specific therapies related to those specific causes. My experience with the failed back syndrome is over 8000 patients. Nearly 2500 of those have come to reparative surgery. This means that in the majority

of patients, no indication for reoperation was found [22]. However, in a very large number, there was an abnormality which could be corrected with the probability of pain relief and/or improvement in neurological function. The majority of those in whom no specific generator could be identified were satisfied and continued to function with their ongoing complaints. Approximately 1000 with more serious complaints were referred for spinal stimulation, and approximately 500 were maintained in chronic pain management programs. Of those in whom specific abnormalities amenable to surgery could be identified, approximately one third were symptomatic because the original surgery had failed to correct the underlying abnormality. Another third had developed a significant direct complication of previous surgery, and the final third had developed a new problem such as transition syndrome. These possibilities should be kept in mind when designing a protocol for the study of the patient who has failed previous treatments.

That actual protocol is very similar to what will be used with a patient with first-time complaints. A history, particularly of previous treatments, is important. The physical examination provides a baseline but rarely as anything of diagnostic value. Imaging studies should include plane dynamic films, CT for bony anatomy, and MRI. CT myelography is required more frequently in these patients because of the artifact induced by the presence of fixators. Two- and three-dimensional reconstructions can overcome the fixator artifact. In evaluating these studies, the three important questions are: (1) did the original surgeon accomplish the goals of the indicated operation? (2) is there a definable complication which could explain this patient's complaint? and (3) is there a new disease which can explain the patient's complaint? [18]

Diagnostic blocks can be helpful. Individual root blocks can define painful roots to correlate with imaging abnormalities. Field blocks of hardware can identify when the fixator is the cause of the pain. Facet blocks and diskography above and below fusion areas or blocks of apparent pseudoarthroses may be helpful in making a decision about the causative abnormality. Only when a clearly reparable problem can be demonstrated should surgery be selected. In my experience, these repeat procedures are as effective as original procedures to the fourth reoperation. That is, three procedures do not impact upon the eventual outcome but beyond three outcomes will be less salutary [18].

50.13 Use of Pain-Relieving Procedures

There are two procedures to be used for pain control when reoperation is not feasible and symptoms are severe enough to warrant.

Spinal cord stimulation is the most popular and has the longest history [23]. The technique has been employed for more than 40 years now and in my experience is very successful given specific parameters of selection. The patient should have a definable cause of the problem for the complaint and no serious unresolved psychosocial issues. Drug misuse should not be an issue. Stimulation is better for radicular pain than for back pain, and pelvic pain is the most difficult to relieve. Patients are selected by trials of temporary stimulation and those who achieve good relief are candidates for implanted devices. The overall long-term outcome is approximately equivalent to reoperation, and spinal stimulation is nearly always an alternative if neurological loss is not an important issue [24–32].

By contrast, the implanted drug delivery systems have been much less satisfactory in my experience. I have no patient who has achieved lasting control with such a problem. Therefore, I reserve them for the last resort when all else is failed and the patient is desperate for another trial of pain control [5].

50.14 Psychosocial Features of Chronic Pain

The effects of chronic pain are well known [33, 34]. Demoralization, depression, and anxiety are common consequences of unrelieved pain. They

do not necessarily imply that these were primary problems or cause the pain complaint.

On the other hand, pain is a common complaint with depression and other psychosocial issues [6]. The importance of these so-called comorbidities is that they may interfere with the appropriate evaluation of the patient and that patient's outcome of therapy. Pain is a subjective complaint, and, therefore, the complaints must be valid if treatments are to be prescribed and outcomes assessed. The major point is that these comorbidities must be assessed in advance and appropriately treated lest they influence both decision making and posttreatment evaluation.

The issue of litigation and disability is important in many countries. In the National Low Back Pain Study, we identified that every patient working at the time of surgery for herniated lumbar disk returned to the same job without restriction postoperatively. For those patients involved in litigation, not one returned to work during the first 2 years after surgery. However, the anonymous outcomes assessed by every measure were identical for the two groups. The effect of litigation upon complaints and the resolution of those complaints must always be considered [19].

Malingering or exaggerations are also known among these patients. The actual incidence of true malingering is probably small but must be remembered whenever a patient appears to be exaggerating the pain complaints through pain behavior. The signs suggestive of exaggeration were described by Waddeil and those observations remain valid. Pain behavior is a red flag which needs to be considered. Florid pain behavior may be nothing more than the patient's desire to impress upon physician how important the problem is, but it may have much more serious connotations which need to be evaluated. Whenever depression, anxiety, or demoralization appear to be important as factors in the patient's complaints, it is valuable to have the patient seen by a mental health professional to deal with those issues. Florid pain behavior strongly suggests the need for psychiatric consultation and potentially for the cognitive and behavioral therapies which will be of value. In my experience with failed back syndrome, the need for these complex pain therapies is relatively small, but the important issue is that any patient in whom important comorbidities are suspected, psychiatric and/or psychological evaluation may be helpful [35].

50.15 The Tarlov Cyst

In the recent past, I have recognized that the number of patients with symptomatic Tarlov cysts may be substantially higher than is generally been suspected. These cysts were described in the 1930s, and by midcentury, it was well accepted that many were symptomatic. MRI subsequently demonstrated a number of cysts which were not symptomatic, and the appreciation that some could be was gradually lost. Now it is common for radiologists and neurosurgeons to state that these cysts are never symptomatic. We have identified groups of patients in whom the cysts are obviously symptomatic. These fall in three categories.

Dural ectasia in patients with known connective tissue disorders such as Marfan's syndrome is frequently symptomatic and produces loss of sacral root neurological function.

Dural diverticula, which may be variations of internal meningoceles, are often seen. These are large midline structures, usually confined to the sacrum, unlike the ectasias which often penetrate the sacrum and appear as presacral masses. The dural ectasias are typically found in women; the dural diverticula are typically found in men. The diverticula are often associated with progressive neurological deficit mimicking tethered cord syndrome.

Patients with large perineural cysts on individual nerve roots can also be symptomatic. The typical clinical picture is of pain in the distribution of the affected roots and appropriate accompanying neurological loss.

I have successfully operated upon these patients for many years though the numbers remain quite small (approximately 75). Recently, we have begun a study for aspiration of apparently symptomatic cysts and subsequent filling with a fibrin sealant. The outcomes are promising, but longer evaluations required to determine

what the eventual outcome will be. The important issue is that large Tarlov cysts should not be dismissed as incidental findings. Some will be symptomatic and adequate treatment will relieve the patients.

50.16 Minimally Invasive Procedures

There are a number of procedures introduced over the many years of my practice for the treatment of low back pain, degenerative disk disease, herniated disk, and related conditions. The injection of chymopapain, an enzyme to dissolve the internal structure of the nucleus and possibly herniated disk fragments, failed because of the small incidence of fatal anaphylactic reactions and neural toxicity. A new form of this enzyme therapy without either drawback is currently being studied and may be an important new adjunct in therapy of back pain related to disk degeneration and herniation.

There have been a number of attempts to remove the nucleus of the disk percutaneously. These have included laser destruction, mechanical excision, and heat. There are no adequately controlled studies to demonstrate significant value of any of these techniques. Heat and the injection of hypertonic solutions have also been used to try to solidify existing nuclear structures and thus improve the biomechanics of the spine. No adequately controlled studies exist to verify the value of these techniques.

Perineural and periarticular steroid injections are commonly employed. It is the experience of many spinal experts that these provide immediate relief of pain in many patients with compressed nerve roots or arthritic facets. The studies are mixed and mainly flawed by lack of selectivity in the patient inclusion criteria. Nevertheless, it is the experience of many that these injections will be of immediate value in many patients with acute and some patients with chronic problems. There is virtually no evidence that the eventual clinical course of these patients will be modified, but pain relief can often be immediate and provide for more rapid mobilization of the patient.

Prolotherapy which is the injection of hypertonic solutions designed to strengthen ligaments in the back has limited theoretical value in my opinion. I know of no definitive studies which demonstrate long-term value of the technique.

Radiofrequency destruction of the medial branch of the posterior primary ramus for the treatment of facet-based spine pain was introduced in the early 1970s and has proven to be very successful in a relatively small number of patients. The patient who is a candidate should have demonstrated facet arthritic changes, excellent relief of pain by temporary blockade of the innervation of those joints, and failure of periarticular steroids. About 60 % of such patients will achieve lasting relief with simple percutaneous denervation carried out on an outpatient basis [36]. Unfortunately, a relatively small number of patients appear to have pain generated almost exclusively from lumbar facets. Most have a more complicated set of pain generators.

50.17 Newer Concepts of Diskogenic Pain and Its Treatment

Motion and nerve root compression have been the established causes of back pain amenable to surgery. Several newer concepts are suggested to be important in the generation of lumbar pain.

Transient pain from muscle and ligament injury or reaction to injury is well known and typically relents with conservative care. Recently, abnormalities of spinal contour have been shown to be causes of chronic severe pain. Scoliosis with and without rotation has long been known to be associated with pain. Abnormalities of sagittal contour with displacements of the normal spinal center of gravity either anteriorly or posteriorly are increasingly understood to be a cause of chronic pain. These are usually related to degenerative disk disease and may occur with and without spondylolisthesis. Correction of disorders of sagittal contour and scoliosis can reduce ligamentous tension, inflammation, and muscle distortions all of which produce pain [37].

There is increasing evidence that the inflammatory products of the herniated or degenerating disk also induce pain [38]. Products of the inflammatory cascade are found in nerves, the dorsal root ganglion neurons, and even in the spinal cord neurons [39]. Nociceptors are sensitized. Normally quiescent cells are sensitized and respond to all kinds of stimulations by signaling pain. This local inflammatory response may explain why annular tears and small disk protrusions without obvious significant nerve root compression can cause apparent back and radicular pain of severe degree. It is increasingly likely that one of the reasons why locally injected steroids can be so effective in eliminating symptoms is their antiinflammatory influence upon the inflammatory cascade. This concept is supported by laboratory research but remains to be verified in humans [40]. The inflammatory products of the injured disk have been demonstrated. At present, the only practical treatment would be oral administration of antiinflammatory drugs, local measures for the relief of the inflammation, and local steroid injections, which are so often successful in relieving symptoms with acute disk injuries.

The newest field of research in diskogenic pain relief involves reconstitution of annulus and/or nucleus with stem cells or related cellular techniques [41]. There are promising animal models. Protein growth factors, gene transfers, and cellular therapies utilizing stem and mature cells are all strategies being investigated. Tissue engineering is another possible reconstructive technique for sealing tears and strengthening the fibroblastic response. Sealants may exclude the inflammatory process from the surround. None of these have been applied to humans sufficiently to judge potential as yet [42–45].

A future scenario is likely to be injection of a nucleolytic to dissolve a disk herniation followed by injections to reconstitute the nucleus and annulus. First steps are now being taken to make this possibility a reality.

There are no data which allow the evaluation of surgical biological therapies for these degenerated but not herniated disks as yet. It seems likely that diskectomy with stabilization or replacement of the injured disk with an artificial substitute would be useful but as yet even that has not been systematically investigated for the simple degenerated disk. The biological alternatives would be minimally invasive and thus even more appealing.

50.18 The Guidelines of My Spinal Practice

Low back pain is a common adult complaint throughout the developed world. The majority of acute low back pain episodes will relent spontaneously. Evaluation is not needed immediately if there are no red flags. A small number of patients with acute disk herniation will require surgery based upon severity of pain and real or impending neurological deficits. Many can be relieved of radicular pain by perineural steroid injection and/or a short course of oral steroids. Rapid mobilization and return to function are helpful. A small number of patients will not improve after 1–3 months, and surgery for demonstrated pain generators is highly successful. Major indications for surgery currently are instability and neural compression. The role of disk degeneration, facet arthritis, and skeletal deformity continues to be explored, but corrective procedures for all three are often of value. The majority of patients with degenerative spinal disease do not need fusion. Simple posterior fusion is often satisfactory, and fixators should be employed for specifically defined purposes. The presence of back pain is not an indication for fusion alone. Patients who fail procedures should be reevaluated to be certain that the original procedure was successful, no complication has occurred, and no new disease has developed. Those with serious psychosocial and behavioral issues should be referred for comprehensive evaluation and treatment. Pain management with narcotics will be useful for some who might otherwise be disabled. The majority can be managed with nonnarcotic analgesics, restriction of activities, and education concerning the realities of a chronic pain back problem. There are many unproven therapies available for these people, and it is important that they all understand what is accepted therapy,

what is proven to be a value, what is investigational, and what is of no proven value. The so-called conservative measures commonly employed in back pain may provide immediate improvement in symptoms but have no lasting effect upon the natural history of the problem. Many acute patients in whom surgery might be contemplated will escape operation if surgery is delayed for 1–3 months following onset of symptoms. A requirement for physical therapy prior to surgery is without merit based upon my experience and literature reviewed. The key issue is that surgery corrects specific abnormalities and should be reserved for those individuals in whom those specific abnormalities can be demonstrated. Surgery for symptoms is not indicated and will rarely be successful. Surgery for the correction of demonstrated abnormalities should relieve related symptoms.

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Lessons Learned from a Life

51

H. Michael Mayer

51.1 The World of Spinal Surgery: Then

In 1982 when I started my career as a young resident at Mario Brock's Department of Neurosurgery at the Free University in (at that time "West"-) Berlin, the "world of spinal surgery" seemed to be easy.

Neurosurgeons performed lumbar (micro-) diskectomies and cervical keyhole (sometimes rather "mousehole") foraminotomies and anterior diskectomies with fusion using autologous bone grafts like Cloward or Smith and Robinson had taught them.

For spinal tumors and metastases, total laminectomies very often were the treatment of choice.

Orthopedic surgeons concentrated on deformity correction. The Harrington rods and the Luque technique were the standard procedures for the treatment of deformities. For trauma surgeons, the treatment of spinal fractures and injuries was at that time a difficult endeavor. Conservative treatment in casts, wires, and rods without the possibility of reduction, and uninstrumented fusion were the most popular treatment modalities. For short-level fusions, a more logical but "dangerous" technique of putting screws into the pedicle and connecting them with rods or plates had just been invented by two European spine surgeons [1, 2] who were about to use this techniques in clinical trials.

In summary the treatment of disk herniations, spinal cord compression of any kind, fractures, and deformities were the main fields which were covered by spinal surgery. Moreover, diagnostic measures were limited. X-rays, myelography, and scintigraphy were standard procedures. The spinal computerized tomography (CT) scan was something new and not used as a standard diagnostic tool at that time.

Patient selection was easy, diagnosis was difficult and invasive, surgical technology was poor, and looking back very critically to those years, the treatment outcomes were poor as well. Surgical treatment of the spine was characterized by high complication rates, loss of correction in deformity cases, the necessity of recurrent operations, and pain. These were the years were a new syndrome was established: the "failed back surgery syndrome" (FBSS). Although we are aware that also today we see patients with persistent pain following spinal surgery, we now know that the term FBS "syndrome" is a semantic error

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_51

because "syndrome" implies an underlying clinical and morphological entity which is not the case in patients suffering from persistent symptoms following back surgery. Today we are able to find out the specific pain source in virtually every patient.

For most of neurosurgical and orthopedic residents, spine surgery was a potentially dangerous and unknown territory, poorly understood, and not at all an attractive choice for subspecialization. Neurosurgical residents were fascinated by brain surgery or aneurysma clipping, and orthopedic residents focused on the trendy field of arthroscopic knee surgery or total hip replacement – fields with a great future.

So what kind of idiot could I have been to get interested in spinal surgery?

And here we come to the *first lesson* I have learned:

Lesson 1: Don't Always Follow the Mainstream

One of the first operations I was allowed to perform at the beginning of my neurosurgical training was a cranial burr hole to insert an intraventricular catheter for intracranial pressure measurements in a brain-injured patient. My second operation was a lumbar diskectomy. These two procedures were at the beginning of the 1980s the typical "resident's cases." Besides the marginal technical differences the main difference I noticed between these two "procedure categories" was that, outcome- and complication-wise, there was not really much to lose in a nearly brain-dead patient, but you could well "destroy" the professional and social life of a patient with a simple disk herniation if the operation was not done properly.

It wasn't really clear to me at that time, why we youngsters were allowed to perform lumbar diskectomies which outcomes could have such a big impact on a patient's life, whereas the excision of a glioblastoma (with a survival rate for the patient which was at that time less than 9 months with or without treatment) was considered to be high-level neurosurgery.

I believe the answer to this policy which was practiced in the majority of neurosurgical departments throughout Europe lies in the fact that the contact time of a disk patient with neurosurgery was short. Pre- and postoperative treatment were completely in the hand of either physiatrists or orthopedic surgeons, neurologists, and pain specialists. Unless it was a recurrent disk herniation or a postoperative pseudo-meningocele, we very rarely saw a patient with a "failed back surgery."

Anyway, I got interested in disk surgery and in the question how the common surgical technique of diskectomy could be improved. It was in the early days of 1983 when John A. McCulloch visited the Neurosurgical Department at the Free University of Berlin and showed us a new technique which was called "chemonucleolysis" [3]. I was fascinated by the idea that a posterolateral percutaneous intradiscal injection of an enzyme which was obtained from the papaya fruit and which was called "chymopapain" could have the same clinical outcome as "open" diskectomy. Until that time, my whole scientific activities had been focused on intracranial pressure, brain metabolism measurement, and intracerebral blood flow under various experimental conditions such as ischemia, brain abscess or brain injury. Now I got interested in a "spinal" topic.

I learned the technique and was allowed to perform it. My scientific interests focused on perioperative intradiscal pressure-volume tests, anesthesiologic aspects, clinical results, and complications such as allergic reactions [4–7].

The results were good, the complication rates were low, and chemonucleolysis was about to become a new minimally invasive standard technique in spinal surgery.

Then I had to learn my *second lesson*:

Lesson 2: Successful Treatments May Fail Without Medical Reasons

Why is this important? The neurosurgeon and orthopedic surgeon's thinking in the middle of the 1980s of the last century was more or less mechanical. A slipped disk causes pressure on the nerve root. If you remove the disk, the nerve root is relieved. The biochemical aspects of disk herniations and root pain were unknown that time. Now if chymopapain is injected into the disk, it hydrolyses the bonds of the matrix mucopolysaccharides and "dissolves" the nucleus

pulposus. This leads to a reduction of the intradiscal pressure and thus to a reduction of the pressure on the nerve root. However, it can take some time until this clinical effect is evident for the patient as well as for the surgeon. Now, being patient is not really typical for surgeons. Even though chemonucleolysis achieved good clinical results with low complication rates, it never had the popularity which it should have deserved. Moreover, the reimbursement was much lower as compared to surgical diskectomy.

Three things happened in the middle of the 1980s which initiated the failure of chemonucleolysis. (1) There was a report of a patient who had developed a paraplegia after erroneously intrathecal injection of chymopapain [8, 9]. (2) There were some case reports on anaphylactic reactions to chymopapain [10]. Chymopapain is also an ingredient of "meat tenderizers" or cleaning fluids for contact lenses, so there is a certain sensitization among the normal population. (3) In 1985 a new percutaneous technique was described to mechanically aspirate nucleus pulposus from the center of the lumbar disk [11].

So, I lost chemonucleolysis temporarily out of sight because I was about to learn my *third lesson*:

Lesson 3: The Shortest Way Is Not Always the Best Way

I had realized that the spectrum of spinal surgery in neurosurgery would be too small to build a career on. After 3 years, I interrupted my neurosurgical training to start my orthopedic training at the Department for Orthopedic Surgery at the Free University of Berlin to learn spinal fusion techniques as well as anterior approaches to the thoracic and lumbar spine. The advantage of having being skilled already in microsurgical techniques was priceless. Although it was accidentally that I did part of my neurosurgical training first, I learned the lesson that if you are able to practice microsurgery, it will definitely be easier to learn macro-surgical techniques. I enjoyed doing hip and knee surgery through small skin incisions (which I had to justify everyday because nobody was practicing or was even thinking about minimally invasive approaches for total hip or knee replacement at that time …). I could learn all types of anterior trans- and retroperitoneal approaches to the lumbar spine because the philosophy of biomechanically stable circumferential fusion had become popular by the work of René Louis from the mid-1970s [12]. I could experience the first steps with a new posterior correction and stabilization system called "CD" according to its inventors Cotrel and Dubousset, two surgeons from France [13, 14]. I learned anterior transthoracic approaches for anterior scoliosis correction with the Zielke system [15]. Orthopedic surgery made fun, but after 3 years I was in the situation that I had completed two half resident's programs and I had to make a decision.

Between 1985 and 1987, Onik's automated percutaneous lumbar diskectomy (APLD) became popular on both sides of the Atlantic Ocean. However, it turned out that obviously the indication spectrum for a central decompression of the lumbar disk was narrow and that the majority of disk herniations could not be treated with this procedure.

The percutaneous approach however was fascinating. I was wondering whether an endoscopic procedure which would follow the principle of arthroscopic surgery could be an innovative approach to lumbar disk herniation. It turned out that I was not the first to have such an idea; however, since the orthopedic patient population at that time did not include a lot of disk patients and since my chief was a traditional hip surgeon who did not support my ideas, I decided to find somebody to support me. It was my former chief Prof. Mario Brock who, due to his experience with chemonucleolysis, was also fascinated by the idea of an endoscopic approach to the disk.

As I said, it was not really my own idea. Parviz Kambin in Philadelphia, USA, was about to organize the first international workshop on "Arthroscopic Microdiskectomy" in 1987 in Philadelphia. I attended this workshop and met with Hijikata from Japan who had performed percutaneous diskectomies since early 1973 [16] and I met Profs. Schreiber and Suezawa from Switzerland who had performed the first endoscopic diskectomies worldwide [17].

In summer 1987, I performed the first endoscopic diskectomy in Germany and spent the following years until the early 1990s with this scientific topic. I learned that a selective diskectomy is possible under endoscopic control with various types of instruments. In experimental and clinical trials, I learned about the use of different laser technologies for endoscopic diskectomy. I learned that using a laser does not really influence the clinical result of endoscopic diskectomy (but it helped me to write my PhD thesis) [18, 19].

I completed my neurosurgical training and could show, in a prospective, randomized controlled trial, that percutaneous endoscopic diskectomy achieves similar results as compared to microsurgical diskectomy (with the same indication criteria) [20].

I was happy but not yet a spine surgeon. I realized that I had to leave neurosurgery again to learn the rest of the orthopedic part of spinal surgery.

And there I learned another (the *fourth*) *lesson*:

Lesson 4: Don't Sacrifice the Surgical Goal for a New Technique

I was fascinated by small surgical approaches to the human spine. In 1991 Obenchain, an American gynecologist, described a laparoscopic approach for lumbosacral diskectomy [21]. This was more or less the trigger for laparoscopic and thoracoscopic fusions and approaches which were refined in the following years. The long learning curves, demanding technology, complication rates, and high non-fusion rates were the reasons, why laparoscopic fusion did not stand the proof of time. One of the major problems with laparoscopic surgery was that this fascinating approach was combined with the application of threaded fusion cages. These cages never proofed to be sufficient as a stand-alone implant for spinal fusion even if they were applied through "open" approaches. So the fact that the surgical goal to achieve a solid spinal fusion was sacrificed for the new minimally invasive approach was the main reason for the failure of laparoscopic techniques although the idea was fascinating. However, thoracoscopic surgery survived and is now a routine for anterior treatment of fractures and other pathologies of the thoracolumbar spine.

I was frustrated with my first laparoscopic experiences and focused my attention to the development of mini-open anterior approaches to the thoracic and lumbar spine [22, 23]. Again I could apply "microsurgical thinking" to develop a new approach. Mini-open anterior lumbar interbody fusion turned out to be a universal approach for different pathologies without the necessity to use one single type of implant.

It even turned out to be the access technique of choice for modern artificial disk implants.

The era of modern total disk replacement began in 1999, and again I learned another important *lesson* (*#5*):

Lesson 5: Progress in Spinal Surgery Needs the Right Implants, the Right Surgeons with the Right Technology at the Right Time

I had the honor to attend one of the first Charité total disk implantations at the Charité Hospital of the Humboldt University in "East Berlin" in 1984 which was performed by Karin Büttner-Janz and Professor Schellnack, the two inventors of the "Charité disk." At that time, nobody realized that it would take nearly 15 years until this technology would "make it around the world." There have been several reasons why it took so long for a good idea to become accepted. It was the implant material and design which had to be further improved. It was the anterior transabdominal surgical access which was way too aggressive at that time to justify the implantation of a new implant for degenerative disk disease. And last but not least, it was the diagnostic uncertainty which was a very high threshold for surgeons to recommend aggressive types of surgical procedures. I remember that all these arguments were important for us not to start with total lumbar disk replacement at that time. However, the topic was so fascinating that we decided to organize the first international symposium on "The Artificial Disk" which we performed in Berlin in on November 9, 1989 [24]. It was an historic event, not necessarily because of the scientific topic but because of the date. During our faculty dinner on the evening of November 9, 1989, the Berlin Wall opened and we had the opportunity to be part of a historical moment when we went to

the Brandenburg Gate that night. Actually one of our overseas faculty members thanked us later on for "the best social program he ever had…."

Although politically it was the right time, total disk replacement had to wait.

However, 10 years later, I was fascinated by the idea to apply our minimally invasive anterior approaches with the new generation of total disk replacement. It was in the mid-1990s when Thierry Marnay visited me in Berlin to discuss minimally invasive anterior approaches for the implantation of anterior fusion devices and total disk replacement.

When Prodisc L second generation was developed, I learned *lesson # 6*:

Lesson 6: Total Disk Replacement Works

In 1997 I was chief staff surgeon and vice director of the Department of Orthopedic Surgery at the Free University of Berlin. I had become a spine surgeon and was ready to take over full responsibility. Fortunately I got the chance to build up a spine center at one of the most traditional and well-known orthopedic hospitals in Germany: the Orthopädische Klinik München-Harlaching in Munich, Germany.

I took over the new job in March 1998 and began to structure a spine center. Besides the various managing tasks, I, for the first time in my professional life, had the freedom to practice new techniques. In 1999 we implanted the first artificial lumbar disk through a mini-open retroperitoneal approach. It was a great moment to realize that my access technique actually met the needs for this new implant concept. Motion/function preservation in combination with a minimally invasive surgical access technique turned out to be the key for the success story of total lumbar disk replacement. Although the overall midterm outcomes of total lumbar disk replacement in the last 10 years are more or less comparable to spinal fusion, there is a subgroup of patients who show and represent the cutting edge of this new technology combination. Looking back at spinal fusion results, I had never seen high-level athletes who returned to their full performance strength after lumbar of cervical fusion. Now I could see a professional soccer player who played in 60 matches in the year after total lumbar disk replacement. I could see a patient becoming Olympic champion 7 months after artificial cervical disk replacement, and I had saw patients who could run marathons with an artificial lumbar disk [25–28].

Our enthusiasm in "motion preservation" urged us to organize the first international scientific meeting on "Spine Arthroplasty" in 2001 in Munich. Munich was the birthplace, and this meeting was the birth place of the Spine Arthroplasty Society (SAS) which was founded during this meeting.

In the following years, the idea of spine arthroplasty grew, the annual meetings of the SAS have become the yearly highlights of the scientific scenery for motion-preserving technology and have also become the forum for the rapidly growing industry behind it.

In 2001 we all did not realize that total disk replacement was just the beginning of a new era in spinal surgery. The hype of replacing fusion surgery with reconstructive technology has triggered other developments such as dynamic pedicle-screw fixation, interspinous "extension stoppers," interspinous spacers with interlaminar fixation, etc.

And here is *lesson #7*:

Lesson 7: We Cannot Beat Nature

If we look at outcome studies for various types of treatment in degenerative low back pain, we will soon realize that the successful so-called long-term results all range between 60 and 80 %. This is true for passive waiting as well as for all types of invasive treatment. And – it is logical. Degenerative changes of the spine are self-limiting pathologies which symptomatology is temporary in the majority of the patients. If you add on whatever kind of more or less aggressive treatment to this "natural course," how can you expect the "end result" to be better than the "uninfluenced" course?

This led me to *lesson 8* which says:

Lesson 8: Surgical Therapy in Degenerative Diseases of the Spine Can Only Modulate the natural Course

The "classic" in this sense are the outcomes of lumbar diskectomies. It is well known from the

literature and from randomized controlled trials (RCT) that the midterm and long-term results of lumbar diskectomy (open, micro, endo) are virtually the same as in non-operated patients. The results converge after 4 years. However, would this justify to tell a patient who is in severe radicular pain due to a lumbar disk herniation or who is suffering from neurological deficits to wait 4 years for the "end result?"

Definitely not! Even if the result of diskectomy is the same as for conservative therapy and even if the risk of surgery is higher than the risk of just waiting, this result can be achieved much quicker through the decompression of the affected nerve root.

The concept of indirect decompression of the central and lateral spinal canal by the implantation of an interspinous spacer and extension stoppers arose in 2003 with the first clinical application of X-Stop [29]. In the past years, this concept has been further elaborated and now a great number of interspinous implants are currently in clinical studies or already in routine use for the treatment of spinal stenosis and/or low back pain. They neither have a significant stabilizing effect nor do they promote spinal fusion. This means that these implants most probably will have a temporary clinical effect.

And this is *lesson # 9* I learned:

Lesson 9: Spinal Implants with a Temporary Clinical Effect May Be Acceptable for the Surgeons and the Patients

It is a daily experience I make since a couple of years: patients want to get rid of their pain quickly and reliably. The less invasive a type of treatment is, the higher is the acceptability. How would we or the patient classify, for example, the percutaneous implantation of an interspinous spacer for the treatment of dynamic lumbar spinal stenosis? Most of the patients consider this 12 min procedure more as an aggressive or invasive type of conservative therapy than as a minimally invasive type of surgery. Even though the perspective is only a temporary relief of symptoms, the patient seems to accept this kind of treatment provided that the need for another surgery in case of recurrent symptoms is not impaired by the fact that bridges have been burnt down.

51.2 The World of Spinal Surgery: Now

The last lesson is *lesson # 10*:

Lesson 10: The Spine World in 2014 Is More Colorful

When I learned the first lesson in my "spine life," the world of spinal surgery was black and white. For a given pathology, there were one or two treatment options. Today we are facing a wide variation of conservative and surgical treatment modalities. This makes the life of a spine surgeon easier and harder. It is easier to choose among different options, but it is more difficult to determine which treatment option is the best in each individual case. But this is what makes spinal surgery so fascinating and what will keep us busy scientifically and clinically for the coming years.

Innovative ideas are not getting less, but the obstacles and difficulties to realize them get more. Failures of most of the global players in the spinal Medtech industry to realize that innovation and progress has always been patient/surgeon – and not engineer – driven have led to the development and marketing of a number of needless and senseless implant systems and concepts in the last 15 years. This on the other hand has expectedly increased the alertness and criticism of payers, insurance companies, and healthcare providers toward new products. The adherence of major companies to the currently dominant and overregulated markets has initiated a downward spiral for innovative spine surgery in the western world.

However, this opens new opportunities for countries and companies which do not comply with this trend. We should always remember that all major steps forward in orthopedic surgery started very nontraditional, off-label, off-budget, uncontrolled, remarkably innovative, and unhibited by failures and relentless.

I would like to thank my great teachers and fellow colleagues who have lit the fire for spine surgery and who have helped me to learn my lessons.

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Lessons from 35 Years in the Trenches

52

Edward C. Benzel, Kene Ugokwe, and Nina Z. Moore

52.1 Introduction

Mastery of the art and science of the spine surgery is a career-long endeavor. Spine surgeons are exposed to experiences throughout their career that are not necessarily a part of their formal training, yet mold their practice and their academic life. Though a solid understanding of the biomechanical and surgical principles is essential, the lessons learned from "experience" are equally valuable and when coupled with prior knowledge result in "wisdom." These "lessons learned" are not limited to the act of surgery but also include the perioperative period. Surgeons can get caught up in the "act of surgery," while ignoring essential nonoperative factors. The patient selection process and the "social aspects" of surgery and the decision-making process are critical components of the "art of surgery." The "social aspect" of care takes into account the patient's desires, expectations, and feelings. It involves an obligatory ongoing dialog with the patient and the patient's family. This chapter focuses on the senior author's reflections regarding the art and science of surgery, as interpreted by the junior authors.

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52.2 The Preoperative Period

The game is won or lost in the outpatient clinic.

Patient selection for surgery can be challenging. This is clearly an understatement. To simplify this process for lumbar degenerative disk disease, one might divide patients into several categories: nonoperative, potentially operative, and definitively operative. Nonoperative patients often have an undiagnosed chronic pain syndrome. These individuals often have numerous pain complaints (multiple unrelated somatic complaints) that are not attributable to a specific dermatome or myotome. Their pain is often characteristically atypical, e.g., burning pain. One of the most significant mistakes in the lumbar degenerative disease decision-making process is to treat chronic pain as if it were acute pain. These patients often have a low energy level and complain of nonrestorative sleep. Unfortunately,

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_52

they may also have "pathology" on imaging studies. This "pathology" often tempts the surgeon to recommend surgery. The outcome is often predictably suboptimal. The bottom line here is to maintain a low threshold for establishing the diagnosis of a chronic pain syndrome and to treat the patient accordingly – usually without surgery.

Operative patients can be divided into two groups based on a simple question. Would the surgeon have this surgery if he/she were the patient? If the surgeon honestly answers this question, the rest of the process is greatly simplified. During a national spine meeting approximately 8 years ago, audience members during a plenary session were asked if they would recommend surgery for a case presented to the group. Eighty percent of the surgeons responded in the affirmative. When asked if they would have the same surgery themselves, only 20 % of the audience responded in the affirmative. This is damning to the profession of spine surgery. Performing an operation that one would not undergo him/herself, at the very least, raises questions regarding the surgeon's specific operative indication process and the motives for such. There are, of course, patients that harbor a clear-cut indication for surgery and are, therefore, much easier to select. Regardless of the strategic plan derived, the spine surgeon should be fiscally responsible when crafting the plan of attack on the patient's malady. The surgeon should act (i.e., manage and advise the patient) as if he/she were paying the bill.

52.2.1 Nonsurgical Management

Most patients should undergo aggressive nonsurgical management prior to any consideration for surgery. Surgery should be most often employed as a treatment of last resort. It is imperative that the surgeon be familiar with, and be willing to prescribe, relevant nonsurgical clinical modalities. Offering such should not be construed as a sign of failure, but rather as an indication of good judgment. Physical therapy by a familiar and competent physical therapist is an often underutilized tool. Other nonoperative techniques that should be considered are epidural steroid injections, traction, TENS units, and nonnarcotic meds including muscle relaxants and NSAIDs. An appropriate exercise program should consist of a core-strengthening and flexibility training that also incorporates weight loss, cessation of smoking, and aerobic exercise. The spine surgeon should be keenly aware of the needs of the patient and the value to the patient provided by consultants and modalities. An open line of communication between the surgeon and the therapist is critical. A trial of membrane stabilizers (e.g., gabapentin or pregabalin) should also be considered in the appropriate patient (e.g., patients with neurogenic claudication or neuropathic pain) prior to operative management. Finally, the adverse consequences, whether they be short or long term, of spine surgery must not be taken lightly. Remember, "One can always do surgery, but one cannot undo surgery."

The best surgical candidates are those that meet the criteria for surgery and have demonstrated that they are medically compliant. Cessation of smoking, weight loss, and active participation in physical therapy programs are all means by which one can assess the patient's compliance. The absence of a commitment to such (i.e., noncompliance) correlates with poor outcome regardless of treatment employed. The patient and the surgeon must work together in order to achieve optimal results.

52.2.2 Education

The surgeon must not underestimate the importance of the well-informed patient and family. Surgical success is measured not only by the physical outcome but also the patient's interpretation of the outcome. Patients and their families must be presented with realistic expectations and be well informed regarding the potential risks and complications of surgery so they can make well-informed decisions and be prepared prior to the day of surgery. If complications occur, the involved and informed patient and family will be much more likely to

understand and work collaboratively with the surgeon to overcome the obstacles encountered. Additionally, it is important to establish a healthy and genuine relationship with patients. Expressions of empathy and active listening yield more accurate medical histories, as well as improved professional relationships between the patient and the surgeon. It is important for the surgeon to inform the patient of any conflicts of interests so the patient can take that information into account during the decision-making process. This serves as a means by which the surgeon can regulate his/her own clinical bias and help avoid the perception of any impropriety [1].

When the aforementioned aspects are appropriately considered in the clinical decision-making process, an optimally tailored approach to care is easily achievable.

52.3 The Intraoperative Period

From an operative perspective, a strategy that embodies the concept that "more is better" does not always hold true. Sometimes simplicity is best. More complex surgery does not ensure a decreased return to surgery rate. Doing less is not a sign of weakness, inefficiency, or incompetence, but may be a sign of maturity. The "older (mature) surgeon" adage of "the more I do, the less I do" applies here.

52.3.1 The Surgical Team

The surgeon must work as a team member and as the leader of the team. The importance of teamwork cannot be overemphasized. This team approach is critical both in and outside the operating room. It establishes open lines of communication with all involved surgical team members. As the leader of the team, the surgeon must convey expectations, concerns, and overall operational strategies to the anesthesia and nursing teams in a timely and calculated manner. The surgeon must maintain composure regardless of the situation. Information should be exchanged in a nonthreatening and nonconfrontational manner. All members of the team look to the surgeon for guidance and leadership. The absence of composure sends a powerfully negative message to the remainder of the team that may induce panic and a suboptimal overall team effort. Communication with the patient's family is also important during surgery. Updating the family members during the operation reduces family stress and solidifies the doctor-patient relationship.

52.3.2 Unexpected Intraoperative Findings

It is not uncommon for intraoperative findings to be unexpected, based on preoperative imaging and clinical information. Surgeons are expected to be creative and to improvise in such situations, thus demonstrating their ability to adapt to adverse and unexpected circumstances.

It is important to think in terms of the "future" as well as the "present" when making intraoperative decisions. For example, fusing extra levels may be good for the "present," but be associated with excessive long-term consequences. Such long-term negative consequences may be preventable by appropriately considering extent of surgery. The operative decision-making process should be guided more by the principles of providing long-term relief of symptoms than by those symptoms associated with instant gratification. The surgeon should always consider the potential problems associated with an operation. Every attempt should be made to avoid creating a problem of equal or greater magnitude.

The surgeon should be mindful of how the intended operation will affect the patient's spine alignment and balance. Appropriate lumbar lordosis helps avoid adjacent segment disease. Fusions should be performed only after the effect on adjacent levels is appropriately considered. The surgeon should avoid extra or "prophylactic" surgery – making every attempt to perform the surgery for which the patient was consented. The surgeon should also be mindful of the patient's wishes, culture, and religion preoperatively,

intraoperatively, and postoperatively. The surgeon's expectations should ALWAYS be aligned with those of the patient.

52.3.3 Intraoperative Complications

If an intraoperative complication occurs, it is best that such be disclosed to the patient and their family, regardless of how trivial it may seem. The term complication should encompass unexpected outcomes. Such outcomes should be directly addressed. Honesty, forthrightness, and clarity of thought and action are key virtues in these situations.

Staging an operation is often prudent in cases with excessive operative time or blood loss. Staging surgical procedures is clearly a decision that is surgeon based, but made in collaboration with other members of the team (i.e., the anesthesiologist). The arguments for and against such must be carefully considered.

After every operation, it is imperative that the surgeon show gratitude and appreciation to the rest of the surgical team. A simple gesture such as a "thank you" or a "great job everyone" goes a long way. It makes the team members feel appreciated and it makes them look forward to the next interaction.

52.4 The Postoperative Period

Patients and their family members universally look forward to seeing their surgeon postoperatively. They nearly always have questions and concerns and are nearly always anxious. Successful surgery is associated with a strategically planned postoperative course. The communication and enactment of a sound postoperative plan are essential. Wound care management, pain control, physical therapy plans, continued weight loss, and smoking cessation should all be part of the plan, when appropriate.

It is particularly important to establish and maintain an ongoing dialog with patients that have had suboptimal outcomes or who have terminal conditions. Avoidance of these patients often causes anger and leaves them with a sense of abandonment. Always provide honest responses to questions. Surgeons must provide comfort by objectively guiding the decision the patients must make. This simple act provides relief and security for patients and their family. As Rabbi Kushner [2] once said, "Caring about others, running the risk of feeling, and leaving an impact on people, brings happiness. Being kind to others is a way of being good to yourself." He emphasized the two major fears that terminal patients harbor: pain and abandonment. These can be addressed by adequately and appropriately treating the pain and by having an extra sit-down talk or two with the patient. Such talks are universally appreciated. They make the surgeon feel good, as well. Remember Kushner's words: "…Being kind to others is a way of being good to yourself."

One final comment regarding suboptimal outcomes: the patient who does not improve as expected from surgery deserves special consideration. It is extraordinarily important to reassess their problem. One must consider the notion that the patient did not improve because they did harbor the diagnosis that correlated with the surgery performed. The presence of a chronic pain syndrome is likely the most common reason for failure of lumbar spine surgery for pain. If the surgeon operates on a lumbar spondylolisthesis, but the patient's complaints are those of a chronic pain syndrome, the outcome is seldom positive. In this case, surgery is not the treatment of choice and is essentially doomed to failure.

52.5 Summary

This chapter provides reflections into the lessons learned from a career in spine surgery. It is, however, important to note that these lessons can be applied not only to spine surgery but to all surgical specialties. Regardless of the contents of this chapter, as spine surgeons and as physicians, we must all remember that we must "first do no harm" and second to "do unto others as you would do unto yourself." It is important to be honest and to do what is right for our patients. We

leave you with five important principles, outlined by Robert Grossman [3], which we believe all spine surgeons should live by:

1. There is no such thing as a simple neurosurgical spine operation. A neurosurgical spine is identical to an orthopedic spine.
2. It is easier to stay out of trouble than to get out of trouble.
3. The time expended in avoiding complications will be more than compensated by the time saved in not having to treat them.
4. The patient's well-being is paramount. Therefore, the surgeon should never hesitate to request consultation, or assistance, during surgery.
5. Surgeons should always operate as if the patient were their family member.

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History of Lumbar Endoscopic Spinal Surgery and the Intradiskal Therapies

53

Yong Ahn, Gun Choi, and Sang-Ho Lee

53.1 Introduction

In the field of spinal surgery, preservation of normal tissues has become an important issue with understanding human physiology more comprehensively. And the main goal of the latest spinal surgery is neural element decompression and stabilization of spinal motion segments without any normal tissue damage and its negative long-term consequences. To achieve these, many types of surgical technologies have been developed for minimizing their invasiveness. Especially, the introduction of endoscope to spinal surgery was an encouraging sign of achieving splendid development of minimalism. With recent advance and experience, several advantages such as reducing blood loss, operation time, recovery period, and time to return to work have differentiated percutaneous endoscopic spinal surgery from conventional open surgery. However, conventional operations have been reported to be associated with good results and such has been accepted as a "golden standard" until now. Today, the spectrum of minimally invasive spinal surgery with a percutaneous endoscope is expanded from simple disk operations to include deformity operations. In this chapter, a historical account of percutaneous endoscopic lumbar disk operations is summarized in terms of their technical landmarks.

53.2 Era of Percutaneous Diskectomy (Fig. 53.1)

The concept of *posterolateral percutaneous diskectomy* was firstly introduced in 1973. Parvis Kambin conducted percutaneous indirect spinal canal decompression by nucleotomy using Craig's cannula in a nonvisualized posterolateral

Financial support: This study was supported by a grant from the Wooridul Spine Foundation.
The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in this chapter.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_53

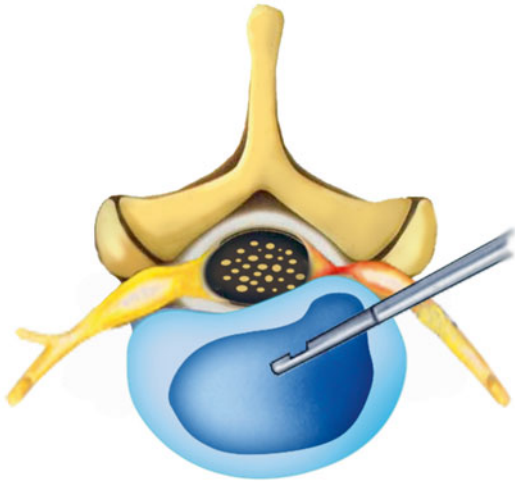

Fig. 53.1 Posterolateral percutaneous diskectomy

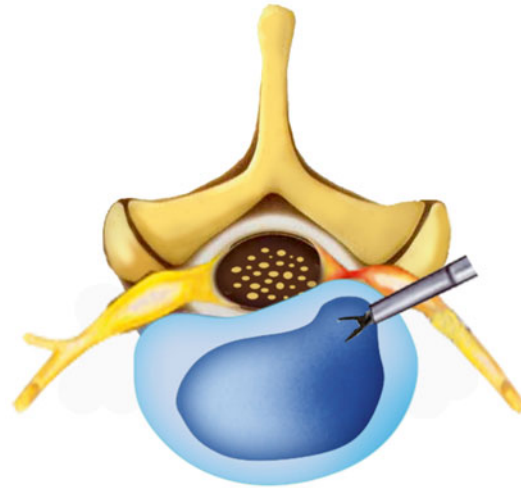

Fig. 53.2 Transforaminal endoscopic diskectomy for contained disk herniation

approach [1]. Hijikata firstly published the technique of nonvisualized posterolateral percutaneous diskectomy in 1975, which was a standalone procedure [2]. In 1983, the direct lateral approach for percutaneous nucleotomy was performed by William Friedman in which he reported the association between this procedure and a higher rate of bowel injury [3]. In the mid-1980s, Onik et al. introduced a motorized aspiration shaver to the percutaneous diskectomy technique [4], and then, Onik and Maroon reported the clinical outcome of "*automated percutaneous diskectomy*" using the Nucleotome [5, 6].

53.3 Era of Endoscopic Diskectomy (Contained Disk Herniation) (Fig. 53.2)

After the percutaneous diskectomy age, an endoscope termed the *diskoscope* was applied to the percutaneous diskectomy technique for direct visualization. Hausmann and Forst introduced a nucleoscope for viewing the intervertebral disk space [7]. Schreiber and Suezawa firstly reported a transdiskoscopic nucleotomy technique [8]. In the study, some of the patients underwent percutaneous diskectomy performed under the diskoscopic visualization. In 1988, Kambin et al. reported the first intraoperative diskoscopic views of herniated nucleus pulposus and he suggested that the visualization of the epidural space would be very important in his later articles [9]. In 1989, Schreiber et al. used a *biportal approach* with a diskoscope and injected indigocarmine dye into the disk to discriminate abnormal nucleus pulposus and annular fissure [10].

In 1990, Kambin also described an important anatomical feature regarding the transforaminal approach – the so-called *triangular working zone* in which there is neither vessel nor nerve [1]. The safe zone is bordered anteriorly by the exiting nerve root, inferiorly by the end plate of the lower vertebra, posteriorly by the superior articular process of the inferior vertebra, and medially by the traversing nerve root. The definitive description of the triangular working zone enabled the introduction of larger endoscope with larger instruments and more sophisticated decompression without exiting nerve root damage.

Mayer and Brock described the technique of *percutaneous endoscopic lumbar diskectomy (PELD)* for contained disk herniation using an angled lens scope allowing dorsal vision around the annular tear [11]. This was similar to Schreiber's biportal approach. They removed the herniated nucleus with rigid or flexible forceps, as well as with automated shaver system under

intermittent endoscopic control (diskoscopy). Since then, the so-called PELD is one of the representative terms of endoscopic lumbar diskectomy techniques.

53.4 Era of Endoscopic Diskectomy (Noncontained Disk Herniation) (Fig. 53.3)

Mathews 1996 [12] and Ditsworth 1998 [13] opened the era of real *transforaminal approach*. Ditsworth described the technique in which a working channel endoscopy passes completely through the foramen into the spinal canal and the surgeon directly removes free fragments and decompresses the nerve root and dural sac [13]. Since then, a truly transforaminal approach, as opposed to just going through part of the foramen and into the disk, has been developed and the target disk pathology is broaden from contained disk herniation to noncontained disk herniation.

In 1996, Kambin and Zhou published a technique of endoscopic decompression for the treatment of lateral recess syndrome. They decompressed the nerve roots, compromised by lateral recess stenosis, by annulectomy and osteophytectomy with forceps and trephines in using angled endoscopes (0- and 30-degree endoscopes) [14].

They described that in the case of large central disk herniation at the level of L5–S1, sequestered disk herniation, or migrated disk herniation, open surgery was required [14, 15].

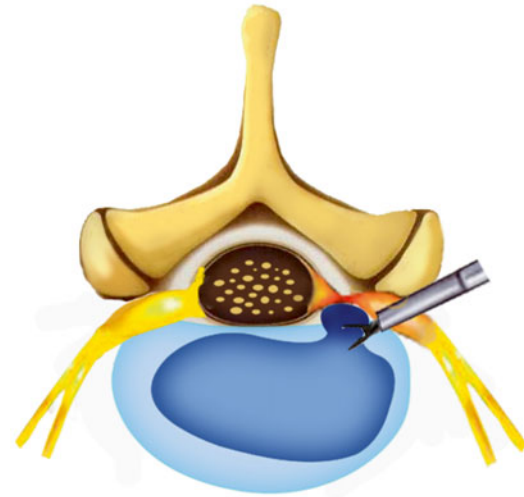

Fig. 53.3 Transforaminal endoscopic diskectomy for noncontained disk herniation

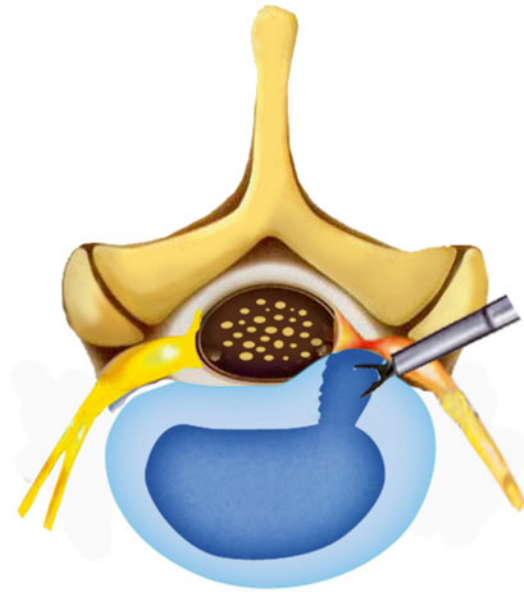

Fig. 53.4 Transforaminal endoscopic selective diskectomy

53.5 Era of Endoscopic Selective Diskectomy (Noncontained Disk) (Fig. 53.4)

The basic concept of the percutaneous endoscopic surgery has been evolved from an indirect intradiskal decompression to a direct epidural or selective neural decompression. The working space has been extended from central nucleus to periannular and finally epidural space [16]. In the new millennium, various advanced endoscopic techniques have been developed. *Selective endoscopic diskectomy* was named by Kambin et al. [17] and Yeung [18] independently. Yeung used the Yeung Endoscopic Spine System (YESS™) which has a rigid rod lens and integrated, multichannel, wide-angled endoscope [19]. They described the selective endoscopic diskectomy technique

for extruded lumbar disk herniation. They also introduced a foraminoplastic approach at the L5–S1 level. In 2003, the endoscopic surgical system became more contemporary as launching YESS designed around the transforaminal endoscopic approach for intradiskal and epiduroscopic procedures. Yeung and Yeung also described the utility of provocative intraoperative diskography, thermal diskoplasty and annuloplasty, and annular resection for creation of an annular window to perform foraminoplasty using abrasive drills, burrs, and lasers [20]. Some authors reported the endoscopic technique for various situations such as recurrent disk herniation, disk herniation at L5–S1 level, migrated disk herniation, or upper lumbar disk herniation. Ahn and Lee described the endoscopic technique for recurrent disk herniation and upper lumbar disk herniation [21, 22]. Sometimes, the standard posterolateral approach might be associated with problems in reaching the epidural space due to anatomical peculiarities. This problem of poor visualization of the epidural space was solved with an extreme lateral approach described by Reutten et al. [23]. They pointed out that the usual transforaminal access is posterolateral and associated with problems in reaching the epidural space directly with unhindered vision, and then they described an extreme lateral access into the spinal canal using the full-endoscopic uniportal transforaminal approach. At the same time, Schubert and Hoogland described a foraminoplastic approach with bone reamer to remove the migrated and sequestrated disk herniation [24]. They used a bone reamer to undercut the part of superior facet to reach the epidurally extruded disk fragment. Choi and Lee introduced a technique of interlaminar approach to L5–S1 level or migrated disk herniation from L4 to 5 level [25, 26]. Lee et al. applied a classification system for the migrated disk herniation and demonstrated the clinical outcomes according to the disk migration zone [27].

In 2006, Lee et al. studied the limitation of endoscopic diskectomy in the aspect of the size and location of disk herniation [28]. They concluded that open surgery may be considered for herniations with high-canal compromise and high-grade migration. Lee et al. also described percutaneous endoscopic intraannular subligamentous *herniotomy* [29]. The concept of herniotomy is removal of whole iceberg, not just the tip of the iceberg. It is important to prevent recurrent disk herniation or incomplete removal which is one of the main concerns about minimally invasive endoscopic surgery [16].

53.6 Era of Endoscopic Foraminal Decompression (Fig. 53.5)

Although various foraminoplastic approaches were introduced, most of the techniques were not for true foraminal decompression, but for approach to the intracanal pathologies. Therefore, the history of foraminal endoscopic decompression started in the late 1990s. Knight et al. introduced *endoscopic laser foraminoplasty* for various foraminal nerve root entrapment syndromes [30–32]. The basic concept of foraminoplasty is reshaping foramen by ablating soft tissues such as foraminal ligaments and osteophyte using side-firing laser under endoscopic visualization. Ahn et al. described a *percutaneous endoscopic lumbar foraminotomy* technique using bone reamer and laser [33]. Schubert and Hoogland also reported the use of a bone reamer for foraminoplasty in the case of migrated disk herniation [24]. However, the previous techniques have limitations for definite foraminal decompression. The use of laser is effective for only neural entrapment caused by soft tissue or fragile osteophyte. However, it may be less effective for severe bony foraminal stenosis. Blind use of bone reamer also has inherent limitations such as bone bleeding and neural injury because it is a blind technique without any direct vision control. Nowadays, some authors reported more advanced endoscopic foraminal decompression techniques that can be performed for severe foraminal stenosis cases. The use of endoscopic burr and endopunches enables a safer and more effective full-scale foraminal decompression [16, 34].

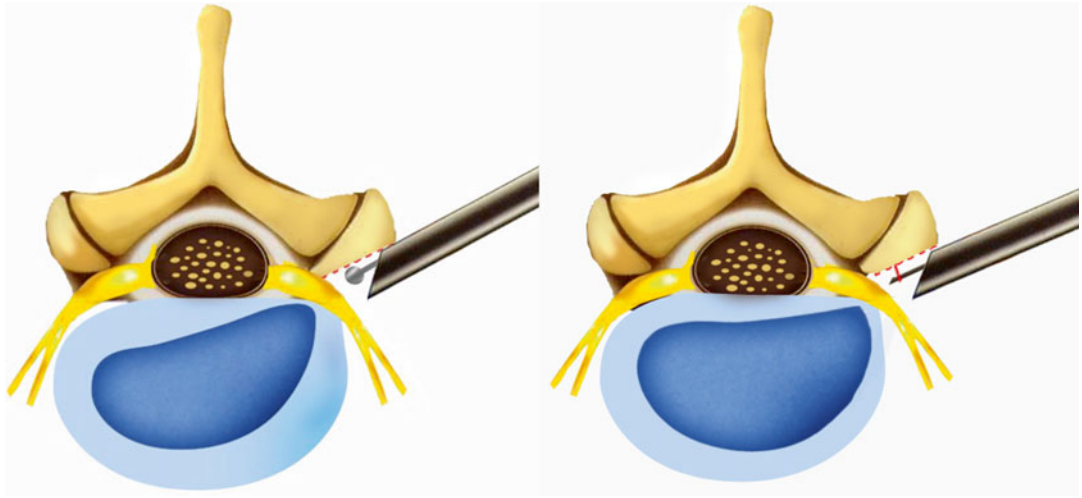

Fig. 53.5 Percutaneous endoscopic lumbar foraminotomy

53.7 Era of Endoscopic Treatment for Diskogenic Back Pain (Fig. 53.6)

Most previous studies on percutaneous endoscopic surgeries have mainly described the technique which treats the lumbar radiculopathy caused by nerve root compromise. Several pioneers tried to treat diskogenic back pain with percutaneous endoscopic techniques. In 2004, the surgical technique of minimal access posterolateral transforaminal selective endoscopic diskectomy and bipolar radiofrequency thermal annuloplasty to interrupt the purported annular defect pain sensitization process was introduced to treat the patients with chronic lumbar diskogenic pain [35]. In this study, a total of 113 patients were recruited; however, the results showed lack of clinical benefit from this procedure. In 2010, Ahn and Lee reported the outcome predictors of percutaneous endoscopic lumbar diskectomy and thermal annuloplasty (PELDTA) for diskogenic low back pain, in which 83.5 % patients showed symptomatic improvement and the success rate was 70.9 % [36]. In their conclusion, PELDTA could be effective for the patients with chronic diskogenic low back pain. Lee and Kang used laser-assisted spinal endoscopy (LASE) kit for the percutaneous intradiskal decompression to evaporate and shrink the posterior and central nucleus for improvement of lumbar pain [37]. Percutaneous endoscopic laser annuloplasty, a new minimally invasive technique, used LASE for direct coagulation of the painful inflamed granulation tissue with new vessels and nerves in 30 patients with diskogenic low back pain. They reported favorable outcomes for carefully selected groups of patients with diskogenic low back pain. Although the theoretical background is fascinating, the clinical application of this technique is not, as of yet,

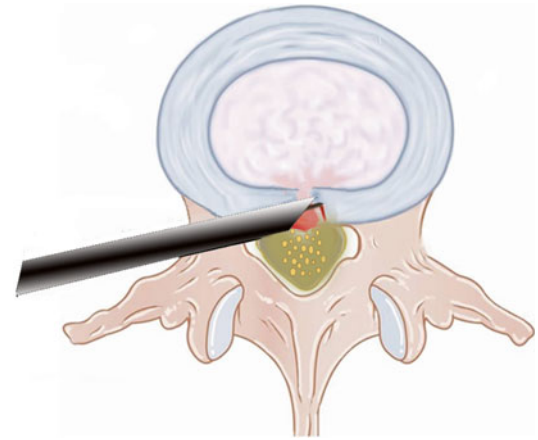

Fig. 53.6 Percutaneous endoscopic lumbar annuloplasty for diskogenic back pain

established. The patient selection and surgical technique should be more standardized to produce a reliable clinical result in the future.

53.8 Era of Laser Diskectomy and Radiofrequency Ablation

The application of the laser to minimally invasive or percutaneous lumbar surgery is very attractive to spine surgeons because of the ability to deliver a large amount of energy through a small fiber to a focused spot area. The laser tissue interaction can be classified into three types: photochemical effects, photothermal effects, and photomechanical and photoionizing effects [38]. Until now, for percutaneous laser disk decompression (PLDD), lasers in the near-infrared region (Nd:YAG, Ho:YAG, and diode lasers) and with visible green radiation (frequency doubled Nd:YAG, called "KTP laser") were reported to be effective [38]. The basic technique of PLDD is similar for all trials. The procedure is conducted under local anesthesia of the skin and underlying muscles. After assessment of the correct disk level by using fluoroscopy, a hollow needle is inserted 10 cm from the midline, pointing toward the center of the disk. A laser fiber (0.4 mm) is inserted through the needle into the center of the nucleus pulposus. Laser energy is then delivered into the nucleus pulposus to vaporize its content and reduce intradiskal pressure [39].

In the mid-1980s, Ascher and Choy developed percutaneous laser diskectomy technique [40, 41]. Ascher firstly applied laser into the disk surgery using a neodymium:yttrium-alluminum-garnet (Nd:YAG) laser [40]. The procedure included fluoroscopically guided insertion of an 18-gauge needle into the disk space through which 400-nm laser fiber was advanced into the disk space. Approximately 1200 J of energy in short bursts to avoid heating the adjacent tissues was delivered to ablate a small intradiskal tissue. Through the spinal needle, the vaporized tissue was escaped. Finally, an adhesive bandage covered the needle site and patient was discharged. In 1990, Davis performed laser diskectomy with the potassium titanyl-phosphate (KTP) 532-nm laser in 40 patients and reported 85 % success rates [42]. Choy et al. introduced the new technique of percutaneous laser disk decompression (PLDD) in 1992 [43]. They reported the clinical outcomes of 333 patients with 78.4 % of good to fair results. Subsequently, Mayer and Brock suggested a combined technique between laser ablation and endoscopy in order to keep observing the amount of removing disk tissues during surgery [11]. There was a report on comparison study between Ho:YAG laser diskectomy and conservative treatment in 1993 [44]. Even though they could not identify a significant difference in terms of complications, they concluded that the laser diskectomy was a safe procedure to be effective in relieving symptoms in some patients. There was also a comparison study between the Ho:YAG and ND:YAG laser in 1994 [45]. They demonstrated that Ho:YAG laser was the best for compromising between efficacy of absorption and convenience of fiber-optic delivery. In 1995, Casper et al. reported an 84 % success rate at 1-year follow-up in the patients treated by the side-firing Ho:YAG laser [46]. In 1998, Knight et al. reported endoscopic laser foraminoplasty using a side-firing Ho:YAG laser for chronic low back pain and sciatica [30]. Then, Hellinger started to use the Ascher technique for Nd:YAG laser ablation in 1999, who had treated more than 2500 patients for 13 years and his overall success rate was approximately 80 % [47]. In 2000, Yeung reported an 84 % success rate in his experiences with more than 1000 patients whose herniated lumbar disks were treated by KTP laser [48]. Nowadays, the laser can be used as a supplementary role in ablation of bone and soft tissue. It can be also used for thermal laser annuloplasty in the treatment of diskogenic back pain.

53.8.1 Radiofrequency Ablation

High-frequency radiofrequency (RF) ablation has progressed with developing several applications in spinal surgical field. To dissect and coagulate the tissue, high-frequency RF keeping low

temperatures during surgical works was developed. Also on demand for targeted application and precise tissue ablation, Trigger-Flex Bipolar System (Elliquence, New York, USA) was developed, which is compatible with other endoscopic spinal surgery system.

RF ablation is considered a promising alternative to lasers in terms of their cost, safety, and convenience issues. In 2004, Tsou et al. reported the surgical outcomes of 113 consecutive patients with diskogenic low back pain, minimum 2-year follow-up, in which they used low-temperature RF tissue ablation [35]. There were no aborted procedures, unexpected hemorrhage, device-related complications, neurologic deficits, or instability.

Nowadays, the high-frequency RF with low-temperature tissue ablation has been involved as a part of endoscopic spinal surgical system, and it is suggested that this RF ablation is very effective in controlling bleeding and shrinking tissue.

53.9 Randomized Trials

Through the history of percutaneous endoscopic lumbar surgery, there are only four randomized controlled trials in which the effectiveness of percutaneous endoscopic diskectomy was compared to conventional open diskectomy [49–52]. In 1993, Mayer and Brock firstly reported a randomized trial evaluating the effectiveness of percutaneous endoscopic diskectomy for contained disk herniation compared to microdiskectomy [51]. They concluded that percutaneous endoscopic diskectomy appeared to offer an alternative to microdiskectomy for patients with "contained" and small subligamentous lumbar disk herniations. Hermantin et al. ($n=60$) demonstrated that the satisfaction rate between the endoscopy group and the open diskectomy group was the same [49]. However, the period of postoperative disability or narcotic use was significantly shorter in the endoscopy group. Hoogland et al. conducted a prospective randomized study recruiting 280 patients with lumbar disk herniation treated by endoscopy alone or endoscopic diskectomy with intradiskal injection of low-dose (1000-U) chymopapain [50]. Ruetten et al. ($n=178$) used full-endoscopic transforaminal diskectomy using 4.2-mm working channel endoscope, and they demonstrated that the results were comparable to those in conventional open-disk surgery [52]. However, the current level of evidence on the effectiveness of transforaminal endoscopic diskectomy is low because most studies have substantial design weaknesses in the randomization method or outcome measures with a high risk of bias. Only one adequately randomized controlled study has been identified thus far [49]. Therefore, high-quality randomized controlled trials with sufficiently large sample sizes are required to provide valid information on the effectiveness of endoscopic diskectomy in the future [16, 53].

53.10 Future Perspective

The technical improvement of percutaneous endoscopic lumbar surgery has been splendid in surgical approaches, design of optics, and surgical instruments. Because of the rapid technical advancement, the paradigm of percutaneous endoscopic spine surgery is shifting. In earlier generations, the main topic of the percutaneous endoscopic surgery is soft disk herniation. Any stenotic component with lumbar disk herniation is regarded as a contraindication or a predictor of poor outcome for this technique. However, the indications are broadening to the degenerative lumbar stenosis. The percutaneous endoscopic decompression technique for various lumbar stenosis and even deformity correction will likely continue to evolve. Furthermore, this technique may be combined with various minimally invasive spine procedures such as motion-preservation technology, regenerative medicine, or biologic therapy for traumatic and degenerative spine disease.

Acknowledgments The authors would like to express a special acknowledgment to Ho Kim, B.S. and Jae Eun, Park, B.S. for preparing figures and manuscripts.

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The Importance of a Registry in Spinal Surgery

54

Emin Aghayev, Christoph Röder, Helton L.A. Defino, Carlos F. Herrero, and Max Aebi

54.1 Mainstays of Patient Care

The mainstays of patient care throughout the ages used to be intuition, psychology, and charisma. In this environment, which was characterized by trust on the part of the patients and society and self-confidence and dedication to the cause on the part of the clinician, considerable advances in medical therapy were made. Only a few players in the medical arena made initiatives for a systematic assessment of what was done and what the result of those treatments were. Among them was Florence Nightingale, a nurse, who applied statistical methods for analyzing preventable deaths in the British military during the Crimean War as early as 1854. Ernest Codman, a US physician and the father of what is today considered as outcome management in patient care, became famous in the early 1900s for his "end-result system" which stated that every patient needs to be followed up to assess the benefits and complications of the received treatment. Finally, Maurice E. Müller, cofounder of AO/ASIF (Arbeitsgemeinschaft für Osteosynthesefragen/Association for the Study of Internal Fixation), published his concept of a multi-site trauma registry with centralized database for assessment of surgeon performance, efficacy of surgical techniques, and postmarket surveillance of implants in 1963 [1].

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54.2 Quality Control and Outcome Research

54.2.1 Definition of Quality in Health Care

To those not involved in quality improvement in a professional capacity, it might appear relatively simple to define quality; however, more than

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_54

2000 years after Plato invented this term, there is still great debate regarding the meaning of the word [2]. The American Society for Quality (ASQ) defines quality as "a subjective term for which each person or sector has his or her own definition" [3]. According to a user-based approach, quality can be defined as "meeting or exceeding customer satisfaction" [4]. Quality is a multidimensional construct, and the dimensions are specific for each category. The US Agency for Healthcare Research and Quality defines quality in health care as "doing the right thing, at the right time, in the right way, for the right person, and having the best possible results [5]."

The quality measures in health care assess four components:

- Structures (resources such as staff or equipment)
- Indications (making the right therapeutic decision for a given pathology and its stage)
- Processes (therapeutic interventions, prescribing, interactions with patients)
- Outcomes (end results of health care such as mortality and patient satisfaction) [5, 6]

The measures used to obtain the patients' views can be classified into three categories:

- Preferences
- Evaluations
- Reports

Wensing and Elwyn defined preferences as patient ideas about what should occur in healthcare systems. Evaluations are patients' "reactions" to their experience of health care and reports are objective observations (e.g. how long the patients had to spend in the waiting room). The choice of the type of measure depends on the aspect being assessed and the purpose of the evaluation (educational, certification, accreditation, quality control, or quality improvement) [7]. One of the most widespread means of measuring processes and outcomes is the assessment of patient satisfaction (evaluation category). Outcome satisfaction is also one of the criteria for assessing the validity of process measures. Indeed, according to Chassin [8], a measure of process is valid when it is related to health outcomes (e.g., mortality, patient satisfaction, etc.). Hence, the responses to questions concerning satisfaction with treatment, typically used in treatment outcome studies, can also be seen as outcome measures in the quality control and improvement context.

54.2.2 Overlap of Outcome Research and Quality Control

Quality control is an important concept in all medical disciplines, but a factual implementation and application in a stringent and meaningful way is still lacking in many cases. The growing emphasis on an evidence-based approach in the medical setting has led to a corresponding increase in the number and quality of studies in the twenty-first century examining the efficacy of surgical and nonsurgical treatments. These studies are usually conducted in university hospitals and clinics that have an in-house research staff or that cooperate with academic research institutions. The studies are not commonly perceived by the care provider (hospitals and clinics) as being something from which they can benefit, from an economical point of view; in contrast, carrying out such research can sometimes be seen as a drain on resources. The research activities on treatment outcomes are merely seen as something that may indirectly benefit the institution in terms of prestige and corporate social responsibility. However, the possibility of economic benefit from corporate social responsibility activities is not a sufficiently persuasive argument for increasing investment in research; otherwise, all the public and private hospital and clinics would likely have their own research departments or research staff. Significantly, in all of this, one important factor is typically overlooked: research projects in the field of treatment outcomes and their predictors can be useful to the provider in a much more direct way in terms of quality improvement and the control of service performance [9].

54.3 "Observational" Versus "Experimental"

The main goal of outcome research and quality control is the collection of distinct evidence, and an appropriate study design is one of its main prerequisites. The study designs can be divided into observational, such as a registry, and experimental ones, such as an RCT (Fig. 54.1).

Levels of evidence are defined by the study design and execution, and designs have been variously graded by their potential to eliminate bias [10, 11]. A hierarchy of study designs was first proposed by Campbell and Stanley [10]. The concept of evidence levels has been widely promoted since then to grade recommendations for clinical practice. The dogma of an RCT and RCT-based meta-analyses having superior evidence over an observational study has long been held as gospel despite numerous appeals to reconsider and to adapt the evidence levels [11–16]. The reasons for this may be that the only available evidence pyramids focuses on efficacy studies, which allow for an accurate assessment of cause and effect. The terminology "observational" connotes that the data were collected without interference, so the decision to assign patients to an exposure is not random and may be self-determined by confounding variables that are highly correlated with the outcome. As a result, an observed significant difference in outcomes may not necessarily be attributable to the choice of treatment alone but to the confounding variable (or to some combination). Thus, according to the current evidence-based medicine practice, a small sample-sized RCT would bring undoubtful superior evidence than a large observational study. RCT study design has a high acceptance in all clinical disciplines despite a long list of its limitations such as ethical considerations, organizational burden, complexity of random allocation, complexity of blinding, time and personal resources consumption, compromised integrity of the clinical context, difficulty in studying rare events and outcomes in distant future, limitations in evaluation of population-based interventions [11], sample size limitation for definitive results [17], patient refusal of participation, narrowing of the studied population, and limited external validity [18], as well as financial efforts. This is also despite the fact that so many efforts are required to answer only one main posed hypothesis in an RCT and the fact that the number of non-randomizable clinical questions is by far much higher than the number of randomizable ones.

In orthopedic surgery and traumatology, among other medical disciplines, it is often diffi-

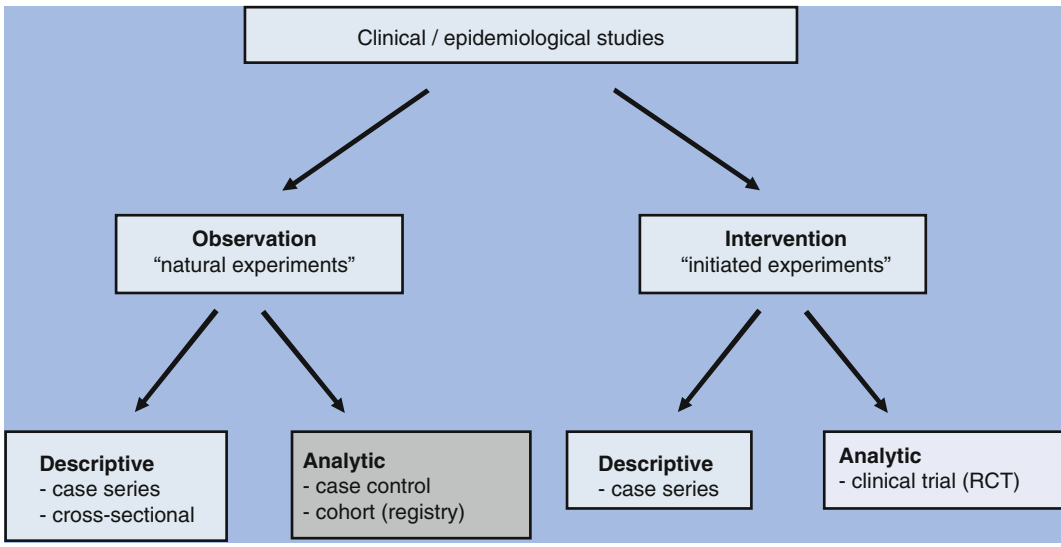

Fig. 54.1 Anatomy of medical research

cult to provide an ethically justifiable patient randomization for differing and often insufficiently studied treatment methods. In medical disciplines other than surgical ones, like in conservative treatments or in pharmacology, the effect of a treatment is often assessed in comparison to a placebo. In surgical disciplines and particularly in orthopedic implantology, placebo comparisons are difficult to imagine. This is a nonnegligible and important organizational restriction of a randomized controlled study design. There are particular questions in implantology which may justify an RCT; however, the method of choice for implant comparisons is a registry with sufficient participation to ensure high external validity, i.e., generalizability of results to the routine clinical settings [19]. Particularly when introducing new implants and aiming at postmarket surveillance, an observational approach allowing for benchmarking of new and older implants appears to be the most reasonable one [19].

Moreover, one should be aware that a large observational cohort and an RCT are per se designed to answer different questions, and their different goals and setups result in their different characteristics (Table 54.1). Importantly, while an RCT answers the question "can it work?" an observational study addresses the question "does it work?" [20] In a large dataset, one could add "in whom does it work best?" as one of the key questions that the large observational comparisons can answer, since they include better and poorer indications for a certain therapy, as it is mostly the case when an innovation is adopted by the larger medical community. Table 54.1 summarizes characteristics of an RCT versus registry.

On the other hand, strong evidence exists on the similarity of the results in RCTs and in observational studies. Benson and Hartz reviewed RCTs and observational studies between 1985 and 1998 and found that in a vast majority of therapeutic comparisons, the estimates of the treatment effects from observational studies and randomized controlled trials were similar [13]. In the same time, Concato et al. reviewed literature between 1991 and 1995 and concluded that the results of well-designed observational studies with either a cohort or a case-control design do not systematically overestimate the magnitude of the effects of treatment as compared with those in randomized controlled trials on the same topic, as it is anticipated [12]. In orthopedics, Bhandari et al. have shown that, when adjusted for important risk factors, the results of observational studies ($n = 13$) on revision and mortality rates after internal fixation of femoral neck fracture were similar to those in RCTs ($n = 14$) [21]. Equality of the results in an RCT and in a cohort study was shown also in spinal surgery based on the results from SWISSspine registry [22] and the Spine Tango results of a single center [23].

The proponents of an observational study design are often opponents of an experimental approach and vice versa. In 1996, Black wrote that there is no perfect study design and that "the false conflict between those who advocate randomized trials in all situations and those who believe observational data provides sufficient evidence needs to be replaced with mutual recognition of the complementary roles of the two approaches" [24]. Spinal surgery is one of the youngest and, in the same time, one of the fastest growing clinical disciplines with high and further growing epidemiological and financial impacts on society. The evidence demand in spinal surgery is therefore high, and there is a compelling need for quality assurance, outcome research, and postmarket surveillance of spinal implants.

54.4 "Spine Tango": An International Spine Registry for Quality Assurance, Outcome Research, and Postmarket Surveillance of Implants

54.4.1 History and Objectives

In the late 1990s, the founder of the first spine unit in Switzerland – Prof. Dieter Grob – was asked by the cantonal government of Zurich to conduct an outcome study of the results of surgical interventions on the spine. The investigation was completed and the data provided to the spon-

Table 54.1 Characteristics of an RCT and a registry

Characteristics	RCT	Registry
Type of evidence	Efficacy	Effectiveness[a]
Principal question	Can it work? (the first step of evidence generation)	Does it work? (verification in clinical practice)
Internal validity (methodological quality)	+++	+/++ (expandable with, e.g., monitoring, audits, or validation with secondary data, etc.)
External validity (transferability/generalizability)	–	+++
Bias	Low to very low	High to low depending on set-up (appropriate set-up and evaluation methodology reduces bias)
Levels of evidence	1a, 1b	2b-4, depending on methodology
Hypothesis-based approach	Yes	Usually no
Duration of observation period	Predefined	Predefined or open end
Focus of research/measurement	Sharp, narrow (hypothesis driven)	Broad
Quality assessment	Not intended (strictly defined indications, process quality at least derivable, outcome quality depends on effectiveness, a given indication, and process)	Structure, indication, process, outcome
Early warning system	Not possible	Possible
Long-term follow-up	Feasible	Feasible (depending on set-up only for a representative sample)
Coverage	Only among participants	From individual center/surgeon over representative clinic sample to full national/regional coverage
Benchmarking	Only benchmarking of RCT arms	Various (depending on the final composition of participants regional to nationally representative benchmark)
Type of quality assurance	Internal, external vs. benchmark of participants	Internal, external vs. representative regional or national benchmark
Efforts	Very high	Low
Cost per case	High to very high	Low
Cost per study	High to very high	Low-cost basis
Availability of potential patients	Usually low	Usually high
Patient compliance	Potentially low	High
Use of generated data	Only in the framework of the scientific goal/hypothesis	Open-hypothesis generation possible
Comparator	Given per definition	Ranges between none to numerous comparators, depending on registry set-up

[a]Unclear terminology, Cochrane called it "efficiency," better always specify what is meant (evidence derived from controlled experiment versus evidence derived from routine clinical practice)

sor. There was no further feedback or consequences as a result of this study. This triggered the idea of conducting a similar project on a larger scale. The Institute for Evaluative Research in Medicine in Bern, Switzerland, had by the time already an over 20-year experience with orthopedic registries, as the first detailed hip arthroplasty registry, the so-called IDES (International Documentation and Evaluation System), was set up in Bern in 1974 by Prof.

M.E. Müller. Prof. Max Aebi, who took over the institute lead in 2000, and who was a close friend and collaborator of Prof. Dieter Grob, put the vision of a first international spine registry to reality.

All over the world, efforts were being made to set up orthopedic registries on regional, state, or even national levels. Spine surgery represents a challenge for all registry endeavors. The variety of levels, pathologies, accesses, and surgical techniques confounds all attempts to invent a short yet comprehensive questionnaire. Consequently, the project launched by Grob and Aebi was first based on sketches and discussions on form content, large personal commitment and motivation, and by the most modern approach of the time – the internet-based approach. This effort was later introduced to SSE, the Spine Society of Europe as "Spine Tango," and the society adopted the registry in the early 2000s.

Goals of the Spine Tango are:

- *Quality assurance and quality improvement*
- Presentation of the *state-of-the-art* European spinal therapies, including all pathologies, levels, accesses, single as well as two-staged surgeries, and nonsurgical treatments
- *Outcome research* and *prospective observational evaluation* of different surgical and nonsurgical techniques as an alternative to randomized controlled trials
- *Benchmarking* on national and international levels
- *Postmarket surveillance of implants*

In the mid- and late 1990s, Swedish spine surgeons also implemented a spine registry based on a short questionnaire dedicated to low back pain [25]. This effort become a national one and included other spinal pathologies with various treatments in the early 2000s [26–28].

Spine Tango is probably the first spine registry initiative to face the challenge of developing a comprehensive questionnaire covering all major spine pathologies and treatments, as well as spanning all anatomical levels. To accomplish this task, a technically demanding computer application was a prerequisite. The consensus and piloting process for the Spine Tango surgical questionnaires' "surgery," "staged surgery," and "follow-up" took about 5 years and needed around 4000 completed forms. The result are two double-sided A4 questionnaires (surgery, staged surgery) and one single-sided questionnaire for follow-up that can all be completed online or using scannable paper questionnaires. At the same time that the physician-based content was finalized, a working group at the Schulthess hospital in Zurich, Switzerland, had developed and validated the COMI (Core Outcome Measures Index) instruments for neck and low back based on a proposal by Deyo et al. [29], which became the officially recommended patient-based outcome instruments in the framework of the Spine Tango registry [30]. Until today, the Spine Tango database has grown to over 70,000 cases and currently includes 70 hospitals from 16 countries in Europe, the USA [31], but even Latin America, Asia, and Australia [32].

The cumulated numbers of the main Tango forms increase exponentially (Fig. 54.2). During the first three active years about 10,000, the second 3 years about 25,000, and during the last 3 years about 40,000 primary cases were documented.

54.4.2 Content

The refined set of questions still allows for a documentation of the broad spectrum of pathologies and treatments in spine surgery. This is made possible by means of a list of main pathologies and their specifications and the so-called surgical matrix, a terminology system reducing the interventions to their basic principles – decompression, fusion, stabilization rigid, stabilization motion preserving, percutaneous procedures, and others. The duplication and, hence, separation of these principles into anterior and posterior ones complete the matrix. The exact content of the surgeon- and patient-based Tango forms was already previously described [33–35], and the forms are available on the Eurospine Web page [36]. Kessler et al. have developed the first version of

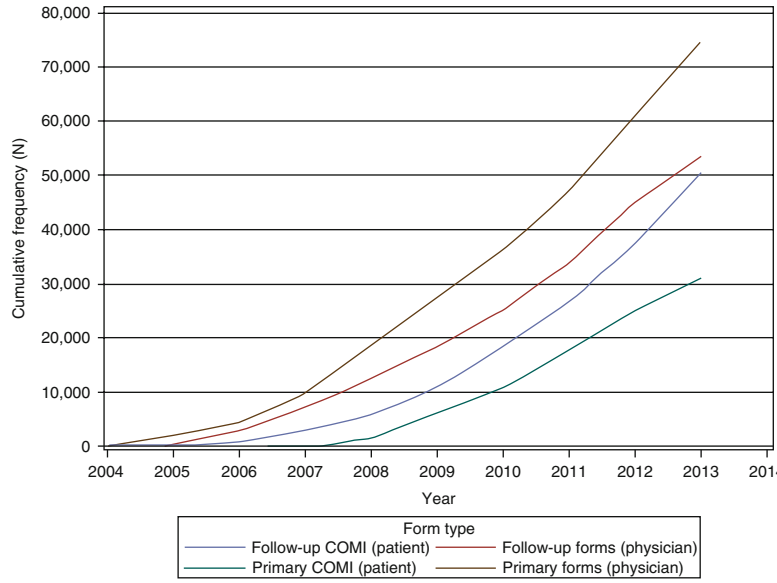

Fig. 54.2 Growth rates of different form types in Spine Tango

documentation content for conservative spinal treatments for Spine Tango in 2011 [37].

54.4.3 Technology

Spine Tango has long left the early stage of a simple Web page for data entry and has grown into an international project with a sophisticated IT (information technology) structure and a multitude of clinical and scientific experts serving the user community and developing the registry further. The central database is part of the powerful scientific MEMdoc documentation portal hosted by the University of Bern; it offers various methods for clinical, implant, and radiographic data collection and a multitude of possibilities for data downloads and online statistical queries. An important step was the implementation of so-called modules, national satellite servers that filter out sensitive data for protecting user and patient privacy in the respective country before sending the clinical dataset to the central server in Switzerland [33]. Such modules are meanwhile installed in Germany, Austria, Italy, Poland, Belgium, Switzerland, Great Britain, Australia, USA, Mexico, and Brazil. Users whose country does not yet have such a national filter server may use the international module [36].

54.5 Benefits of Spine Tango

In 2004, Aebi and Grob wrote that it was increasingly understood that in any technology-driven surgical discipline, patients should be documented in a standardized way if they are recipients of novel inventions and implants. This to have a common language for reporting outcomes, complications, and unforeseen incidents which can be better recognized in a large, common data pool serving as an early warning system [38]. These words could be considered as the conception framework of the Spine Tango endeavor. The registry has now grown into one of the largest international clinical registries with one of the highest number of participating countries. Based on modern information technology, the participating spine surgeons have built a database in which numerous spinal treatments and, importantly, treatment indications are backed up by facts. Within the registry, each participating surgeon, department, and hospital has its own performance record. The analyses based on Spine Tango data reach from single center-based studies [39–41], overbenchmarking against the pooled data of other hospitals [34] to comparative studies across spine registries [42]. Also, from a methodological point of view, the analyses

range between methodological papers [43] and registry-based technical notes [34], over case series [39–41] and subgroup analyses to propensity score-based weighted comparison of multiple treatment options [44].

The online tools such as data download, online statistics, follow-up calendar, and annual and benchmarking reports aim at facilitation of real-life quality assessment, outcome research, and performance monitoring for the users. Some European and non-European national societies recognizing the value of the registry are evaluating the possibility of introducing Spine Tango as their national quality assessment and outcome research tool and make it mandatory for certified spine centers.

In the perspective of quality control, the registry is able to provide evidence on indications, processes, and outcomes. Assessments of quality of structures (e.g., resources such as staff or equipment) are only a secondary goal but remain feasible for certain questions and to a certain extent.

In the societal perspective, the collection of state-of-the-art evidence with high external validity has a direct impact on clinical practice and treatment quality as well as outcome improvement. An example from the Swedish Hip Registry showed that serious complications and revision rates have declined significantly by making information from the registry available to the entire community of surgeons in Sweden [45]. The Tango dataset is reaching reasonably high numbers, which should now allow for systematic data analyses, evaluations, and dissemination of the results. This requires, however, time and resources. The Spine Tango committee of Eurospine is engaged in promoting publication of the observed results in the registry. Additional to studies based on one registry, cross-registry studies are possible and may help in generation of stronger evidence [42].

54.6 Criticism of a Registry

The most relevant criticism to a registry in terms of the evidence level of findings is the unmonitored collection of heterogeneous data prone to selection bias. In an unmonitored voluntary registry, selection bias cannot be excluded. Audit and monitoring of data recordings are the main tools in reducing selection bias and controlling and improving the quality of the observational data. Aiming at collection of high-quality data, the Spine Tango committee plans to introduce the so-called pool of accredited participants. Those are participants who have a minimum 80 % case documentation rate. A case is defined as a combination of a preoperative COMI form, the surgical intervention form, and at least one postoperative COMI and physician follow-up form at an interval of 3 months after surgery or later. For the non-surgical participants, a case is defined as a pretreatment COMI form, the conservative treatment form, and an end-of-treatment assessment with a COMI form. On-site audits by an independent party will then be performed for those participants. One should be aware of the enormous efforts required for making a large international registry a monitored study. A snap sample monitoring, however, seems to be a rather feasible endeavor.

Making documentation mandatory within hospital or national boarders is a further instrument against selection bias. As was mentioned above, some European and non-European national societies are evaluating the possibility of introducing Spine Tango as their national quality assessment and outcome research tool and making documentation mandatory. These policy changes are, however, lengthy and difficult negotiations, and their political dimensions and controversies should not be underestimated.

Many industry partners are interested in the Spine Tango registry as well. It is increasingly being recognized as a unique tool for postmarket surveillance of medical implants and therapies. Recent clinical disasters in plastic surgery with PIP implants and in hip surgery with DePuy metal-on-metal implants have impressively demonstrated the necessity of registration in implantology [46, 47]. Systematic analyses of registry data can result in early warning mechanisms much earlier than single surgeons or hospitals will raise their suspect.

The evaluation of registry data requires solid statistical methods. Comparative registry-based

studies need to be at least of multivariate-adjusted character to account for observed confounding factors [44, 48]. The analysis of a propensity score-matched sample can even mimic that of an RCT [49]. Furthermore, the representativeness of the selected study sample within Spine Tango should always be proven where appropriate. However, the representativeness of the documented and the treated patient populations in the participating clinics cannot be assessed, similarly as the representativeness of the international spine surgery can probably not be claimed yet.

One should remember that the primary goal of documentation in the registry is the user's own quality assurance and quality improvement. The data remains anonymized and belongs to the physician. An honest documentation is in the interest of the users themselves. Scientific data monitoring is regularly performed in Spine Tango to assess clinical indicators for honest documentation, such as proportions of complications per participating hospital, treatment type, diagnosis, etc. A good indicator of honest documentation is the proportion of dura lesions. The proportion of dura lesions in Spine Tango appears to be well comparable or even slightly higher than that in the Swedish Spine Registry [44], which is a national spine registry with a 90 % coverage rate [26].

54.7 Financing of a Registry

Having a long experience in medical registries, the Institute for Evaluative Research in Medicine was and is hosting registries with various financing models. A certain evolution in the financing models of registries was observed over the last decades. In the oldest financial model of the IDES registry, documentation of total hip and knee arthroplasty was paid by the initiator, Prof. M. E. Müller. The money was coming from earnings of hip prostheses, which were supposed to be monitored in the registry. The registry collected 48,000 primary total hip arthroplasties, 12,000 revision arthroplasties, and 77,000 follow-up evaluations [50]. This type of registry was voluntary, but direct financial support of the documenting sites was attractive for participating centers, and it caused such high documentation numbers at a time when quality assurance and postmarket surveillance were not hot topics yet.

A more complex model was used within the SWISSspine registry [22, 42, 51]. After the moratorium on total disk arthroplasty and kyphoplasty in Switzerland, the SWISSspine registry was launched according to the principles of coverage with evidence development. The registry is administered under the auspices of the Swiss Society for Spinal Surgery, but it was mandated by the Swiss Federal Office of Public Health for evaluating these specific spinal therapies. The implant producers operating in Switzerland became the financial supporters of the registry as this was the only way to bring their products to market and have them reimbursed by the basic health insurance. The sales figures and documentation numbers are compared by an independent trustee officer and reported to the Federal Office of Public Health. Also, an annual registry report is provided. Based on the observed results, balloon kyphoplasty was already released from the evaluation in 2009 [22, 52].

Meanwhile the so-called National Association for Quality Control in hospitals and clinics in Switzerland (ANQ) has been founded in Switzerland, whose main task is national population-based observation of selected quality indicators. The association has its own budget out of which, among others, the large national registry for surgical site infections Swissnoso [53] is paid. Although hip and knee prosthesis do meanwhile belong to the list of quality assessment programs of ANQ, a new financial model had to be created due to the limited ANQ budget. According to this model, every participating hospital is charged 20 CHF (+ VAT) for each knee or hip implantation [54]. The money is used for organizing documentation, data collection, on-site and first level support, reporting, administration of the registry, and communication. The planned inclusion of other implant-based surgeries will reduce this charge. This model is beneficial from the perspective of patients who are indirectly participating in quality assurance and quality improvement and from the perspective of hospitals who are assuring their quality assessment as it is anchored in the Swiss healthcare law.

The Spine Tango registry with its abovementioned goals is running under the auspices of Eurospine, the Spine Society of Europe. The society and its members are financing the registry. This fact underlines the feasibility of large international registries embedded within a professional society. The type of registry remains voluntary. The mature user tools in the registry, such as annual and benchmarking reports, online statistics with benchmarking, data download, follow-up calendar, etc., bring meaningful benefits to the participating colleagues in their daily practice.

54.8 Outlook

The benefits of the collected data in terms of evidence generation range from epidemiological and descriptive analyses [33], subgroup analyses [48], and matched case-control studies to the development of clinical outcome prediction models [55]. A first model on prediction of complications after spine surgery was recently published by a research group from Seattle based on data from two hospitals [55]. Development of outcome prediction models represents an important step in utilization of the collected evidence and making it publicly available. Spine surgeons need to be able to make evidence-based predictions regarding the outcome of their surgical procedures, based on reliable prognostic information, and to share and discuss it with their patients. The risks and benefits of different treatment modalities must be adequately communicated to the patient. This is particularly important in view of recent developments toward shared decision-making, where physicians and patients both actively participate in selecting the therapeutic intervention. The use of validated risk prediction models to inform decisions for surgery will potentially improve treatment outcomes and save healthcare costs by providing information that can be used to avoid unnecessary treatments and to improve the selection of the most beneficial treatment for individual patients. These models will also provide societal benefits by providing the best available data about surgical outcomes in an accessible format that can be individualized according to patient characteristics to support more detailed patient informed consent. The development of prediction models based on data from Spine Tango has started and should provide results soon.

The Spine Tango benchmarking project was recently initiated by the registry research group. The project aims at analyzing the most frequently encountered treatments for the most common degenerative diseases of the spine, in order to find out if and to what extent surgical spinal interventions “do” [20] work in day-to-day clinical settings. Disk herniation and spinal stenosis, making up about two thirds of all degenerative diseases recorded with Spine Tango, are the first pathologies the benchmarking project will assess.

Conclusions

Spine surgery is one of the fastest growing medical specialties with high epidemiological and financial societal impacts. There are compelling needs for evidence generation and quality assurance. Those aims require nothing other than a standardized documentation as one common language. An important scientific and methodological approach under such conditions is a registry, whereas objective data from care providers should be reasonably accompanied by subjective data from the patients. Not only high-quality data collection but also pragmatic methodological evaluation approaches are required for generation of sound evidence.

The European Spine Tango endeavor with over 10 years of technical and content development represents a unique international registry concept and data pool with large potential for evidence generation in spine surgery. The strengths lie in the large sample size, internationality, “common language” for conservative and surgical procedures, mature technical documentation solutions and tools, as well as a wide network of physicians. These aspects limit the potential of selection bias to a considerable extent. An introduction of accredited participants with (nearly) complete documentation coverage and follow-ups should help to

further increase the quality of the collected data and at the same time help to measure the influence of potential selection bias in non-consecutively documenting hospitals. The fact that this large registry is financed by member fees of a professional society underlines the feasibility of such registries. Besides the dissemination of the collected evidence in scientific publication and conference proceedings, one of the next major steps should be the development of valid outcome prediction models. A joint endeavor in a "common language" is the current result of the registry and is the best prerequisite to assure its successful future.

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Lessons from a Life: The Journey of Spinal Neurosurgery in the United States

55

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55.1 Introduction

Given the rapid, continued development of increasingly sophisticated devices for internal spinal fixation, it is easy to overlook the fact that the history of spinal instrumentation spans only a short period. Although there is evidence that spinal disorders were recognized as a cause of significant morbidity from early antiquity, surgical attempts to address these disorders were extraordinarily rare [1]. Despite the great strides that occurred during the medieval and Renaissance periods in characterizing the anatomy and mechanical characteristics of the spine, surgical approaches to the spine were long considered daring, reckless endeavors, associated with unacceptably high mortality and morbidity, and ultimately doomed to failure. As a result, treatment for spinal disorders historically relied upon a variety of external braces and devices that were uncomfortable and unsuccessful in equal measure and avoided internal correction almost entirely.

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With the development and dissemination of anesthetic and antiseptic techniques in the nineteenth century, the practice of surgery transitioned from a frenzied, messy, and excruciatingly painful affair associated with significant mortality and postsurgical infection to a more careful and considered approach [2, 3]. No longer rushed to take decisive action with incomplete information, surgeons were free to innovate, and it was in this fertile bed that spinal instrumentation took root as a method to correct spinal instability and deformity. This chapter tells the story of spinal instrumentation from its humble beginnings in the late 1800s to the present day and includes a discussion of the crucial advances in construct design, materials, and techniques that have permitted the development of the wide array of technology available to today's spinal surgeon.

Unfortunately, we cannot hope to include mention of every incremental advance in instrumentation. This chapter is only a brief glimpse at the progression of spinal instrumentation since its birth, and thus we strive to describe those advances that substantially contributed to that progression. Likewise, there is unfortunately limited space in which to describe each innovation in detail. Nevertheless, the history of spinal instrumentation is a fascinating story that provides important context for understanding instrumentation technology today.

J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4_55

55.2 The Birth of Spinal Instrumentation

The first recorded successful attempt at spinal instrumentation was performed in Ottawa, Kansas, in 1888 by W. F. Wilkins. Wilkins performed surgery on a newborn infant who had sustained a vertebral dislocation with traumatic rupture of a lumbar intervertebral disk. After reducing the disk herniation, Wilkins stabilized the spine by wiring the pedicles together with carbolized silver wire, and the infant recovered uneventfully [4].

A similar technique was subsequently employed by Berthold Ernest Hadra in Texas in 1891, though he was not aware of Wilkins' procedure at the time. Hadra was a Prussian-born surgeon who had immigrated to the United States after serving as an assistant surgeon in the Prussian army during the Austro-Prussian war [5]. He used silver wire to join the spinous processes of the sixth and seventh cervical vertebrae in a 30-year-old patient with an unstable cervical fracture-dislocation and neurological deterioration. The procedure was initially a success, although the surgery was repeated 3 weeks later when the wires loosened. Undaunted, Hadra posited that his interspinous wiring method was a success and could be adapted for use in the treatment of "any deviation of a vertebra" [6].

As it happened, the closing of the nineteenth century found physicians facing widespread outbreaks of tuberculosis worldwide. Progressive spinal deformity and neurological compromise as a result of extrapulmonary tuberculosis, first described by Percivall Pott in 1779, had long been treated with externally applied braces and devices, but remained a debilitating malady that surgeons of the day struggled to address. Pott himself had advocated surgical drainage of paraspinal tuberculosis abscesses as a solution, although this procedure did nothing to correct deformity and was associated with the development of secondary infections and draining sinus tracts [7].

Inspired by his relative success with interspinous wiring, Hadra suggested that his procedure might have applicability in the treatment of Pott's disease, although he had not attempted this himself [8]. Two years later, French neurosurgeon Antoine Chipault performed the first internal fixation for this very purpose. In 1898, Lovett published a report of his experience in five patients with tuberculosis spondylitis, describing a procedure in which he denuded adjacent spinous processes and then wired them together with silver wire [9]. However, despite achieving stability initially, this process resulted in short-lived success and patients frequently required a second surgery [10].

Inspired by the work of Hadra and Chipault, Fritz Lange of Munich was himself beginning to consider the problem of internal splinting for tuberculous spines. He envisioned an "artificial spinal column of steel," composed of bilateral tin-plated steel rods wired to the spinous processes. After his first attempt in 1902 resulted in postoperative complications from the sharp ends of the silver wire used to secure the rods, he set to work trying to characterize the optimum materials for use in his procedure. After several years of animal experiments, he settled on 5-mm-thick, 10-cm-long, tin-plated steel rods secured to the spinous processes with silk thread [11].

55.3 Electrolysis and the Development of New Materials

Ultimately, Lange abandoned metal rods for a celluloid material because of problems with corrosion. By the turn of the twentieth century, he and others recognized that a major limitation to the use of metals for internal spinal fixation was the tendency for metals to corrode when placed in the body. In addition, it was observed that such metals produced pathological changes in local tissues that impaired healing and subsequent stability. While many hypotheses were advanced to explain these changes, it was not until the 1930s that the true culprit was widely appreciated: electrolysis [12].

It was well known that materials such as silver, aluminum, nickel, and stainless steel were not only weakened by electrolysis but also produced local bone erosion that significantly hampered attempts to achieve fixation. In 1936,

Venable and Stuck began investigating the causes for the breakdown of metal implants, and in 1938 Venable published a definitive description of the process of electrolysis as it related to fracture fixation [13]. Venable and Stuck experimented with several metals over a 3-year period and ultimately recommended Vitallium, a cobalt-chromium-molybdenum alloy developed in 1932 that withstood the corrosive effects of electrolysis and produced no pathological changes in the bone [14].

Before that time, there had been little interest in discovering the optimal attributes of a material for implantation, despite the fact that the first use of a metal implant had occurred more than a century earlier. Once it became clear that the choice of materials had profound implications for the strength and durability of the implant, research began in earnest to understand the ideal chemical properties of implanted materials and to develop stronger materials that could resist corrosion. Stainless steel alloys were quickly developed that were better able to resist electrolysis, yet maintained much of the mechanical properties that made steel preferable for fracture stabilization and spinal instrumentation.

In 1951, Leventhal introduced the idea of using titanium in orthopedic procedures, noting its impressive strength and lack of pathological tissue changes [15]. Moreover, the mechanical properties of titanium and its alloys more closely approximated those of bone, making it an attractive candidate material for implantation in bone [16]. Surgeons also found that titanium produced less artifact on radiographic imaging than stainless steel or Vitallium [17]. Since that time, titanium alloys gradually became the primary material used in spinal fixation. The later widespread use of magnetic resonance (MR) spinal imaging solidified the place of titanium, which is compatible with MR imaging, in spinal instrumentation. Current researchers are investigating the role of ceramics and synthetic polymers in creating strong, lightweight constructs for orthopedic procedures [18]. One such polymer in wide use today is polyetheretherketone, the chemical and mechanical properties of which make it especially attractive in spinal and orthopedic surgery.

55.4 Spinal Fusion

In 1911, Fred Albee and Robert Hibbs, both orthopedic surgeons in New York, independently struck upon the importance of arthrodesis in halting the progressive deformity of Pott's disease when they each developed procedures that used autologous bone grafts to achieve bony fusion of the spinous processes, thereby obviating the need for wires. In both procedures, this process corrected deformity and reinforced the dorsal spinal elements. The Albee procedure used tibial grafts as struts between the spinous processes of adjacent vertebrae [19], while Hibbs used bone from the spinous processes themselves to bridge vertebrae [20, 21]. The theoretical advantages of these procedures were immediately obvious, and their potential for halting spinal deformity from other causes was quickly recognized, such that these techniques were widely adopted soon after their invention. In 1914, Herbert Galloway became the first surgeon to use fusion techniques to correct paralytic scoliosis [22]. Nevertheless, these initial efforts at fusion resulted in unacceptably high rates of pseudarthrosis, and as a result, these procedures were often modified by others to include silver wiring to minimize graft movement and maximize arthrodesis [23].

The 1930s saw the development of more elegant techniques for spinal fusion, including interbody fusion of the lumbar spine. In 1933, Burns published his description of anterior lumbar interbody fusion for an L5–S1 spondylolisthesis [24]. Beginning in 1939, Cloward would go on to develop the posterior lumbar interbody fusion approach [25]. Such procedures were developed and refined over the course of the next 30 years. While all were promising methods for halting the progression of spinal deformity, all were also initially associated with fairly high rates of pseudarthrosis.

55.5 Paul Harrington and the Modern Era of Spinal Stabilization

Importantly, the foregoing sections illustrate the point that spinal instrumentation and fusion were developed more or less independently. These

earliest methods for addressing deformities of the spine were limited in two ways: (1) They generally halted the progression of deformity, rather than correcting it, and (2) they failed to marry the techniques of spinal fusion, which provided the durable stabilization sought by these early pioneers, with spinal instrumentation, which helped to maintain the alignment and rigidity necessary to promote arthrodesis. It was not until the 1960s that the interdependence of these two parallel advances would become fully and widely recognized, and the modern era of spinal stabilization would begin. In the immediate aftermath of World War II, American physicians faced a recurrence of widespread poliomyelitis epidemics. In the late 1940s and early 1950s, polio crippled approximately 35,000 individuals each year, with the development of an effective vaccine still several years away. Aside from the immediate complications of polio, many sufferers subsequently developed progressive and debilitating thoracic scoliosis, often with attendant cardiorespiratory compromise that made treatment with braces and casts impossible. The treatment of these patients occupied spinal surgeons of the day.

One such individual was Paul Randall Harrington, an American orthopedic surgeon in Houston, Texas. After finishing his residency in orthopedic surgery in 1942, he joined the US Army, serving as the chief of orthopedic surgery for the 77th Evacuation Hospital. At the war's end in 1945, Harrington settled in Houston, where he worked at the Jefferson Davis City-County Hospital. City-County saw many polio patients and by 1953 had become the second Respiratory Center in the nation.

Recognizing that a large number of the polio patients seen at City-County often developed scoliosis, Harrington began in 1947 to develop a method to stop the progression of these patients' deformity and improve their cardiopulmonary function. Harrington's first attempts used screws to fix the facet joints in a corrected position, a technique introduced by Toumey [26], and King [27], as a means of providing rigid internal fixation to aid in arthrodesis. While Harrington's facet-screw procedure appeared promising at first, ultimately this method proved a failure, and he was forced to seek an alternative means for correcting the deformity [28]. The next iteration of Harrington's approach involved hooks connected to a threaded rod, by which he was able to apply distracting corrective forces. The hooks were placed at the spinous processes of the vertebrae at the superior and inferior extremes of a curve, with the rod spanning the concavity of the scoliotic curve.

Harrington continued to refine his surgical technique and instrumentation over the next 15 years, making the early instrumentation by hand. When his early handmade constructs failed, he partnered with engineers to develop sturdier instruments that could withstand the repetitive stress to which they were subjected. Ultimately, Harrington's work led to the creation of a system of stainless steel rods and distraction hooks. As he continued to develop an instrumentation system that could address the spinal deformity from polio, Harrington also began to apply it to cases of idiopathic scoliosis [29].

Despite the initially satisfactory correction of the deformity, Harrington was cognizant of the fact that hardware failure was inevitable, often as early as 6 months postprocedure. To achieve lasting deformity correction, he recognized that his instrumentation would have to incorporate a fusion within its extent. Rather than using hooks and rods as a dynamic means of establishing correction, he determined that instrumentation should serve as a means of permitting arthrodesis [28].

By demonstrating that instrumentation was merely a temporary means to the end of spinal fusion, rather than an end in itself, Harrington laid the foundation for future developments in spinal instrumentation. His experience revealed that instrumentation failure is inevitable, but that permitting arthrodesis can achieve long-term stability. By acknowledging the "race between instrumentation failure and the acquisition of spinal fusion," Harrington united the parallel advances in internal fixation and spinal fusion, thereby ushering in the modern era of spinal stabilization [28].

Almost immediately, Harrington's rod system became the state-of-the-art spinal instrumentation

through the 1970s. Indeed, use of Harrington instrumentation continues to the present day. The utility of the procedure was easily recognized, and the indications were soon extended beyond polio and idiopathic scoliosis to include trauma [30, 31], degenerative processes, and malignancy [32, 33]. With its widespread adoption, however, came the recognition of its limitations. Most notably, the effectiveness of distraction rods in correcting coronal curvature of the spine came at the expense of the natural sagittal curvature of the spine, resulting in loss of lumbar lordosis, the so-called flatback syndrome [34, 35]. Additionally, the procedure required that patients spend several months in plaster braces postoperatively. Lastly, repeated stresses occasionally resulted in hook dislodgement or rod breakage [36].

55.6 Segmental Spinal Fixation and Development of the Pedicle Screw

If Harrington provided the bedrock on which the modern era of spinal instrumentation was built, much of the foundation was laid by Eduardo Luque in the mid-1970s. Luque, an orthopedic surgeon in Mexico City, sought to address some of the limitations of the Harrington rod system. His work ultimately led to the introduction of segmental spinal fixation. Whereas Harrington used straight rods with hooks at either end of the deformity, Luque used a contoured steel rod, attached to the vertebrae at several points with sublaminar wiring. By doing so, Luque was able to more evenly distribute the forces across the construct, which not only increased the rigidity of the construct and reduced the potential for hardware failure but also offered the potential for greater correction and reduced the need for postoperative bracing. Most importantly, however, segmental spinal fixation permitted deformity correction without sacrificing sagittal curvature [37].

While spinal surgeons recognized the promise of Luque's segmental fixation technique, their enthusiasm was tempered by concern for potential neurological injury caused by the sublaminar wiring used to secure the rods. Indeed, reports of complications such as epidural hematoma and direct trauma caused by passing the sublaminar wire left surgeons searching for alternative means of achieving segmental fixation [38, 39]. To address these concerns, Drummond et al. published a description in 1984 of a technique using a button-wire implant threaded through a hole drilled at the base of the spinous process [40]. Although the construct was not as strong as Luque's sublaminar wiring construct, it had the advantage of reducing the potential for neurological injury, thereby making it a more attractive alternative to spinal surgeons of the time.

A major advance during the refinement of segmental fixation techniques was the introduction of pedicle screws as a means to secure the constructs to the vertebrae. As mentioned previously, the first accounts of the use of screws for internal fixation of the spine as an adjunct to fusion were published in the early 1940s by Toumey [26] and King [27]. Both used short bone screws that traversed the facet joints of the segment to be fused bilaterally. King reported a pseudarthrosis rate of only about 10 %, although Thompson and Ralston subsequently reported much higher rates of pseudarthrosis using a similar technique [41]. Thus, the technique did not gain widespread acceptance, and Bosworth suggested in 1957 that the benefits of screw fixation did not justify the difficulty in placing the screws [42].

H. H. Boucher, a Canadian spinal surgeon, believed that the concept of screw fixation was nevertheless sound. He developed and implemented a method of screw fixation using longer screws to traverse the facet joint and enter the pedicle and vertebral body below. In 1959, he published a paper describing his experience with this technique over a 12-year period for single- and multiple-level fusions and to treat spondylolisthesis [43]. Although he reported excellent results, he conceded that screws were a temporary solution and were likely to loosen over time, but that well-placed screws could offer superior fixation to minimize pseudarthrosis.

In Paris, Raymond Roy-Camille, under the guidance of Robert Judet, used pedicle screws as fixation points for a multiple-segment poste-

rior plate system. Although he performed his first surgery in 1963, he did not publish the results until 1970 [44]. His system of plates and pedicle screws was applied to a variety of spinal disorders, and its success confirmed the superiority of pedicle screw segmental fixation [45]. He is largely credited with pioneering the use of pedicle screws in segmental instrumentation.

The advantages of pedicle screws over facet screws, hooks, and wire fixation are manifold. Biomechanically, pedicle screws gain better purchase and are capable of withstanding a wider range of forces across multiple vectors [46, 47]. Additionally, unlike hooks and wire fixation, which require posterior vertebral structures, they may be placed even after a laminectomy, a benefit that permitted the extension of instrumentation techniques to address various degenerative spine conditions.

In the United States, the first surgeon to popularize the use of pedicle screws for segmental fixation was Arthur Steffee, an orthopedic surgeon in Cleveland, Ohio. In the early 1980s, Steffee et al. noted that the pedicle acted as a "force nucleus" for the vertebra and was the conduit by which the forces acting upon the posterior vertebral elements could be transmitted anteriorly [48]. Accordingly, he posited that the pedicle was an ideal structure for placing a screw in a segmental fixation construct. Steffee placed headless screws in the pedicles and modified standard long bone fracture plates with slots that could slide onto the screws. He secured the plates in place with nuts, thereby pioneering "variable screw placement."

In Paris during roughly the same time, Cotrel and Dubousset were developing a segmental fixation system that used rods, as opposed to the plates that their contemporaries were using. Initially, their system used hooks at multiple segments, secured with bolts [49], and while this offered satisfactory correction, the bolt-locked hook system proved difficult to remove. Eventually, they adopted monoaxial pedicle screws as fixation points for their rods [50], allowing for easier adjustment or removal of the construct. Thus, Cotrel and Dubousset married the advantages of segmental rod fixation of the spine with those of pedicle screws. While plate constructs were preferred for their strength in spinal instrumentation, rods offered much greater flexibility and a lower profile, thus allowing surgeons to more precisely correct deformities in three dimensions and leaving more room for bone grafting.

Since that time, further development of spinal instrumentation has largely centered around refinements of segmental rod fixation using pedicle screws as fixation points. Today's surgeon has a myriad of choices of instrumentation systems from multiple manufacturers. Advances in screw design, from the monoaxial screw used by Cotrel and Dubousset to uniaxial screws and the polyaxial screws in greater use today, have greatly aided spinal surgeons in creating even more complex constructs. Uniaxial screws, as the name implies, are mobile in one plane at the junction of the head and the shaft, making them ideal for derotation of the spine in the axial plane. Polyaxial screws have freely mobile heads, allowing surgeons to align the heads to the rod, providing greater ease of integrating fixation points into the construct. Additionally, minimally invasive techniques and instrumentation systems have been developed that allow multilevel instrumentation through small paraspinal incisions.

55.7 Dynamic Spinal Stabilization

Since the advent of the pedicle screw, spinal instrumentation with fusion has been increasingly used to treat degenerative spine conditions, based on the hypothesis that eliminating spinal motion across diseased segments could eliminate spinal pain and neurological symptoms. As use of this procedure has increased in frequency, however, surgeons have come to appreciate not only that the success of fusion does not guarantee clinical improvement but also that immobilizing spinal segments has an effect on the spinal levels adjacent to the fusion [51]. By altering the distribution of forces in the spinal column and increasing the relative mobility of the adjacent segments,

rigid spinal fusion has the untoward effect of subjecting adjacent spinal segments to abnormal mechanical conditions, causing pain and deformity, and often necessitating subsequent surgeries [52–55].

While rigid spinal fusion remains the surgical standard for addressing degenerative spinal conditions, currently there is widespread development of so-called dynamic stabilization systems that seek to redistribute the load away from diseased spinal levels while maintaining mobility at those levels. With these systems, adjacent levels are not subjected to increased relative motion, which reduces pathological changes and pain in the segments. At present, there are a number of approaches to dynamic stabilization, including anterior disk prostheses, such as the Prestige and Bryan (Medtronic plc, Dublin, Ireland) cervical disk prostheses and the Maverick (Medtronic plc) lumbar prosthesis, as well as posterior constructs utilizing flexible connections between pedicle screws, such as the Dynesys (Zimmer Spine, Zimmer Biomet Holdings, Inc., Warsaw, IN), the AccuFlex (Globus Medical Inc., Audubon, PA), and the CD Horizon Agile (Medtronic plc). It is not clear what role these systems will play in the future; currently, insufficient data exist to determine whether any or all are superior to spinal fusion in treating degenerative spine disease and reducing complications at adjacent segments.

Interestingly, the first use of dynamic stabilization of any sort occurred in the 1950s, when Paul Harmon began to perform disk arthroplasties, replacing diseased disks with spheres made of Vitallium [56]. These spheres, later called "Fernström balls" after Ulf Fernström, who used stainless steel spheres in the 1960s [57], did not gain widespread acceptance at that time, although Fernström and later McKenzie [56] reported excellent results. The technique was not commercialized further at that time, although the use of spheres for disk arthroplasty has reemerged in the form of Satellite Nucleus Replacement spheres (Medtronic plc), which are available in both cobalt chrome and polyetheretherketone.

55.8 Cervical Spine Instrumentation

Despite the fact that the history of spinal instrumentation truly begins with techniques for wiring cervical vertebrae, most of this chapter has thus far focused on the development of spinal instrumentation as it pertains to the thoracolumbar spine. It is, however, worth briefly mentioning some of the major advances in cervical instrumentation.

With regard to posterior cervical spine instrumentation, in 1939, Gallie developed a technique for fusion of C1–C2 for cases of trauma whereby an Albee or Hibbs' graft was secured and compressed between the C1 and C2 posterior arches by sublaminar wiring [58]. This technique, while associated with fairly high fusion rates, nevertheless suffered from the same potential for neurological injury that limited later techniques using sublaminar wiring, as mentioned above. In addition, the wiring did not fully eliminate rotational motion between C1 and C2, occasionally leading to a failure of bony fusion [59]. Brooks and Jenkins modified this technique in 1978 using a pair of ilium grafts wedged between the posterior arches of C1 and C2, again using sublaminar wire [60]. This technique resulted in better resistance to rotational motion, but passing wire under the laminae of multiple levels was associated with significant risk for neurological injury.

While the Gallie method was largely effective, sublaminar wiring required considerable skill. In 1975, Tucker reported the use of the Halifax clamp, a construct that used sublaminar hooks connected by a screw to compress the posterior elements [61]. The Halifax clamp could be rapidly applied and was comparable to the Gallie technique, although its bulk made it somewhat unwieldy and its sublaminar hooks encroached on the spinal canal [62].

Magerl in 1984 introduced transarticular screw placement for internal fixation of C1–C2. He passed sagittally oriented screws from the inferior articular facet of C2 through the facet joint to engage cortical bone of the anterior arch of C1 [63]. This technique avoided the need for passage of wires or clamps and provided immediate bilateral fixation.

Combined with a Gallie-type bone graft, this technique resulted in stable fusion of C1–C2.

In 1989 Roy-Camille et al. reported on a novel, lateral, mass screw-and-plate system for stabilizing the cervical spine [64]. This original concept was later modified by An and Coppes [65], Anderson et al. [66], and Jeanneret et al. [67] to minimize the likelihood of injury to the nerve roots or the vertebral artery. The screw-and-plate system had limitations, especially in the treatment of complex spinal disorders such as spondylosis. However, the late 1980s and 1990s ushered in the development and implementation of screw-rod constructs [68, 69]. These systems allowed for placement of polyaxial screws that accommodated a variety of anatomical abnormalities, and the connection of the screws via rod systems allowed for immobilization. Further refinements in technique, including introduction of cervical pedicle screws, have improved biomechanical stability of posterior cervical constructs [70].

In 1991, Dickman and Sonntag described a modification of the Gallie technique that again used wire to secure an ilial graft between the posterior arches of C1 and C2. Instead of passing wire under the posterior arches of multiple levels, as Gallie and Brooks had, they used the spinous process of C2 to secure the wire inferiorly, thereby requiring sublaminar passage of wire at only one level [71]. In 2001, Harms and Melcher [72] described a posterior C1–C2 fixation technique, previously reported by Goel and Laheri [73]. The Goel-Harms construct consists of C1 lateral mass screws and C2 pedicle screws. A C2 translaminar modification of the Goel-Harms construct has been reported more recently [74, 75].

For anterior approaches, in 1967, Böhler reported using anterior cervical plating to treat cervical spine trauma, and, since that time, anterior plating has become a popular technique for treating many different conditions, including degenerative conditions, trauma, and infection [76]. Over time, refinements in plate design and screw placement, as well as graft design and construction, have increased the utility and versatility of anterior plating for cervical spine fixation and greatly reduced complications [77].

55.9 Fusion Grafts and Bone Morphogenetic Protein

Since 1911, when Albee [19], and Hibbs [20] described their techniques for achieving arthrodesis of the spine, surgeons have explored several different methods for using bone grafts in spinal surgery. Both autografts, obtained by harvesting bone from the patient, and allografts, which are obtained by harvesting bone from another donor, have classically been used to achieve spinal fusion. The most common sites are local to the site of surgery, such as the iliac crest and the rib. Autograft has proven superior in terms of its ability to stimulate bone formation [78] and is generally preferred over allograft. However, harvesting of autograft is invasive, requiring a surgical incision at the donor site, potentially leading to long-standing postoperative pain or numbness, increased risk of infection, and cosmetic defects at the donor site [79–81]. Such potential complications have led to a long-standing search for materials to replace or augment bone grafts.

The better results obtained by grafting autogenous bone are related to three properties of bone healing and growth. Osteogenicity—the capacity to form bone via the presence of osteoblasts—is a property of freshly harvested autologous bone or bone marrow. Osteoconductivity is a material's ability to serve as a scaffold for new bone formation and growth, a property shared not only by autogenous bone but also by allografts and even ceramics and synthetic polymers. Osteoinductivity refers to the presence of factors, the so-called bone morphogenetic proteins (BMPs) in the graft that stimulate osteogenesis in the recipient bed, as well as the differentiation of mesenchymal stem cells into osteoblasts [82]. Therefore, the ideal graft for spinal fusion would include all three characteristics, which are inherent in autologous bone, while minimizing or avoiding the potential complications of an autograft harvest.

To that end, researchers have developed bone graft extenders and replacements that aim to improve fusion results. Bone graft extenders are generally purely osteoconductive, lacking osteoinductivity or osteogenicity. These are typically used to augment autologous bone grafts and may

be composed of materials such as calcium phosphate, calcium sulfate, or composites of calcium phosphate and collagen. Demineralized bone matrix, first described by Marshall Urist in 1965 [83], is obtained from a demineralized allograft and contains minute amounts of osteoinductive BMPs. Thus, it may be used to effectively extend and augment autologous bone grafts. Bone graft extenders have demonstrated promise in improving fusion rates while reducing the amount of autograft needed to perform the fusion [84].

Bone graft replacements seek to entirely eliminate the need for harvesting autografts, while improving fusion rates. This is achieved by using highly osteoinductive materials, namely, recombinant human BMPs (rhBMP), approved by the FDA in 2002 for fusion of the anterior lumbar spine. After animal trials revealed promising results using rhBMPs [85–87], human trials of rhBMP-2 and rhBMP-7 commenced in the early 2000s. At present, it is unclear what role rhBMPs will ultimately occupy in surgical treatment for spinal fusion, as studies have yielded inconsistent results [88–91], reports of higher complication rates [92], and recent evidence that the use of rhBMP may be associated with a higher incidence of benign tumors [93].

55.10 Summary

From the earliest use of interspinous wiring in the cervical spine in the late 1800s through the intervening decades, spinal instrumentation has progressed dramatically. Today's surgeons have access to a myriad of options for internal fixation throughout the entire spinal column. As our understanding of the spine has increased and materials and techniques have improved, surgical treatment for a variety of debilitating and deforming spine conditions has continued evolving at an astounding rate.

Against such a backdrop, it is difficult to predict what the future of spinal instrumentation will look like and, furthermore, which of today's new technologies will contribute to shaping that future. Nevertheless, with the spinal instrumentation technology available today, and the promise of even more effective, elegant constructs in the future, this is truly an exciting time in spinal surgery.

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J.L. Pinheiro-Franco et al. (eds.), *Advanced Concepts in Lumbar Degenerative Disk Disease*,
DOI 10.1007/978-3-662-47756-4