A. Alexandre
M. Masini
P. P. M. Menchetti
Editors

Advances in Minimally Invasive Surgery and Therapy for Spine and Nerves

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Edited by
Alberto Alexandre
Marcos Masini
Pier Maria Menchetti

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Alberto Alexandre
European Neurosurgical Institute, Centro per lo studio e la cura delle malattie
del sistema nervoso periferico
31000 Treviso, Italy

Marcos Masini
School of Medicine, University of Planalto Central and South Lake
Hospital, SCN Qd 05 Bl. A Sala 912, Brasilia,
Distrito Federal, Brazil

Pier Maria Menchetti
Florence University, Via Jacopo Nardi, 15, 50132 Firenze, Italy

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Preface

On behalf of the International Study Group on Spinal Degenerative Pathologies (ISSDP) (head Dr Alberto Alexandre) and the Committee for Peripheral Nerve Surgery of the World Federation of Neurosurgical Societies (head Dr Eduardo Fernandez) and sponsored by EU. N.I., European Neurosurgical Institute, the Sixth Symposium on Peripheral Nerve Microsurgery and Minimally Invasive Treatments for Spinal Diseases was held in Treviso with wide international participation.

The course was also supported by the European Association of Neurosurgical Societies and by the Latin-American Federation of Neurosurgery.

Peripheral nerve problems were discussed and problems concerning differential diagnosis were highlighted, i.e. differential diagnosis in special situations such as between radicular and peripheral nerve trunk lesions, pinpointing the significance of different diagnostic tools. Minimally invasive techniques, utilized nowadays to minimize bone demolition, scarring and risk of recurrence, were carefully analyzed. Microdiscectomy was compared with the results of intradiscal techniques, and new methods were discussed in the face of problems such as epidural fibrotisation, microinstability, osteoporotic or neoplastic or postraumatic vertebral lesions. The different minimally invasive methods were discussed with participation of radiologists, orthopedic and neurological surgeons as well as physical medicine specialists coming from different countries.

A new, exciting field of interest is the use of autologous blood elements in order to favor healing processes in spinal degenerative processes, where demolitive surgery tends to be substituted by nourishment of tissues and reorganisation of function.

Authors from different countries in the world have contributed to this volume, for which we express our thanks. This bespeaks the wide interest that exists in the matter of minimal invasiveness and shows how widely this philosophy of treating patients is entering into neurosurgery.

We are especially grateful to Prof. Armando Basso for his attentive, continuous intellectual support of our philosophy of work underlying the different clinical and surgical problems, and his contribution to building up a more physiological and anatomically-minded way of treatment.

Also, we thank Acta Neurochirurgica for having dedicated this special issue to the Course in Treviso. Once again this is a good opportunity for underlining the importance of a common understanding of peripheral-nerve and spinal surgery problems in order to obtain a more perfect differential diagnosis between problems so closely related and which have quite a similar physiopathology.

Treviso, Italy — Alberto Alexandre
Brasilia, Brazil — Marcos Masini
Firenze, Italy — Pier Maria Menchetti

Contents

Surgical Anatomy of the Sacral Hiatus for Caudal Access to the Spinal Canal

Andrea Porzionato, Veronica Macchi, Anna Parenti, and Raffaele De Caro

Abstract The sacral hiatus is used for access to the spinal canal in many neurosurgical and anesthesiologic procedures. The aim of the present paper is to give a review of its anatomical characteristics relevant to permit correct and uncomplicated accesses. The sacral hiatus is posteriorly closed by the superficial dorsal sacrococcygeal ligament (also called sacrococcygeal membrane) which has to be pierced in order to gain the sacral canal. The mean distance between the hiatal apex and the dural sac has been reported to be 45–60.5 mm in adults and 31.4 mm in children. The mean sacral space depth has been observed to be 4.6 mm in adults and 3.5 mm in infants. On the basis of anatomical measurements of the sacral hiatus, lower insertion angles have been suggested in infant with respect to adult subjects (21° vs. 58°).

Keywords Sacral hiatus · Sacral bone · Epidural injections

Introduction

The sacral hiatus is used as neurosurgical and anesthesiologic access to the spinal canal in many procedures such as myeloscopy/epiduroscopy [1–6], for both diagnostic and therapeutic (lysis of adhesions, local injection of anesthetics and steroids) purposes, and caudal epidural block (e.g., [7]). Knowledge of the anatomical characteristics and variations of the sacral hiatus is essential in order to permit a correct and uncomplicated access to the sacral canal. Nevertheless, to the best of our knowledge a review of the surgical anatomy of the sacral hiatus, with particular reference to the above procedures, is not yet present in the literature. The aim of the present study was to revise the literature about this topic in order to synthetise the useful anatomical information for access to the sacral canal through the sacral hiatus.

The anatomy of the sacral canal and hiatus have been studied in cadavers or dry sacral bones (e.g., [7–10]) and in the living, through magnetic resonance (e.g., [11, 12]) and ultrasound (e.g., [13]) imaging. The dorsal surface of the sacrum shows a raised median sacral crest made up of four (or three) spinous tubercles fused together. The fifth (or four and fifth) tubercle is not present but a communication with the sacral canal is visible, i.e., the sacral hiatus. This hiatus is due to failure of the laminae of the fifth (or sometimes also fourth) sacral vertebra to fuse in the median plane. Laterally to the median sacral crest and up to the sacral hiatus, the fused sacral laminae are visible. More laterally, the intermediate sacral crests are formed by four tubercles due to the fusion of the sacral articular processes. The inferior articular processes of the fifth sacral vertebra are free, project downwards at the sides of the sacral hiatus, are called sacral cornua and are connected to coccygeal cornua by means of intercornual ligaments. The sacral hiatus is closed by the superficial dorsal (or posterior) sacrococcygeal ligament (also called sacrococcygeal membrane), which runs from the free margin of the sacral hiatus to the dorsal surface of the coccyx and correspond to the ligamenta flava of the spine. Conversely, the deep dorsal (or posterior) sacrococcygeal ligament is the continuation of the posterior longitudinal ligament. It is localized inside the sacral canal going from the posterior aspect of the fifth sacral segment to the dorsal surface of the coccyx. The lateral sacrococcygeal ligaments complete the foramina for the fifth sacral nerve running from the rudimentary transverse processes of the first coccygeal vertebra to the lower lateral angle of the sacral bone [14]. The filum terminale emerges below the sacral hiatus, and after passing along the dorsal surface of the fifth sacral vertebra reaches the coccyx. The fifth sacral spinal nerves also emerge through the sacral hiatus, medially to the sacral cornua [15]. The sacral hiatus is covered by skin, subcutaneous fatty tissue and the sacrococcygeal membrane [16].

A. Porzionato, V. Macchi, and R. De Caro (✉)
Section of Anatomy, Department of Human Anatomy and Physiology, University of Padova, Via A. Gabelli 65, 35127, Padova, Italy
e-mail: rdecaro@unipd.it

A. Parenti
Section of Pathologic Anatomy, Department of Medical Diagnostic Sciences and Special Therapies, University of Padova, Padova, Italy

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Sacral Hiatus Measurements for Spinal Canal Access

The mean length of the sacral hiatus has been found to be 32.1 mm (range: 12–53) on adult dry sacral bones [7] and 22.6 mm (range: 11–36) on adult sacral bones studied through Magnetic Resonance Imaging (MRI) [12]. The width of the sacral hiatus at the level of the sacral cornua has been reported to be 10.2 mm (2.2–18.4) by Sekiguchi et al. [16] and 17.5 mm (7–28) by Senoglu et al. [7]. The distance between the hiatal apex and the tip of dural sac has been observed to be about 45 mm [17] or 60.5 mm (range: 34–80) [12]. Senoglu et al. [7] analysed the distance between the sacral hiatus and the level of S2 foramina as this is the most common level of the caudal extremity of the dural sac: the distances from the apex and base of the sacral hiatus to the S2 foramina were 35 mm (11–62) and 65 mm (39–85), respectively [7]. Moreover, it has been observed that the triangle formed between the superolateral sacral crests and the apex of the sacral hiatus is equilateral with mean length of the sides of 66.5–67.5 mm, these measurements being considered useful landmarks for localizing the apex of the sacral hiatus when ultrasonography or fluoroscopy are not possible [7]. The mean depth of the sacral hiatus at the level of its apex has been reported to be 6.0 (range: 1.9–11.4) by Sekiguchi et al. [16] and 4.5 mm (range: 1–7) by Senoglu et al. [7]. However, the anteroposterior (sagittal) diameter of the sacral canal at the level of the apex of the hiatus has been found to be 2 mm or less in 1–6.25% of cases [7, 16, 17]. On MRI, the maximum antero-posterior diameter of the sacral canal at an angle of 90°, corresponding to 4.6 mm (range: 1–8), has mainly been found in the upper third of the sacrococcygeal membrane [12]. Crighton et al. [12] on the basis of the above measurements identified the best fit angle to enter the sacral canal through the sacral hiatus in 57.9° (range: 40°–74°).

MRI imaging analysis on children (mean age: 134 months; range: 10–215) showed mean length of the sacral hiatus of 24.3 mm (range: 12.1–44.3) and maximum anteroposterior diameter of 4.92 mm (range: 2.0–10.0) [11]. The mean distance between the upper margin of the sacrococcygeal membrane and the dural sac was 31.4 mm (range: 13.6–57.1). Another study on children (median age: 19 months; range: 2–84) performed through ultrasound imaging showed median intercornual distance of 17.0 mm (range: 9.6–24.6) and sacral space depth of 3.5 mm (range: 1.0–8.0) [13]. In this children series, the optimal insertion angle was identified in 21° (range: 10°–38°).

The sacral hiatus may present some anatomical variations which can interfere with correct entrance in the caudal spinal canal. Agenesis of the hiatus has been found in mean percentages of 4–7.7% [7, 12, 17, 18]. The limitation in the access to the sacral hiatus due to cartilagineous tissue has been reported to be solved in two cases by mini-surgical approach consisting in dissection until the hiatus and removing of cartilagineous tissue with a Kerrison rongeur [3].

Cysts of the Sacral Canal

Some cyst types may also be present in the sacral canal, sometimes extending to the sacral hiatus. Although pathological entities and not anatomical variations, they are worthwhile to be considered due to their frequent asymptomatic presence, with possible complications of an access through the sacral hiatus. Nabors et al. [19] classified spinal meningeal cysts into three types: type I, spinal extradural meningeal cysts without spinal nerve root fibres; type II, spinal extradural meningeal cysts with spinal nerve root fibres; type III, spinal intradural meningeal cysts. According to Nabors et al. [19], cysts could show or not a communication with the subarachnoid space. Conversely, for Cilluffo et al. [20] the term “diverticula” is to be preferred if such a communication is present. Moreover, if the cyst wall is made up of arachnoid mater the term arachnoid cyst should be preferred, using the term meningeal cyst only if the cyst wall is constituted of dura mater [21]. Spinal arachnoid cysts are congenital lesions which are usually asymptomatic until patient’s second decade of life [21]. Spinal arachnoid cysts without communication are rare and are more frequently located at spinal levels higher than L2 [18, 22, 23]. Only six genuine sacral epidural arachnoid cysts have been reported in the literature [24–28]. More frequent in the sacral canal are perineural or Tarlov cysts (Nabors type II), which form themselves between the perineurium and endoneurium of the spinal posterior nerve root sheath of the dorsal root ganglion and contain spinal nerve root fibres within the cyst wall or cavity [29–32]. These cysts are also mostly asymptomatic, show an incidence of 4–9% [29] and are more frequently found at the S2 or S3 levels [33]. Large Tarlov cysts may erode surrounding bone [31, 34].

Conflict of interest statement We declare that we have no conflict of interest.

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Radiologic Anatomy of the Sacral Canal

Veronica Macchi, Andrea Porzionato, Aldo Morra, Carla Stecco, and Raffaele De Caro

Abstract The extradural space is currently investigated through fluoroscopy and ultrasound for surgical approach, whereas magnetic resonance imaging has been used to provide detailed information. The aim of the present paper is to describe the radiologic anatomy of the sacral canal through a review of its appearance in the different radiologic techniques. CT is able to visualise also the sacrum and the content of the sacral canal, triangular in shape in the transverse images, being able to establish the measurement of the transverse area of the dural sac and of the canal diameter. On the sagittal CT scans, the sacrococcygeal membrane appears as a hypodense structure, between the posterior end of the sacral vertebra and the posterior tip of the coccyx. In magnetic resonance imaging, on T2-sagittal plane images, the sacral canal appears hyperintense, due to the presence of the liquor. The dural sac appears as a hypointense band and its termination as hypointense cul de sac in the context of the hyperintensity of the sacral canal. The sacrococcygeal membrane appears as a hypointense band between the posterior end of the sacral vertebra and the posterior tip of the coccyx. On ultrasound imaging, in the transverse sonographic view, two hyperechoic reversed U-shaped structures correspond to the two bony prominences of sacral cornua, between which there were two hyperechoic band-like structures. The band-like structure on top is the sacrococcygeal ligament. The band-like structure at the bottom is the dorsal surface of the sacrum. The sacral hiatus corresponds to the hypoechoic region observed between the two hyperechoic band-like structures.

Keywords Sacral hiatus · Sacral canal · Extradural space

V. Macchi, A. Porzionato, C. Stecco, and R. De Caro (✉)
Department of Human Anatomy and Physiology, Section of Human Anatomy, University of Padova, Via A. Gabelli 65, 35121 Padova, Italy
e-mail: rdecaro@unipd.it

A. Morra
Department of Radiology, Euganea Medica, Padua, Italy

Introduction

Spina bifida occulta is a condition where there is incomplete fusion of the neural arch of the vertebra, usually in the lumbosacral region [1]. When this condition occurs in the sacrum, the level of non-closure of the lamina of the sacral bodies is variable [2]. Many sacra have S5 or also S4 open, exposing the dorsal surface of the fifth sacral body [3]. Many radiological studies have investigated the prevalence of this condition in the sacrum in various populations, also analysing X-rays that were originally taken for other diagnostic purposes [4], or combined X-ray and computed tomography to determine the level of sacral crest closure [5], raising the question as to whether a standard frontal X-ray image of the whole of the sacrum gives a clear enough image to confidently diagnose spina bifida occulta at all levels [6].

The extradural space has also been investigated through fluoroscopy [7] or ultrasound [8–14] for surgical approach, whereas magnetic resonance imaging has been used to provide detailed information on the anatomy of the extradural space in living subjects [15].

The aim of the present study is to describe the radiologic anatomy of the sacral canal through a review of its appearance in the different radiologic techniques.

X-Rays

In an antero-posterior projection of the pelvis, the sacrum appears as a large, triangular bone, derived from the fusion of five vertebrae; its blunted, caudal apex articulates with the coccyx. In the lateral radiograph, the sacrum shows its pelvic concavity, opened infero-anteriorly, which continues with the supero-anteriorly opened concavity of the coccyx [16]. Thus, the sacrum does not lie in the coronal plane, because of the sharp lumbosacral angle. Moreover, the bone is more vertical in males than in females and the female sacrum is more curved, especially in the lower half of the bone [17].

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A tilt of the X-ray beam 10–15° [17] or 20° [18] cephalad allows the best possible view of this bone, and the angle may need to be increased if there is a greater posterior tilt of the sacrum, for example in a female patient [17]. In a comparative study between X-ray and cadavers dissection, Albrecht et al. [6] found that a single antero-posterior view with 10–15° cephalad angulation provided the clearest image of the whole sacrum.

In an antero-posterior (Fig. 1) X-ray of the sacrum, the sacral hiatus appears as a more radiotransparent zone at the lower end of the sacrum, due to the presence of the inverted U- or V-shaped foramen, formed by the failure of the vertebral arch at fifth sacral vertebra to meet in the median plane. The sacral hiatus is covered by fibrous tissue (sacrococcyx membrane) [3]. A complicating factor in diagnosing images of this area is the presence of intestinal gas, fecal matter, and the full urinary bladder overlying the sacrum. This can make it difficult to see the sacrum and hence make it difficult to diagnose. For this reason, radiography positioning texts [17–19] recommend that the patient both empties the bladder and has a cleaning enema before a sacral X-ray. This rarely occurs in practice, especially if the X-rays are not specifically requested for the sacrum.

Fluoroscopy is most commonly used in interventional spine procedures [20] and is frequently used in confirming the location of caudal epidural needle. It has been advocated that caudal epidural needle placement should be confirmed by fluoroscopy alone or by epidurography [7]. Radiographic contrast administration can confirm the location of the caudal epidural needle with the Christmas tree-like appearance, due to the bath of the contrast dye of the external aspect of the dura mater and nerve roots [8]. Radiation exposure is the major concern when obtaining fluoroscopic images; actually pulsed imaging is preferred during fluoroscopy because it can reduce overall exposure by 20–75% [7].

Although myelography has been replaced in large part by MR imaging, it remains indicated in some instances (for instance the presence of metal hardware that precludes examination of the spinal canal and cord by magnetic resonance imaging or computed tomography). Subarachnoid contrast agent for myelography is most commonly introduced by a lumbar approach and in these cases lateral fluoroscopy can be helpful in determining an entry site on the skin slightly caudal to the hiatus at about the S5 level, allowing for alignment of the needle nearly parallel to the posterior aspect of the upper sacral vertebral bodies [21].

Computed Tomography

Computed tomography (CT), with its cross-sectional scan provides the capability to visualize the sacral canal, formed by sacral vertebral foramina, and appears triangular in axial images. Its caudal opening is the sacral hiatus. In the sagittal CT images, the sacrococcygeal membrane appears as a hypodense structure, between the posterior end of the sacral vertebra and the posterior tip of the coccyx (Fig. 2). CT is able to visualise also the content of the sacral canal, being able to establish the measurement of the transverse area of the dural sac and of the canal diameter [22]. Solomon et al [23] studied the opening of the sacral canal in 2 population groups: born 1940 to 1950 and 1980 to 1990 and have reported that the individuals born later have significantly more open sacral arches when compared with those born 40 years earlier, especially in the midsacral region. Also,

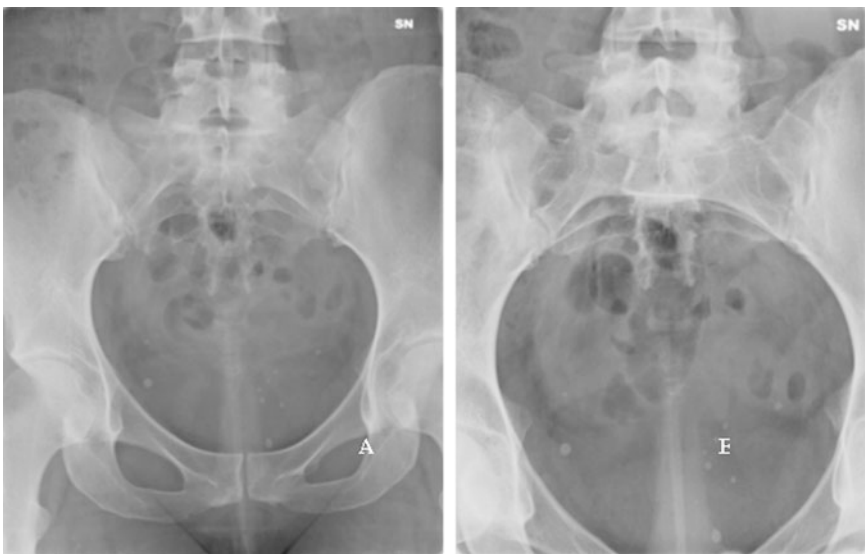

Fig. 1 Antero-posterior radiograph of the sacrum showing the sacral hiatus

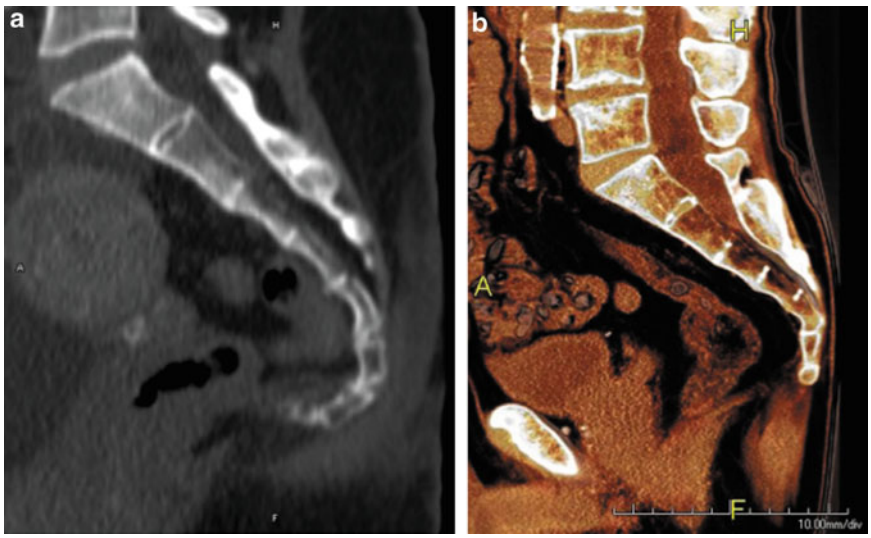

Fig. 2 CT sagittal image (**a**) and volume rendering reconstruction (**b**), showing the caudal space, the sacrococcygeal membrane appears hypodense (*asterisk*)

males have open sacral arches in the rostral segments of the sacrum more than females. CT can be used as guide for sacroplasty for the proper cannula placement prior to cement injection [24]. CT is able also to show with great details the soft tissues and on in vivo CT studies, Scapinelli [25] documented the appearance of the lumbo-sacral meningo-vertebral ligaments, most commonly on transverse images, as a median sagittal septum, easily identifiable when the extradural fat that it crosses is abundant.

Magnetic Resonance Imaging

Magnetic resonance (MR) imaging offers a detailed representation of the sacral canal and of its content (cauda equina and the filum terminale, and the spinal meninges) with a high quality tissue contrast and on multiple planes. Opposite the middle of the sacrum, the subarachnoid and subdural spaces close: the lower sacral spinal roots and filum terminale pierce the arachnoid and dura mater at that level [3]. The images of the sacrum have been obtained on sagittal and transverse planes. It can also be visualised whole or in part during the exams of the lumbar vertebral columns. Usually a phase array spine coil is used and the patient is in the supine position. The relevant anatomy of the sacral canal is demonstrated by the T2-sagittal plane images [15, 26, 27], in which the sacral canal appears hyperintense, due to the presence of the liquor. The dural sac appears as a hypointense band and its termination as hypointense cul de sac in the context of the hyperintensity of the sacral canal. The sacrococcygeal membrane appears as an hypointense band between the posterior end of the sacral vertebra and the posterior tip of the coccyx (Fig. 2). McDonald et al. [15] reported that the median level of termination of the dural sac is located at the level of the middle one third of the S2, extending from the upper border of S1 to the upper border of S4. The mean level for males was also the upper one-third of S2 and for females the middle one-third of S2. Crighton et al. [27] reported that the distance of termination of the dural sac from the beginning of the sacrococcygeal membrane was 1.4 cm (Fig. 3).

Ultrasonography

Diagnostic imaging including plain radiography, computed tomography, and magnetic resonance imaging can provide accurate anatomic information regarding the location of the epidural space, but their use is impractical in most clinical settings where epidural analgesia is used. In contrast, the safety and feasibility of bedside ultrasonography during pregnancy or in neonates or children are well established [8–14]. The sacral canal is studied with patient in prone position and a linear-array ultrasound transducer by using the "acoustic window" [10] in both the longitudinal midline and cross-sectional planes to identify the sacral hiatus. In the transverse sonographic view, two hyperechoic reversed U-shaped structures correspond to the two bony prominences of sacral cornua, between which there are two hyperechoic band-like structures. The band-like structure on top is the sacrococcygeal ligament. The band-like structure at the bottom is the dorsal surface of the sacrum. The sacral hiatus corresponds to the hypoechoic region observed between the two hyperechoic band-like structures [8, 11]. The longitudinal view is obtained by rotating the transducer 90°. In the longitudinal sonographic view, the hyperechoic structure corresponds to the ventral end of the sacrum, and the deep hyperechoic band like structure corresponds to the posterior surface of the sacrum. The hypoechoic band-like structure between the two hyperechoic zones corresponds to the sacrococcygeal ligament.

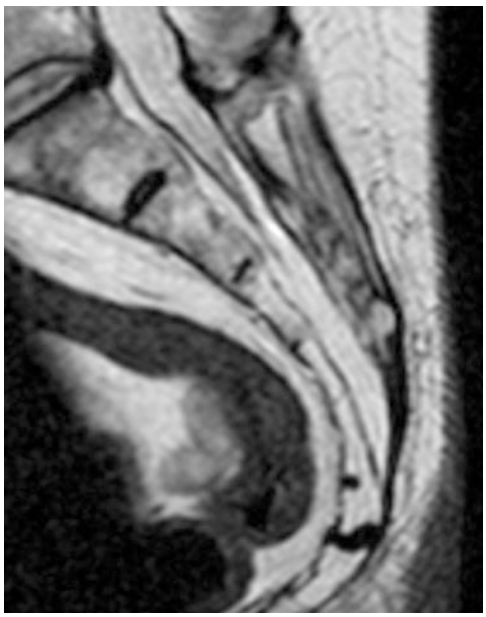

Fig. 3 MR sagittal image of the caudal space

To avoid the most important limitation of the ultrasound-guided caudal epidural injection, i.e. inadvertent intravascular injection [28, 29], color Doppler ultrasonography can be added. The color Doppler ultrasonography shows unidirectional flow (observed as one dominant color) of the injection of the solution through the epidural space beneath the sacrococcygeal ligament, with no flows being observed in other directions (observed as multiple colors) [14].

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Imaging in Degenerative Spine Pathology

Cesare Colosimo, Simona Gaudino, and Andrea M. Alexandre

Abstract The lack of radiation, high soft tissue contrast and capacity for multiplanar and three-dimensional imaging have made magnetic resonance imaging (MRI) the imaging modality of choice for evaluating spinal cord diseases. In diagnostic imaging of the spine, MRI is clearly superior to both conventional radiography (CR) and computed tomography (CT) and it should be preferred as first diagnostic examination when degenerative spine pathologies are suspected.

The other technological equipments (CT, CR, dynamic orthostatic X-ray, myelography, discography and skeletal scintigraphy) have to be selectively chosen and adapted to the individual patient.

Both "container" and "contents" of the spine should be primly evaluated. Finally, a correlation between clinical and radiological features seems to be mandatory for selecting the correct therapeutic choice, since the reliability of the MRI as potential prognostic indicator has been demonstrated.

Keywords Degenerative spine pathology · Spine imaging · Neuroimaging of the spine

MRI, CT and Radiography: Indications and Diagnostic Protocol

Technological weapons that can be used by a (neuro)radiologist in degenerative pathologies of the spine (DSP) include three major techniques: magnetic resonance imaging (MRI), computed tomography (CT), radiography (X-ray); and some others that have a supporting role: myelography and myelo-CT, discography, skeletal scintigraphy and nuclear medicine. In fact while MRI, CT and X-ray are widely used for DSP, the others have particularly strict indications. Myelography and myelo-CT can be used in case of myelopathy, dynamic evaluation or in patients with contraindications to MRI (e.g. pacemaker). Discography is an important tool before percutaneous procedure, while the criticism to discography is related mainly to its invasive nature, reliability of the response, and lack of specificity [1, 2]. Skeletal scintigraphy provides a panoramic view of the spine, and has an important role in dynamic evaluations such as the use of marked granulocytes to discover infections. During the last two decades the diagnostic protocol used for degenerative spine pathologies has changed completely; in fact, in the early 1990s, the sequence of the exams proposed was: X-ray for a general evaluation of bone structures, CT for additional information about soft tissue, while MRI was reserved to well-selected cases. In the middle of the 1990s X-ray was keeping the role of first exam, whereas CT had started to be used electively in lumbar tract and MRI was preferred in cervical myelopathies. Nowadays the situation has changed and MRI is slowly used as first diagnostic exam, followed by CT and then by X-ray. It is difficult for a standard X-ray to maintain the role of screening because of its poor sensibility and specificity and especially because of radiation exposure. CT should be used as a completion, above all in patients suspected for bone or joint alterations. Dynamic X-ray in orthostatism is suggested in case of suspected instability (Fig. 1).

Therefore, despite important differences depending on the tract of spine that is to be examined, MRI should be chosen as first exam wherever available.

MRI and CT: Requirements and State-of-the-Art

Which MRI?

It should be a high field MRI, with dedicated phased-array coils, with efficient and fast gradient echo sequences.

C. Colosimo (✉), S. Gaudino, and A.M. Alexandre
Department of Bioimaging and Radiological Sciences, Catholic University of Sacred Heart, Policlinico "A.Gemelli", L.go A.Gemelli, 00168 Rome, Italy
e-mail: colosimo@rm.unicatt.it

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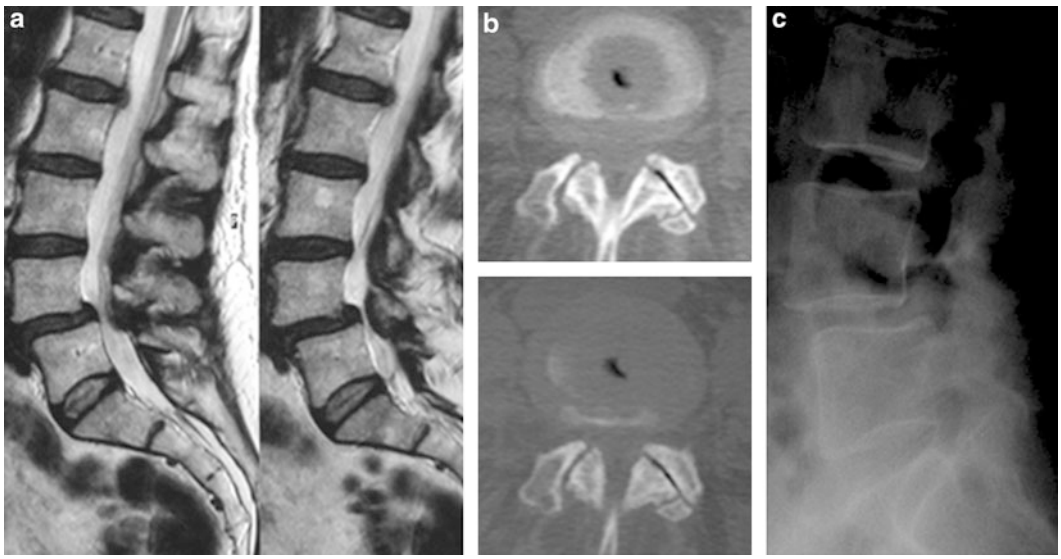

Fig. 1 Imaging of the spinal instability. Sagittal T2-weighted images demonstrate L4-L5 discopathy and L1-L2 herniated disc; the associated decreased antero-posterior canal dimension is suspected for spondylolisthesis (**a**). Axial CT demonstrating a zygapophyseal sublussation (**b**). Dynamic orthostatic X-ray confirms L4-L5 instability (**c**)

Multiplanar imaging offers several significant advantages, therefore at least sagittal and axial sections, with T1 and T2-weighted images and 3 millimetre thickness, seems to be mandatory to us (Fig. 2). In case of bone alterations other techniques that suppress adipose tissue signal can be used (e.g. SPIR/SPAIR, FAT-SAT, STIR); in fact, for these lesions the best approach to characterization and to precisely defining their extent and relationships is to combine unenhanced non-fat-suppressed T1-weighted imaging with fat-suppressed T2-weighted or STIR imaging, and post-contrast SPIR T1-weighted imaging [3] . If a lumbar spinal canal stenosis is noted, a myelo-MRI is needed to quantify the spinal cord compression. In selected patients the use of intravenous contrast agent can be very important, above all after spine surgery [4]. Finally orthostatic MRI, when necessary, is preferable to an axial loader technique since the first is more physiological (Fig. 3).

Which CT?

First of all CT should be used only in selected patients after an MRI, and particularly to focalize the attention on bone structures, however a multislice CT scanner, at least a 16-64-slice system, is required, as well as 2D and in some case 3-Dimensional (3D) multiplanar reconstruction images. The spine must be studied with both "bone" and "soft tissue" algorithm, even if thickness acquisition can differ in relation to the pathology that is to be investigated. Injection of contrast agent should be avoided since it can be used with fewer risks and even less radiation during MRI.

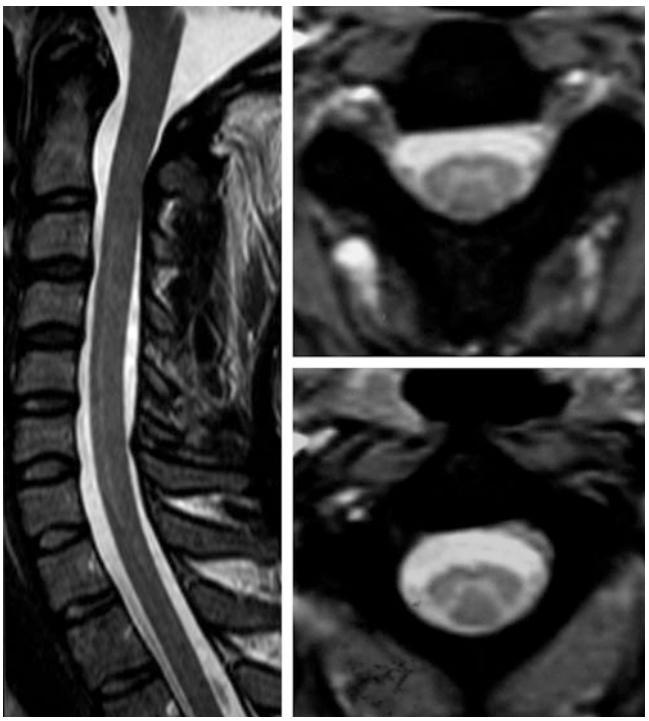

Fig. 2 Sagittal and axial high quality T2-weighted Magnetic Resonance images of the cervical spine permit an high-resolution anatomic evaluation of the cervical spine

Container and Contents, Finding and Report

Spine imaging must give a complete evaluation of "container" degenerative modifications, that is modifications of vertebrae, discs, facet joints and ligaments, moreover it is

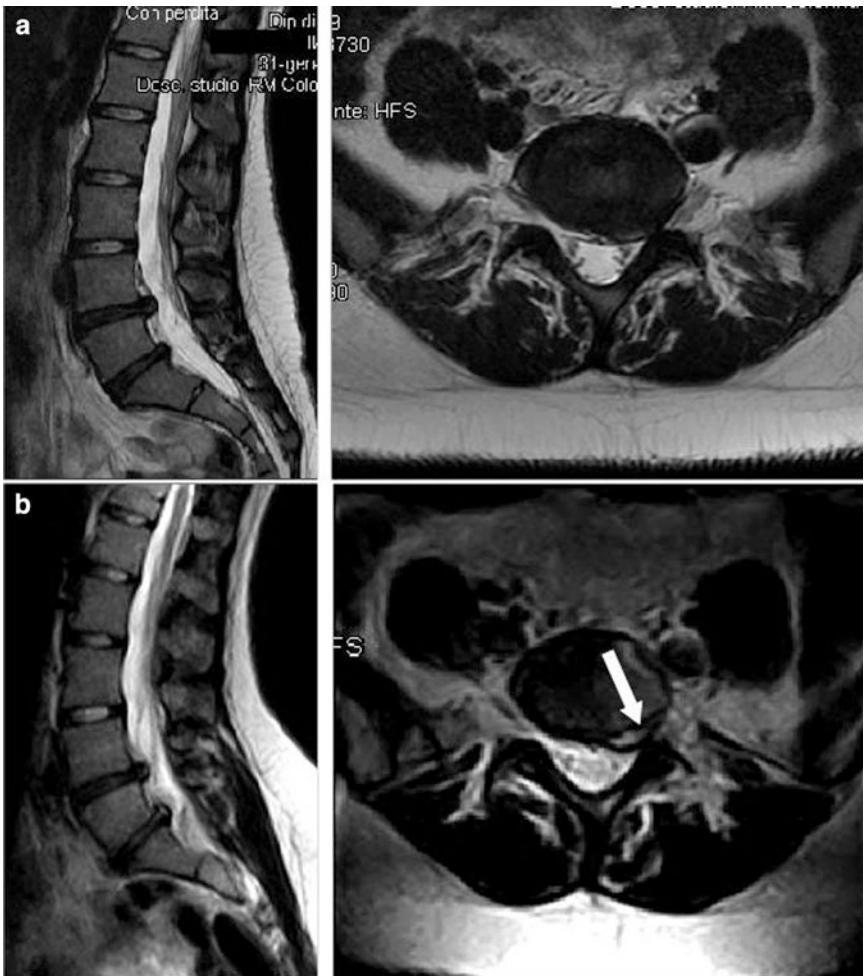

Fig. 3 Comparison between sagittal and axial MRI projections obtained in standard **(a)** and orthostatic **(b)** positions. The disc herniation, and the compression of the adjacent root is more evident during orthostatism (white arrow). (Courtesy of Prof. M. Gallucci. Dept. of Neuroradiology. University of L'Aquila)

extremely important to define and to describe accurately the effects on the "container", that is on the spinal cord, nerve roots, nerve ganglion, meninges and vascular structures. With regard to this second point it is better to separate diseases and imaging of the cervico-dorsal spine, which regard properly the spinal cord, and diseases and imaging of the lumbo-sacral spine, which involve specifically nerve roots. Finally even the smallest sign of instability must be recognised and quantified if it is present.

Cervico-Dorsal Spine

MRI sequences should be chosen in relation to the pathology that is to be studied, indeed every patient has a different situation and sequences must be adapted to the individual case, in this context we want also to underline the importance of the quality of an image in clarifying a diagnostic question (Fig. 4).

Demonstration of "soft" herniated disc and differential diagnosis between disc herniations and osteophytes requires gradient echo (GRE) axial images, and often 3D T1 and T2-weighted images, only in some cases is a CT examination preferable. In case of myelopathy, 3D GRE T2-weighted axial images are the most important sequences to visualize the extent and degree of the spinal cord compression, above all employing techniques that suppress adipose tissue signal.

Although with all equipment you can obtain images in flexion and extension, the contribution given by dynamic orthostatic X-ray still remains irreplaceable.

Disc herniations must be properly defined as: central, postero-lateral and lateral/intraforaminal. Other elements that must be always considered are: presence of osteophytes, unco-arthropathy, calcification of posterior longitudinal ligament and yellow ligament hypertrophy. Spinal canal stenosis, lateral recesses stenosis and neural foramina stenosis must be considered distinctly.

The term "spinal cord compression" (SCC) must be cautiously used; it is compulsory demonstrating or, on the other hand, excluding any radiological sign of spinal cord distress; in fact when spinal cord distress is full blown signs are clearly of vascular origin, with a major involvement of the grey matter in the context of an atrophic spinal cord (Fig. 5).

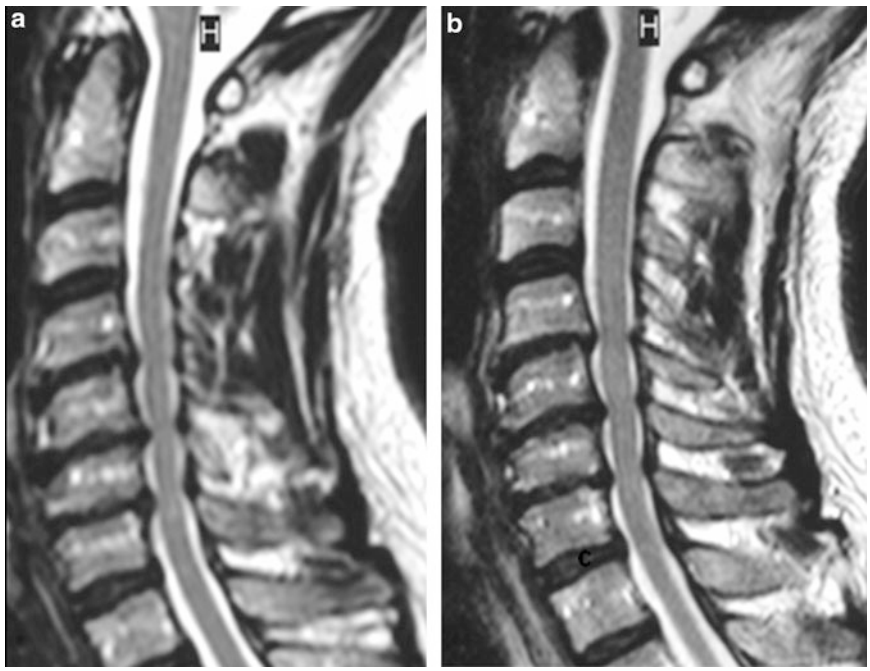

Fig. 4 The importance of the quality of MRI images. Sagittal turbo-spin echo (TSE) T2-weighted images studied in a 1,5 T equipment with a phased-array coil. The cervical spine of the same patient studied with different parameters (matrix acquisition and Turbo Factor). In (**b**) disappears the sign of spinal cord compression at C6-C7 level that could be misinterpret in (**a**)

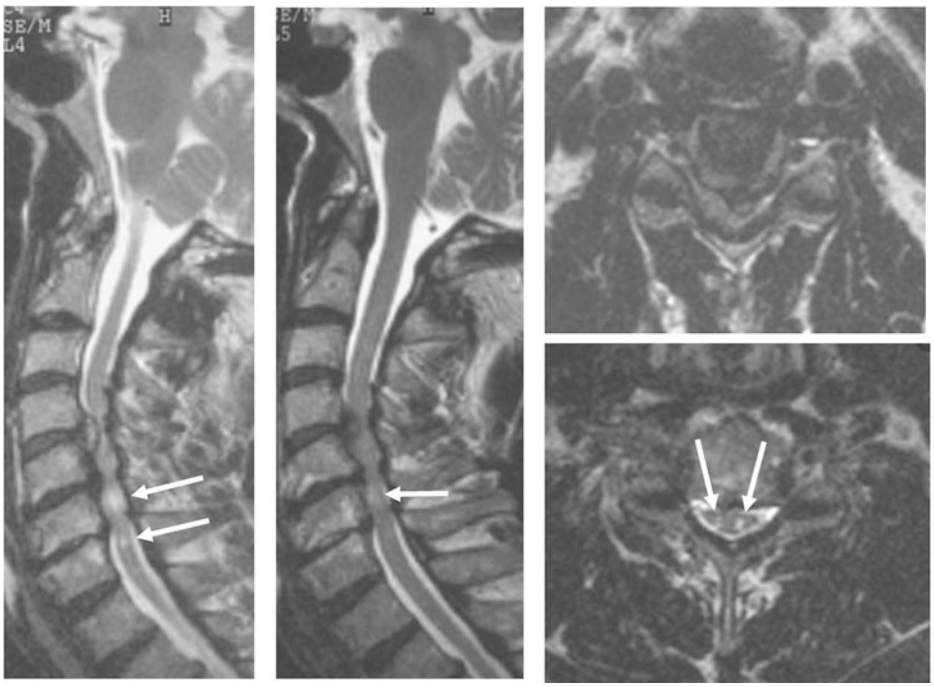

Fig. 5 Sagittal and axial T2-weighted MRI, showing a chronic cervical spondylotic myelopathy, with a symmetrical suffering of the central grey matter at multiple levels

Lumbo-Sacral Spine

When a non specific low back pain is present, MRI should be performed as the first examination [5]. Sagittal image scanning must include both neural foramina, and the choice between T1 or T2-weighted axial images should be based on what kind of equipment the (neuro)radiologist can rely on. The value of T2 relaxation times, especially, has been proved to characterize the structure of lumbar intervertebral discs [6].

Whenever bone changes are present it is mandatory to apply adipose tissue suppression techniques, or complete

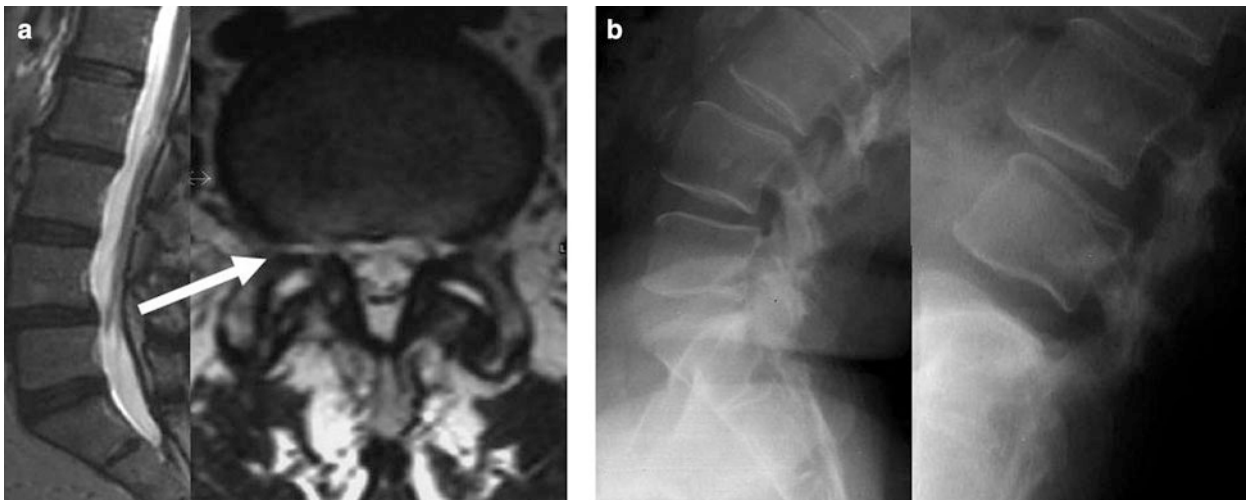

Fig. 6 Minimal signs of spondylolisthesis (white arrow) can be appreciated in sagittal and axial T2-weighted MRI **(a)**. Dynamic orthostatic X-ray confirms aretrolisthesis of L5 **(b)**

the study with a CT. The use of contrast agent should be reserved to well-selected patients, even if it can be very useful to highlight bone, intra-articular and muscular findings. Even though minimal signs of spondylolisthesis are noted in a standard supine MRI, as for example exaggerated fluid in facet joints [7], bone instability must be suspected and a dynamic orthostatic X-ray or an orthostatic MRI, if it is available, must be suggested to the patient (Fig. 6).

Lumbar discs alterations represent only a small part of degenerative spine pathology, in fact the same attention should be given to modifications of other spine structures such as ligaments, zygapophyseal joints and vertebral body (Fig. 7). These structures are involved by a mechanism cycle of degeneration that is instigated by small changes in the mechanical integrity of the intervertebral disc [8]. In any case, compression effects on spinal canal, lateral recesses, neural foramina and their contents (thecal sac, nerve roots and ganglion) must be underlined if they are present. Even dural venous plexus modifications must be searched for. If a central spinal canal stenosis is diagnosed, the extent of the stenosis can be confirmed by the presence of varicose and thicker nerve roots above the site of compression.

Disc Degeneration and Lumbar Disc Herniation

Changes in discs are related to aging; in fact desiccation, fibrosis and cleft formation in the nucleus, fissuring and mucinous degeneration of the anulus, defects and sclerosis of endplates, and/or osteophytes at the vertebral apophyses are frequently seen in the asymptomatic patient during radiological examinations. Clinical features must be considered to determine whether degenerative changes on imaging are pathologic and what may or may not have contributed to their development [9], even if the distinction between aging changes and pathologic changes remains unclear [10]. The role of imaging is to provide accurate morphologic information and influence therapeutic decision making [11]. Disc degenerations should be classified with standard criteria using the Thompson Grading Scale, where, following a set of parameters, an X-ray radiographic inspection of the disc is conducted and the gross morphology is used to determine the extent of degeneration [12]. The term herniated disc means a focal lesion, and confusion with a bulging disc must be avoided. Unfortunately common classifications of herniated disc disease are not widely accepted; the absence of universal nomenclature standardization with respect to the definition of a disc herniation and its different categories, especially regarding type and location, is still a major problem that will only be overcome when major national or international scientific societies join efforts to support a particular scheme [13, 14]. Radiologists are asked anyway, to specify the localization (median, paramedian, posterolateral, lateral or foraminal and "far-lateral"), the fragment migration direction (cranial or caudal) and the continuity with the original disc. Any signal intensity or signal density can be associated with a herniated disc, even fluid or gas signal ones; these signal alterations can rapidly modify or even disappear.

Lumbar Instability

In the last decade diagnostic imaging has become an "obsessive" research of instability, while before it was almost ignored. Radiological instability signs have to be

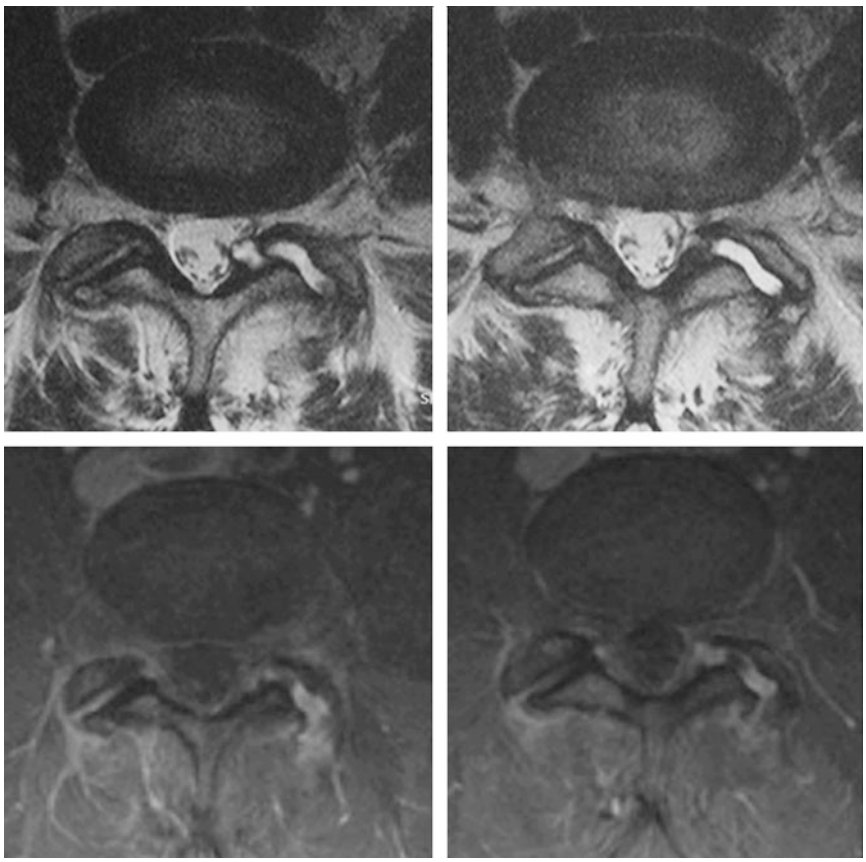

Fig. 7 T2 and T1-weighted axial images pointing out remarkable zygapophyseal joints and muscular degenerations

correlated with the patient's symptoms. Axial loader systems are not physiological and risk to "create" an instability, therefore orthostatic MRI and particularly dynamic orthostatic X-ray should be preferred. In this context multislice CT maintain a preferential role thanks to its resolution, as a complementary examination to MRI, in visualizing zygapophyseal joints, spondylolysis and pre-spondylolysis. Measurement technique of Dupuis et al. maintains a central role to quantify the entity of the instability [15].

Conclusions

Nowadays and in a recent future MRI should be preferred as first diagnostic examination when degenerative spine pathologies are suspected [1]. The other technological equipments (CT, X-Ray, dynamic orthostatic X-ray, myelography, discography and skeletal scintigraphy) have to be selectively chosen and adapted to the single patient. Radiologists should analyze both "container" and "contents" of the spine. Finally a correlation between clinical and radiological features seems to be mandatory for selecting the correct therapeutic choice, since the reliability of the MRI as potential prognostic indicator has been demonstrated [16].

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Operative Management of Lumbar Disc Herniation
The Evolution of Knowledge and Surgical Techniques in the Last Century

F. Postacchini and R. Postacchini

Abstract Removal of a herniated disc with the use of the operative microscope was first performed by Yasargil (Adv Neurosurg. 4:81–2, 1977) in 1977. However, it began to be used more and more only in the late 1980s (McCulloch JA (1989) Principles of microsurgery for lumbar disc disease. Raven Press, New York). In the 1990s, many spinal surgeons abandoned conventional discectomy with naked-eye to pass to the routine practice of microdiscectomy. The merits of this technique are that it allows every type of disc herniation to be excised through a short approach to skin, fascia and muscles as well as a limited laminoarthrectomy. For these reasons, it has been, and still is, considered the "gold standard" of surgical treatment for lumbar disc herniation, and the method used by the vast majority of spinal surgeons. In the 1990s, the advent of MRI and the progressive increase in definition of this modality of imaging, as well as histopathologic and immunochemical studies of disc tissue and the analysis of the results of conservative treatments have considerably contributed to the knowledge of the natural evolution of a herniated disc. It was shown that disc herniation may decrease in size or disappear in a few weeks or months. Since the second half of the 1990s there has been a revival of percutaneous procedures. Some of these are similar to the percutaneous automated nucleotomy; other methods are represented by intradiscal injection of a mixture of "oxygen-ozone" (Alexandre A, Buric J, Paradiso R. et al. (2001) Intradiscal injection of oxygen ozone for the treatment of lumbar disc herniations: result at 5 years. 12th World Congress of Neurosurgery; 284–7), or laserdiscectomy performed under CT scan (Menchetti PPM. (2006) Laser Med Sci. 4:25–7). The really emerging procedure is that using an endoscope inserted into the disc through the intervertebral foramen to visualize the herniation and remove it manually using thin pituitary rongeurs, a radiofrequency probe or both (Chiu JC. (2004) Surg Technol Int. 13:276–86).

Microdiscectomy is still the standard method of treatment due to its simplicity, low rate of complications and high percentage of satisfactory results, which exceed 90% in the largest series. Endoscopic transforaminal discectomy appears to be a reliable method, able to give similar results to microdiscectomy, provided the surgeon is expert enough in the technique, which implies a long learning curve in order to perform the operation effectively, with no complications. All the non-endoscopic percutaneous procedures now available can be used, but the patient must be clearly informed that while the procedure is simple and rapid, at least for the disc L4–L5 and those above (except for laserdiscectomy under CT, that can be easily performed also at L5–S1), their success rate ranges from 60 to 70% and that, in many cases, pain may decrease slowly and may take even several weeks to disappear.

Keywords Microdiscectomy · Percutaneous techniques

A Short Historical Review

After the enormous scientific contribution provided by "*De Ischiade Nervosa. Commentarius*" of Cotugno [1] (1764), in which the author first ascribed sciatica to the involvement of the sciatic nerve, almost one century passed before herniation of the intervertebral disc was identified by Luschka [2], who, however, did not relate the pathologic findings to the clinical features of the disease.

The first discectomy was performed by Krause in 1908 at the Berlin Augusta Hospital on advice of the neuropathologist Oppenheim [3]. The patient obtained an immediate, complete relief of pain. The tissue responsible for the symptoms, however, was mistaken for an enchondroma.

F. Postacchini (✉)
Department of Orthopaedic Surgery University Sapienza, Rome, Italy
e-mail: franco.postacchini@uniroma1.it

R. Postacchini
Department of Orthopaedic Surgery, University Tor Vergata, Rome, Italy

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In 1911 Goldthwait and Osgood [4] reported on the case of a patient with paresis of the lower limbs, operated by Cushing, who found a disc protrusion which was interpreted as the cause of impingement of the nervous structures and thus responsible of the patient's sciatica and cauda equina syndrome. In the 1920s, Schmorl [5] started to study 10,000 human spines and described the protrusion of disc tissue in the vertebral body as well as disc herniation in the spinal canal; however he did not attribute any clinical significance to the latter findings.

In 1930 Alajouanine and Petit-Dutaillis [6] presented a case of sciatica associated with an intraspinal lesion at the Surgical Academy of Paris and suggested that what had previously been identified as a tumour actually was herniation of the nucleus pulposus. The first patient whose preoperative diagnosis was "ruptured intervertebral disc" was operated in 1932 by the neurosurgeon Mixter and the orthopaedic surgeon Barr [7]. Two years later, the authors correlated disc prolapse with the neurologic disorders associated with this condition and stressed the therapeutic role of the surgical treatment. In the following years, Filippi [8] analysed the changes occurring in the disc after removal of the nucleus pulposus, while De Sèze [9] stated that the nerve root is affected within the spinal canal before it enters the intervertebral foramen.

In 1938, Love and Walsh [10] reported on the clinical results of surgery in 100 patients with disc herniation and for the first time, a on recurrent herniation; in 1940, their cases reached 300. In 1948 Lane and Moore [11] reported on the removal of lumbar disc herniation through a transperitoneal approach.

The Explosion of Surgical Treatment

In the 1960s and 1970s, removal of a herniated disc became one of the most frequent operative procedures performed by orthopaedic surgeons and neurosurgeons. The preoperative diagnosis was made by myelography and electrodiagnostic studies, but most often it was based only on the clinical history and physical examination. It was common practice to operate any patients with radicular pain of even very recent onset. A few surgeons made the diagnosis by asking the patient to bend forward and scheduled an operative treatment simply on the finding of sciatic pain elicited by trunk flexion.

Since the level involved was often unclear, it was common practice to explore the last two lumbar discs in order not to miss a herniated disc. Many mild disc protrusions were thus operated on and when no herniation was found an etiologic role in the genesis of radicular symptoms and nerve root irritation or compression was attributed to epidural varices.

In most cases radical discectomy was performed. It consisted in the complete removal of the nucleus pulposus as well as the cartilaginous end plates by curettes used to grasp the cartilage as extensively as possible to avoid regrowth of the nucleus. Usually the result was a severe decrease in the height of the intervertebral space.

The Advent of Percutaneous Techniques

In the early 1960s Smith [12] published an experimental study showing that the intradiscal injection of chymopapain in rabbit dissolved the nucleus pulposus. In 1963 he successively treated the first patient with the enzyme. However, only in the late 1970s and 1980s this method of treatment, called chemonucleolysis, became more and more popular and hundreds of thousands of patients with a herniated disc received intradiscal chymopapain. And hundreds of studies were carried out, which found the therapeutic efficacy of the procedure to reach 70–80% [13]. This method was widely used in USA and Europe, but often also by inexperienced doctors. This was probably the main reason for the dramatic increase in complications, particularly the most severe ones, of the procedure, namely anaphylactic shock and cord lesions. This led, in the 1990s, to the progressive decrease in the use of chymopapain, which was then withdrawn from the market in many countries.

Parallel to the decrease in popularity of chemonucleolysis, a new percutaneous technique, first performed by Hijikata and Yamagishi [14] in 1975, began to be used in few centres, i.e. the manual removal of nucleus pulposus by a percutaneous posterolateral approach to the disc using small sized pituitary rongeurs. This technique, however, did not gain popularity, at that time, because another, technically simpler method – the percutaneous automated nucleotomy with the Onik instrumentation – was introduced in the market [15]. The latter technique rapidly reached the same popularity as chemonucleolysis because of its safety and the high percentage of satisfactory results initially reported. Subsequently, however, many studies demonstrated that the percentage of success of this procedure did not exceed, on average, 65%, a figure not significantly higher than that obtained with conservative management. In addition, this method, as the previous ones, was essentially indicated for contained herniation, that is a fairly small proportion of herniated discs. During the 1990s, this method was thus almost completely abandoned, even if the concept on which it was founded was considered valid by many researchers. The concept was that it might be sufficient to decrease the intradiscal pressure by making a hole in the

annulus fibrosus and removing a limited portion of the nucleus pulposus to obtain a gradual decrease in the disc protrusion.

The Era of Microdiscectomy

Removal of a herniated disc with the use of the operative microscope was first performed by Yasargil [16] in 1977. However, it began more and more used only in the late 1980s [17]. In the 1990s, many spinal surgeons abandoned the conventional discectomy with naked-eye to pass to the routine practice of microdiscectomy. The merits of this technique are that it allows every type of disc herniation to be excised through a short approach to skin, fascia and muscles as well as a limited laminoarthrectomy. Due to the excellent lighting of the operative field and a magnified view, the surgical manoeuvres can be performed with greater precision, the causes of compression of the neural structures can be more easily identified and fewer risks are run to cause undue trauma to the emerging nerve root or thecal sac. For these reasons, it has been, and still is, considered the "gold standard" of surgical treatment for lumbar disc herniation, and the method used by the vast majority of spinal surgeons.

The Knowledge of Natural History

In the 1990s, the advent of MRI and the progressive increase in definition of this modality of imaging, as well as histopathologic and immunochemical studies of disc tissue and the analysis of the results of conservative treatments have considerably contributed to the knowledge of the natural evolution of a herniated disc. It was shown that disc herniation may decrease in size or disappear in a few weeks or months. The process occurs in contained, extruded (subligamentous, transligamentous or retroligamentous), or migrated herniations, the latter being the condition in which a fragment of disc tissue migrates at a distance from the disc. Migrated herniations disappear in approximately 75% of patients in 2–4 months, whereas extruded herniations decrease in size or disappear in some 60% of cases. By contrast, only in some 30% of patients with contained herniation, the latter disappears in the course of few to several months.

In migrated or extruded herniations, phagocytosis of herniated tissue, carried out by macrophages contained in the epidural tissue and/or originating from less differentiated epidural cells or arriving in the spinal canal with the epidural vessels, appear to play a primary role. In contained herniations, the main mechanism leading to a decrease in size or disappearance of the herniation is likely to be represented by dehydration of the herniated nucleus pulposus. This may account for the higher frequency with which young patients, who tend to have a greater hydration of the nucleus pulposus, often present a decrease in size of their herniation. In contrast, contained herniations of highly degenerated and thus less hydrated nucleus, or herniations mainly represented by portions of annulus fibrosus, have little tendency to decrease in size or disappear spontaneously.

The New Operative Procedures

Since the second half of the 1990s there has been a revival of percutaneous procedures.

Some of these are similar to the percutaneous automated nucleotomy and are based on a similar concept on which the latter was founded, namely to perform a "hole" in the annulus fibrosus and to either remove or destroy a limited amount of nucleus. They include, among others, the "Reliefer," which is a very similar device to the Onik one, "Laserdiscectomy" (first performed by Choy [18] in 1986) carried out by inserting the laser probe in the centre of the disc, and the "Nucleoplasty" which uses radiofrequency to generate a temperature of 50–60° that produces a thermic coagulation of the disc tissue, as well as biochemical changes in the latter.

Other methods are represented by intradiscal injection of a mixture of "oxygen-ozone" [19], or laserdiscectomy performed under CT scan [20]. The mechanism of action of the former is still somewhat unclear, but it appears to produce biochemical changes in the components of the nucleus and to exert anti-inflammatory effects which may affect the nerve root compressed by the herniation. The latter consists of delivering laser energy directly into the herniated portion of the disc which is reached by a very thin laser probe introduced through the spinal canal.

However, the really emerging procedure is that using an endoscope inserted into the disc through the intervertebral foramen to visualize the herniation and remove it manually using thin pituitary rongeurs, a radiofrequency probe or both [22]. This technique has the merit of being able to remove not only contained herniation, but also extruded or even migrated fragments of the disc. Additional advantages, compared to microdiscectomy, are that the procedure avoids any damage to the paravertebral muscles and excision of the posterior bony elements of the spine, particularly the articular processes, and that only a limited portion of the intervertebral disc is removed thus preserving to a large extent the integrity of the disc.

An alternative endoscopic procedure can be performed by posterior approach with dilators of different diameters introduced into the paravertebral muscles to reach the laminae, which are partially excised to gain access to the spinal canal [21]. This technique is very similar to microdiscectomy with no significant advantage compared to the latter and has thus never reached a wide popularity.

Present Trends in the Management of Lumbar Disc Herniation

Based on the present knowledge of the natural history of lumbar disc herniations, a large part of these conditions do not need any surgical procedure.

This holds particularly true for migrated herniations (free fragment of disc) because the clinical symptoms decrease in severity and then disappear in a large part of patients in the course of 1–2 months. In these cases, there is an indication for surgery in the presence of excruciating pain or severe motor or sensory deficits which may not recover completely by delaying or avoiding surgery. When resorting to an operative treatment, there is an indication for microdiscectomy in the presence of a free fragment into the spinal canal, or in the intervertebral foramen (intraforaminal herniation) or lateral to the foramen (extraforaminal herniation). In the latter instances, the herniation can be removed through an interlaminar approach by removing the articular processes to such a limited extent as not to produce any vertebral instability. Microdiscectomy can also be used to remove the herniation by a paraspinal or paralateral approach to the intervertebral foramen, a technique that implies a minimal removal of bone of the posterior vertebral arch.

Considerations similar to those made for migrated fragment of disc tissue are valid for extruded herniations which, however, more often need surgery since they have less tendency to disappear spontaneously and more frequently produce severe radicular pain and neurologic deficits. Also for these conditions, microdiscectomy is most often the treatment of choice. A valid alternative can be the endoscopic discectomy through a transforaminal approach. In the presence of a small fragment of tissue extruded just behind the disc, the method of CT-aided laserdiscectomy can also be carried out. In this case, the patient should be informed that the percentage of success of the procedure does not exceed 70%. The same holds true for other intradiscal non-endoscopic techniques, which however appear to have, compared with laserdiscectomy under CT, a lower percentage of satisfactory results. It should be borne in mind that all these procedures rely to a variable, but often large, extent on the tendency of symptoms to undergo spontaneous resolution in the course of a few weeks or months.

In contained herniation, conservative management should usually be prolonged for 2–3 months in the absence of excruciating pain and neurologic deficits. If symptoms do not resolve, there are three main options: microdiscectomy, endoscopic transforaminal discectomy, percutaneous non-endoscopic procedures. Microdiscectomy is still the standard method of treatment due to its simplicity, low rate of complications, and high percentage of satisfactory results, which exceed 90% in the largest series. Endoscopic transforaminal discectomy appears to be a reliable method, able to give similar results to microdiscectomy, provided the surgeon is expert enough in the technique, which implies a long learning curve in order to perform the operation effectively, with no complications. All the non-endoscopic percutaneous procedures now available can be used, but the patient must be clearly informed that while the procedure is simple and rapid, at least for the disc L4–L5 and those above (except for laserdiscectomy under CT, that can be easily performed also at L5–S1), their success rate ranges from 60 to 70% and that, in many cases, pain may decrease slowly and may take even several weeks to disappear. These techniques should thus be avoided in patients with severe leg pain who ask for immediate or rapid resolution of symptoms as well as in those with large herniations that have low chances of undergoing a significant decrease in size with the procedure.

Conclusion

In 1932 Mixter and Barr first operated on a patient with a preoperative diagnosis of lumbar disc herniation. In the following decades discectomy for a herniated lumbar lumbar disc was among the most commmon operations performed by orthopaedic surgeons and neurosurgeons. Chemonucleolysis with chymopapain was the first minimally invasive treatment for lumbar disc herniation, with a mean success rate of 75%. It becames extremely popular in the 1970s and 1980s, until it was replaced by surgical techniques which did not expose to the complicacions of chemonucleolysis, namely the allergic ones.

Microdiscectomy, introduced in the late 1970s became more and more popular in the late 1980s and since the 1990s it has become the “gold standard” of surgical tratment of lumbar disc herniation because it can be successfully employed for any type of herniation. In the second half of the 1990s and the present decades many new minimally invasive techniques have been developed, which however can give satisfactory results in not more than 60–70% of patients with a contained herniated disc or a herniation

with a small extruded fragment of disc. It should be considered, anyway, that at least a part of the successes with these methods are due to the natural tendency of the herniation to disappear spontaneously. The most valid of the new surgical procedures appears to be the endoscopic discectomy through a transforaminal approach, which however, in contrast to miscrodiscectomy, cannot be performed in all cases of disc herniation.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Philosophy and Concepts of Modern Spine Surgery

Soriano-Sánchez José-Antonio, Marcos Baabor-Aqueveque , and Francisco Silva-Morales

Abstract The main goal of improving pain and neurological deficit in the practice of spine surgery is changing for a more ambitious goal, namely to improve the overall quality of life and the future of patients through three major actions (1) preserving the vertebral anatomical structures; (2) preserving the paravertebral anatomical structures; and (3) preserving the functionality of the segment. Thus, three new concepts have emerged (a) minimal surgery; (b) minimal access surgery; and (c) motion preservation surgery. These concepts are covered in a new term, minimally invasive spine surgery (MISS) The term "MISS" is not about one or several particular surgical techniques, but a new way of thinking, a new philosophy. Although the development of minimally invasive spine surgery is recent, its application includes all spine segments and almost all the existing conditions, including deformities.

Evidence-based medicine (EBM), a term coined by Alvan Feinstein in the 1960s (Feinstein A (1964) Annals of Internal Medicine 61: 564–579; Feinstein A (1964) Annals of Internal Medicine 61: 757–781; Feinstein A (1964) Annals of Internal Medicine 61: 944–965; Feinstein A (1964) Annals of Internal Medicine 61: 1162–1193.), emphasizes the possibility of combining art and science following the strict application of scientific methods in the treatment of patients (Feinstein A (1964) Annals of Internal Medicine 61: 944–965; Feinstein A (1964) Annals of Internal Medicine 61: 1162–1193.), which may represent the advantages of objectivity and rationality in the use of different treatments (Fig. 11). However, EBM has many obvious defects, especially in spine surgery it is almost impossible to develop double-blind protocols (Andersson G, Bridwell K, Danielsson A, et al (2007) Spine 32: S64–S65.). In most cases, the only evidence one can find in the literature is the lack of evidence (Resnick D (2007) Spine 32:S15–S19.), however, the lack of evidence does not mean its absence. Only then, with a rigorous self-analysis, we may take a clear path towards a new philosophy in spine surgery. Of course, feedback from patients through satisfaction and clinical scales can guide our direction and provide the energy needed to maintain the enthusiasm (Fig. 12).

Keywords Dynamics of the spine · Evidence-based medicine · Image guided procedures · Minimally invasive surgical techniques

S.-S. José-Antonio (✉) and F. Silva-Morales
The American British Cowdray Medical Center, Avenue Carlos Graef Fernández no. 154 Consultorio 106 y 107 Tlaxala Santa Fe, Delegación Cuajimalpa, CP 05300, México D.F.
e-mail: neurojass1@hotmail.com

M. Baabor-Aqueveque
Hospital Clinico Universidad de Chile, 11 de Septiembre no. 1363 Oficina 1502 Providencia, Santiago de Chile. Universidad de Chile
e-mail: marcosbaabor@yahoo.com

Philosophy and Concepts of Modern Spine

We must recognize that many aspects of spinal surgery have changed over time. The world itself has changed. The mortality rate has decreased and life expectancy has increased at a rate of approximately 3 months per year in accordance with the University of Cambridge, and as a result, world population has increased from just over three billion in 1965 to almost seven billion at present and with a projection, according to the WHO, around nine billion by 2050. This explains the gradual increase in the number of people beyond the fifth and sixth decades of life and diseases specific to those ages. Population growth, urbanization, industrialization and poverty, on the other hand, explain the increase in accidents and violence, especially in underdeveloped countries. This is why today we noticed an increased incidence of degenerative, traumatic and vertebral column metastatic diseases.

The information acquisition process has undergone an evident metamorphosis from the large paper-based library collections to virtual libraries, as well as the overwhelming amount of information online that can be obtained nowadays

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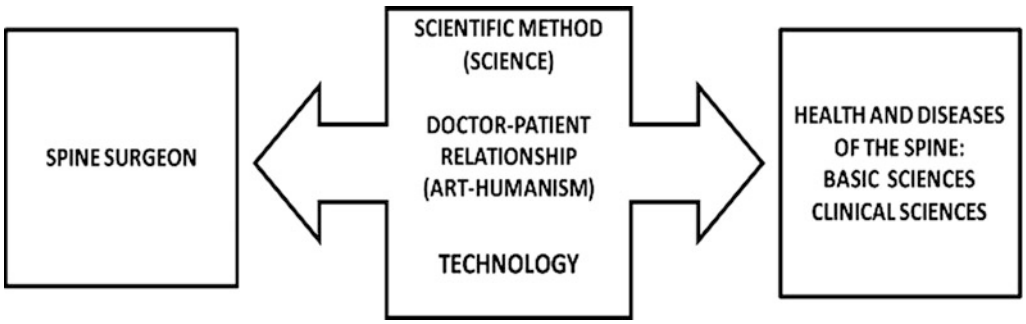

Fig. 1 Elements of knowledge on spine surgery: experienced person, object of knowledge, and interaction with each other

from anywhere on earth thanks to the internet. Today, the concern is not the amount of information on a specific topic but the methodological quality of the same, as will be discussed later.

Knowledge is defined as the abstraction of the phenomena that surround us and serves to transform the universe and subordinate the nature to the needs of man; it has a progressive changing and perfectible nature [4]. In the case of spine surgery, the three critical components of knowledge are the individual, namely the spine surgeon, who knows the object of knowledge; that is to say the health status and disease of the spine and the interaction between the two, which is carried out through scientific knowledge but also through art and humanism against the sickness and with the help of the techniques and technology [6, 8] (Fig. 1).

In few areas of medicine have been so many advances in knowledge in recent times, as in spine surgery [16]. As examples, we have moved from the approximate anatomical drawings and descriptive anatomy of the spine to the deep knowledge of surgical anatomy, functional anatomy (biomechanics) and radiological anatomy. It is worth to mention that in the basic sciences have been great advances in histology, biochemistry, genetics, immunology, physiology, biomechanics, etc. Which have increased our understanding on the complex structure and function of the intervertebral disc, which in turn has opened the hope to new possibilities of more specific and thorough treatments in the future, such as biological treatments; even though we must recognize that we too need to understand, to the point that it has not even been possible to define the meaning of degenerative disc disease and differences as far as the natural aging process [1].

The acquisition of images is other fundamental aspect that has undergone major changes; we have evolved from simple biplane studies to sophisticated three-dimensional studies such as computed tomography and magnetic resonance imaging, which allow us the precise identification of normal and pathological anatomy, including virtual anatomy, as in the case of neuronavigation. And of course today we have intraoperative images in real time whose purpose is not only diagnostic but also therapeutic, and this in turn has created the opportunity for new options of treatment for patients including interventional radiology and image-guided surgery. That has made it possible to limit the iatrogenic damage of vertebral and paravertebral structures through the precise delimitation of intraoperative target; thus contributing to the origin of the minimally invasive surgical techniques that aim to improve the prognosis of patients (Fig. 2). We should not forget to mention other advances such as movement studies, which help us to better understand the dynamics of the spine, and metabolic studies such as PET, etc.

Of course, there is no doubt that clinic history remains the cornerstone for the integration of diagnosis but the quality of the current auxiliary studies allows us to establish not only topographic and pathological, but also functional diagnostics, with which we can make an approximate projection about the possible outcome of our treatments. But even in a situation where the pathological changes, in diagnostic images, can be severe, often it is hard to define what is the pain-generating specific structure. We must remember that pain is the main symptom, and often the only one, for which the patient visits a practitioner. Its origin can be unique or multiple (intervertebral disc, articular facets, nerve roots, ligaments, muscles, bones) but too often the reason that leads us to decide on a treatment or surgical intervention. In this sense, the selective diagnostic blockades, fully underpinned as forecasts by multiple work of evidence based medicine, offer us the unique opportunity to confirm or refute our clinical suspicions and make a more rational treatment plan aimed at relieving the patient´s complaints and not only the changes in the image. With the possibility of materializing accurate diagnosis, we are forced to have clear objectives and especially a specific target during surgical procedures (Fig. 3). Today, it does not seem valid to change the diagnosis or surgical plan during the procedure.

Spine surgery-applied technology has been developed at neck breaking speed, including radiolucent tables that allow ideal positioning of the patient, intraoperative images in real and virtual time (tomography, fluoroscopy, MRI,

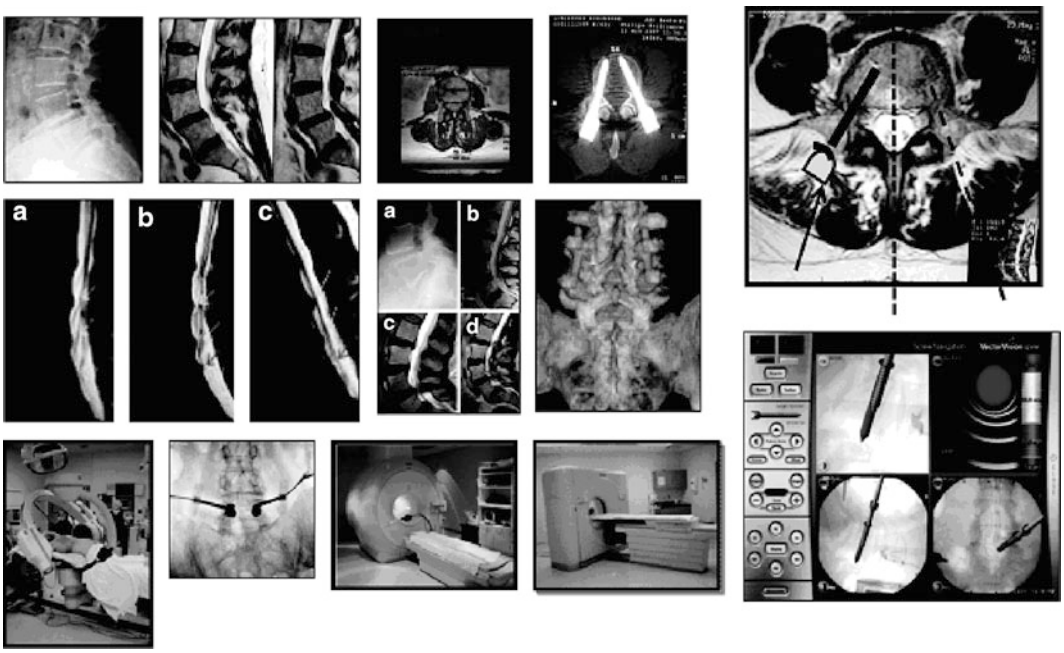

Fig. 2 The knowledge from static to dynamic images, from real to virtual images, from diagnostic to therapeutic images

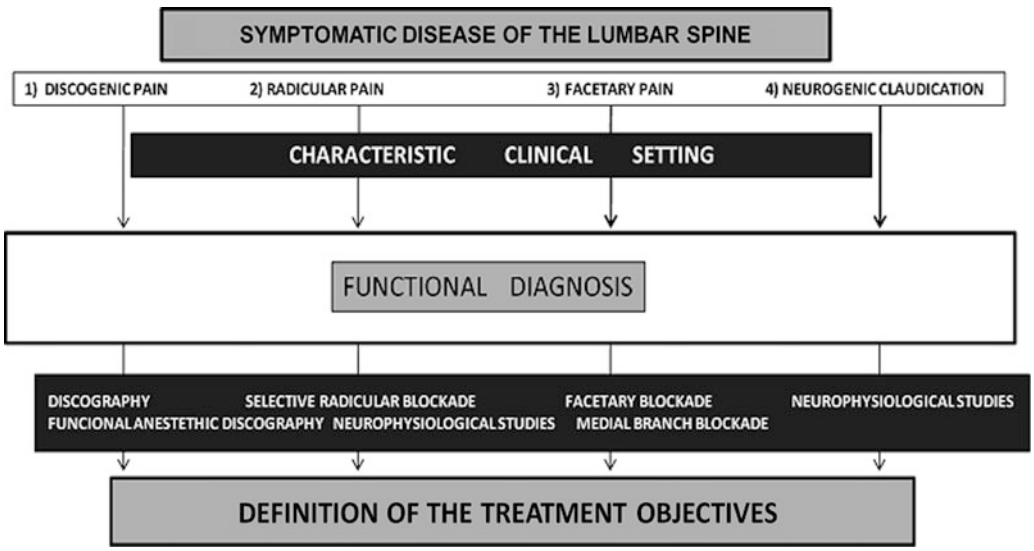

Fig. 3 The research of pain generating structure is the main basis for developing the treatment plan

neuronavigator), lighting and magnification systems of the surgical fields (microscopes, endoscopes, tubular systems for minimal access, etc.) [11, 13] and sophisticated instruments for separation, retraction, coagulation and implementation of devices in order to achieve the surgical objectives through small existing anatomical sites and from the skin outer surface (Fig. 4).

The main goal of improving pain and neurological deficit in the practice of spine surgery is changing for a more ambitious goal, namely to improve the overall quality of life and the future of patients through three major actions (1) preserving the vertebral anatomical structures; (2) preserving the paravertebral anatomical structures; and (3) preserving the functionality of the segment. Thus, three new concepts have emerged (a) minimal surgery; (b) minimal access surgery; and (c) motion preservation surgery. These concepts are covered by a new term: minimally invasive spine surgery (MISS) (Fig. 5). To better understand these terms, it is worth remembering that all surgical procedures consists of two main elements: the surgical access and the specific surgical procedure [11]. The surgical access implicates the pathway through which the surgery target is

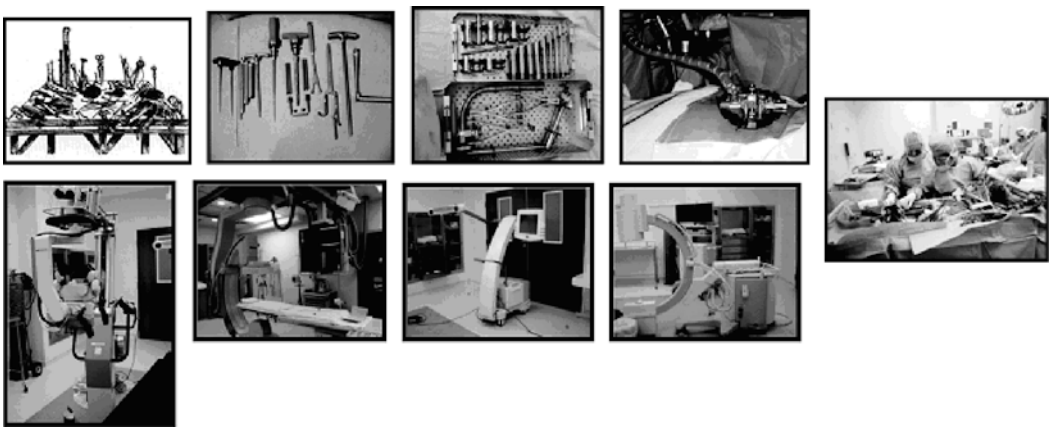

Fig. 4 The development of technology aimed at surgery practice

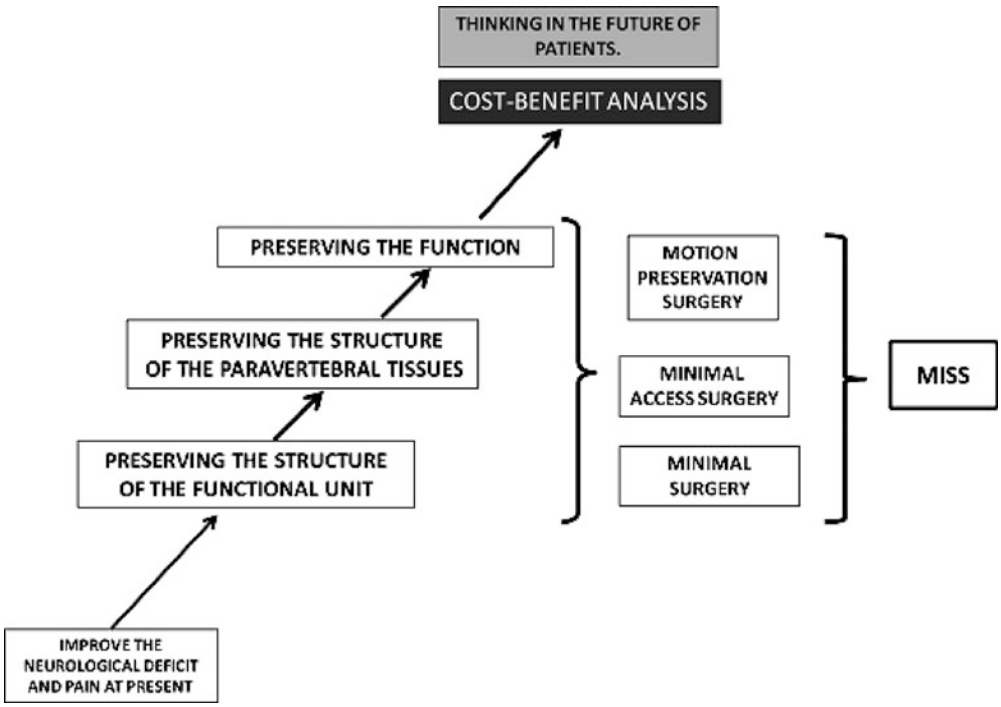

Fig. 5 Evolution of spine surgery goals and specific actions to achieve them. The concept of minimally invasive spine surgery

reached [11]. If it is as small as possible it can be considered minimal, but especially if existing inter- or trans-muscular anatomical pathways are used, and if insertions and muscle vascularity as well as ligaments and joint capsules are respected [11]. The fulfillment of all the goals of surgery must be guaranteed, including mini-open and microscopic, endoscopic, percutaneous accesses. Regarding the surgical procedure it is considered minimal if causing minimal consequences on the functional unit of the spine, the opposite case is considered maximal, as in the case of fusion (Fig. 6). One of the important aspects of minimally invasive procedures in the spine is that many of those are image guided and include automated steps, which favor reproducibility. Therefore, they may be less operator dependent, which in the future may result in more consistent and comparable results among surgeons or between institutions.

The MISS is not destined to interchange a major procedure by a smaller one; that would be a shortsighted view of its scope. Really it means – on the basis of reduced risk- a sooner intervention in the natural history of a particular ailment and always with the ideal of preserving the functional unit, reducing risks and improving the quality of life and the future of the patients (Fig. 7). The term "MISS" is not about one or several particular surgical techniques, but a new way of thinking, a new philosophy. Although the development of minimally invasive spine surgery is recent, its application includes all

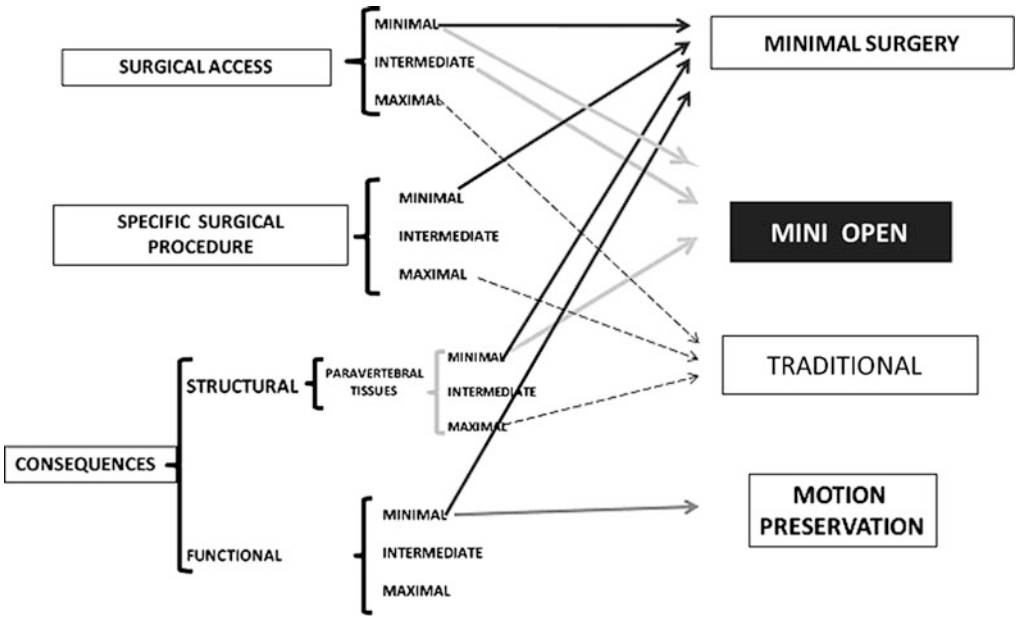

Fig. 6 Simple classification of spine surgery based on surgical access and specific procedure

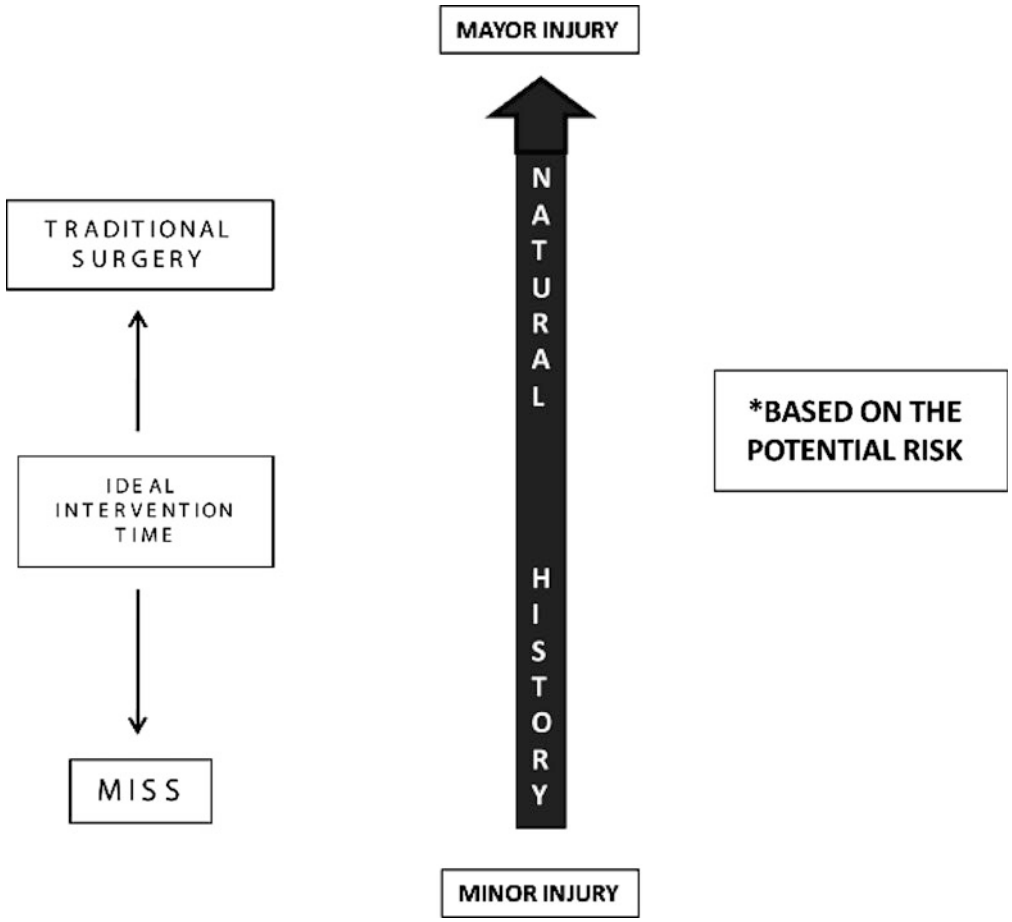

Fig. 7 Preserving as far as possible the structure and function, and intervening at a most opportune time of the natural history are the most important concepts of MISS

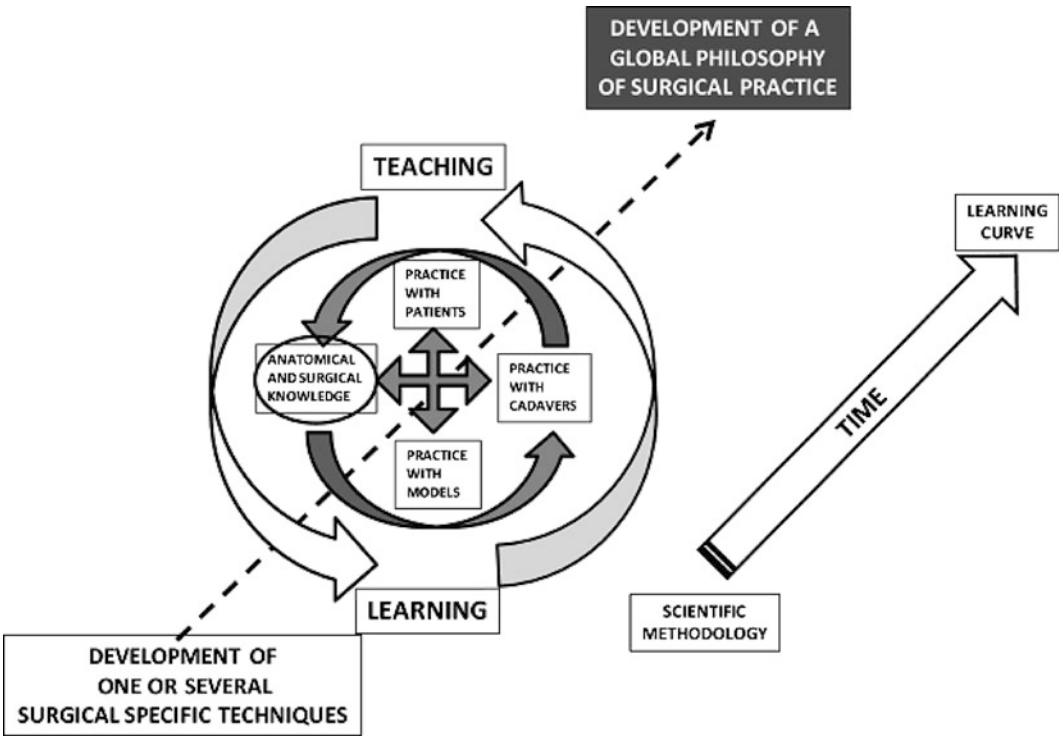

Fig. 8 The use of a teaching model and the adoption of a learning curve in spine surgery as strategies to achieve the development of a new philosophy

spine segments and almost all the existing conditions, including deformities.

The traditional teaching/learning model of spine surgery has also undergone changes, especially because today information access is easy, which has favored the possibility of theoretic self-education. But in practice, it is necessary to assume that the trials in models and laboratory specimens are indispensable [5, 8] and the necessary acquisition of a learning curve, which is proportional to the experience and skill of the surgeon and the complexity of each procedure, but above all the time (Fig. 8).

In the complex setting of spine surgery, its different elements have undergone substantial changes. The main actors are still patients and spine surgeons. The patients, beyond the demographic and epidemiological changes, now have free access to all the scientific and unscientific information appearing in abundance in the media and generally have a basic knowledge that allows them to question the diagnosis and treatments and be more applicants regarding the search for better expectations and the best cost. Surgeons must choose between the massive amount of information and the large number of available techniques, all you need is to integrate the diagnostic and therapeutic criterion favoring better the prognosis of patients. To this end, it is necessary assuming the commitment *sine qua non* of the constant medical update and the professional practice under a transparent ethics based on the science for implementation of the technology. Here, it should be noted that the need of further facilitating the practice of spine surgery and improving the results has led to the development of other key stakeholders, the industry, that has had a logarithmic growth from Harrington's bars, Luque's frames, Fërmstron intervertebral disc prosthesis and the Knowles first intervertebral spacer of the decades of 1950s–1960s to overwhelming cascade of currently available devices on the market and beyond that can improve or not forecasting of procedures, has increased the costs of patient´s care [14]. The reality today is that we still have not learned and understood a generation of devices when the next generations are already arriving. This is driven by the assumption and undeniable pretext of research for the benefit of patients, but also the apparent company purpose of increasing sales and thus profits. These increased costs in spine surgery practice [14] are a serious concern to two other actors on stage (1) insurance companies that are obviously always pointing towards the containment of costs, sometimes even irrespective of the benefit magnitude; and (2) governments for whom the economic burden is becoming unbearable and who are now competing for a radical change in the fundamental concept in the practice of traditional medicine into a scientific, rational, that is evidence-based medicine [14, 15] (Fig. 9).

It is clear that in a framework where personal interests, fashion, financial interests, etc., the scientific interest must prevail for solving problems (Fig. 10). In the traditional practice of medicine, often the solution of problems is

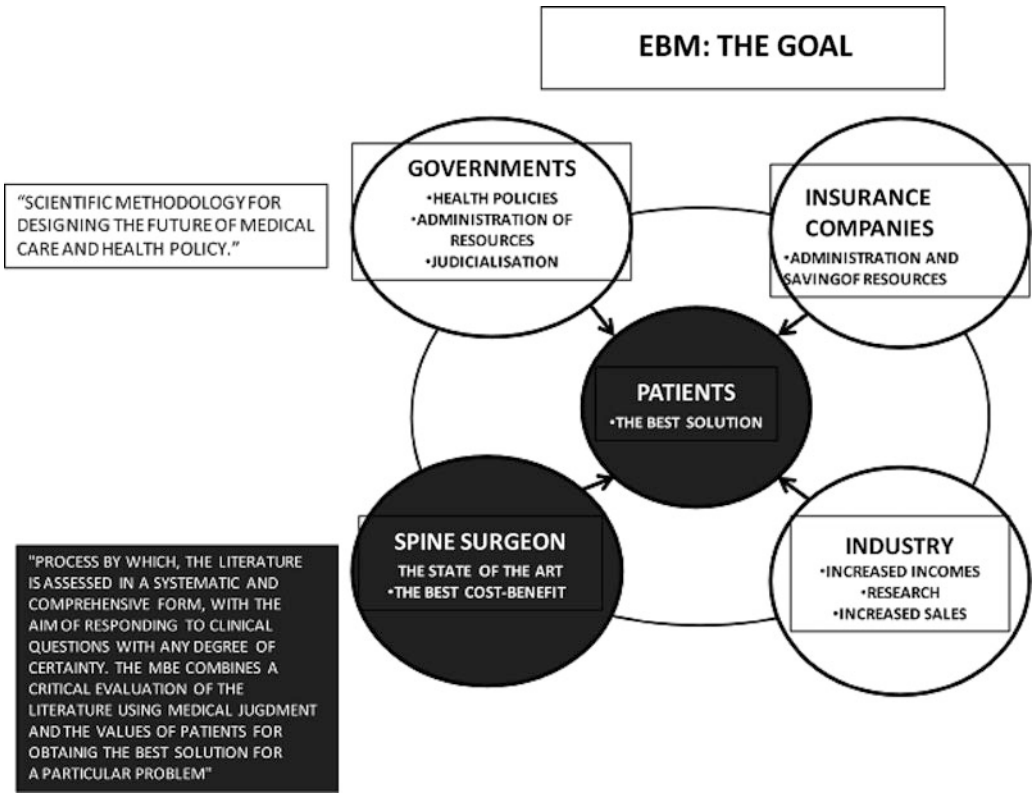

Fig. 9 Usefulness of evidence-based medicine for different players in the setting of spine surgery

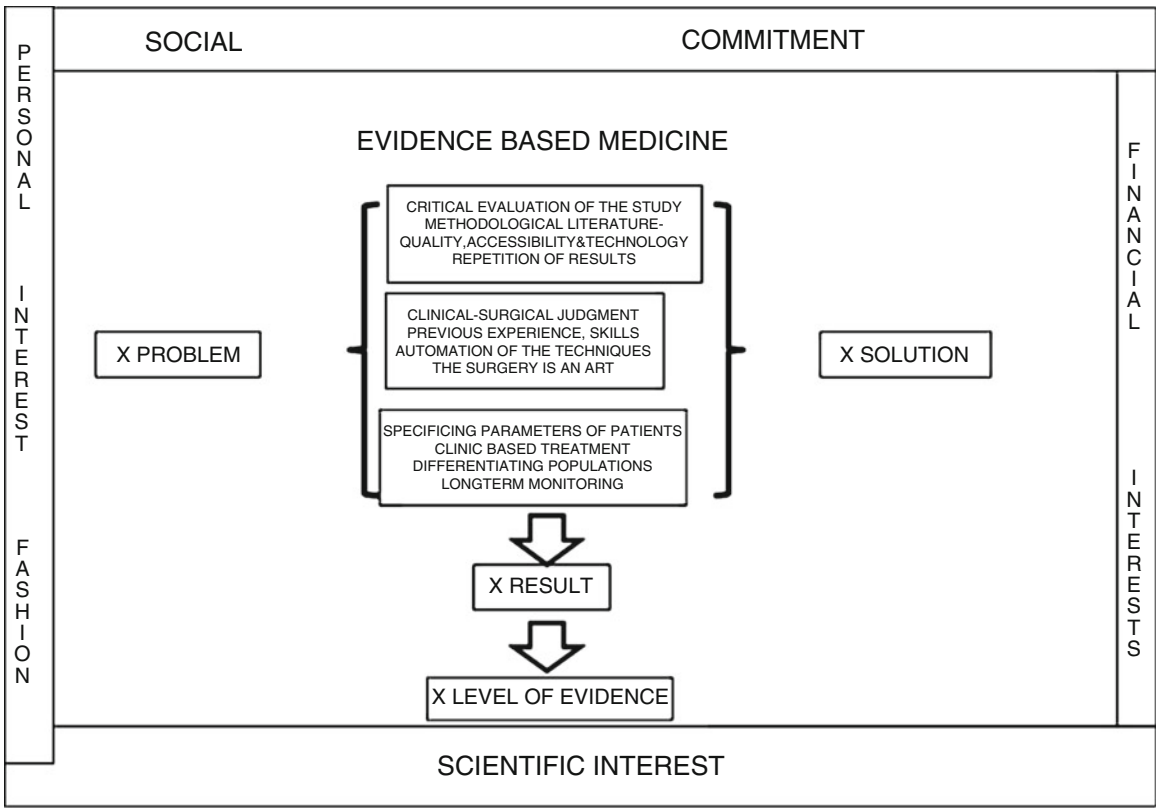

Fig. 10 Scientific interest as the main argument for the development of evidence-based medicine

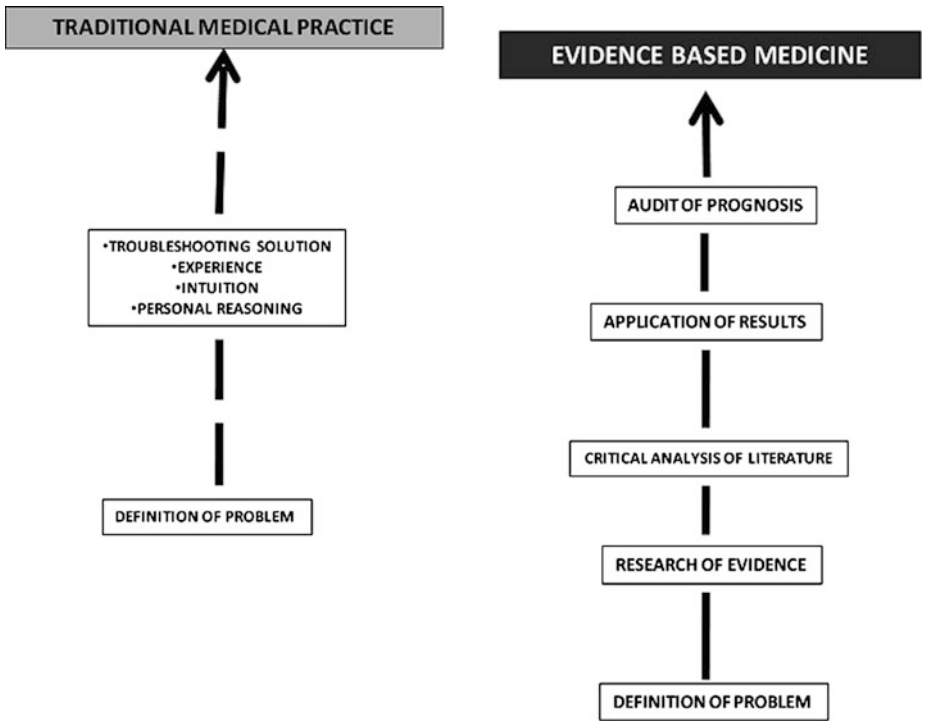

Fig. 11 Methodology is the main difference between the traditional medical practice and evidence-based practice

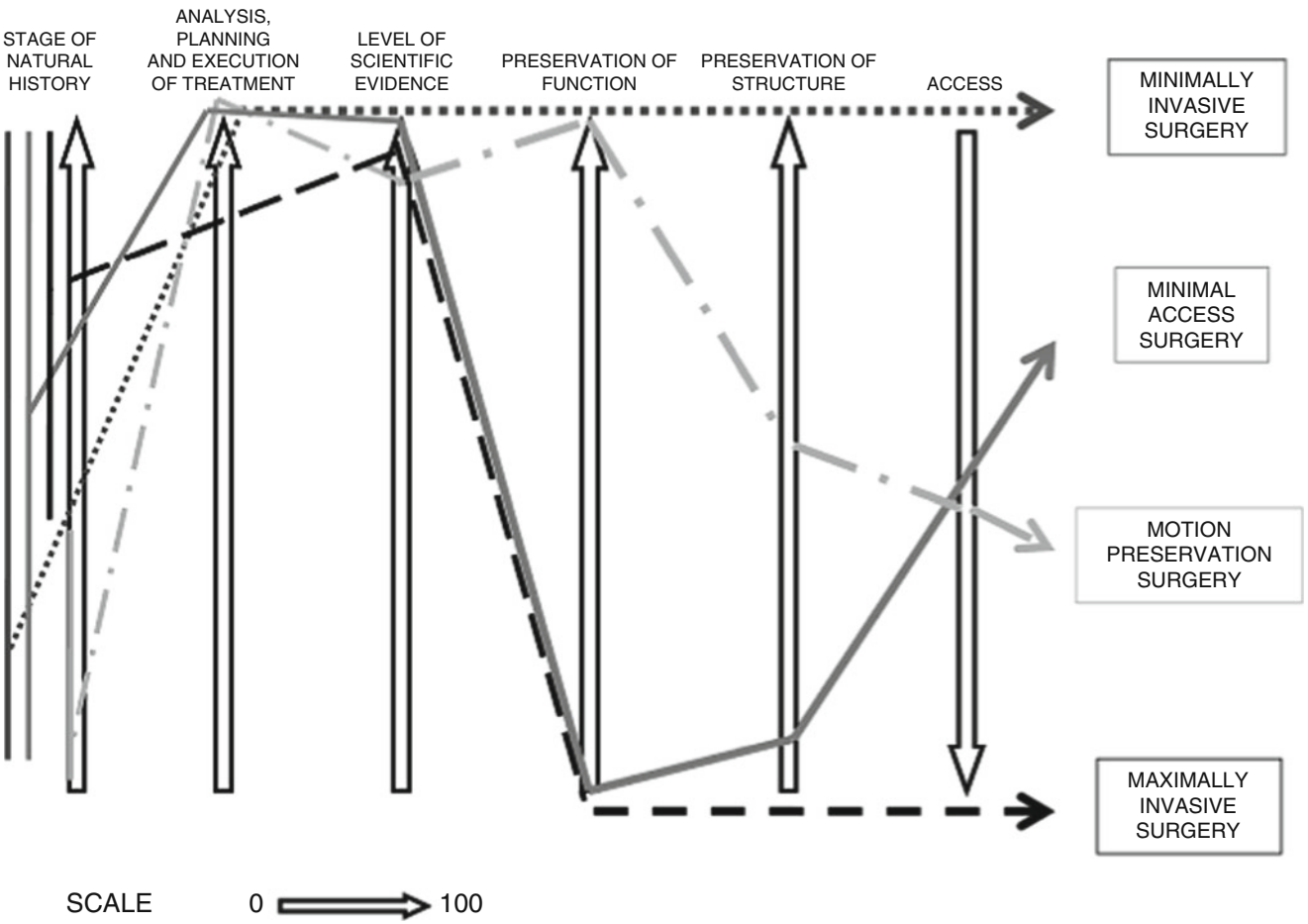

Fig. 12 Scale guide suggested to recognize and define our performance as spine surgeons and evolve for developing a better surgical practice

based on personal experience and intuition [14]. Evidence-based medicine (EBM), a term coined by Alvan Feinstein in the 1960s [5–8], emphasizes the possibility of combining art and science following the strict application of scientific method in the treatment of patients [7, 8], which may represent the advantages of objectivity and rationality in the use of different treatments (Fig. 11). However, EBM has many obvious defects, especially in spine surgery it is almost impossible to develop double-blind protocols [2]; also incongruous is the industry-open participation in order to prove the usefulness of their products in many of these studies [10]. Not to mention the low number of studies meeting appropriate methodological quality, so many of the current management guidelines are based on a small and insufficient number of cases [3, 14], compared with the whole quantity of all surgeries in the world. In most cases, the only evidence that one can find in the literature is the lack of evidence [12], however the lack of evidence does not mean its absence. The cold analysis of the statistics too can lead to a dehumanized approach of medicine.

It would be ideal to graph scales for each patient forcing us to monitor continuously [2, 12] during our professional practice as spine surgeons, our own actions directed to provide "the best" to the patient [9], including the stage of the disease, the natural history in which we intervene, the tools used to complete a diagnosis, scientific analysis of the literature in which we argue our treatment plan [2], the size and route of surgical access and consequences of specific procedure on the functional unit. Only then, with rigorous self-analysis, we may take a clear path towards a new philosophy in spine surgery. Of course, feedback from patients through satisfaction and clinical scales can guide our direction and provide the energy needed to maintain enthousiasm (Fig. 12).

Conclusion

There are many changes in the field of the modern spine surgery, which includes concepts such as evidence based medicine applications, identification of the pain generator, minimally invasive surgery, as well as the great advances in basics sciences specially genetics and biomechanics. Obviously all of them supported by new technologies for diagnosis and treatment. All this linked concepts are the basis of the new philosophy of the modern era of spine surgery.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Minimally Invasive Treatment for Refractory Low Back Pain, Targeted by Epidural Endoscopy with O_2/O_3 and Steroid Therapy

Marcos Masini and Aldo Calaça

Abstract *Purpose:* Epidural endoscopy is an efficient option among conservative modalities in the management of refractory low back pain. The purpose of this paper is to evaluate retrospectively the effectiveness of the treatment of this condition with targeted O_2/O_3 and steroid therapy.

Material and Methods: The procedures were performed in 32 consecutive patients who failed to show significant response of at least 6 weeks or longer to treatments that included anti-inflammatory and analgesic drugs, physiotherapy and posterior epidural steroids and/or facet joint injections. These procedures were performed during the year 2006 and all the patients have been followed up for at least 2 years.

Results: Patients evaluated by Visual Analogue Scale (VAS) pre and immediately post procedure advised an improvement of mean 80% of their previous pain status. Follow-up revisions with 1, 3, 6, 12 and 24 months showed persistent improvement percentage at mean 60%. The Oswestry Disability Index showed significant changing in status pre and post procedure related to the pain control condition. No serious complications were related to the procedure.

Conclusions: Targeted Epidural endoscopy associated with injection of O_2/O_3 and steroids is a safe and efficient minimally invasive procedure to be used in patients with refractory low back pain. The association with ozone (O_2/O_3) and steroids seems to result in a long lasting pain relief, giving to the physician and to the patient a wider window to work on the treatment of other frequently associated causes (emotional, socio-economic and environmental) of refractory back pain.

M. Masini (✉)
School of Medicine University of Planalto Central and South Lake Hospital, Brasilia, Distrito Federal, Brazil
e-mail: marcos.masini@uol.com.br

A. Calaça
Department of Neurosurgery, Santa Casa Hospital, Maceio, Alagoas, Brazil

Keywords Epidural Endoscopy · Low back pain · Ozone–Oxygen therapy · Steroid therapy

Introduction

Ten percent of the patients suffering from low back pain have no improvement after 6–8 weeks of conservative treatment [23]. Also the clinical picture, image diagnoses, patient decision and the treating physician's experience will define the next treatment choice. It is not an easy decision. Clinical signs and image can be challenging. Sometimes there is no explanation for patient's symptoms or they are contradictory, mainly in patients already submitted to surgical procedures of the spine [3, 15, 22].

Epidural endoscopy is an option among conservative modalities in the management of refractory low back pain. It can be used for its diagnosis and treatment, and was included in the armamentarium in 1966 by Saberski and Kitahama [20]. The technique permits to navigate, diagnose and treat the exact place of conflict without additional (other tissues) lesions.

The physician has to understand the importance of the inflammatory mediators in the genesis of the low back and radicular pain [17, 18] and know about the many modulators used in the treatment considering anesthetics, steroids, clonidine, and O_2/O_3 mixture application directly in the place of pain origin. The purpose of this paper is to evaluate retrospectively the effectiveness of the treatment of this condition with targeted epidural endoscopy injection of O_2/O_3 and steroid therapy.

Material and Methods

This retrospective study evaluated the results of procedures performed in 32 consecutive patients who failed to show significant response to at least 6 weeks or longer of

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treatments that included anti inflammatory and analgesic drugs, physiotherapy and posterior epidural steroids and/or facet joint injections. These procedures were performed during the year 2006. Patients with facet joint pain or sacroiliac joint pain as major causative factors of disability were excluded. Age, gender, time of onset, cause, duration of pain, history of previous surgical interventions was collected. All patients had image study analysis with plain x rays in anterior posterior and lateral/oblique positions, magnetic resonance and/or computerized tomography (or both) of lumbar spine. Patients with associated irradiating pain had electromyography of the lower extremities. Pain in pre and post procedure evaluation was made using visual analogue scale (VAS), immediately grading the improvement in percentage at 1, 3, 6, 12 and 24 months post procedure so that all the patients had a follow-up of minimum 2 years. The Oswestry Disability Scale was applied before and after 3 months of the procedure. The Microsoft Excel Statistical Pack was used to analyze the data. The charts of all patients were reviewed by a third person who was not involved in their treatment and contacted them for re-evaluation purposes.

All procedures were performed under light sedation by an anesthesiologist and in a conventional surgical theatre and sterile operating room with monitoring systems. The patients were positioned in prone and the lumbosacral area prepared and draped as a sterile field. The epidural space was entered through the sacral hiatus with a Touhy18-gauge-90-mm needle after local anesthesia with 5 cc of lidocaine 0.5% without vasoconstrictors. A 0.9 mm wire was inserted through the needle and advanced with fluoroscope to L5/S1 level. The needle was taken out and followed by a 3-mm incision around the wire with the advancement of a 3.8-mm × 17.8-cm dilator over the guide wire. The internal part of the dilator was then taken out, and the video guided catheter with two working channels with 3.0-mm × 30-cm (Myelotec) was introduced with video endoscopic (0.8-mm fiberoptic spinal endoscopy) and fluoroscopic guidance to the level of the suspected pathology. The catheter and fiberoptic "Myeloscope" were manipulated and rotated in multiple directions with visualization of the nerve roots at various levels. The widening of the epidural space was carried out by slowly injecting normal saline (maximum of 120 ml) and manipulation of the catheter under the endoscope and fluoroscopic visualization. It was not necessary to inject contrast medium for correct positioning of the catheter. Upon confirmation, the procedure was accomplished with the injection of Clonidine (0.5 µg/kg); Marcaine 0.5% 4 ml; Depomedrol (steroid) 2 ml (80 mg); Fentanila 0.5 ml(25 µg/ml). Ozone (O_2/O_3 mixture) 20 ml with a concentration of 20 µg/ml is injected at the end. The catheter was taken out and an absorbable suture applied to the wound. The patient was evaluated and oriented to back school by the physiotherapist and discharged on the same day. The patient was maintained under anti-inflammatory/analgesics for 10 days, antidepressant drugs for 2 months or as long as necessary and submitted to hydrotherapy of 10–20 sections.

Results

The 32 patients included 18 females and 16 males with the majority of patients being in the third, fourth and fifth decades of life (Fig. 1). All these patients failed to show any significant response to at least 6 weeks or longer of treatments that included anti-inflammatory and analgesic drugs, physiotherapy and posterior epidural steroids and/or facet joint injections. Clinically the patients had untreatable low

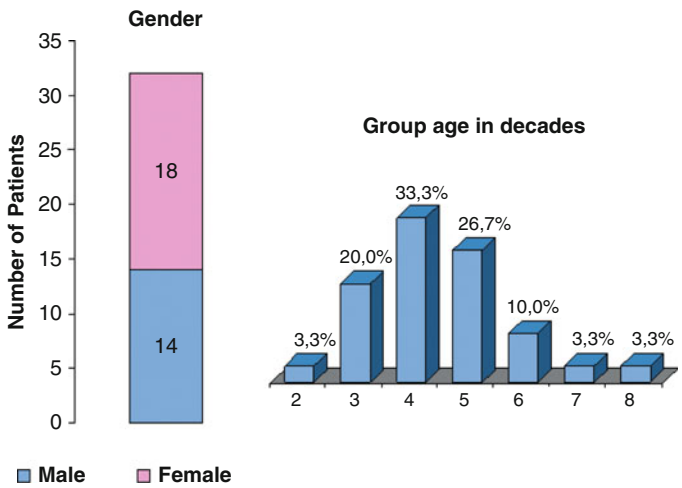

Fig. 1 *Gender and Age data.* The *left bar* shows the total number of patients (n = 32) included in the research, separated by gender. The *upper part* represents 18 females and the lower one 14 males. The *graph on the right side* shows that a bigger portion of the patients was between 41 to 59 years old

back pain without progressive neurology and no indication to open surgical procedure. Plain X rays, magnetic resonance and computerized tomography of the spine did not show any pathology with surgical procedure indication and demonstrated that 19 (61%) patients had previous surgical procedure with instrumentation of the spine. In these cases, the posterior approach to the epidural space was practically impossible due to scarring and instrumentation.

Patients evaluated by VAS scale pre and immediately post procedure advised a mean improvement of 80% of their previous pain status. Follow-up revisions with 1, 3, 6, 12 and 24 months showed persistent improvement with a mean of 60%. There is a decline of 15% between the moment of the procedure and 1-month-evaluation, which was maintained during the following 3 and 6 months. There is a tendency to keep the good result in these patients. It may be concluded from this that patients with improvements realised in the first month will not lose it during the next month, allowing a wide window to complete the treatment utilizing other modality options. Data also suggest a better improvement in females than in males, probably related to the way they assume the completion of the treatment and to the life style of each group (Fig. 1).

The Oswestry Disability Index applied after 3 months showed improvement of status pre and post procedure with 22 (70%) of the patients having better work capacity. This index follows the pain reduction analysis. All patients were classified as group 5 initially due to the excruciating pain, meaning that they were unable to work or assume activities. After 3-month analysis, 70% were classified as group 1 showing normal capacity for activities. The lower index was 3, which means that they were still in rehabilitation programs with improvement to be expected. In other treatment modalities the time between the procedure and recovery takes longer than 3 months, and usually the patients keep some degree of inability after the treatment, never reaching group 1 index (Fig. 2).

No serious complications were related to the procedure. No adverse effect of the drugs used in injection. No infections. No motor deficit or sphincter disturbance. In one patient it was decided to proceed with an open surgical procedure, the other 31 patients were kept in clinical treatment as described previously (Fig. 3).

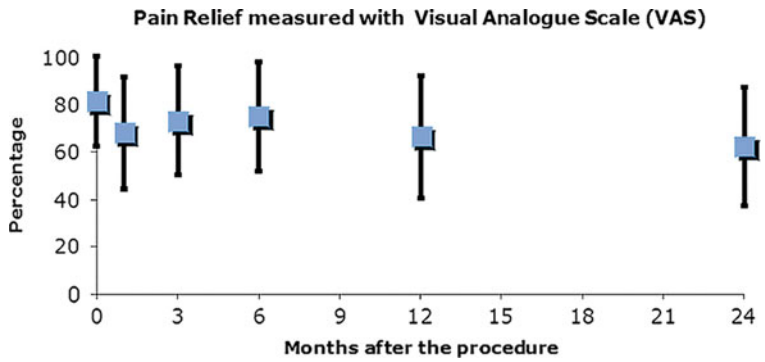

Fig. 2 *Improvement VAS*. Each *square* shows the mean percentage of pain improvement after the procedure in VAS and the deviation in group and *bars* – for the time frame analysed. Therefore, just after the procedure (zero time), the patients showed a pain relief of 80% mean. The data also suggests a better improvement in females than in males, probably related to the way they assume the completion of the treatment and to the life style of each group

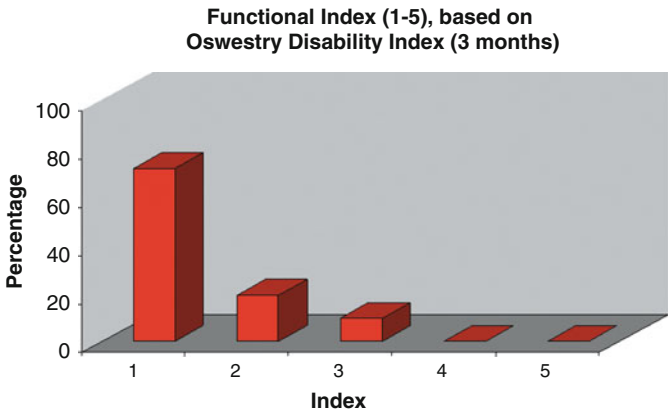

Fig. 3 *Functional/ODI*. The graphic shows the improvement in Oswestry Disability Index after 3 months of treatment. All patients were classified as group 5 initially due to the pain, meaning that they were unable to work or assume activities. After 3-month analysis, 70% were classified as group 1 representing total capacity for activities. The *index line in 3* means patients that were still in the rehabilitation program

Discussion

Saberski et al. [19] in 1995 mentioned that epidural endoscopy is not limited to injections but can also be used as an instrument for diagnosis in many situations such as hematomas, abscess, tumors, inflammations and adhesions. It can be used to drain cists, to make biopsies and remove scars. It is known that adhesions develop after nucleus pulposus extrusions causing chronic chemical radiculites [8, 16]. The mechanical movements of the disc associated to a fissure of the annulus releases proteoglycans, which causes an autoimmune reaction next to the root maintaining the inflammatory process. The inflammatory reaction is evoked consecutively through histamine, bradykinins or prostaglandins which sensitize the nerve root and the ganglion keeping the chemical pain [10, 11]. Distortions caused by the disc fragment or the scar process do not allow adequate blood supply to the region. Drugs will not arrive to stop or reverse the inflammation. Catabolites will not easily leave the region due to bad vascular drainage. Kayama et al. [8] suggested that the intra neural vascular compromise is probably the cause of nerve conduction distortion and pain generation which can be alleviated by reducing radicular edema and the local inflammatory processes.

Sakai et al. [21] reported that after contrast injection in the epidural space in patients with previous surgical procedure all of them presented some kind of block in the diffusion around the roots which did not happen in places not submitted to procedure. They also confirmed that patients underwent epidural endoscopy and injection of steroids and anesthetics had a reduction in their pain and dysfunction of fibers A? and A? associated with chronic sciatica.

Geurts et al. [4] described their experience using clonidine with analgesic and antineurophatic properties at the dorsal ganglion and antinociceptive property at the posterior horn of the spinal cord. They describe a good clinical response with clonidine associated with hialuronidase in epidural endoscopy for incapacitating low back pain. They confirmed that among 20 patients with normal magnetic resonance, 8 patients had some epidural scars and adhesions.

The intra-discal effect of ozone is based on its direct effect on proteoglycans under the release of water molecules, which is followed by cell degeneration and shrinkage of tissue. The activation of fibroblasts causes additional scarring and a subsequent reduction in the herniated disc tissue under strain. Around the root ganglion space, ozone improves the tissue oxygenation and through the immune modulating effect, reduces the release and activation of cytokines, bradykines and prostaglandins and other pain stimulators [1, 2, 13].

Manchikanti et al. [9] used steroids and anesthetics through epidural endoscopy with 50% of initial pain reduction but no significant residual result after 6 months. The association with ozone injection is probably the explanation for our long lasting results after 2 years of follow-up.

Oder et al. [14] studied the nucleolysis with ozone combination with steroids and analgesics in 620 patients with lumbar pain. They also confirm the sustainable results with significant pain relief mainly in patients with bulging discs. Muto et al. [12] in 2008 reported their experience with 2,900 cases of patients treated by discolysis with O_2/O_3 intradiscal, periganglionic and periradicular injection. They describe an initial success of 80% of substantial pain relief in disc protrusions and no major complications related to this method. This is the conclusion we have sustained from this work.

Igarashi et al. [7] reports the effect of epidural endoscopy and injection in the treatment of 58 patients with lumbar stenosis relating the improvement of the patients to sympathetic block and better blood supply in the compressed roots.

Heavner et al. [6] describes two cases of intravenous injections of contrast medium during epidural endoscopic procedures and relates to vein lesions and absence of wall collapse associated to fibrotic adhesions. Gill et al. [5], in 2005, reviewed 12 cases of retinal venous hemorrhagic complication associated to epidural endoscopic injection and concluded the it could be associated to the speed of volume injection. Their conclusion is that the injection should not exceed 1 ml/s. Even with no complication in our patient group, this is very interesting knowledge to follow during the procedures.

Conclusions

Targeted epidural endoscopy associated with injection of O_2/O_3 and steroids is a safe and efficient minimally invasive procedure to be used in patients with refractory low back pain. The association with ozone (O_2/O_3) and steroids seems to result in long lasting pain relief giving to the physician and to the patient a wider window to work on other frequently associated causes (emotional, socio-economic and environmental) of refractory back pain.

Conflict of interest statement We declare that we have no conflict of interest.

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Epidural Injections: Past, Present and Future

Marcos Masini

Abstract In the past, if someone had pain and a "defect" was noted on the myelogram or CT, surgery was immediately warranted. During this era, neural compression was considered to be the sole reason for all spinal pain. The surgical community firmly believed in the presence of a concrete-structural alteration to explain the pain and spinal arthrodesis was introduced. Over time, it became obvious that many patients did not improve after surgical interventions. Epidural injections were performed, formerly without fluoroscopic localization, and then with precise targeting.

The spine care clinicians incorporated mediation of inflammation and neuromodulation as pathways to achieve pain control in order to pave the way for functional restoration. Epiduroscopy is presented as the most recent , complete and effective means for treating persistent low-back pain.

Keywords Epidural injections · Epiduroscopy · Neuromodulation · Pain treatment

Introduction/History

Early on, spine care was solely dictated by the concrete-structural/psyche paradigm. This has been replaced by a paradigm shift that emphasized functional optimization over structural alteration. Before 1980 spine care was dominated by the concrete-structural findings. Non operative option available to patients was to confine the patient to strict bed rest while attached to traction. Mobilizing was thought to be deleterious.

The premise was very simple. If someone had pain and a "defect" was noted on the myelogram or CT, a surgery was immediately warranted. Over time, it became obvious that many patients did not improve after surgical interventions. This was related to psychological imbalance [4]. In a limited fashion, epidural steroids injections were introduced to reduce residual or persistent pain. During this era, neural compression was considered to be the sole reason for all spinal pain. The surgical community firmly believed in the presence of a concrete-structural alteration to explain the pain, and spinal arthrodesis was introduced into the surgical care of the spine. Salvage fusions were developed to deal with the iatrogenic persistent pain pictures. As I usually say: "if you do not know how to repair the locker, you should nail and close the door."

The next era started with pain programs to deal with the chronic pain patients created by multiple failed surgeries. Epidural injections were performed without fluoroscopic localization. Some centers started using injections on pre-operative patients. Injections were done in the facets (zygapophyseal) joints and sacroiliac joints. The introduction of advanced imaging techniques as computed tomography allowed an accurate assessment of the lateral recess, facet joints, joint cysts, and a better knowledge about the many forms of disc pathology. Injection techniques became more precise.

Anatomic work defined the enervation of the facet joint and opened the pathways to considering spinal pain along neurophysiologic lines. On the basis of the imaging advances, the neuroanatomic findings and the chemical mediator discoveries and the reported non operative treatment successes, a new spine care paradigm began to evolve.

The spine care clinicians incorporated mediation of inflammation and neuromodulation as pathways to achieve pain control in order to pave the way for functional restoration. The new paradigm did not "de facto" require the surgical alteration of spinal structure be present or be repaired to reach its purpose [5]. The lack of randomized trials to support injection therapy or injection pain localization has repeatedly been pointed out.

M. Masini (✉)
School of Medicine, University of Planalto Central and South Lake Hospital, Brasilia, DF, Brazil
e-mail: marcos.masini@uol.com.br

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At the present time the treatment algorithm incorporates the injection procedures to facilitate functional improvement and the beginning of the rehabilitation program. Now we have new drugs, including ozone in the front treatment. With associated epiduroscopy we can *really* see the lesions and place the drug exactly in the anterior epidural space where the conflict exists [1–3, 6, 7]. We can confirm or make visual diagnosis, we can mechanically treat the conflict, we can wash out the chemical substances that are promoting the pain symptom and place the drugs exactly where the inflammation is.

We can act immediately, thus avoiding the chronic sensitization of central and peripheral nervous system pain pathways with a minimally invasive technique.

Conclusion

I believe that the horizon is currently much brighter for those with chronic back pain.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Long Term Intrathecal Infusion of Opiates for Treatment of Failed Back Surgery Syndrome

Nilton Alves Lara Jr., Manoel J. Teixeira, and Erich T. Fonoff

Abstract Failed Back Surgery Syndrome (FBSS) is a multidimensional painful condition and its treatment remains a challenge for the surgeons. Prolonged intrathecal infusion of opiates for treatment of noncancer pain also remains a controversial issue. The authors present a prospective study about the long-term treatment of 30 patients with nonmalignant pain treated with intrathecal infusion of morphine from February, 1996 to May, 2004. Self-administration pumps were implanted in 18 patients and constant-flow pumps in 12. The mean intensity of pain reduced from 9.5 to 4.6 according to the visual analogue scale ($p<0.001$); the mean daily dose of morphine necessary for pain control became constant after the sixth month of treatment. No difference was observed in the results between patients treated with bolus or constant infusion. Side effects were more frequent at the beginning and became tolerable after the first month of treatment. There was improvement of the quality of life measured by SF-36 (30.8–49.6) and in all dimensions of the Treatment of Pain Survey, except for working capacity. The follow-up period ranged from 18 to 98 months (mean = 46.7 months). It was concluded that intrathecal infusion of morphine is a useful and safe tool for long-term treatment of chronic nonmalignant pain.

Keywords Failed back surgery pain · Implantable pumps · Intractable pain · Opiates · Treatment of pain

Introduction

The evolved definition of failed back surgery syndrome (FBSS, also known as post-laminectomy syndrome) is persistent or recurring low back pain, with or without sciatica following one or more lumbar operations [1]. It is a multidimensional condition; a spectrum of organic disease processes complicated by secondary financial gain and learned chronic behavior. The medical, social, legal and economic implications are enormous [2].The causes of back pain are largely unknown. Correlations with diagnostic studies are uncertain. The lack of precise diagnoses is reflected in a multiplicity of nonspecific treatments, mostly of unproven value. Management of FBSS is thus to an extent empirical and commonly involves a stepwise progression from the lowest risk treatments [3]. As a result, patients who have failed to find relief may eventually come to be treated on a trial basis with oral opiates; however, a study of long term oral opioids for low back [40] and neuropathic pain found good results in only 16.7% of cases [4].

In 1979, Wang et al. [5] injected opiates in the spinal intrathecal space of humans for treatment of pain for the first time. Uncomfortable frequent punctures and the high risk of infection encouraged the development of safer and simple methods for drug delivery into the spinal canal such as the implant of catheters connected to subcutaneous reservoirs to allow applications without spinal punctures [6–12]. Among other advantages, intrathecal infusion of drugs allows delivery of analgesics or adjuvant analgesic medication close to the site of action, resulting in increased effectiveness, longer duration of action and reduced doses as well as side effects [13, 14]. Prolonged spinal infusion of drugs has become widespread in the treatment of patients with oncologic pain [8, 11, 15–19, 39]. The good results observed in cancer pain patients have encouraged its application in non-oncologic pain patients [16, 18, 20]. However, its effectiveness in the treatment of these patients have been questioned by some of authors [16, 18, 19, 21]. To date, the majority of these studies have been retrospective, involving a relatively small number of cases and short follow-up periods [8, 13, 21–23]. Additional investigations are necessary to prospectively evaluate the long term effectiveness of the method in patients with non-cancer pain as FBSS.

N.A. Lara (✉), M.J. Teixeira, and E.T. Fonoff
Division of Neurosurgery, University Of São Paulo, São Paulo, Brazil
e-mail: niltonlara@uol.com.br

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Patients and Methods

From within the Pain Center of the Department of Neurology of the Faculty of Medicine of São Paulo University, 78 patients with defined etiology, with severe and incapacitating painful FBS not improved with systemic use of common analgesics, non-steroidal anti-inflammatory analgesic drugs (NSAIDs), tricyclic antidepressants (amitriptyline or nortriptyline), anticonvulsants and opiates (codeine, tramadol, oxycodone) were selected for implantation of pumps for long term intrathecal infusion of drugs between February, 1996 and May, 2004. All patients signed the informed consent form, approved by the Ethics Committee of the Hospital. Patients with previous or present history of alcohol or drug addiction or with acute or chronic infections that could hinder device implantation were excluded. All 78 patients were treated for 2 weeks with home self-administration of 3 mg of morphine Hcl diluted in 3 ml of 2% lidocaine b.d. through an epidural D6 catheter.

The pumps were implanted in patients who had more than 50% of the original pain relieved without side effects during the test period.

We randomly implant according to availability in our institution self-administration pumps, Cecor [Cordis-USA] and Algomed [Medtronic-Minneapolis-USA] models, constant flow pump Arrow M-3000® (Arrow-Massachusetts-USA) and electronic Synchromed® pump (Medtronic-Minneapolis-USA).

The visual analogue scale (VAS) and the McGill Pain Questionnaire [24] (MPQ) were used to evaluate pain preoperatively, throughout and at the end of the follow-up period, which lasted 18–98 months (mean = 46.7 months, sd = 21.4, median = 38, $p < 0.001$). The quality of life prior to the procedure and at the end of the follow-up was evaluated with the "Treatment Outcomes in Pain Survey" (TOPS) [25] and with "The Medical Outcomes Study 36 Short-Form Health Survey" [26].

Systemic drugs used prior to the implantation of the pumps and at the end of the follow-up, dosages of morphine and satisfaction of the patients were also evaluated.

The occurrence of side effects was evaluated along the follow-up period.

Results

Fifty-eight percent of the 30 patients selected for implantation were male. Their ages ranged from 21 to 85 years (mean = 48.4; sd = 13.80; median = 45.0) and pain complaints had persisted for 12–204 months (mean = 53; sd = 37.5; median = 36.0).

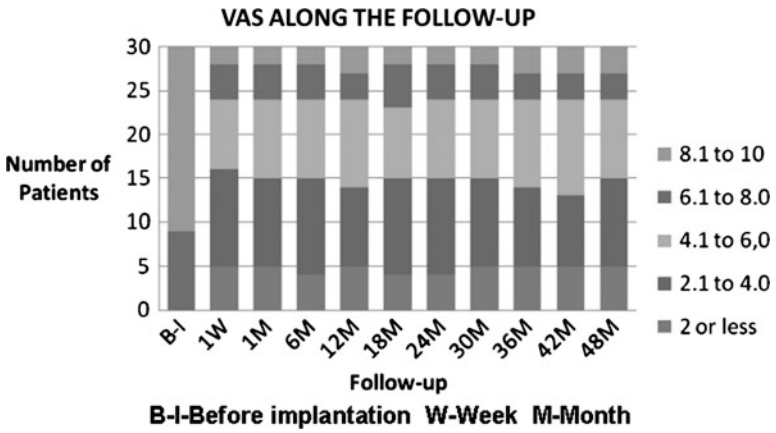
Sixty five (81.3%) patients were treated with self-administration pumps, that is 24 (30%) with Cecor® [Cordis-USA] and 41 (51.3%) with Algomed® [Medtronic-Minneapolis-USA] model, and 6 (7.5%) with the constant flow pump Arrow M-3000® (Arrow-Massachusetts-USA) and 13 (16.3%), with the electronic Synchromed® pump (Medtronic-Minneapolis-USA). The infusion was continuous in 19 (23.3%) patients and in bolus in 61 (76.3%).

There was sustained pain VAS intensity improvement as shown in Graph 1.

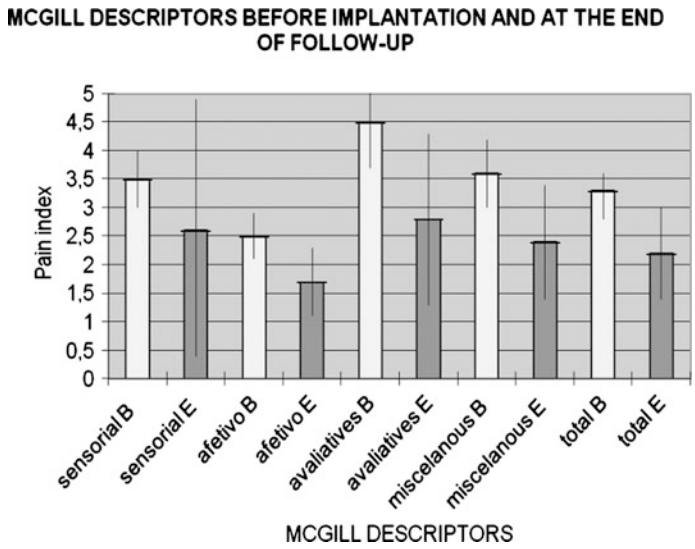
The improvement of pain was the same in patients treated with continuous or bolus infusion ($p = 0.597$).

At the end of the follow-up there was a significant reduction of the mean number of the sensorial, affective, evaluative and miscellaneous descriptors of the MPQ of patients, even when they were divided into groups according to their pain conditions (Graph 2).

There was also improvement in all domains of the SF-36 Questionnaire from 30.8 (sd = 10.1; median = 29.3; minimum = 10.7; maximum = 54.0) to 49.4 (sd = 18.6; medium = 50.6; minimum = 10.7; maximum = 87.9) ($p < 0.001$) and in all domains of the TOPS ($p < 0.001$), except for Objective Work Disability ($p = 0.392$) (Table 1).



Graph 1 Distribution of the number of patients according to VAS during the follow-up



Graph 2 McGill descriptors before implantation and at the end of follow-up

Table 1 TOPS domains before implantation and at the end of follow-up

Domains	Initial		Final		*P*
	Media	sd	Media	sd	
Pain symptom	22.74	1.9	13.74	7.35	<0.001
Functional limitations	5.47	0.96	3.16	2.12	<0.001
Perceived family disabillty	18.26	5.96	14.63	6.32	<0.001
Objective family disability	16.95	2.66	14.79	2.65	<0.001
Objective work disabillty	7.74	3.46	7.16	3.69	0.392
Total pain experience	14.63	7.09	50.2	17.6	<0.001
Life control	11.47	5.4	17.37	5.18	<0.001
Passive coping	13.95	4.09	11.42	3.22	<0.001
Solicitous responses	14.68	5.56	13.21	5.58	<0.001
Upper body limitations	9.84	2.95	10.84	2.36	<0.001
Work limitations	16.11	3.68	12.47	5.44	<0.001
Fear avoidance	19.63	4.13	11.95	4.14	<0.001
Patient satisfaction with outcomes	6.68	3.13	12.95	3.55	<0.001
Health care satisfaction	24	7.06	25.89	6.05	<0.001

At the end of the follow-up, 70 (87.5%) patients were satisfied with the treatment that is 94.4% of them treated with bolus infusion and 85.5% of them treated with continuous infusion ($p=0.442$).

There was a significant reduction in the number of patients using systemic analgesics or adjuvant drugs ($p<0.001$) (Graph 3).

The mean daily dose of morphine at the end of the follow-up period in 68 (85%) patients ranged from 0.1 to 15 mg/day (mean = 2.99; sd = 2.70; median = 2.50). The daily mean consumption changed over time ($p<0.001$); it was higher at the end of the 18th and 24th month in relation to the 1st week and 1st month of the follow-up ($p<0.05$), but was the same in the 6th, 12th, 18th and 24th months (Graph 4).

The consumption of morphine in the pump was the same in patients treated with continuous or bolus infusion, at the end of the 1st week, 1st month, 6th, 12th 18th and 24th months (p-values all >0.30) of the follow-up.

Table 2 shows adverse effects at the first week of treatment and after the first month.

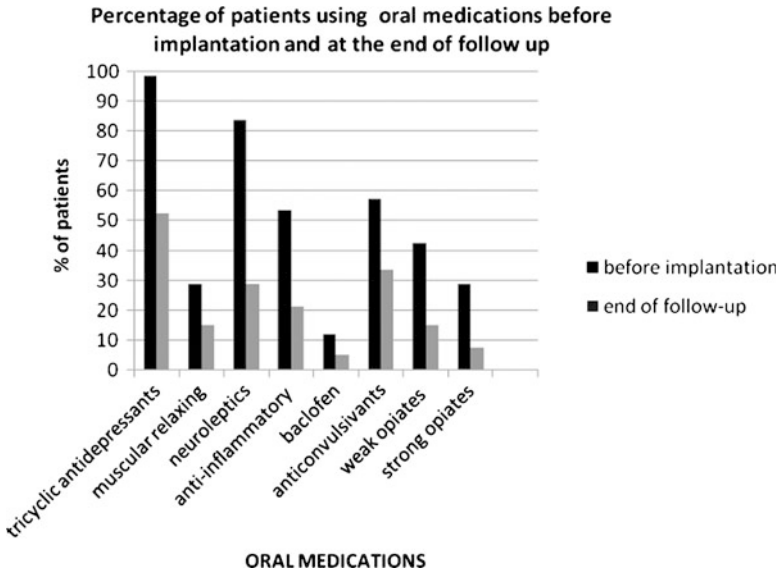
One (3.4%) patient presented bacterial meningitis and 1 (3.4%), compulsive behavior for opiate intake.

During the follow-up, 12 revisions of pumps or of catheters were necessary, of which 10 (33.4%) concerned revision of mechanical problems or replacement of the catheter and 2 (6.8%) were due to treatment of infection caused by the implanted device.

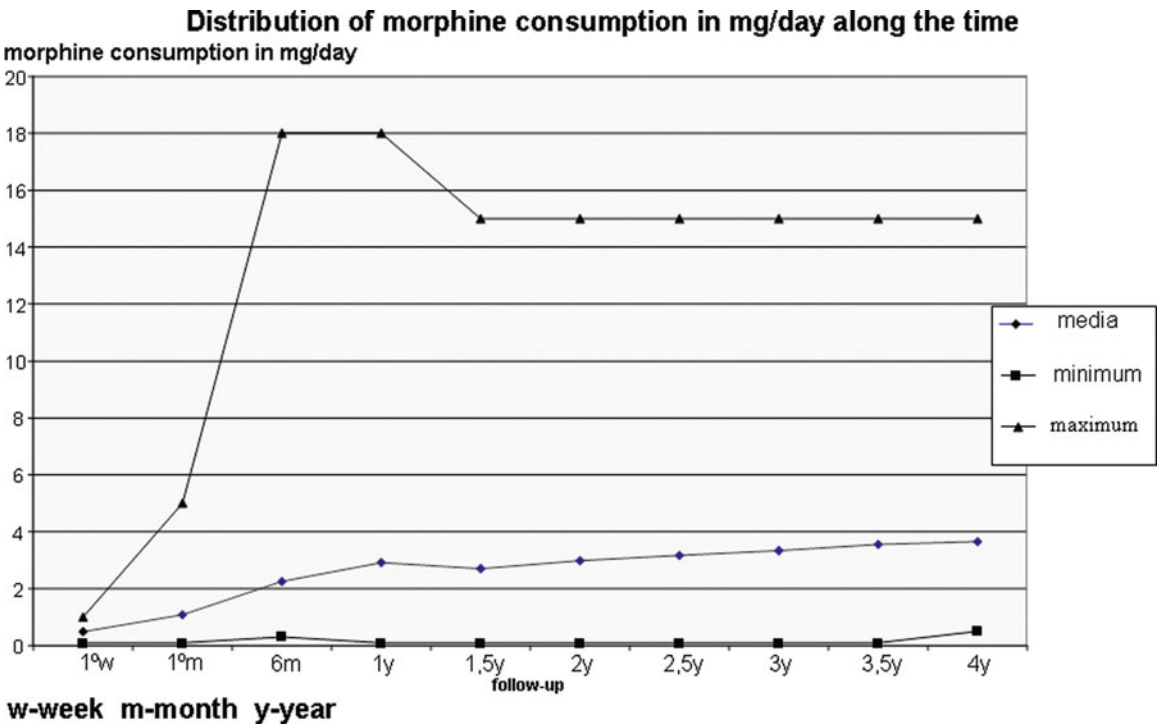
Discussion

Failed back surgery syndrome is a common, yet devastating pain complaint. Patient selection for repeated spinal surgery is not uniform and must be further refined. The best data available today suggest that most of the patients suffering from failed back syndrome are incapacitated by psychiatric, psychological, and social/vocational factors, which relate to the back complaint only indirectly [1]. Improved imaging should delineate disorders more clearly, and advances in surgical technique may improve outcome. It is likely, however, that a number of patients will continue to require long-term pain management.

Spinal infusion of opiates is effective in the treatment of cancer pain [8, 9, 11, 23] and of chronic pain not related to cancer [8, 14–16, 20–22, 27], being an option for FBSS treatment in those individuals who do not improve with oral medications or cannot tolerate them. However, its long-term effectiveness has not been established. Tolerance, physical dependence, addiction, infection and intoxication are concerns related to the use of the method in patients with non-oncologic



Graph 3 Oral medications before implantation and at the end of follow-up



Graph 4 Distribution of the morphine consumption in mg/day through follow-up time

chronic pains. Failed back surgery syndrome was the most frequent indication for pump implantation in a Canadian multicenter review [28].

There are few prospective studies about prolonged intrathecal infusion of opiates in non-oncologic pain patients [15, 21]. Most of the studies were retrospective, not controlled [13, 14, 20, 22, 23] and not randomized and, in many of them, the methods of evaluation were inappropriate.

The patients included in our prospective study had prolonged suffering (mean = 53 months) and severe pain (mean VAS = 9.6), despite the appropriate pharmacological treatment, physical medicine, and psychotherapy.

Mean reduction of pain was about 50% at the end of the follow-up that lasted 18–98 months (mean = 46.7 months) the mean VAS decreased from 9.5 to 4.6 ($p < 0.001$). Pain intensity was reduced from 78.5 to 58.5 in the Anderson and

Table 2 Side effects at the first week and after the first month

Side effects	First week		After first month	
	N	%	*N*	%
Nauseas	43	53.8	8	10.0
Vomits	25	31.3	6	7.5
Urinary retention	22	27.5	4	5.0
Diaphoresis	2	2.5	1	1.3
Constipation	11	13.8	11	13.8
Breathing depression	2	2.5	2	2.5
Xerostomy	1	1.3	0	0.0
Coryza	1	1.3	0	0.0
Sleepiness	2	2.5	1	1.3
Dizziness	0	0.0	1	1.3
Mental confusion	4	5.0	4	5.0
Itch	17	21.3	3	3.8

Burchiel's 1 patient; the improvement was higher than 25% in half of the cases. The average reduction of pain was 39% in Hassenbusch' 23 patients, 61% in Paice's 27 patients and 67.4% in Winkelmuller's 19 patients.

The reduction of pain intensity became stable through the time (Graph 1). There was a significant reduction in the number of the descriptors of MPQ (Table 2). Winkelmuller 19 and Anderson and Burchiel 1 also observed a reduction in the number of the evaluative and sensorial, but not of the affective descriptors of MPQ.

Our patients presented significant improvement of the quality of life (QOL) according to the SF-36 Questionnaire. There was also improvement of all domains of the TOPS Questionnaire [25, 26], except of the working capacity that evaluates the social security benefits of the patients as showed in Table 1. QOL has been evaluated only in recent studies about intrathecal infusion of opiates [15, 20, 22].

Anderson and Burchiel 1 used the "Chronic Illness Problem Inventory" [29]; Winkelmuller 19 just questioned the improvement of QOL with treatment; Hassenbusch et al. 23 used a simple, but not validated questionnaire, which made comparison of their results with other publications impossible.

After the first month of the follow-up, the mean daily dose of morphine required in the pumps was kept stable. The daily mean dose of morphine at the end of the 24th month of the follow-up was 3.0 mg/day, a value quite close to the dose used by other authors [15, 20, 30, 31]. This means, intrathecal opiate tolerance does not occur in long-term use. Yaksh and Onofrio [32] made a postal inquiry involving 19 doctors who treated 163 patients with cancer pain with prolonged intraspinal or intraventricular infusion of opiates; the mean dose of morphine was 4 mg/day during the first week and 17 mg/day at the 12th week. The initial mean daily dose was 8.5 mg/day in the 41 patients of cancer pain Schultheiss et al. [18] treated with bolus infusion of morphine through self-administration pumps; in just 7 of their 26 patients who survived more than 12 weeks it was necessary to increase the original dose. Anderson and Burchiel [15] used several opiates for intrathecal infusion and based on equianalgesic table they concluded that the mean equivalent dose of morphine was 14.59 mg/day at the end of the follow-up. The average dose of morphine at the end of the follow-up in the cases of Winkelmuller [31] was 4.9 mg/day.

We observed a significant reduction in the use of oral analgesics and adjuvant drugs at the end of the follow-up ($p<0.001$). However, Anderson and Burchiel [15] did not find a reduction in the oral intake of drugs after the implantation of infusion devices.

The improvement of pain and the mean daily dose of morphine required in the pump were the same in our patients, either treated with continuous or bolus infusion ($p=0.597$). No other publication focused on the results in relation to the long-term spinal infusion of morphine.

At the end of the follow-up 70 (87.5%) patients were satisfied with the treatment despite the use of bolus infusion and or continuous infusion. There are few studies comparing the mode of infusions [14, 32]. Gourlay et al. [33] did not observe any difference between the results of 29 patients with cancer pain treated with epidural bolus infusion and 28 patients treated with continuous epidural infusion.

The adverse effects were more common during the first week of treatment and became less expressive and did not harm the patients with time, as has been observed in other studies [15, 22, 34]. Only one of our patients who had previously omitted a history of cocaine abuse, presented compulsive behavior for the use of morphine, as was already observed in relation with the oral use of opiates by others authors [4, 35, 36], meaning that the method is safe when the selection of the patients is rigorous.

Many revisions of surgical procedures [33] were necessary to revert mechanical problems of the devices or infection, a finding that is in agreement with other authors [15, 22, 32]. Just one of our patients presented bacterial meningitis. In the multicentric study of Kamran et al. [37], complications were observed in 97 patients with implantable pumps; 6.2% of the patients presented infections, 1.0% bacterial meningitis, and 6.2% mechanical problems. The higher infection rate in our patients probably is the consequence of the longer follow-up period and the reduced concentration of morphine (10 mg/ml or less) used in our cases. Other authors [15, 20, 22] used up to 50 mg/ml of morphine which resulted in fewer pump charges, and hence contamination of the device. Intrathecal granulomas, however, have been associated with higher doses of intrathecal morphine [16, 32, 34, 37]. Fortunately, this complication was not observed in our cases.

Intrathecal pumps are considered to be a procedure with moderate evidence for FBSS treatment, same as for

transforaminal epidural steroid injections, lumbar percutaneous adhesiolysis, spinal cord stimulation and spinal endoscopy [38]. In fact, there is no gold standard for FBSS treatment, but these results seem promising. However, much research work is still necessary regarding prolonged intrathecal infusion of analgesics. The use of drugs such as ziconotide, neostigmine, droperidol, ketamine and ropivacaine need further evaluations. Psychiatric evaluations that could foresee the candidates for pump implantation shall be developed. Further evaluations about the financial viability of long-term treatment are also warranted.

Conclusion

Intrathecal spinal long-term infusion of morphine is efficient and safe in the treatment of FBSS patients. It leads to the improvement of pain and QOL. The dose of morphine became constant after the sixth month of treatment. The side effects were negligible. Surgical revisions were frequent, mostly due to malfunctioning of the devices implanted or infection.

Conflict of interest statement We declare that we have no conflict of interest.

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Modic Changes: Anatomy, Pathophysiology and Clinical Correlation

C.C. Quattrocchi, A.M. Alexandre, G.M. Della Pepa, R. Altavilla, and B.B. Zobel

Abstract Studying discovertebral complex anatomy is extremely important for the understanding of the pathophysiology of disc degeneration which leads to vertebral endplates signal changes, also known as Modic changes.

The sequelae of disc degeneration are among the leading causes of functional incapacity in both sexes and are one of the most common sources of chronic disability in the working years. Even if the presence of degenerative changes in MRI of the spine is by no means an indicator of symptoms, we are concordant in a positive association between Modic changes and low back pain, above all as a relatively specific but insensitive sign of discogenic low back pain.

Keywords Disc degeneration · Disc disease · Modic changes · Vertebral endplates signal changes

Discovertebral Complex Anatomy

The disc is made up of two fundamental structures: the nucleus pulposus and the anulus fibrosus. Although its composition percentage differs in cervical, dorsal and lumbar spine, it is made of three basic components: proteoglycan, collagen, and water. The nucleus pulposus is the water-rich, gelatinous center of the disc, and can tolerate very high pressure values in standing and especially in the seated position. The anulus fibrosus has a much more fibrous structure, containing a much higher collagen percentage and lower water content. It serves as a limiting capsule of the nucleus because of the high pressure that is upon it. It is made of 15–25 concentric sheets of collagen (lamellae). The very outer fibers of the disc, Sharpey's fibers, anchor themselves into the vertebral endplates and into the anterior and posterior longitudinal ligament [34].The disc is avascular, and disc cells depend on molecular diffusion from blood vessels at the disc's margins to supply the nutrients essential for cellular activity and to remove metabolic wastes [51]. This is a key concept in the anatomy and pathophysiology of the discovertebral complex, as it has been proved that a fall in nutrient supply can reduce the number of viable cells in the disc, leading to degeneration [3, 20].

The intervertebral disc can be thought as a soft pad that separates the vertebrae of the spine from one another. Its functions are mainly three: it acts as a ligament by holding the vertebrae together; it acts as a shock absorber to carry axial load; and finally it acts as a pivot which allows spine bending, spine rotation and spine twisting.

Pathophysiology of Degenerative Disc Disease

Understanding the process of intervertebral disc degeneration is extremely important, as other spinal structures can be affected by changes within the disc itself, leading to various pathological conditions, such as ligamentous hypertrophy, facet hypertrophy or arthopathy, vertebral endplates changes, disc herniation, spinal canal stenosis, lateral recesses stenosis or even vertebral instability.

Indeed the term "degeneration" as commonly applied to the intervertebral disc covers such a wide variety of clinical, radiologic, and pathologic manifestations that the word is really only a symbol of our ignorance about disc disease, as Printzker [45] asserted in 1977.

Nowadays the knowledge about degenerative disc disease is quite expanded, and even a classification scheme for

C.C. Quattrocchi (✉), A.M. Alexandre and B.B. Zobel
Department of Radiology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy
e-mail: c.quattrocchi@unicampus.it

G.M.D. Pepa
Department of Neurosurgery, Catholic University of Rome, Via Longoni, 47 00155 Rome, Italy

R. Altavilla
Department of Neurology, University Campus Bio-Medico of Rome, via Longoni, 47 00155 Rome, Italy

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lumbar intervertebral disc degeneration has been proposed [44].

Basically, degeneration is a process that begins early in life and is the consequence of a variety of genetic, physiologic, and environmental (mechanical, traumatic, nutritional) factors, as well as normal aging [38].

Disc degeneration per se is not painful and this is proven by the very high prevalence in the asymptomatic population. However, all the consequences that we mentioned act in combination and the inflammatory response causes the complained low back pain.

A very interesting flowchart of a hypothetical inflammatory cascade for degenerative disc disease has been proposed by Modic and Ross [38]. A variety of mechanisms and mediators are involved, such as TNF, IL-1, macrophage recruitment, monocyte chemoattractant protein-1 (MCP), granulocyte macrophage colony-stimulating factor (GM-CSF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), IL-8, IL-6, matrix metalloproteinases (MMPs), nerve growth factor, calcitonin gene-related peptide (CGRP), nitric oxide (NO), prostaglandin E2 (PGE2), phospholipase A2 (PLA2), substance P and Leukotrienes, all together resulting in pain.

By consequence we can simply understand that low back pain and sensory/motor deficits would appear as the result of both a combination of mechanical deformation and the presence of inflammation.

The degenerative process within discs results in greater axial loading and increased stress on the vertebral body endplates [41]. such changes may secondarily affect the local marrow environment, resulting in vertebral endplate signal changes on MRI, also known as Modic changes [37, 39].

Nomenclature and Definition

Signal intensity changes in the vertebral body marrow adjacent to the endplates are a common observation in magnetic resonance imaging [11].

Vertebral body marrow changes, as described by Modic et al. in 1988 [37, 39], include three main forms: type 1 refers to decreased signal intensity on T1-weighted spin-echo images and increased signal intensity on T2-weighted images, indicating bone marrow oedema associated with acute or subacute inflammatory changes. Types 2 and 3 indicate chronic changes. Type 2 refers to increased signal intensity on T1- weighted images and isointense or slightly increased signal intensity on T2-weighted images, indicating replacement of normal bone marrow by fat. Type 3 refers to decreased signal intensity on both T1 and T2-weighted images, indicating reactive osteosclerosis. This is considered the standard classification world-wide [14].

In all three types, there is always evidence of associated degenerative disc disease at the level of involvement. Moreover Modic changes may also change over time. In fact type I changes may revert to normal or convert to type II changes, suggesting some stabilization of the degenerative process. Type II changes tend to be more stable but may convert to type I or a mixed combination of types I and II. When changes do occur in type II marrow, they are usually associated with evidence of additional or accelerated degeneration or a superimposed process such as infection or trauma [38].

Histopathological correlation shows in type I changes disruption and fissuring of the endplate and vascularized fibrous tissues within the adjacent marrow. Enhancement of type I vertebral body marrow changes is seen with administration of contrast material that sometimes extends to involve the disc itself and is presumably related to the vascularized fibrous tissue within the adjacent marrow.

Type II changes show evidence of endplate disruption too, with lipid marrow replacement in the adjacent vertebral body.

Type III changes correlate with extensive bony sclerosis on plain radiographs. The lack of signal in the type III changes reflects the relative absence of marrow in areas of advanced sclerosis [38].

Similar marrow changes have also been noted in the pedicles; in this case too, changes are probably a reflection of abnormal stresses, by loading or motion [40, 50].

Some authors sustain that endplates sclerosis exists in all types of Modic changes, especially in mixed Modic types, and not only in type III, as endplates sclerosis might not be detected in MRI depending on the amount of mineralization of the bone marrow [32].

Modic classification is both reliable and reproducible, and it is simple and easy to apply for different observers of varying clinical experience [24, 29]. The same conclusion, that is inter-observer reproducibility of a detailed evaluation of Modic changes, is supported also by other studies [8, 9, 22, 25, 30].

The clinical importance of these findings, as Modic et al. explained at the first description, is that they are associated with degenerative disc disease and that they can be distinguished from changes secondary to malignancy or vertebral osteomyelitis. Furthermore the fact that a degenerative disc can be identified without concomitant vertebral body marrow changes indicates that they do not represent an invariable outcome, but part of a spectrum of the same disease [39].

Clinical Correlation

In patients with low back pain there are several mechanisms which often act in combination causing pain; these include instability with associated disc degeneration, facet disease, mechanical compression of nerves by bone, ligament, or herniation, and production of biochemical mediators of inflammation. The concept of the disc as a pain generator was described by Crock [10] as chronic internal disc disruption syndrome; other terms describing the same process are internal annular tear, internal disc disruption, black disc disease, and discogenic pain.

The sequelae of disc degeneration are among the leading causes of functional incapacity in both sexes and are one of the most common sources of chronic disability in the working years. The presence of degenerative changes is by no means an indicator of symptoms, and there is a very high prevalence of this disease in asymptomatic individuals; even the relationship between Modic changes and degenerative disc disease remains unclear.

In this context we should clarify the role of imaging, and in particular the role of MRI, in providing accurate morphologic information and consequently influencing therapeutic decision making.

The relationship among the vertebral body endplate, anulus, and disc has been studied [11, 35, 39] by using both degenerated and chymopapain-treated discs as models, and it seems that type I changes are associated with a higher prevalence of active low back pain symptoms. The exact etiologic mechanism or mechanisms of vertebral endplate changes are thought to be related to stresses, micro or macro-instability or microtrauma between the two vertebral endplates following disc degeneration [38].

Regarding the epidemiology of Modic changes, a recent study evaluating the presence of degenerative imaging findings in lumbar magnetic resonance imaging among young adults has shown that the presence of degenerated disc and bulging are common, whereas Modic changes and herniation are relatively rare (1.4 and 3.8% of subjects respectively, based on a total number of 558 that attended MRI) at 21 years of age; moreover there were no gender differences and type I was more common than type II [48]. The L4–L5 and L5–S1 levels are reported to be those typically affected by Modic changes [6]. Previous studies have reported prevalences of Modic changes ranging from 12 to 58% depending on whether subjects were symptomatic or not [21]. However the prevalence of Modic changes and above all its association with low back pain varies greatly between studies, ranging from less than 1% [28] in adolescents from the Danish general population to 100% [15, 53] in selected patient populations.

A large number of studies and narrative reviews have reported about Modic changes in patient populations with specific LBP (e.g. spondylitis, trauma, tumours and spondyloarthropathies) [18, 19, 23, 52], and in patients with nonspecific LBP, investigating the association between Modic changes and LBP, with the strength of association from none [33] to strong [55].

The wide range in the reported prevalence rates of Modic changes and the different associations with LBP could be explained by differences in the definitions of vertebral endplate signal changes and LBP. They can also be explained by differences in relation to age, sex, and type of study population (clinical or nonclinical population).

Other factors that must be considered to explain the difference in prevalence and association with LBP include year of publication, racial distribution in the study sample, and above all the quality of the study.

A recent systematic literature review found a positive association between Modic changes and LBP in the majority of studies reporting on this subject [21]. furthermore it is important to note that a positive association has been found also in the general [27] and working [31, 46] populations. This is to support the concept that there is a considerable consistency in this association.

If Modic changes are a condition that causes LBP, it seems likely that the prevalence would be the highest in study samples of patients with LBP, lower in study samples from the general and working population and lowest in individuals without LBP [21].

As expected, the prevalence of Modic changes increases with age [30, 39]. This seems plausible as they are correlated to disc degeneration [26, 39] which in turn is correlated to age [2].

The exact reasons why Modic changes may be painful are not known. The lumbar vertebral endplate contains immunoreactive nerves, as shown in studies of sheep and humans [7, 13], and it has been reported that an increased number of tumour necrosis factor (TNF) immunoreactive nerve cells and fibres are present in endplates with signal changes, especially in type 1 changes [26].

The other possibility, as we mentioned before, is that Modic changes are closely related to disc degeneration [1, 30, 39, 42], and immunoreactive nerves have also been shown to be present in degenerative discs [16].

Toyone et al. [49] showed that type 1 changes are highly correlated with low back pain and segmental hypermobility, but type 2 changes are not. Weishaupt et al. [55] sustain that disc degeneration and the presence of a high-signal-intensity zone in the disc, may not correspond directly to painful disc degeneration and should, therefore, not be used to identify symptomatic intervertebral discs. On the other hand, they argue that moderate and severe endplate type I and type II abnormalities on MR images may indicate painful disc derangement in patients with low back pain. Other authors suggest that signal intensity changes along the endplates

may be caused not only by oedema, fissuring of the endplates, and formation of granulation tissue but even in part by endplate avulsion [47].

MR imaging provides a unique means to evaluate the morphologic status of intervertebral discs and their relationship to neural structures in patients with low back pain. Moreover, the technique allows assessment of the biochemical status of the disc on T2-weighted spin-echo and fast/turbo, depending on the MR system manufacture spin-echo MR images. Loss of disc height and loss of brightness of the nucleus pulposus reflect the decreased proteoglycan concentration in degenerated discs [43]. However, although MR imaging provides detailed information with regard to the whole spectrum of abnormalities, the role of MR imaging in the evaluation of discogenic pain has not been well defined [5, 17].

Another study that investigated the predictive value of magnetic resonance imaging of abnormalities of the lumbar intervertebral discs, particularly with adjacent endplate changes, in predicting symptomatic disc derangement, showed that all discs with endplate abnormalities caused concordant pain at discography, which resulted in a PPV of 100% [55]. McCall et al. [36] and Braithwaite et al. [6] reported remarkably similar findings with regard to the prevalence and clinical relevance of endplate abnormalities in patients with discogenic pain.

The likelihood of the clinical relevance of endplate abnormalities in patients with discogenic pain is supported by the low prevalence of endplate abnormalities in an asymptomatic population [54].

Conclusions

In conclusion we want to underline the importance of Modic changes in MR images, as a relatively specific but insensitive sign of a painful lumbar disc in patients with discogenic low back pain.

We must be advised that the high prevalence of anatomical abnormalities in asymptomatic people, combined with the high prevalence of back symptoms in adults, makes coincidental findings likely [12]. By consequence, we must be warned that an observation on magnetic resonance imaging, in the absence of objective clinical findings, may not be the cause of a patient's pain [4].

Disclosure of competing interest: no competing interests.

Conflict of interest statement We declare that we have no conflict of interest.

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Periduroscopy: General Review of Clinical Features and Development of Operative Models

W. Raffaeli, D. Righetti, J. Andruccioli, and D. Sarti

Abstract *Background*: Myeloscopy is a useful approach for both diagnosis and treatment of back pain. However clinicians have underestimated its potential. From the nineties myeloscopy has been used only as a diagnostic tool, without any improvement of the technique. Racz's method is nowadays still used for the lysis of adherence by applying medical solutions without a direct vision inside the spinal channel. In 1998 we showed the limitations of Racz's approach, and in 1999 we developed a new technique, introducing a Fogarty balloon to remove the occlusions of the spinal canal and the resaflex for the lysis of adherence at low temperature (Raffaeli–Righetti technique). In this paper we report a general review of our experience with periduroscopy for the treatment of failed back surgery syndrome (FBSS) and spinal stenosis.

Method: A Fogarty balloon was used to remove fat and/or mild fibrosis occluding the spinal canal, reducing by 50% the volume of the saline solution used in periduroscopy. The Resaflex was subsequently used to lyse adherence and to allow reaching the site of pain origin, using a low temperature (>50°C).

Findings: the fibrosis morphologies of epidural space (ES) were grouped on the basis of common macroscopic and organizational characteristics, which were revealed during myeloscopy. A year after myeloscopy, 59% of FBSS patients, and 67% of patients with stenosis reported a general improvement of their painful pathology, with a pain reduction above 50 in 56% of patients. Forty-eight percent of patients used minor analgesics and 67% of patients went back to work. Only few complications were observed (4%).

Conclusions: myeloscopy technique enlightens pain-triggering mechanisms otherwise unrevealed; it has specific therapeutic value, whereas on the diagnostic side it has not revealed relevant pathologies. Its effectiveness in FBSS patients is high, with the advantage of its relatively easy implementation, limited invasiveness and repeatability.

Keywords Epidural lysis of adherence · Epiduroscopy · Failed back surgery syndrome · Myeloscopy · Racz's approach · Spinal stenosis

Introduction

Myeloscopy is a relatively new approach for both diagnosis and treatment of back pain [1, 2, 10, 16]. Although epiduroscopy has been in use since the nineties, it has not been classified by clinicians as procedure for the treatment of pain yet [12, 16, 20, 22]. Any improvements to allow its employment as surgical treatment of painful back syndromes, in particular for pathologies that are secondary to the surgical operation of rachis (failed back surgery syndrome – FBSS), are still missing [5, 21, 23]. Some authors are still using a technique (according to Racz's method) for the lysis of adherence in FBSS, applying medical solutions without direct vision [6, 11]. We believe that when using this blinded approach it is extremely difficult to avoid laceration of vessel and dura, if there are any abnormalities inside the spinal canal. This method, moreover, does not take into account the underlying morphological substrate; for this reason we believe that it fails to specifically locate the pain triggering zone and hence the extent of tissue exportation.

Based on our experience [12], as from 1998 we defined the role of periduroscopy as a tool to treat and to study dura involvement as painful compartment. In order, to better define the role of myeloscopy, which we think that it is the only technique allowing exploration of the spinal canal and removal of pathologies. We introduced a new technique in 1999. This method, for the first time, used a balloon inside the video-guide [13] to remove materials occluding the epidural space and preventing the vision inside. In 2001, we developed an instrumentation with quantum molecular

W. Raffaeli (✉), D. Righetti, J. Andruccioli, and D. Sarti
Pain Therapy and Palliative Care Unit, Infermi Hospital Rimini, 47900, Rimini, Italy
e-mail: wraffaeli@auslrn.net

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resonance, already submitted for surgical lysis of fibrosis at low temperature [14, 17].

We believe that the peridurolysis technique is nowadays the method to be used as first step for the treatment of complex rachid pain due to failed back surgery syndrome or of pain secondary to spinal stenosis without motor impairment, before using more invasive surgical procedures or implant techniques for neuromodulation, such as spinal cord stimulation (SCS) or intrathecal drug delivery (IDD).

Here we report a general review of our experience, describing the morphological methods that can be found in the different painful pathologies, and the surgical procedures that we use in our center of pain therapy.

Study Design

This is a prospective, single center, single blinded study.

Ethics

Our procedure was approved by the Hospital Ethics Committee and conducted according to the Helsinki declaration principles on human clinical studies. All the patients, after a through explanation of the procedure and the study, gave a written consent.

Materials and Methods

The Sample

This study included patients, followed for pain management at the Unit of Pain Therapy at the Infermi Hospital, Rimini, Italy from 1997 to 2007 and with an indication for peridurоscopy. The sample included 662 patients: 304 with FBSS diagnosis, 209 with spinal stenosis, and 149 with complex pain due to a double pathology, FBSS and stenosis associated with multiple discopathy.

Our criteria for patient selection were the following: inclusion criteria: age >18 years, pain was not responsive to pharmacological, physical, or invasive analgesic treatments (such as peridural blocks); pain was present for at least 2 years after back surgery; no magnetic resonance imaging (MRI), computed tomography (CT) and neurophysiological data available; absence of red flags, motor impairments, sphincter dysfunction, undiagnosed vertebral collapse, persistent fever, or suspected neoplasm; positive response to Raffaeli's low dose method (R-LDM) trial. The trial has been previously described [15, 18]. The tests were judged to be positive if a pain relief >70% using morphine and bupivacaine was attained and no pain relief was observed with placebo.

Exclusion criteria were: presence of surgical and/or medical emergency; non-stabilized central nervous system and/or peripheral nervous system pathologies; previous brain surgery for vasculopathy; diagnosis of primitive and secondary epilepsy, brain vasculopathy (aneurysm, angioma), ocular disease retinal disease, glaucoma, non-drug-related bleeding disorders (coagulopathy); pregnancy; positive response to placebo; evidence of severe psychic disturbance, inability to give informed consent; presence of chronic headache (except menstrual migraine) or cervical stenosis with myelopathy.

Data Collected

The data monitored were pain, personal autonomy, neurological deficit, and drug consumption for pain relief.

Subjective evaluation of the procedure was obtained by a telephone administered self-evaluation, brief questionnaire. Patients were asked to evaluate if they had any benefit from myeloscopy ("Yes"/"No"). If the answer was "Yes," then, they were asked to quantify their pain reduction according to two categories: more than or equal to 50%; or less than 50%. They were also asked for how long this benefit had lasted: if less than 1 month, between 1 and 3 months, 12 months, or more than 24 months. Finally, they were asked if they would agree to have another myeloscopy if required.

A blinded investigator performed a clinical, objective evaluation at 3 months, 1 and 2 years after the myeloscopy.

Anesthesia

The anesthesia procedure was the same for both types of myeloscopy techniques in our study. It was performed with infiltration of 2% lidocaine and hypnotics, at subhypnotic doses of midazolam (5 mg) or propofol (100 mg/20 min), in order to reduce conscious pain perception.

Peridurоscopy Technique

The first phase of peridurоscopy is similar in many authors' procedures, independent of the instrumentation employed, and it is used to visualise the dura space, using fluid infusion via the endoscopic instrumentation. We believe that this important phase should not be performed with a continuous

infusion at low pressure, but with the administration of small boli, in order to dilate the dura space. We describe in detail the phase of dura space visualisation (Raffaeli Fogarty), and of the specialist ablation procedure of the scar tissue (Raffaeli Resaflex technique).

Instrument Insertion: General Technique

The sacrococcygeal anatomical landmark was identified under X-ray guidance (unguided percutaneous procedures are not recommended). The metal guide wire was inserted into the needle, which was advanced by no more than 5 mm. Excessive depth might result in guide entrapment in the nerve roots or fibrotic strands, risking avulsion onset as a consequence of guide withdrawal and/or difficulty in its removal [20].

Instruments Insertion: Specialist Technique

The *lumbar* (interlaminar craniocaudal) *approach* (more invasive and longer in terms of performance times) was adopted only in patients with sacral anatomical abnormalities (tight stenosis of the hiatus, ossified sacrococcygeal ligament).

Description of the procedure [12]: the dilator was pulled along while pushing the insertion tube, in order to introduce the insertion tube/dilator into the metal guide avoiding to damage its edges during this operation. The dilator must never be advanced beyond the 4th sacral vertebra, to avoid limiting the catheter's rotation and thus the endoscopic vision.

The position of the insertion tube was monitored with the fluoroscope in laterolateral and anteroposterior view. If the insertion tube was too lateral, it was withdrawn and repositioned on the midline. The optic fibre was then connected to the camera and the white balance setting was performed. The dedicated catheter was unsealed; the optic fibre was introduced into the canal and focused, ready to record the operation.

Visualisation of the Lumbosacral Canal

The visualisation of the lumbosacral canal was made in two steps. Access to the epidural space was gained by distension with 2–3 ml saline solution boli. The reason for using multiple small boli was to assess any resistance to the fluid (such as barriers or abnormal pressure) and any distension-induced pain (localized pain; nucal pain). Intervals of 30 s were observed every 3–4 boli to allow foraminal outflow. Saline solution was injected slowly in these intervals to improve vision.

Non-traumatic advancement in the epidural space required intermittent epidural irrigation with saline solution at an infusion pressure $\leq$60 mmHg. Infusion pressure should be monitored, but unfortunately systems, such as pressure transducers, allowing continuous monitoring were not available. Clinical monitoring was thus adopted; this was the reason why the procedure could only be performed under local anaesthesia with bland sedation to preserve patient's alertness. The total amount of liquid injected should not exceed 350 ml (average: 220 ml).

The catheter was advanced under direct vision, cleaning the sacral canal of any fat and mild fibrosis. Where anatomical landmarks were identified, it indicated that anatomical abnormalities and/or of meningeal fold adhesions might be present. In those cases, the greatest care should be exercised to avoid dural tears, especially in patients with a short sacrum who had undergone multiple operations.

Phase 1

Preparation of the endoscopic space and dissection were performed according to the Raffaeli-Righetti (RR) technique [17]. Endoscopic exploration and lesion treatment. Mechanical adhesiolysis and/or medication delivery.

The aim of phase I (exploration) was to visualise the dural pannus to avoid blind advancement and to perform endoscopic exploration, mechanical adhesiolysis and medication in back syndromes without the need of radiofrequency resection.

The procedure required slow advancement of the insertion guide by removal of the fat until the site of the lesion was reached. The process of dissection was facilitated by the insertion into the second working channel of a 3F Fogarty balloon (Fig. 1a), which was introduced into the fat mass or the mild fibrosis and then it was expanded with 0.5 ml of saline solution. Filling, dragging and then closing the balloon, followed by fluid injection, enabled the removal of the milder adhesions and exploration of the metameres hidden by fat or scar tissue. The procedure was performed advancing segment by segment, assessing resistance, to expose the pathological sites and thus the fibrotic areas.

Anatomical, Morphological, and Pathological Appearance of the Epidural Space: Non-Pathological Canal

The dural pannus was visualized at the base of the endoscope, and the canal appeared dark. Sometimes, the absence of resistance made it difficult to see the canal, in those cases the instrument was oriented towards the sides and rotated

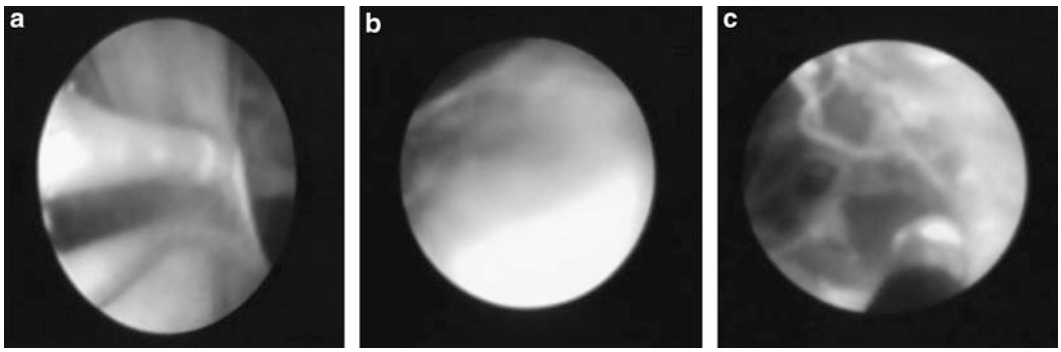

Fig. 1 Myeloscopy: Raffaeli–Righetti technique. The Fogarty balloon is inserted into the fibrosis (**a**). A fibrotic septum is occluding the whole channel (**b**) and is lysed by the Resaflex (**c**), here is shown the Resaflex tip in the right end corner

until the dural pannus (reference point) was visualised. The fluid must be injected towards the wall and the Fogarty procedure performed immediately, in order to avoid fluid dispersion and the risk of consuming the whole dose in the exploration phase.

Anatomical, Morphological, and Pathological Appearance of the Epidural Space: Pathological Canal

The area involved by the scarring process was initially identified by lack of agent diffusion or filling defects and subsequently by direct vision after canal distension with fluid and clearing with the Fogarty (see below in the Raffaeli–Righetti technique).

Once the epiduroscope reached the site that was considered the source of the pain, images were collected with the camera connected to the endoscope. The area, which was close to the scar tissue and/or the inflamed/hyperaemic tissue surrounding the root, was flushed without losing sight of the dura.

Direct fluid injection against a resistance by orienting the scope tip or the Fogarty within and/or towards the lesion allowed performing a first mechanical dissection, to identify abnormalities and to assess pathological findings (scarring, connective strands, hyperaemia/inflammation) before starting the surgical adhesiolysis procedure. We elicited pain upon liquid distention of the sacral space in 55% of FBSS patients, 75% of patients with hyperemic fibrosis and alteration of dura nociception, and 65% of patients with stenosis.

Two types of fibrosis were observed. Type I was mild fibrosis with transverse filmy strands. These can usually be treated by mechanical dissection and dragging with the balloon. Type II was characterised by fibrotic adhesions with webbed or widespread connective septa and partial or total reduction of canal calibre. These were removed with the Resablator.

Phase 2: Surgical Dissection of Adhesions with the Resablator-Magnetic Resonance Imaging (MRI), The Raffaeli–Righetti Technique

The surgical instrumentation included a Resablator and a Resaflex. The preparation of the endoscopic space and the dissection were performed according to Raffaeli's technique [12–14, 17]. Preparation of the operative field: the aim of this phase (exploration) was to visualise the dural pannus to avoid blind advancement and to perform endoscopic exploration.

The procedure required a slow advancement of the insertion guide by removal of the fat until the site of the lesion was reached. In patients lacking a clean, physiological space, this process was facilitated by the introduction of a Fogarty balloon into the second channel, operating about 1 mm outside the endoscope channel.

Utilisation of the Fogarty: the balloon was introduced into the structures surrounding the canal and/or dural pannus (fat, mild fibrosis, adhering tissue); it was expanded by injecting 0.5 ml saline solution and then dragged. This manoeuvre was performed 2–3 times, injecting 3 ml saline solution after each distension. The procedure was aimed at isolating the pathological structures usually covered with fat and peripheral reaction tissue and to assess resistance to canal distension. In this first phase, an initial mechanical dissection of the connective structures was performed by distension of the adhesions sites by introducing the Fogarty and the endoscope tip, filling the balloon and then withdrawing it with a slight rotation while pulling back the catheter.

This mechanical dissection enabled the visualisation of the pathological area, isolation of the different components from the surrounding structures, and identification of the fibrotic septa and/or hyperaemic areas, and the zones where the dura adheres to peripheral connective tissue. It was important to check the fibrotic tissue for septa containing networks of newly formed vessels. These vessels could be hidden in the transverse membranes of reactive and

connective tissue networks, and might be confused with scar tissue septa and cause haemorrhage if damaged.

Resection with the Resaflex probe: after isolation of the individual fibrous septa (Fig. 1b) or the connective tissue adhering to the dura, the site opposing the least resistance point was identified by traction with the tip of the Fogarty, and the tip of the Resaflex probe (Fig. 1c) was inserted at the base of this point. The Fogarty was withdrawn and the probe inserted in the space left empty by the balloon. The probe was oriented towards the base of the septum by rotating its tip, which was angled to allow its identification in situ and its rotation within the lesion, aiming at its base.

After positioning of the tip at the site to be ablated, power with an intensity of 25 W was applied to the first lesion twice consecutively for a few seconds. The ablation tip was then pulled back a few millimetres and repositioned to treat the next lesions (in 3–5 steps of a few seconds), increasing the voltage of 5 W per step. This procedure was repeated until complete or partial vaporisation (it was sufficient to remove the traction exerted by pathological tissue on the dural pouch) of the connective tissue and disconnection of the pathological septum were attained.

The field was then rinsed, and the Fogarty was used to isolate the fibrotic area. It was extremely important not to damage the dural base and to operate only where the dura-adhesion contact point was clearly visible. Finally, the sources of microbleeds were coagulated using the Resaflex's coagulation function. The instrumentation was removed after injecting antibiotic, saline solution and corticosteroids. Procedure duration: 35 min.

Indications for R-R Technique

This new technique for the ablation of epidural adhesions has considerable therapeutic advantages. It should be adopted in all conditions of "functional instability" where fibrotic-connective bands in the epidural space exert traction on the dural pannus, perineural structures and nerve roots.

The vaporisation phase of the technique has allowed exploring its limitations and advantages and to define its characteristics to facilitate the operation.

Magnetic resonance (MR) myeloscopy was a further development that enabled improvement and optimisation of the positive results obtained with standard myeloscopy, especially concerning the reduction of long-term painful recurrences. Compared with traditional procedures, this technique offered therapeutic advantages in terms of pain relief, ease of performance and possibility of repetition.

Clinical Parameters to be Monitored

The clinical parameters that should be monitored during the surgical procedure were nuchal or frontal pain, and axial chest pain and/or constriction.

A total amount of 250–300 ml fluid per operation should not be exceeded. To reduce the amount of fluid employed, the Fogarty can be used immediately for distension after visualization of the canal and identification of the dura and structures.

Pathomorphological Findings

Morphological features of epidural/subdural space (ES) were assessed in two steps. Firstly, during myeloscopy: a dedicated investigator took note of the morphological findings encountered by the operator and printed the relative video images. Secondly, after myeloscopy procedure: the images were analysed by a blinded interpreter and hence compared with similar findings obtained from other patients in order to better classify findings and to look for correspondence between symptoms and pathologic features. In particular we looked for: presence of longitudinal dural septa; degree of stenosis; fibrosis adhesiveness onto the dura; signs of local inflammation and hyperemia; and vascular stasis. Epidural hyperalgesia was assessed indirectly. We have monitored the onset of pain elicited upon injection of ½ ml of saline into the ES; when present, pain intensity was estimated by the awake patient by means of NRS scale (0 = no pain and 10 = worst pain imaginable).

Results

Morphological Features in the Epidural/Subdural Space (ES)

Figure 2 reports major morphological findings in the ES. Normal dura (Fig. 2a) did not present the longitudinal ligament described by Bloomberg [1, 2]. We have occasionally detected images of false septa. In theses cases the dura exhibited a "sail-like" shape as it was probably pulled by an above or underlying fibroid traction (Fig. 2b). Seventy-eight percent of patients with FBSS had fibrosis, 53% of them had septa fibrosis that exerted traction on the dura, whereas 45% of them had a complete fibroid occlusion of the canal at multiple levels. The fibrosis had different morphological characteristics, which defined two different connettival reactions: pluriseptal network or microcirculation

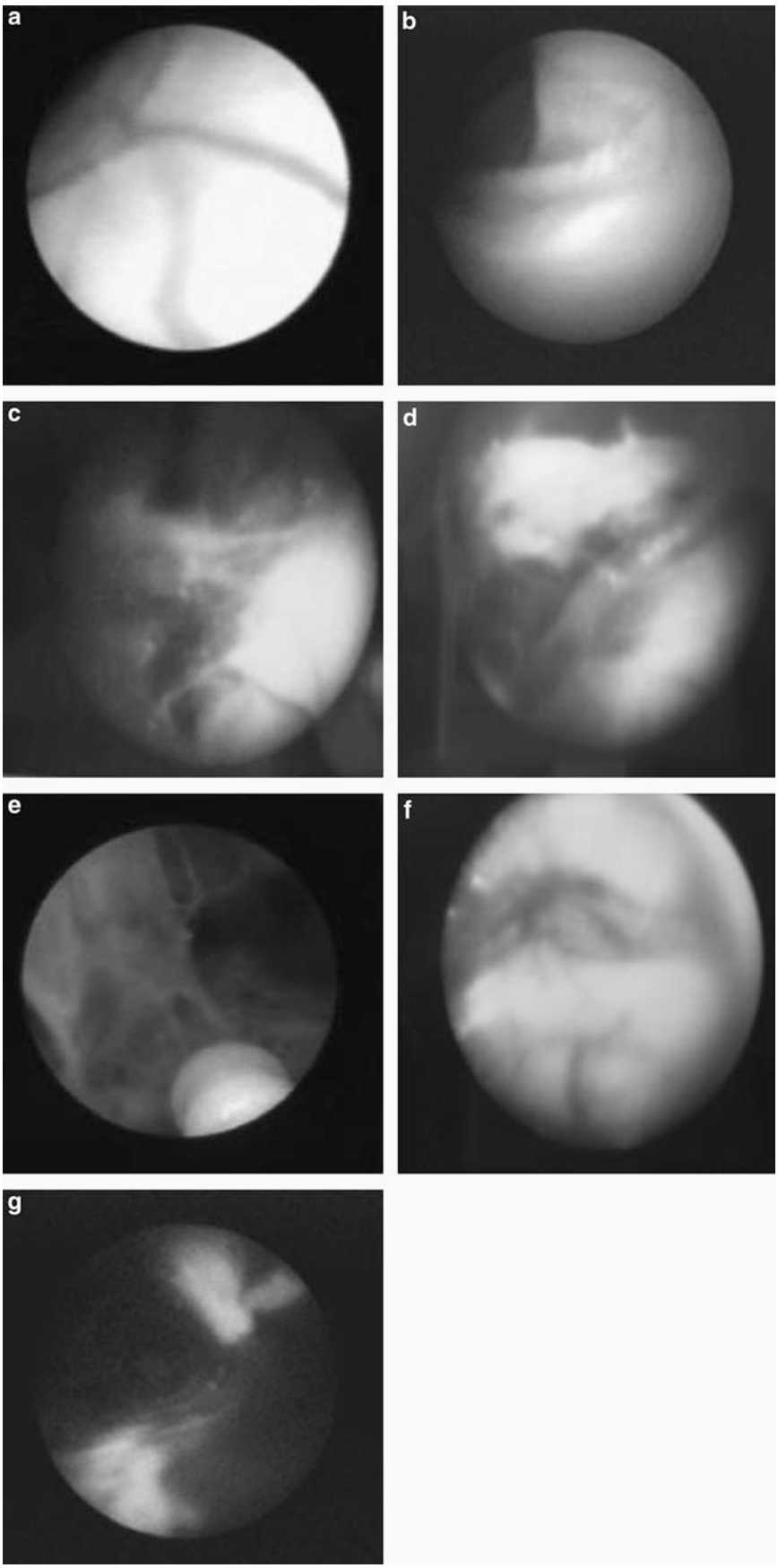

Fig. 2 Morphological features. Normal dura (**a**). Pathological features of the dura included: false septa with the dura exhibiting a sail-like shape (**b**), jagged or cotton-candy-like structures of transparent nature (**c**), organized fibrous structures of hard consistency and adherent onto the dura (**d**), Fibroid bridles with multiple cords forming a deformed transversal network (**e**). Blind compartmentalization of the ES forming obstructive barriers at different levels (**f**), pathologic fibrous elements and hyperemic tissues (**g**). (**b**) was taken from our precedent work [17]

impairments with indirect signs of hyperaemia. Stenosis was coupled with inflammation and hyperaemia aspects in 75% of the cases; with fibrosis in 53%; and with adherence features in 48% of cases.

Fibrosis: Anatomical Appearance

The fibrosis morphologies could be grouped on the basis of common macroscopic and organizational characteristics, which were revealed during myeloscopy. These characteristics were often correlated with the time elapsed from the surgical operation that caused the FBSS and with clinical signs. We have distinguished between the following:

(a) Jagged or cotton-candy-like structures of transparent nature with fibroid elements like bluish flaps, which adhered to the surrounding tissues and loosely to the dura (Fig. 2c). These elements could be further divided into: "honeycomb" and "radial" structures, on the basis of their network shape, spreading from the dura to the ES. These structures caused partial stenosis and during myeloscopy appeared as fragmented stenosis. This pathological morphology was extremely frequent (80–75% of the cases), however, it was not painful on distension but might have been the cause of distal paresthesia.

(b) *Organized fibrous structures of hard consistency and adherent onto the dura* (Fig. 2d), with intrinsic vascularization and diffused vascular stasis. These fibrous structures were mostly distributed at the lateral canal sectors, where they exerted traction onto the nearby dura, resulting in a reduction (2/3) of the ES diameter, which was considered an "anatomical stenosis." During myeloscopy, ES compartmentalization could have a "rat-tail" shape. Dynamic instability was the major clinical feature and distention was painful, since it caused epidural hypertension. For this reason we believe that primary pain in these cases was of mechanical nature.

(c) *Fibroid bridles with multiple cords forming a deformed transversal network* (often paraforamenal) which was associated with multiple inflammatory sites (Fig. 2e). In this case, the distention was painful. Pain could irradiate to distal, sacral, and lumbar structures and might have been associated with episodes of distal paresthesia, suggesting that primary pain had a nociceptive origin. During myeloscopy, these painful features often caused suspension of the procedure.

(d) *Blind compartmentalization of the ES forming obstructive barriers at different levels* (Fig. 2f). During myeloscopy, liquid distension of the sacral compartment caused the same pain distribution pattern of the pain usually experienced in 50% of patients. For this reason, we believe that the presence of abnormal structures in this compartment could account for some of the clinical features of these subjects. Pathologic fibrous elements and hyperemic tissues (Fig. 2g), indeed, were found at S1 level in 80% of patients; whereas complete stenosis of the epidural sacral space, at S3–S4 level, was found in 5% of the patients and was the reason for suspension of the procedure.

Subjective Evaluation

Compliance with the phone interview was good for every patient. A year after myeloscopy with resaflex, 59% of FBSS patients, and 67% of patients with stenosis reported a general improvement of their painful pathology (Fig. 3). Forty-eight percent of patients used minor analgesic for residual pain treatment, and 52% did not use any drug (Fig. 4a), 52% of patients agreed to undergo another myeloscopy in case that symptoms would reappear, 32% did not agree and 16% were undecided (Fig. 4b), pain reduction was more than or equal to 50 in 56% of patients, and less than 50 in 44% (Fig. 4c), 67% of patients went back to work, 26% did not go back to work, and seven were undecided (Fig. 4d).

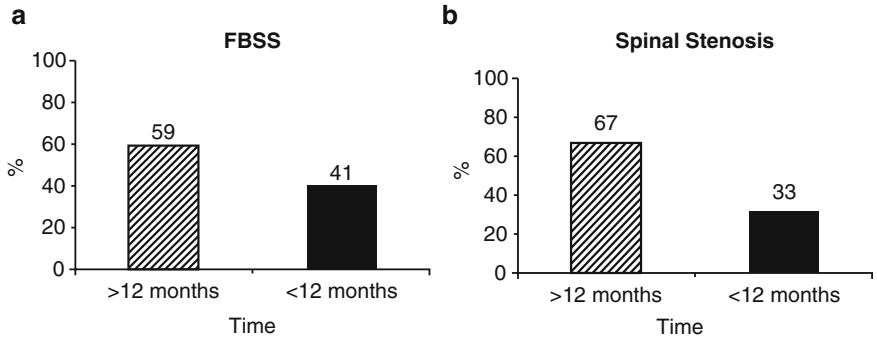

Fig. 3 Duration of pain relief in FBSS and stenosis patients. Fifty-nine percent of FBSS patients (**a**) and 67% of stenosis patients (**b**) had pain relief for more than 12 months, whereas 41% of FBSS patients (**a**) and 33% stenosis patients (**b**) had pain relief for less than 12 months after myeloscopy

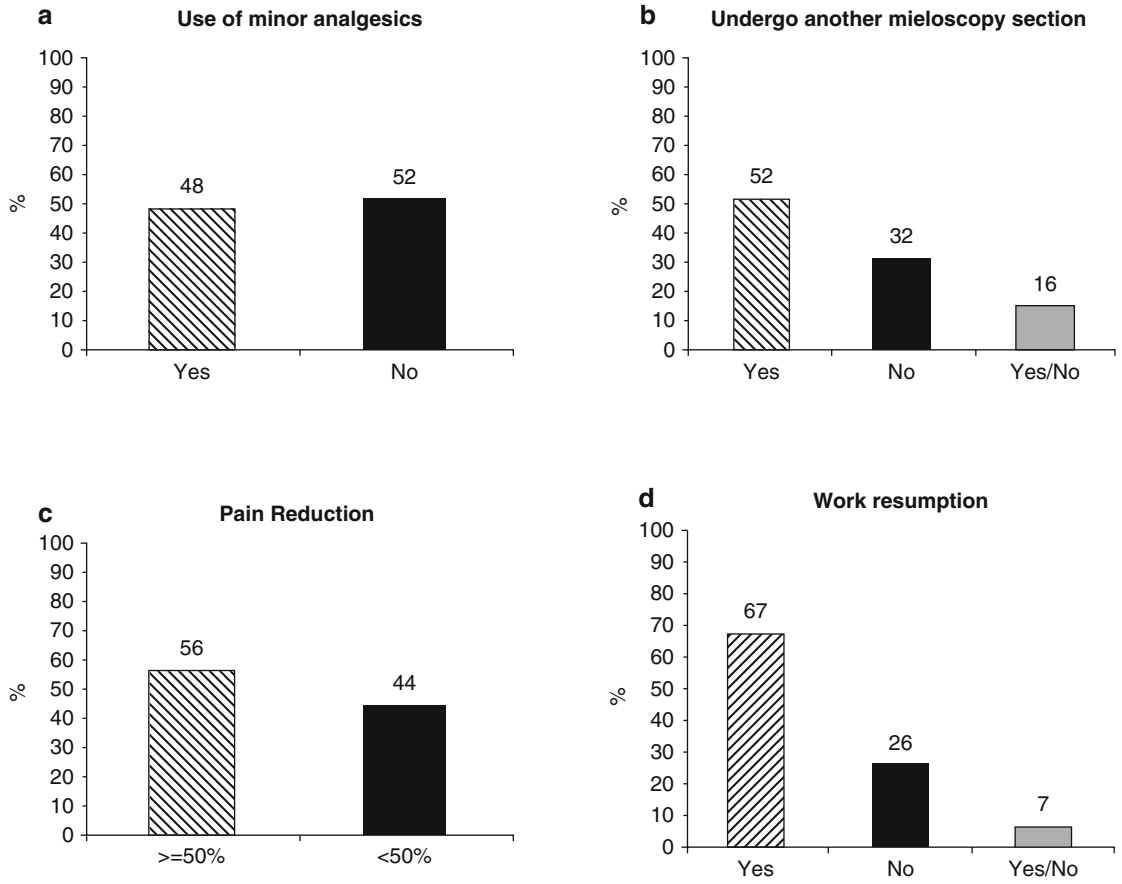

Fig. 4 Results of the phone interview with patients treated with myeloscopy. Forty-eight percent of patients used minor analgesic for pain treatment (**a**). Pain reduction was more than or equal to 50 in 56% of patients, and less than 50 in 44% (**c**). Fifty-two percent of patients agreed to undergo another myeloscopy in case symptoms would reappear (**b**), and 67% of patients went back to work (**d**)

Complications

We did not observe any long-term complications, whereas at short time we had few cases of irritations of the nerves if the canal was explored or the dura was damaged by mistake [16]. In a previous paper [12] we reported a case of air embolism following myeloscopy procedure; perioperative central and peripheral nerve irritation resolved promptly with no sequences.

Hence myeloscopy can be considered a feasible and safe method when: excessive fluid irrigation of the ES is avoided, directly perforating the dura (or indirectly by pulling or pushing rigid fibroid structures) is prevented, and patients' cervico-cranial discomfort is monitored. In agreement with Ruetten and colleagues we believe that major limitation of this technique was due to the obliged access port i.e. the hiatus sacralis. We have used [12] the lumbar interlaminar approach, which we suggest as a second choice when the sacral way is not available, because it is a longer and more invasive procedure. The advantages of the lumbar interlaminar approach on spinal pressures are not certain nor very much studied, as it is not known what is modified through cerebral flush during periduroscopy. Together with collogues at the Veterinary University of Teramo (Italy) we are studying the central cerebral pressure variation in animals (sheep) and the risk connected with the use of resaflex on dura and nerve roots; data are going to be published soon.

Discussion

Following lumbar spine surgery fibrotic tissue commonly replaces epidural fat, and large amounts of scar tissue surrounding nerve roots are found. Scares form as a result of nucleus pulposus extrusion, chronic chemical radiculitis, nerve root inflammation, and surgical bleeding from spinal surgery. Epidural scar tissue may compromise both blood supply and nutrition of nerve root and it may prevent the steroid solution from contacting the nerve root. The peridural scar, especially when extensive, has been considered

responsible for FBSS by several authors. Ross and coworkers [3, 19] report that increasing scar size corresponds to increasing likelihood of recurrent onset of radicular pain. Nevertheless, these authors admit that a scar does not always induce pain and that other factors may be involved. Indeed, although we cannot exclude scars playing a role in radicular pain in certain cases, we strongly believe that this fibrotic tissue, when present, cannot itself indicate an ongoing complex reactive and pain generating peridural phenomena. We believe that pain in FBSS and stenosis is caused by morphological alterations of the dura space. We think, in particular, that it is due to biochemical alterations of the circulation, and to the instability of the meninges traction, where the fibrosis is deeply adherent to the dura and the yellow ligaments. In our experience we found that when pain is caused by inflammation and neurochemical alterations [12–14, 16, 17], there can be benefits without the need to perform a complete lysis. When there is a microfibrosis, indeed, it can easily be removed with the Fogarty. On the contrary, when there is wide connective fibrosis, pain has a mechanical origin and it is responsive to opioid therapy.

Current therapy for FBSS patients can basically be grouped into four strategies. Surgical approach is reported to have low proportions of success in FBSS patients. Some authors report that repeated surgery in FBSS cases fails in 60% of cases, worsens the situation in 20% of cases and results in sufficient benefit in only 20% of cases. Fager [4] has shown similar results more recently. North and coworkers [7–9] also report low benefit from open surgical procedures. Therefore this approach is definitely not recommended, except when instability of the rachis is involved.

International literature reports good effectiveness in pain relief in FBSS patients with significant reductions of analgesics intake with Spinal Cord Stimulation (SCS). Yet, these data are not clear, because the reported percentage of pain relief is referred to patients already selected for their responsiveness to neuro-stimulation and not for the global FBSS population. The initial responsiveness percentages of FBSS patients are 45–55%, which is similar to that obtained with myeloscopy. SCS is a better method for longer pain relief whereas myeloscopy is less invasive than SCS. The two methods address different pain triggering mechanisms; this may explain why they have different response in FBSS. Pain of a primarily nociceptive nature, such as axial back pain, which we showed to be often associated with inflamed ES or with "dynamic instability" of the dura, responds better to myeloscopy. On the contrary, SCS may be more effective when neuropathic irritative pain is involved.

In this study, we confirm with a larger number of patients what we have previously reported [12]: no lumbar ES connective tissue septa exists, as it is described by Bloomberg [1, 2]. In agreement with other authors, we believe that these apparent septal aspects may correspond to abnormal postmortem phenomena and/or to an abnormal "sail-like" expression of the dura [14, 17].

Our findings also suggest that MRI-CT imaging cannot properly reveal every possible FBSS morphology. We showed that these conditions are complex, heterogeneous, and often are not formed by fibrosis alone. Many authors state that fibrosis contribute to pain in 24% of cases, whereas we believe that fibrosis is present in a larger sample of patients, and cause many morphologic alterations, such as vessel stasis and alterations of the dura pannus, resulting in painful pathologies. We also believe that fibrosis can cause instability with traction of meninges in 40–45% of cases, as it is shown in our results [17].

We have described various patterns of fibroid manifestations leading to a variable degree of ES stenosis or occlusion. The epidural structures which this fibrous tissue adheres to may determine different clinical manifestations. Bridles, adherences, organized or cotton-candy-like fibrous elements may adhere onto the dura or perineural structures. In this case flexion, traction or other dura strains (e.g. increased SCF pressure) may elicit pain. We have named this pathologic condition "dynamic instability." In contrast, fibrous adhesions onto inert elements elicit no pain and is called "stable stenosis." Dynamic instability and stable stenosis may coexist. In particular we have noted that in different patients, similar clinical patterns may be sustained by different morphologic impairments; conversely, similar degree of ES reduction may not always be correlated with same pain patterns. Moreover, following myeloscopy, pain relief has been gained without significant removal of epidural fibrosis.

These observations led us to hypothesize that fibrosis may induce pain in at least two different ways: by mechanical compression or inflammation of nervous structures entrapped within the fibroid tissue or by reducing the dynamic solicitations of the dura. The dura wraps dense, collagenous and elastic connective tissue, and for this reason is relatively elastic, freely compressible and mobile. Dynamic changes in dura shape or size are associated with CSF dislocations. Cough or Valsalvas' maneuver, for example, cause an immediate and significant collapse of the thoracic and lumbar dura pouch, with cephalic displacement of CSF. In the "dynamic instability" state, pathologic fibroid structures are anchored onto the dura and limit its ability to respond, even with physiologic solicitations. The dura is literally "frozen" and its natural elasticity and mobility are lost. Any force applied on it (traction or compression) is hence further transmitted and may reach perineural structures, interfere with nerve root nutrition and blood supply, and cause pain. Our findings show that this condition may be further complicated by the presence of local vascular stasis (bridles around vassals), hyperemia and aseptic inflammation. The latter along with local secretion of

pro-inflammatory compounds cannot but enhance nociceptive susceptibility of the "frozen" dura itself. It is obvious that the complex morphologic patterns described cannot be revealed by conventional though advanced indirect imaging technology. Our data show that myeloscopy can provide, along with pain relief, precious information both on the pathogenesis of FBSS and on therapeutic outcomes of spine surgery.

Conclusion

We have exhaustively reported pathologic morphological features in the ES of FBSS patients using the myeloscopy technique. This method enlightens pain-triggering mechanisms otherwise unrevealed. We proved that myeloscopy has specific therapeutic value, whereas on the diagnostic side it has not revealed relevant pathologies. In comparison to the classic resonance, the myeloscopy allow having a morphological sight, and justifies the onset of some painful pathology. It is also useful for the confirmation of the different pathological morphologies: adhesive fibrosis (prevalent in FBSS), and neuroinflammation (prevalent in stenosis).

As a therapeutic tool, it allows a better performance (a maneuver is possible in 35% of the cases), when a channel occlusion is present, it can improve the adherence lysis, and it is safe because it has no major complications. Its effectiveness in FBSS patients (prolonged benefit for over 2 years in some patients), moreover, is not inferior to that of other non-surgical techniques, with the advantage of its relatively easy implementation, limited invasiveness and repeatability. We strongly suggest not using Racz's technique, because the risks of lesions to spinal and vascular structures are too high, on the contrary we recommend myeloscopy as first procedural step in patients with persistent FBSS pain with no signs of instability of the posterior compartment. Given the variability of pathological features identified, the technique is essential for a morphological diagnosis. In FBSS patients, before programming subsequent surgeries, special care must be taken in studying the sacral compartment. It is also necessary to develop new dedicated instruments for myeloscopy and biochemical studies in situ in order to investigate which are the most favorable conditions for myeloscopy indication, and to understand how the different morphologies and scars are formed.

Conflict of interest statement We declare that we have no conflict of interest.

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The Effectiveness of Endoscopic Epidurolysis in Treatment of Degenerative Chronic Low Back Pain: A Prospective Analysis and Follow-up at 48 Months

A. Di Donato, C. Fontana, R. Pinto, D. Beltrutti, and G. Pinto

Abstract The aim of this prospective study was to evaluate the efficacy of endoscopic epidurolysis in the treatment of degenerative chronic low back pain.

Two hundred and thirty four patients affected by chronic low back pain, with VAS $\geq$ 5 and Oswestry Low Back Pain Disability Index (ODI) from 0 to 60% (0–20%, group A; 20–40%, group B; 40–60%, group C) were enrolled and treated prospectively with endoscopic epidurolysis by means of a flexible fiberoptic endoscope introduced into the caudal epidural space and by the intermittent instillation of saline solution added with 150 UI hyaluronidase. Targeted application of ozone (8 ml; 38 γ/ml) and 50 mg ciprofloxacin close to the abnormal areas was also performed. Short and long term efficacy (1 week, 3 months, 6, 12, 24, 36 and 48 months) was prospectively evaluated. VAS score $<$5 and ODI $<$40% were considered as a positive outcome.

The treatment significantly reduced VAS score in all three groups of patients starting from the first week and throughout the entire follow-up period ($P<0.001$). Disability Index (ODI) too showed encouraging results ($P<0.001$) that was particularly evident at 3 months and maintained up to long-term follow-up intervals.

Epiduroscopy by mechanical adhesiolysis and administration on targeted areas of ciprofloxacin and ozone seems to be, in this prospective study, an effective technique to provide a sensible and persisting pain relief and act of improving ODI in chronic low back pain.

A. Di Donato (✉) and C. Fontana
Pain Management Center, Concordia Hospital for Special Surgery, Via Città della Pieve N.19, 00191, Rome, Italy
e-mail: attilio.didonato@fastwebnet.it

R. Pinto and G. Pinto
Department of Anaesthesia and Resuscitation, "La Sapienza" University, Rome, Italy

D. Beltrutti
Pain Management Center, ASL 18, Alba, Bra, Italy

Keywords Chronic low back pain · Endoscopy · Epidurolysis · Epiduroscopy · Radiculopathy

Introduction

Epiduroscopy is a minimally-invasive percutaneous technique that permits direct endoscopic visualization of the epidural space and its delimiting anatomic structures under normal and pathologic conditions. The procedure can be considered a new tool for evaluation and therapy of selected patients affected with chronic, benign lumbosacral pain. The most common clinical conditions associated with chronic lumbar pain are FBSS, spondylolisthesis, stenosis and hernia, all of which are associated with radiculopathy [9, 15].

In the present study, epiduroscopy was performed in patients who did not respond to conservative treatment for at least 6 months (physiokinesitherapy, pharmacological treatment, epidurals with steroids, intraforaminal infiltration with steroids). Such degenerative pathologies are more frequent in older patients whose physical status is not always suitable for surgery, but for whom surgical intervention is indicated.

In this prospective study, we assessed changes in symptoms after epiduroscopic intervention involving mechanical removal of adherences and targeted administration of ozone, ciprofloxacin, and hyaluronidase in patients with spinal degenerative low back pain.

Methods

The study was conducted from December 2001 to December 2005 and involved 234 patients affected with lower back pain attributable to FBSS, spondylolisthesis, stenosis, or hernia were enrolled in this prospective study. All patients

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Table 1 Patients and percentage distribution

	n	%
VAS ≥ 5	234	100
ODI 0–20	44	18.8
ODI 20–40	97	41.5
ODI 40–60	93	39.7

failed conservative therapies lasting at least 6 months and who refused surgical lumbar fusion. All patients presented a VAS ≥ 5 with an Oswestry Low Back Pain Disability Index (ODI) between 0% and 60% (Table 1).

The average age of the patient cohort was 66 years.

Exclusion criteria: Patients with cauda equina syndrome, surgical intervention in the previous 6 months, opioid abuse or dependency, uncontrolled major depression or psychiatric disorders, chronic conditions that could interfere with the interpretation of the outcome assessments such as severe hip or knee arthritis, neuropathy, or other disorders, pregnant or lactating women, history of adverse reaction to local anesthetics, inability to understand the informed consent or protocol, or inability to be positioned in the prone position during the procedure were excluded from the study.

Short and long term efficacy (1 week and 3, 6, 12, 24, 36, 48 months) was prospectively evaluated by an independent certified physical therapist at follow-up interviews and clinical exams; pain scores were measured using a visual analog scale (VAS cm 1–10) [18] modified by the identification of three qualitative scores: very good (VAS 0–2), good (VAS 3–4); and not sufficient (VAS ≥ 5).

Disability was evaluated by the Oswestry Low Back Pain Disability Index (0 to 20%, minimal disability (Group A); 20 to 40%, moderate disability (Group B); 40 to 60%, severe disability (Group C); 60 to 80%, crippled; 80 to 100%, bed bound (or extremely severe symptoms). For the present study, a VAS <5 with an Oswestry Low Back Pain Disability Index (ODI) <40% was considered as a positive outcome.

The Oswestry Low Back Pain Disability Index was evaluated using a questionnaire containing six statements (denoted by the letters A through F) in each of ten sections. The sections probed pain, personal care, lifting, reading, driving, and recreation. For each section, subjects choose the statement that best described their status.

The statements were scored: statement A = 0; B = 1; C = 2; D = 3; E = 4; F = 5. The total scores ranged from 0 (highest level of function) to 50 (lowest level of function). To accommodate patients who did not respond to every section, clinicians could calculate a percentage of disability on the basis of the total possible points. Fairbank and colleagues [4, 5] interpreted the "percentage of disability" scores in the following manner:

0 to 20% – minimal disability
20 to 40% – moderate disability
40 to 60% – severe disability
60 to 80% – crippled
80 to 100% – bed bound or extremely severe symptoms

We have used the following formula in order to calculate the level of disability: point total/50 × 100 = % disability.

The study was approved by the local Ethics committee and informed written consent, describing the details of the trial, was obtained from all patients. Follow-up was evaluated using a clinic record table.

Technique

The patient was placed in a decubitus prone position with a spacer placed under the hips in order to straighten the lumbar vertebral column and render the patient more comfortable. The procedure was performed under local anesthesia with mild sedation. The sacral hiatus was identified using standard techniques with the aid of a fluoroscope in a latero-lateral view.

A sterile field was prepared using an adhesive drape to avoid interference of metal drape clamps with fluoroscopic imaging. The surrounding skin and sacral ligament was infiltrated with local anesthetic. A Tuohy 18 gauge needle was introduced into the sacral canal [14] under fluoroscopic guidance in a latero-lateral view and a J wire was inserted through the needle. Once the J wire was in place, the Tuohy was removed and the site of insertion was enlarged using a #11 scalpel to facilitate passage of the dilator and the endoscopic sheath. The dilator and endoscopic sheath were then introduced in the sacral region using circular movements under slight pressure. Once in the canal, the J wire and dilator were removed and the fiber optic (0.9 mm; 10,000 pixel) was introduced into the video guide in one entrance, while in the other a syringe was connected containing 20–30 ml 0.9% physiological solution. The first peridurogram (Fig. 1) [13] was taken under A-P and L-L fluoroscopic views administering around 8 ml of non-ionic contrast medium (Iopamiro 300 or 360 mg/ml) in order to identify scar tissue, areas of compression, and filling defects that could be targeted by epiduroscopy. Physiological solution was irrigated under pressure for short intervals to aid in leveling the epidural space. The maximum volume of physiological solution used was 200 ml (average 110 ml), which was always sufficient to finish the procedure within adequate safety margins. The saline solution contained 150 IU hyaluronidase to facilitate dissection of adherences and inflammatory tissue.

Complete 360° movement of the endoscope, irrigation of physiological solution, and the use of a grasper (1 mm diameter) permitted the mechanical removal of adherences thus mobilizing nerve roots which was evident by both direct

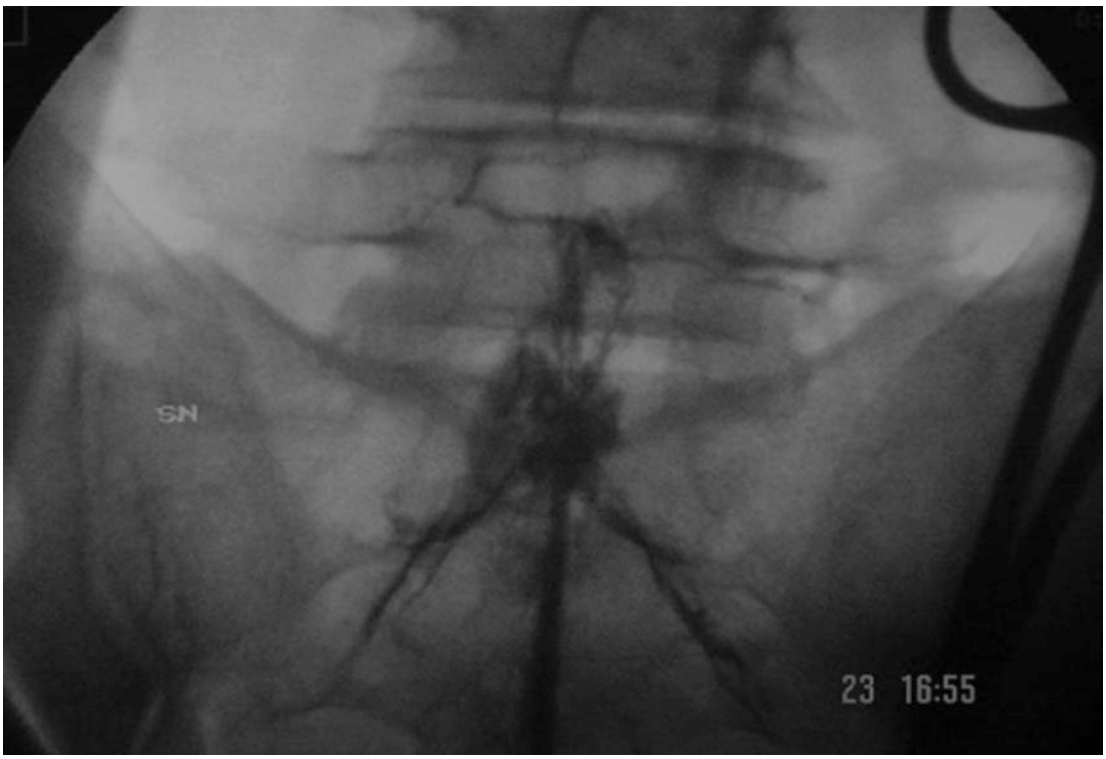

Fig. 1 First epidurogram: absence of contrast spread

observation and the final peridurogram performed at the end of the procedure using the same amount of contrast medium (Fig. 2). Under direct observation, ozone (8 ml; 38 γ/ml) was administered as an anti-inflammatory agent along with ciprofloxacin (50 mg) as an antibiotic to the pathological areas. At the end of the intervention, patients were kept in bed for at least 4 h and all patients were admitted to the hospital for a postoperative observation period of 24 h. Ciprofloxacin (500 mg/day) was given for 5 days following the intervention and celecoxib (200 mg) was given as needed for pain for 1 week. All patients were advised to wear an orthopedic corset for 2 weeks following the procedure.

Statistical Analysis

Statistical analysis was performed using STATISTICA 6.0 software (StatSoft Inc. 1984–2001). On the basis of the ODI score, we divided patients in three independent groups: A with a score of 0 to 20; B with a score of 21 to 40 and C with a score of 41 to 60. We compared the VAS and ODI baseline with the values shown after treatment and the duration of this effect by variance analysis for repeated measures. Newman-Keuls tests were used to determine the significant differences between groups.

Results

It was possible to introduce the endoscope via sacral access in all patients, permitting the precise identification of the origin of lumbar/radicular pain. Short term follow-up at 1 week demonstrated significant relief of pain (VAS) in all patients with an Oswestry Index <40% in 79% of cases. Follow-up at 3 months showed pain relief in 94% of patients with a positive Oswestry Index <40% in 82% of cases. At 6 months, 90% of patients had pain relief with a positive Oswestry Index <40% in 83% of cases. At longer follow-up times (12 months), there was significant pain relief in 74% of cases with an Oswestry Index <40% in 82% of patients. Follow-up at 18 months showed pain relief in 72% of patients and a positive Oswestry Index <40% in 81% of cases. At 24 months, 69% of cases still had significant relief of pain with an Oswestry Index <40% in 78% of patients. At the longest follow-up times of 3 and 4 years, 66% of cases had significant relief of pain with an Oswestry Index <40% in 78% of patients (Tables 2 and 3). The 46% of patients that did not have long-term pain relief went on to have surgical intervention.

As shown in Fig. 3, with respect to baseline values, the treatment significantly reduced the VAS in all three groups of patients starting from the first week ($P < 0.001$); Newman-Keuls test); this beneficial effect on pain lasted throughout

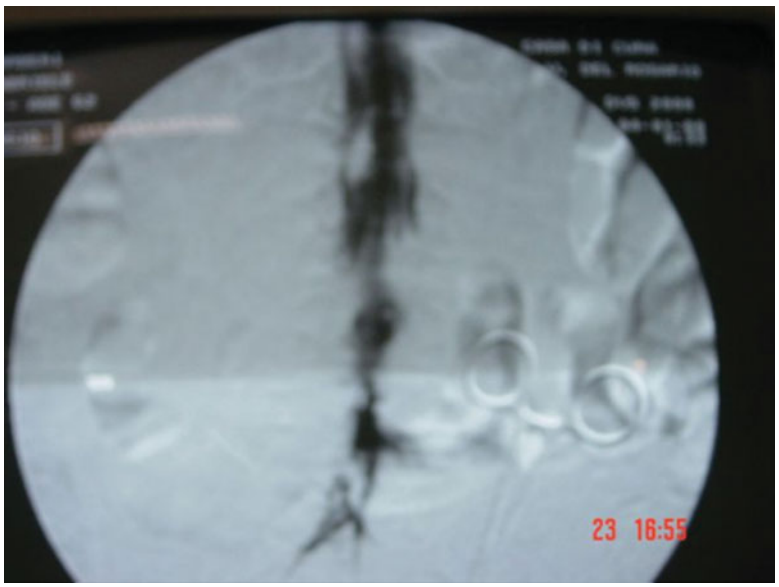

Fig. 2 Increase of contrast spread after endoscopic epidurolysis

Table 2 VAS percentage of positive results at follow up intervals

Follow-up	Positive results %	VAS 0–2	VAS 3–4	VAS ≥5
1 week	100	65	35	0
3 months	94	62	32	6
6 months	90	52	38	10
12 months	74	47	27	26
18 months	72	46	26	28
24 months	69	44	25	31
36 months	66	39	27	34
48 months	66	37	29	34

the entire follow-up period of 48 months ($P<0.001$; Newman-Keuls test). However, epiduroscopy did not have the same magnitude of pain relief in all three groups ($F_{2.231} = 99.09$; $P<0.01$). In particular, in group C, which at enrolment had an ODI between 41 and 60, a progressive increase in the VAS was observed starting from 3 months after intervention, even though it never reached baseline levels.

The changes in the ODI are shown in Fig. 4, in the three patient groups, which have different baseline values. Thus it is not possible to directly compare the three groups, although it can be seen that in groups B and C the treatment led to a statistically significant decrease in the ODI score with respect to baseline values ($P<0.001$; Newman-Keuls test), which after the first 3 months did not undergo significant variations. This trend was common to both groups and was time-dependent ($F_{7.1617} = 12.04$). Group A, which initially had lower ODI scores did not show any statistically significant variations, but did however show a significant decrease in the VAS.

Among the adverse effects encountered, 32 patients (13.7%) had temporary modifications in sacral pain lasting at least 2 weeks, which was related to prior stress of the hiatus and the small sacral canal. In 13 patients (5.5%) non-painful paresthesia was present involving the dermatomes of the nerve root that was subsequently subject to surgical intervention; the paresthesia resolved spontaneously within six days after the intervention. In 2 cases (0.85%), very painful paresthesia was present (VAS 9–10) with altered neurological transmission containing areas of hyper- and hypoesthesia. These two cases included a 34-year-old male with spondylolisthesis and adhering inflammatory tissue covering the root of L5 and a 63-year-old female with a large adherence due to scar tissue at the roots of L4 and L5. The paresthesia resolved spontaneously in both cases at 4 and 8 h after intervention without further sequalae. Accidental puncture of the dura did not occur in any case after passage through the subdural/subarachnoid space, and there were no retinic hemorrhages [18].

Discussion

Based on this prospective study, in chronic low back pain for degenerative disease with neurogenic claudication/radiculopathy, epiduroscopy by mechanical adhesiolysis and targeted administration of hyaluronidase, ciprofloxacin and ozone appears to be an effective technique in providing long term pain relief (an average of 66% at 36 and 48 months) and important decrease of patient's disabilities.

Specifically, in this study, the clinical efficacy of minimally invasive epiduroscopy was pointed out by a considerable improvement in pain relief as demonstrated by a statistically significant ($P<0.001$) VAS reduction from the first week lasting to long follow-up intervals. The Oswestry disability index also showed encouraging results with statistically significant improvements ($P<0.001$) for patients

Table 3 Oswestry disability index percentage of positive outcome at follow-up intervals

Follow-up	Positive results 0–40%	ODI (pz.) 0–20%	ODI (20–40%)	ODI (40–60%)	ODI (60–80%)	ODI (80–100%)
1 week	79	46	33	21	0	0
3 months	82	50	32	18	0	0
6 months	83	50	33	17	0	0
12 months	82	48	34	18	0	0
18 months	81	46	35	18	1	0
24 months	78	40	38	19	3	0
36 months	78	40	38	19	3	0
48 months	78	40	38	19	3	0

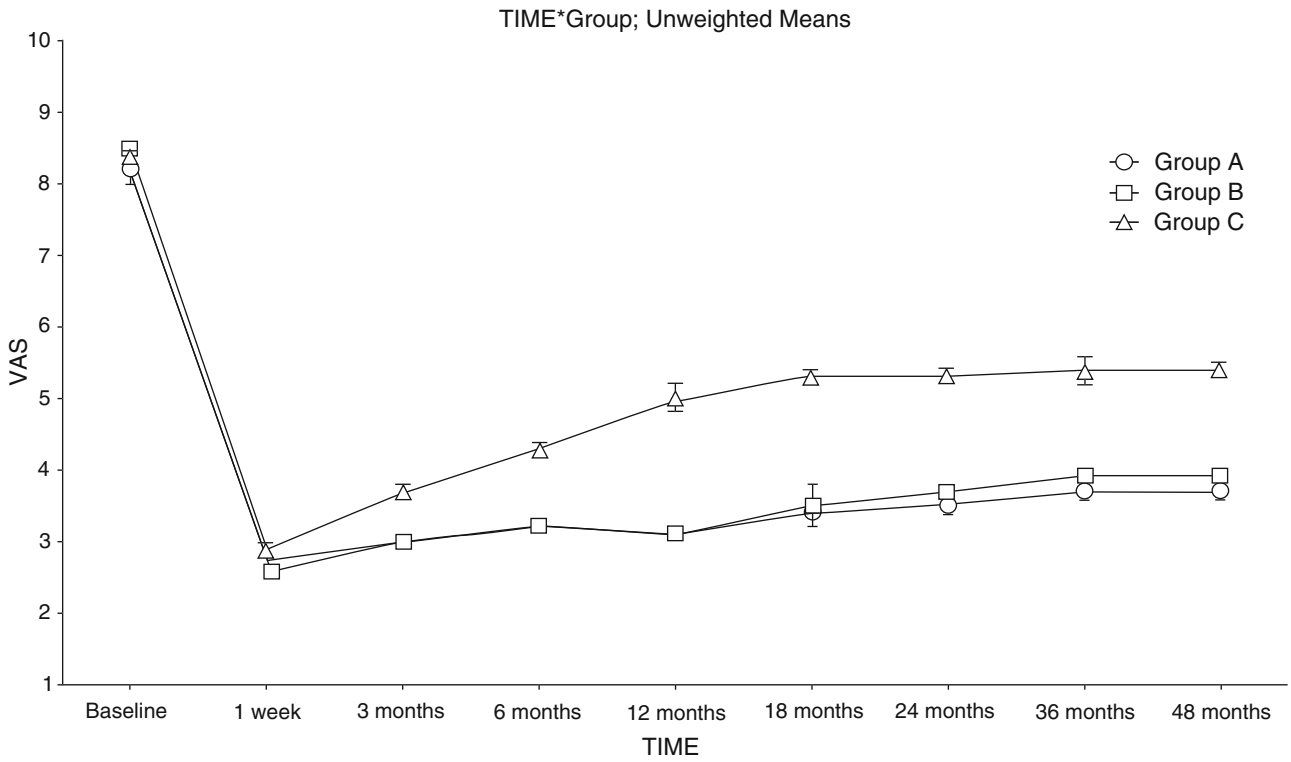

Fig. 3 VAS as function of the elapsed time after the treatment. From the second follow-up the difference between Group C and the others was statistically significant at Newman-Keul's Test ($P < 0.01$)

between 20% and 60% that were evident at 3 months and maintained at 24, 36 and 48 months.

In recent years, several studies have been reported regarding the clinical efficacy of epiduroscopy in treatment of vertebral pathologies. It is difficult to compare the results of these studies given their heterogeneous nature in terms of indications for therapy, surgical methods, co-administration of drugs, postoperative evaluation times, and outcome measures such as quality of life [6, 7, 12]. This is in addition to differences in randomization methods and the presence of a control group [3, 8]. In our study, we did not include a control group since due to the long period of observation and the clinical severity of the pathologies, this would not be acceptable from an ethical standpoint.

All patients had radiographic confirmation (epidurogram at the beginning of procedure) of a degenerative location and complained of neurogenic claudication or radiculopathy correlating with the level of the degenerative tissue present [13]. Moreover, mechanical stimulation of the nerve roots involved in the pathology reproduced the pain referred by the patient during clinical work-up. Direct visualization with fiber optics permitted examination of scar tissue, which was always present in patients with FBSS. Scar tissue and/or inflammatory fibrous tissue was present in the other pathologies examined. These tissues were found to adhere to the structures surrounding roots, were always easily recognizable, and were etiopathologically related to symptoms. The persistence of an inflammatory state associated with a

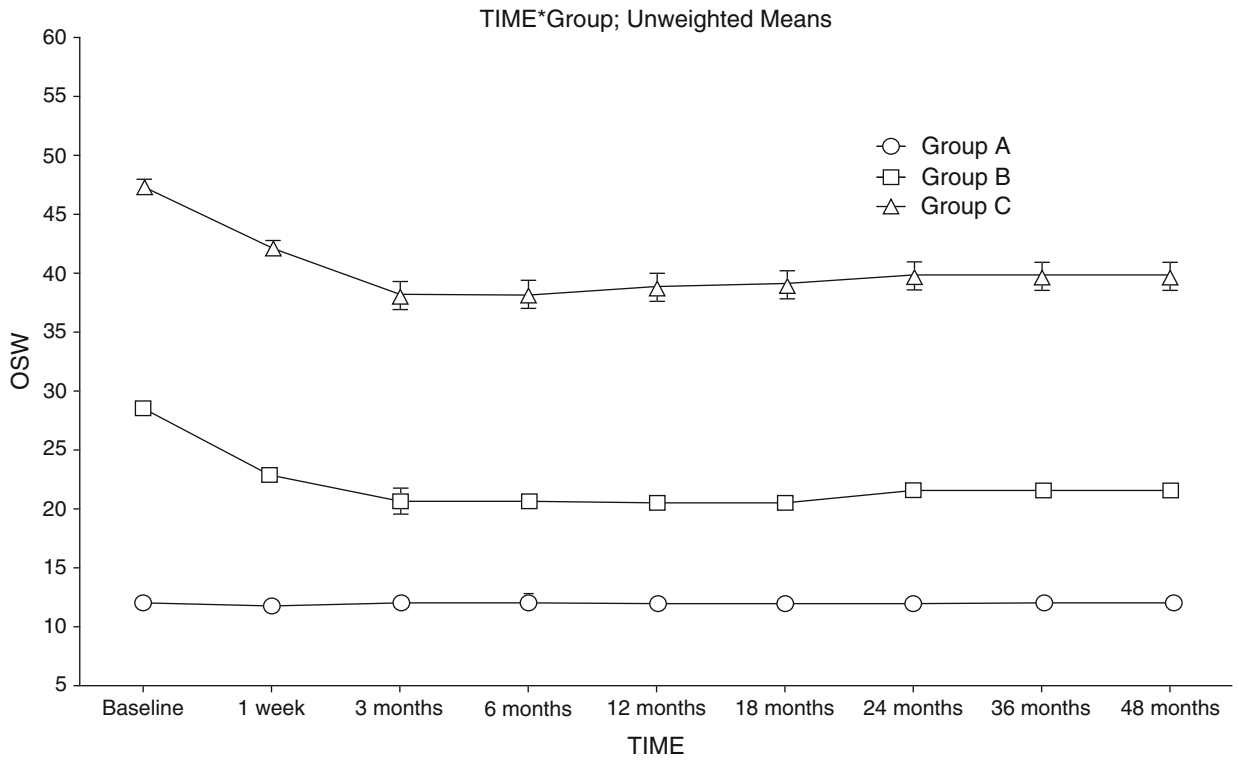

Fig. 4 OSW as function of the elapsed time after the treatment. The difference between the start condition and the next follow-up (from the second to the 48th month) was statistically significant at the Newman-Keul's Test ($P < 0.001$), for group B and C

reduction in fibrinolytic activity leads to the formation of fibrous adherences with ischemic damage to the nerve roots and consequent pain [6, 12, 16]. Using delicate endoscopic movements, the use of graspers through the operative canal, and irrigation using intermittent pulses of 0.9% physiological solution containing 150 IU hyaluronidase aided in separation of the adherences from the nervous structures and their removal. In all cases, endoscopic foraminotomy was performed in pathological areas to attempt to free the roots from eventual intraforaminal adhesions. Thus, recovery and/or the extent of pulsation of the dura could also be followed using peridurograms in addition to the resolution of filling deficits relative to the pathology.

In contrast to other studies in which corticosteroids were invariably used [6, 9, 10], in the present investigation the use of ozone under direct endoscopic visualization of the pathological areas is based on its capacity to normalize the levels of cytokines and prostaglandins [11] with a dramatic reduction in the formation of free radicals, favoring perineural circulation, with a consequent trophic effect on nerve roots [1, 2, 17].

Since the technique is minimally invasive, it can be repeated in case of partial therapeutic success and can even be used in patients with ASA III–IV, as it is performed under local anesthesia and mild sedation.

The technique is easily reproducible and is likely to be preferred by the patient for treatment of severe, chronic, incapacitating pain. We intentionally examined the outcome over a long follow up period, with a large number of patients to evaluate if the procedure can be considered a valid alternative to surgical approaches, and is safe and effective in the long term. The clinical results obtained and described before, offer a relevant confirmation of this purpose.

The technique was associated with a low number of complications, is relatively simple to perform, and does not require extended hospital admission. Thus, minimal work time is lost and the method is likely to be preferred by patients compared to traditional surgery. Based on these results, larger studies dividing patients into well established pathologies are merited, with the possible inclusion of a control group to identify the most suitable patients for the procedure, maybe in shorter observation period.

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Endoscopic Approaches to the Spinal Cord

Erich Talamoni Fonoff, William Omar Contreras Lopez, Ywzhe Sifuentes Almeida de Oliveira, Nilton Alves Lara, and Manoel Jacobsen Teixeira

Abstract Minimally invasive procedures have been used to treat various diseases in medicine. Great improvements in these techniques have provided intraventricular, transnasal and more recently cisternal intracranial accesses used to treat different conditions. Endoscopic approaches have been proposed for the treatment of disk herniation or degenerative disease of the spine with great progress in the recent years. However the spinal cord has not yet been reached by video-assisted procedures. This article describes our recent experience in procedures to approach the spinal cord itself in order to provide either diagnosis by tissue biopsies or inducing radiofrequency spinal ablation to treat chronic pain syndromes. We describe three different approaches proposed to provide access to the entire length of the spinal canal from the cranium–cervical transition, cervico-thoracic canal (spinal cord and radiculi) to the lumbar-sacral intraraquidian structures (conus medularis and sacral roots). We idealized the use of endoscopy to assist cervical anterolateral cordotomies and trigeminal nucleotractotomies, avoiding the use of contrast medium as well as vascular injuries and consequent unpredictable neurological deficits. This technique can also provide minimally invasive procedures to possibly treat spasticity through selective rhizotomies, assist catheter placements in the lumbar canal or debridation of adherences in cystic syringomyelia and arachnoid cysts, providing normalization of CSF flow.

Keywords Cordotomies · Endoscopy · Rhizotomies · Spinal cord

Introduction

The initial evolution of minimally invasive spine surgery dates from the 1929 report by Dandy, in which he "described removal of loose cartilage from the intervertebral disc" [1]. In 1931, Burman [2] introduced the concept of myeloscopy for direct spinal cord observation. It was in 1942 that Pool [3] introduced the concept of intrathecal endoscopy for direct visualization of structures in the spinal canal. However the myeloscopic method did not prove to be actually useful and was abandoned because of the morbidity associated with insertion of a large-bore scope into the spinal cavity. This method remained essentially untouched until Ooi et al. [4] used an endoscope to examine the intrathecal space before surgery. Currently, the use of spinal endoscopy is restricted to the documentation of pathological features of the spine, documentation of decompression of structures, direct nerve inspection, inspection of internal fixation, and delivery of therapeutic agents in the epidural compartment. The current uses of spinal endoscopy have been expanded to include epidural decompression of spinal roots with the use of high intensity laser, epidural biopsies, percutaneous interbody fusion, and decompression of thoracic disc herniations. Spinal endoscopy has been used to perform, for example, thoracoscopy-assisted discectomies, correction of kyphosis, biopsies, drainage of epidural abscesses, and disc space fusion.

In 1974, Olinger and Ohlhaber developed a slim fiberoptic needle endoscope small enough to pass through a 17-gauge spinal needle [5]. Olinger and Ohlhaber proposed that their endoscopic needle could be used for such operations as cordotomy and rhizotomy, permitting direct vision through limited exposures, but they did not actually perform spinal procedures.

E.T. Fonoff (✉), W.O.C. Lopez, Y.S.A. de Oliveira, N.A. Lara, and M.J. Teixeira
Division of Functional Neurosurgery, Department of Neurology of School of Medicine of University of São Paulo, Rua Dr. Ovídio Pires de Campos, 785, São Paulo 01060-970, Brazil
e-mail: fonoffet@usp.br

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Technical Description

Approach to the Craniocervical Transition

Stereotactic posterolateral approach to dorsolateral medulla: Technique for Percutaneous Radiofrequency Endoscopic Guided Trigeminal Nucleotractotomy.

Indications

- Painful anesthesia
- Atypical facial pain
- Postherpetic neuralgia
- Facial pain in Wallemberg's syndrome
- Pain caused by cranioorofacial malignancies

The medulla carries the pain-transmitting nerve fibers and relay neurons related to the processing of cranio-orofacial pain [6], being a key area of the central nervous system for pain surgery.

Trigeminal tractotomy, trigeminal nucleotomy, and nucleus caudalis dorsal root entry zone (DREZ) lesioning have been described as percutaneous or open techniques to destroy centrally the nociceptive fibers from the fifth, seventh, ninth, and tenth cranial nerves or their nuclear relay neurons [7, 8].

For many years, surgical interruption of the trigeminal descending tract was performed using open techniques. Despite their efficacy, mainly in patients with nociceptive pain, the original trigeminal tractotomies present many disadvantages, because they are not efficient in cases of deafferentation pain, nor applicable in poor clinical status high-risk individuals, because they are made under general anesthesia, which also precludes cooperation of the patients during the procedure or monitoring of their neurophysiologic functions, consequentially presents high cost and high complication rate.

The new surgical methods, aiming at the destruction of the trigeminal nuclear cells and not just the trigeminal tract, and the improvement of the classical procedures prompted neurosurgeons to develop less-invasive techniques using percutaneous blind approaches, incurring in less neurological deficits, but still hemorrhage remained a problem related to vascular injury by the operative instruments (Fig. 1).

The videoscopic assisted procedure prevents such complications because it adds a close visualization of the operative field avoiding the contact of the sharp electrode tip with blood vessels. It is possible to clearly visualize the medulla itself, amigdala of cerebellum, cranial and spinal nerve rootlets, arachnoid trabeculi, loops of posterior inferior cerebellar artery and internal face of dura mater.

Positioning and Skin Incision

The patient is awake and placed comfortably in lateral position with flexion of the neck/head over the chest. Only local anesthetics are injected in the site of the skin puncture. There is no skin incision.

Surgical Technique

Detailed stereotactic programming of the procedure is essential for a good target. StereoCT of the head and craniocervical transition is obtained with the frame fixed to the head. The CT images are reconstructed and fused to the volumetric MRI of the encephalon including C2 level. The target in the postero-lateral medulla is determined by measurements (3–5 mm lateral to the midline) in the stereotactic computer system. The radiofrequency (RF) probe and the endoscope trajectories are oriented 30–50° angle laterally between C1 and occipital bone edge on foramen magnum (Fig. 2a, b). The cistern magna provides fairly wide space for the endoscope and the RF electrode. The ablative procedure is performed after careful electrophysiological/stimulation mapping for target refinement avoiding superfluous lesion, consequently minimizing undesired neurological deficits [8]. Additional electrical impedance measurements provide information if the penetrating electrode is in contact to the white (tract) or gray (nucleus) matter of the medulla. This technique allows the procedure to be X-ray and contrast free.

Pitfalls, Pearls, Considerations

- Trigeminal tractotomy is very effective in patients with craniofacial cancer pain, even when the pain is present in the sensory areas of the seventh, ninth, and tenth cranial nerves.
- The improvement rate expected with the procedure is of 80% [7, 8].
- The results of the treatment in cases of atypical facial pain are disappointing [7].
- If pain recurs the procedure can be repeated later.
- Postoperative ipsilateral ataxia related to spinal-cerebellar tract trespassing occurs frequently, but usually is transient [7, 8].
- Contralateral thermoanalgesia is observed in 25–33% of the patients [8, 9].
- Dysarthria and Horner's syndrome are rare.
- Fever is common when radio-opaque contrast media is injected [10].

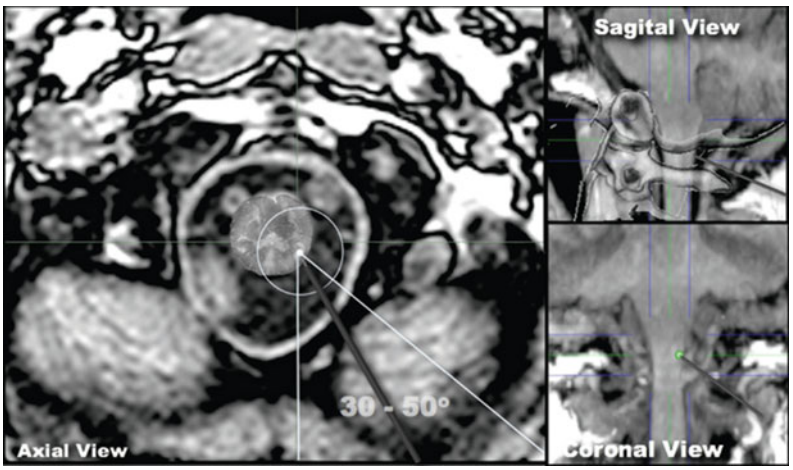

Fig. 1 Representation of the computer templates of a stereoCT/MRI fusion and illustrative histological section of the distal medulla for a stereotactic guided trigeminal nucleotractotomy. T1-weighted images and CT fusion show the safe angle and trajectory of the guide cannula for either the RF electrode or the fine endoscope in axial, sagittal, and coronal view

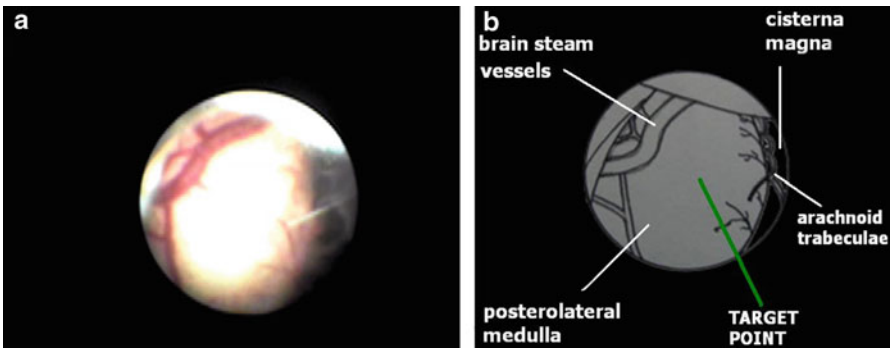

Fig. 2 (**a**) Endoscopic view of postero-lateral aspects of the medulla (distal brainstem), cisterna magna and the cerebellar amygdala. The target point for penetration in the RF probe is shown in *right* in front. (**b**) Illustration and structure labels and the target point for the radiofrequency electrode penetration

Approach to the Upper Cervical Spinal Cord (Atlas–Axial Access)

Endoscopic guided lateral approach to the spinal cord: Technique for Percutaneous Radiofrequency Anterolateral Cordotomy

Indications

- Unilateral intractable pain related to advanced cancer in lower body.
- Bilateral intractable pain may also be well treated by dual and staged procedure.

Recent evolution of general oncology has provided longer survival rates to cancer patients, though increasing their exposure to the development of various pain syndromes often resistant to medication or to opioid infusion pumps. Although not many pain centers propose functional ablative procedures, in our experience they are still needed for the palliative control of pain syndromes in selected patients. Procedures as percutaneous anterolateral cordotomy are currently performed under indirect visualization by X ray (fluoroscopy or CT) guidance requiring intrathecal contrast injection [17]. To visualize the spinal cord, a myelography is performed before a lesion-electrode is introduced; for technical reasons, oily contrast media is used. However, these contrast media are no longer in use for conventional diagnostic myelographies because they are known to cause adhesive arachnoiditis [11] with disastrous neurological consequences. We propose in this report a new technique of percutaneous cordotomy under videoscopy guidance that provides a closer look at the anatomical landmarks in the upper spinal canal and neural structures in spinal cord vicinity, avoiding intrathecal contrast with all its risks and vascular injuries.

Positioning and Skin Incision

We employ the technique described by Rosomoff [12, 13] with some modifications. The patient is placed in the supine position and the head is secured in the Rosomoff head holder with a slight flexion of the neck.

Surgical Technique

The operation is carried out under local anesthesia and light sedation. The patient must be sufficiently responsive and cooperative during sensory testing in the eletrostimulation mapping later in the procedure. Preliminary fluoroscopy (Fig. 3b) guides the location of the local anesthetic injection and the skin puncture which is around 1 cm below and distal to the mastoid process (Fig. 3a) directing to the anterior–lateral aspects of the spinal canal in the atlas–axis (Cl–C2) interspace. A thin cannula (17-gauge) is inserted perpendicularly and its direction is monitored by fluoroscopy and the CSF leak confirms the intrathecal space.

A thin endoscope (0.9 mm) is inserted through the 17-gauge cannula allowing direct identification of the dentate ligament (Fig. 4a), the lateral aspects of spinal cord, the nerve rootlets, the arachnoid membrane and the blood vessels (Figs. 4–6). The RF electrode is inserted into the lateral aspect of spinal cord between the dentate ligament and the anterolateral sulcus of the cord identified by the emergence of the spinal rootlets (Fig. 4a, b). The exact spinal target is finely asserted by the electrostimulation mapping. The patient must refer the sensation of the stimulus on the region affected by the pain, contralateral to the puncture side. The topography of the spinothalamic tract is finely studied during this procedure to observe the medio-lateral orientation of the representation of the upper and lower body (Fig. 7). When the right target is obtained, a restricted thermal ablation of the tract is performed. Pinprick sensation is tested in the body after each ablation and additional lesions may be performed according to the functional results of pinprick and thermal analgesia. Immediate and sustained pain relief is often obtained right after the procedure.

Pitfalls, Pearls, Considerations

- The endoscopic approach may eventually be limited by a narrow spinal canal, constitutional or epidural infiltration by neoplastic disease. This narrowness of the vertebral canal [3], may restrict the distance between the spinal cord and the dura (<1 mm) preventing endoscopic view.

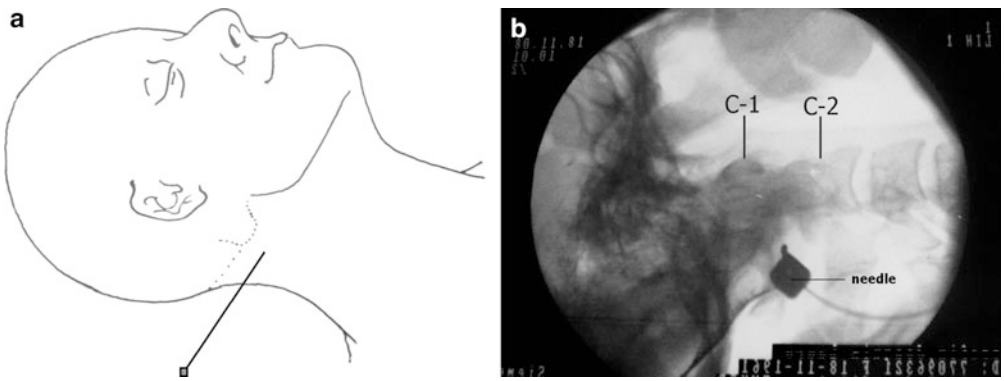

Fig. 3 (**a**) Positioning for cordotomy and the site of puncture. (**b**) Fluoroscopic lateral view of the atlas–axis interspace and the guided cannula (needle) inserted into the intrathecal space

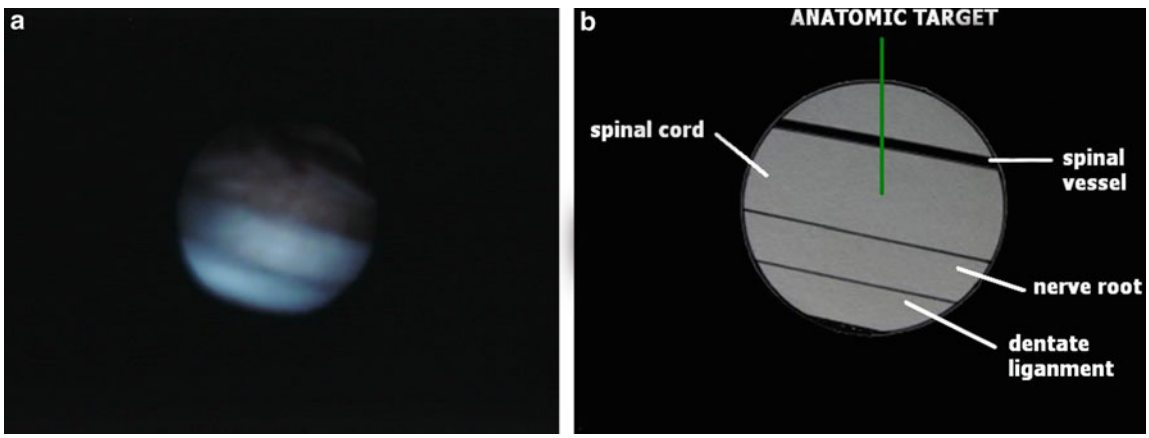

Fig. 4 (**a**) Endoscopic view of the target point of penetration in the pial surface of spinal cord nerve root and dentate ligament. (**b**) Illustration and structure labels

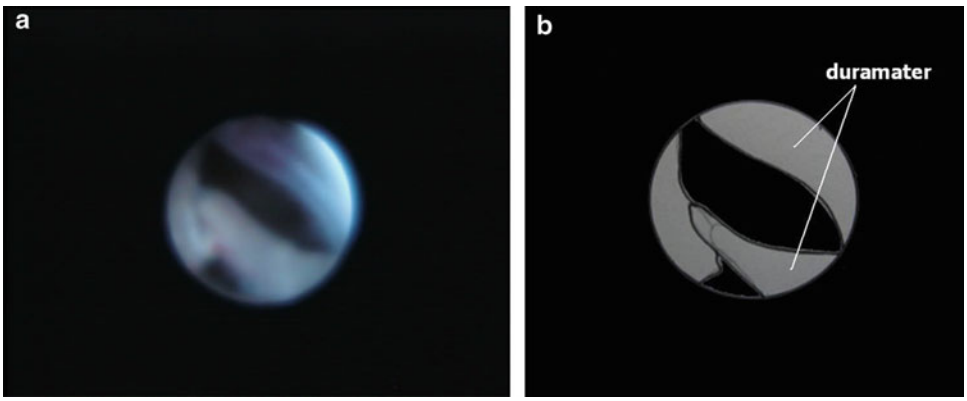

Fig. 5 (**a**) Endoscopic view of dural opening from epidural space. (**b**) Illustration and structure labels

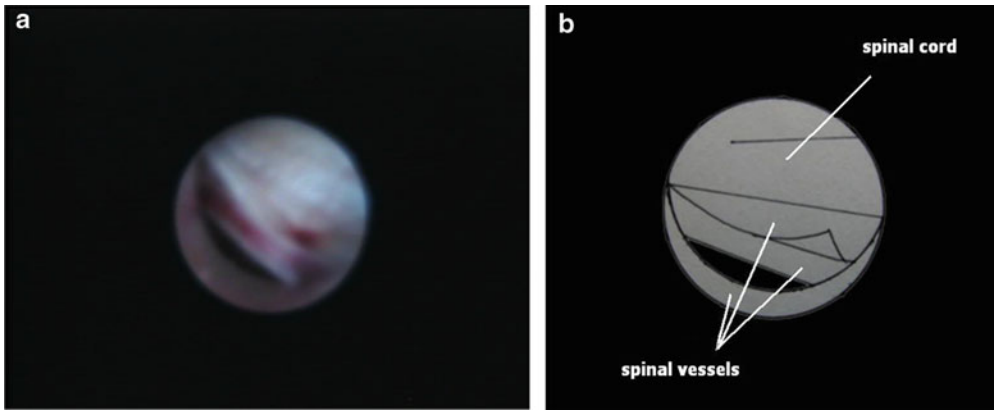

Fig. 6 (**a**) Endoscopic view of the spinal cord, rootlets and radicular vessels through the clear cerebral spinal fluid during an endoscopic cordotomy. (**b**) Illustration and structure labels

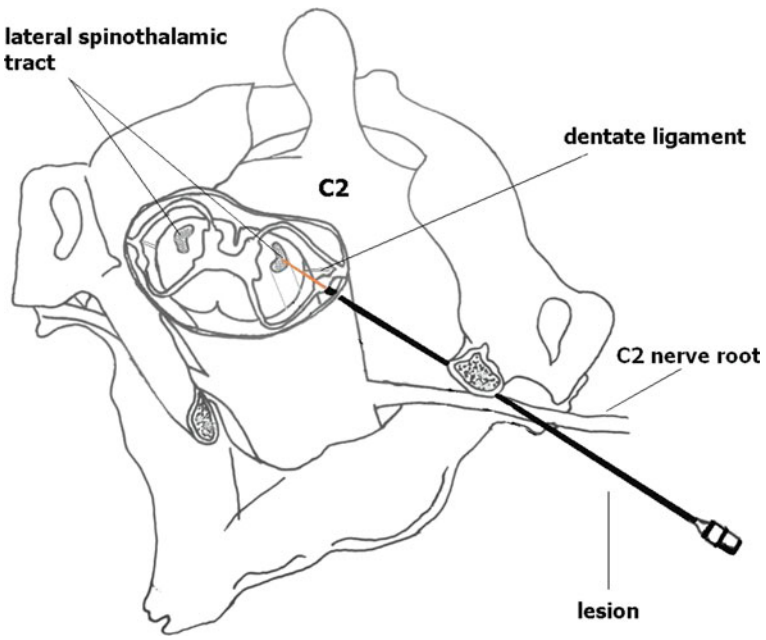

Fig. 7 Illustration of guide cannula (endoscope) trajectory penetrating the *dura* and the electrode towards the spinal cord aiming at the spinothalamic tract

- Bilateral and midline pain, except when it is predominantly lateralized to one side, requires bilateral cordotomy.
- Mild headache and neck discomfort lasting one or two days usually happen.
- Horner's syndrome on the same side and spinal cord ablation confirms that the procedure was accomplished and it is often not noticed by the patient [14–16].
- The patients should be warned that transient ataxia may develop on the side of lesion and cautioned regarding the expected skin thermoanalgesia.
- Urinary disturbances and muscles weakness may occur very seldom and are usually transient.

Approach to the Cervico-Thoracic Region of Spine

Endoscopic guided posterolateral approach to the cervical and thoracic spinal cord and lesions of the spinal canal: Technique of Posterior Translaminar Approach to Spinal Cord Biopsy and Endoscopic Dorsal Rhizotomy.

Indications

- Undiagnosed lesions of spinal cord and canal from the cervical to thoracic spine.
- Severe and intractable spasticity in the lower limbs and neurogenic bladder.

Positioning and Skin Incision

The patient is placed in prone position, a small incision (3 cm) is made two levels below or above the interested site, and a partial hemilaminectomy is performed preserving the intra- and supraspinal ligaments. Another puncture below or above the primary incision is required to insert the endoscope through dilatation (2 mm). (Figs. 8–10)

Surgical Technique

After the restricted hemilaminectomy, the dura mater is opened (2 mm) allowing the flexible endoscope to enter the intrathecal space. The access is intended to be two levels below or above in order to permit best mobilization of the endoscope inside the dural space. Aspiration and irrigation is

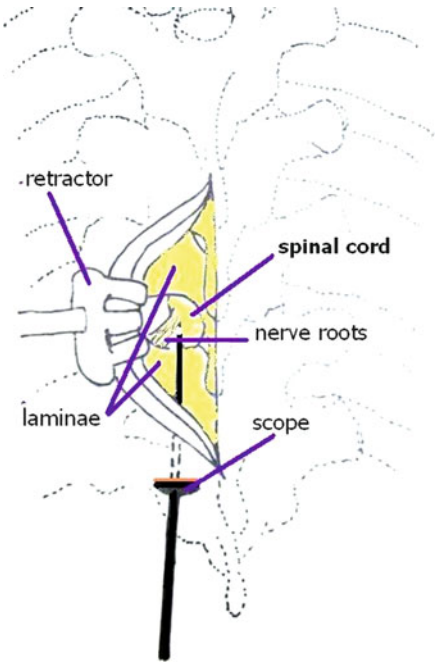

Fig. 8 Illustration of the skin incision, hemilaminectomy and dural opening. The endoscope penetrates the skin through a puncture 3–4 cm from the main incision. This method allows the endoscope to enter the spinal canal through a wide-open angle, providing a smooth progress and easier mobilization of the directional endoscope tip

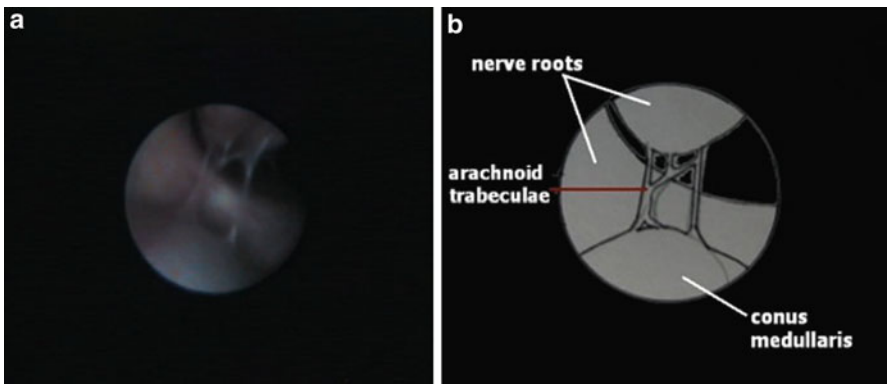

Fig. 9 (**a**) Endoscopic view of the *conus medullaris*, nerve roots and arachnoid trabeculae. (**b**) Illustration and structure labels

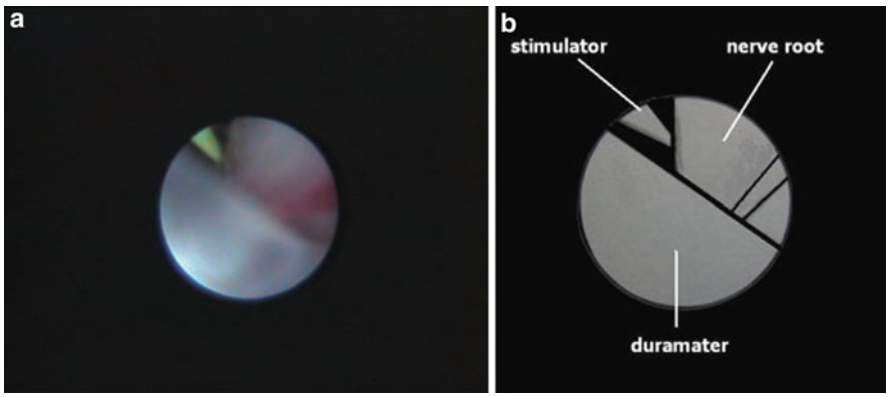

Fig. 10 (**a**) Endoscopic view of the nerve roots and stimulating electrode during a selective rhizotomy for the treatment of spasticity. (**b**) Illustration and structure labels

needed in order to provide clear vision of neural structure within the CSF.

Diagnostic procedures including tissue biopsy require that a punch forceps is introduced through one of the endoscope channels, while the other is used for fiber optics for illumination and visualization. Small tissue samples (<3 mm) are collected under direct visualization of the intended target, by a very delicate forceps. As the volume of tissue fragments is very small, a representative sample may require many of them to provide good material for histological diagnosis.

Selective dorsal rhizotomy for treatment of spasticity may also be performed assisted by endoscopic method. However, special instruments are required, as isolated electrodes for electrical stimulation testing and radiofrequency selective ablation of nerve rootlets (Fig. 10a) as well as delicate seizers for sharp dissection and cuts. The electrophysiological testing is very important for a good outcome and what makes the procedure selective. The endoscopy may reproduce the same procedure performed under microscopic assistance; however it requires other skills, techniques and different instruments.

Approach to the Lumbar Spinal Canal (Intrathecal Space)

Percutaneous endoscopic guided posterior interlaminar approach to the spinal cord, conus medullaris and lumbosacral roots: Technique of approach to Spinal Cord Biopsy and Endoscopic Dorsal Rhizotomy.

Indications

- Undiagnosed lesions of spinal cord, conus medullaris and lesions in the spinal canal and intrathecal space in the lumbo-sacral spine.

Positioning and Skin Incision

The patient is placed in prone position. Under fluoroscopic view, a regular interlaminar puncture with a 17 gauge needle providing access to the intrathecal space.

Surgical Technique

After the needle was introduced into the interlaminar space in the desired lumbar level, reaching the CSF. In order to maintain the canulation of the same space, a 0.8-mm blunt guide wire is then inserted through the needle under fluoroscopic guidance. This operation is potentially morbid to the sacral nerve root, so the surgeon must be very gentle in this introduction. The guide wire must not be advanced more than 1 cm. Using the Seldinger technique, the 4-mm (8.5 F) introducer with a dilator is introduced over the guide wire into the sacral epidural space. After removal of the dilator and the guide wire, a 2.7-mm endoscope containing two channels (fiber optics and a work channel) is introduced into the intrathecal space through a coated introducer. Now under endoscopic visualization (Fig. 11a, b) the endoscope is gently steered and advanced in a cephalic direction (Fig. 12a, b). Fluoroscopic visualization localizes the tip of the endoscope according to the spinal level and the latero-lateral position within the canal. In order to obtain a good visual field, aspiration and saline irrigation is continually made during the procedure. Tissue biopsy is performed by a fine punch forceps which is introduced through one of the endoscope channels, while the other is used for fiber optics for illumination and visualization. Small tissue samples (<3 mm) are collected under direct visualization of the intended target, by a very delicate forceps (Figs. 13a, b, 14a, b). No dural closing technique seems to be required for these procedures. None of the patients in this initial experience had CSF leak or postural cephalgia (Table 1).

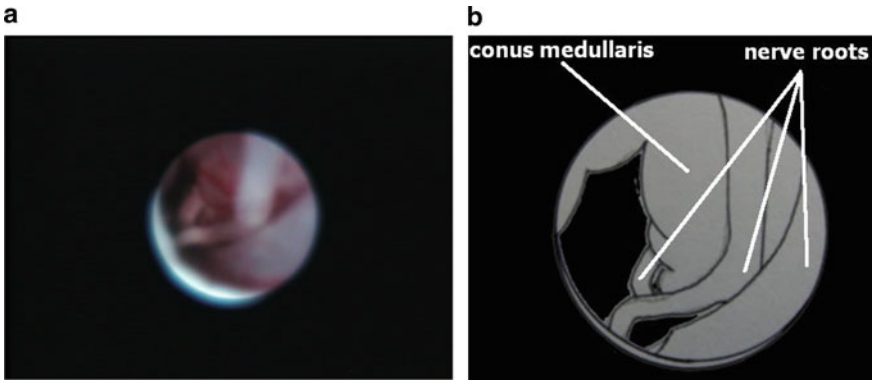

Fig. 11 (**a**) Panoramic view of the conus medullaris and nerve roots. (**b**) Illustration and structure labels

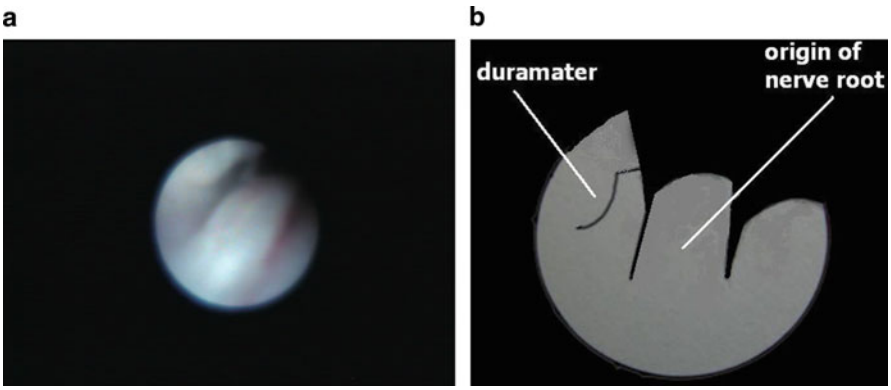

Fig. 12 (**a**) Endoscopic view of the origin of L5 nerve root in the spinal cord. (**b**) Illustration and structure labels

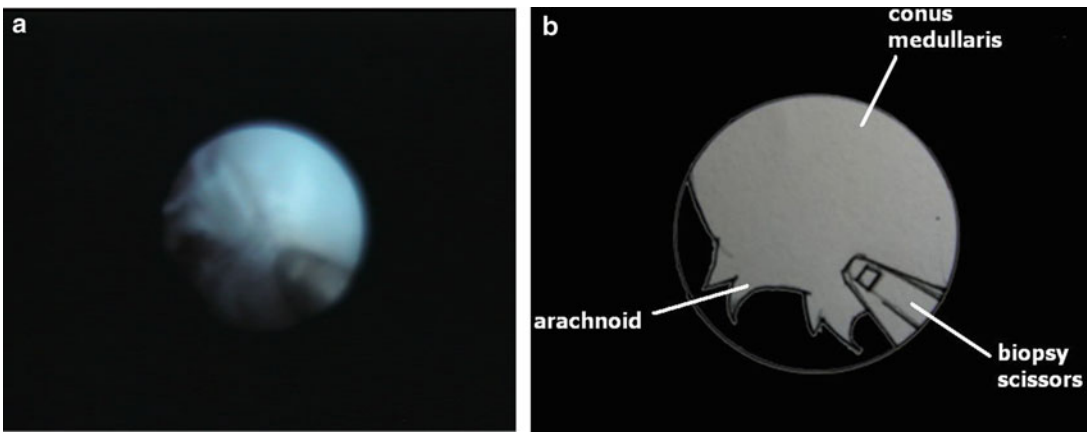

Fig. 13 (**a**) Endoscopic view of the conus medullaris and the site for the intended biopsy and the punch forceps. (**b**) Illustration and structure labels

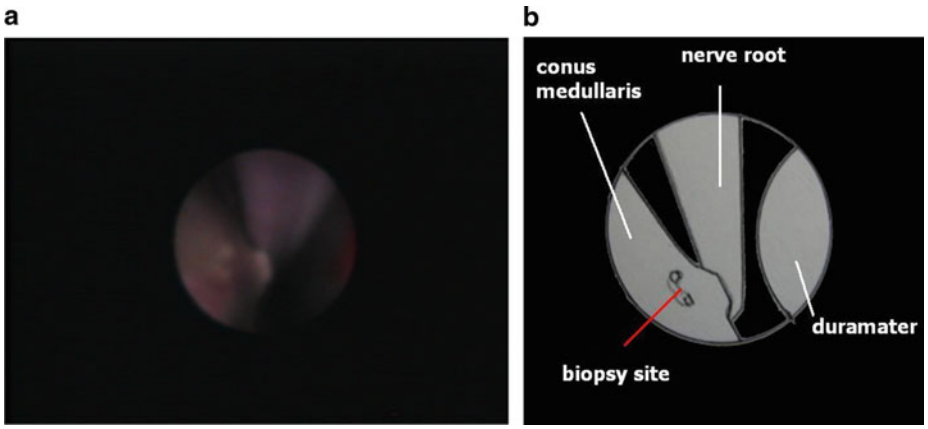

Fig. 14 (**a**) Endoscopic view of the conus medullaris and the biopsied site in a case of intraspinal schistossomiasis. (**b**) Illustration and structure labels

Table 1 Series of patients submitted to spinal cord and spinal canal endoscopic procedure. in cases *F* – Female *M* – Male

Patient	Age	Procedure	Etiology	Surgical access	Intraoperative observation	Outcome
1M	55	Therapeutic (Endoscopic Cordotomy)	Intractable oncologic chest pain in the right side. Lung carcinoma	Percutaneous endoscopic cordotomy C1–C2 with 17G needle in the left side	Endoscopic visualization clear spinal cord and dentate ligament	Satisfactory control of pain
2M	56	Therapeutic (Endoscopic Cordotomy)	Itractable oncologic chest pain in the left side. Lung carcinoma	Percutaneous endoscopic cordotomy C1–C2 with 17G needle in the right side	Viewed spinal cord, dentate ligament, spinal roots. Cordotomy was made with improvement of pain	Satisfactory control of pain
3F	19	Diagnostic (Spinal Cord Biopsy)	Pain in lower limbs and progressive crural paraparesis. Injuries uncertain in T3	T7 median incision of 3 cm size guided by radioscopy. Entry of the endoscope until T3, where the biopsy was performed	Clear visualization of the target for biopsy, avoiding spinal vessels	No CSF fistula No neurological complications Diagnosis: high-grade spinal cord glioma
4F	47	Diagnostic (Endoscopic Inspection)	Weakness in left lower limb. Epidural uncertain injury in L4–L5–S1	Percutaneous access through the sacral hiatus. Entry of the endoscope until L5–S1 where the biopsy was performed	Fibrous lesion made difficult providing satisfactory fragments for diagnosis	Fibrous tissue with Inconclusive biopsy. No fistula or postural cephalalgia
5M	45	Diagnostic (Spinal Cord Biopsy)	Lower limb paresis and pain. Spinal cord herniation in T3–T4?	T7 median incision of 3 cm size guided by radioscopy. Entry of the endoscope until T3, where the biopsy was performed	Visualization and confirmation of the diagnosis of spinal cord herniation	No fistula or postural cephalalgia. No changes in neurological status
6M	47	Therapeutic (Endoscopic Cordotomy)	Oncologic pain in left lower limb. Carcinoma of the prostate	Percutaneous endoscopic cordotomy C1–C2 with 17G needle in the right side	Viewed spinal cord, dentate ligament, spinal roots	Satisfactory control of pain
7M	43	Therapeutic (Endoscopic Cordotomy)	Oncologic pain in left upper limb. Multiple squamous cell carcinoma	Percutaneous endoscopic cordotomy C1–C2 with 17G needle in the right side	Viewed spinal cord, dentate ligament, spinal roots. Cordotomy was made with improvement of pain	Ataxia in left upper and lower limbs that improved in a few days
8F	33	Diagnostic (Spinal Cord Biopsy)	Crural paraparesis and neurogenic bladder. Injuries uncertain in L1–L2	Percutaneous access through the sacral hiatus. Entry of the endoscope until L1–L2 where the biopsy was performed	Enlarged spinal cord diameter. Clear visualization of the target for biopsy, avoiding spinal vessels	No fistula or postural cephalalgia. Intraspinal Schistosomiasis
9M	63	Therapeutic (Endoscopic Nucleotractotomy)	Post herpetic trigeminal neuralgia	Stereotactic percutaneous Endoscopic assisted trigeminal Nucleotratotomy	Significant reduction of pain and further control with oral medication	Satisfactory control of pain
10F	45	Therapeutic (treatment of infusion pump complicatiion	Intrathecal morphine catheter broke up and was released in the subarachnoid space	Percutaneous access through the sacral hiatus. Entry of the endoscope in the lumbar region with direct visualization of the catheter	Technical impossibility (inadequate microtweezers) Did not permit to withdraw the catheter	Rescue of the catheter was not possible

Conflict of interest statement We declare that we have no conflict of interest.

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Application of Pulsed Radio Frequency to the Dorsal Horn and Dorsal Roots

Omar Omar-Pasha MD

Abstract In the world of neuromodulation for pain management, the new multifunctional electrode presented in this article, together with the associated procedure described, considerably extends the range of therapeutic options in the hands of pain physicians. Besides the definite therapeutic effect, the lower rate of complications and side effects, further factors also make this new procedure and device appear an attractive diagnostic and therapeutic modality.

Keywords Dorsal horn stimulation · Functional DREZectomy · Multifunctional electrode · PASHA-electrode® · PRF spinal cord modulation

Introduction

The treatment of chronic pain remains a challenge in modern medicine. Whenever pharmacologic and other conservative treatments of chronic pain fail, ablative and interventional methods are attempted on the assumption that interrupting nerve conduction prevents central pain cognition [21]. Chemical procedures such as injecting phenol or alcohol [8] have been almost completely replaced by cryosurgical and especially thermosurgical interventions because of their superior dosability and placement accuracy [17, 25]. High-end therapies such as spinal cord stimulation or intrathecal drug infusions are expensive and not free of complications [22]. There is still a large gap between the standard therapies and these high-end methods [2].

When using the thermosurgical approach, radiofrequency thermocoagulation (RFTC) is the method of choice. The temperatures applied usually reach 70–85°C [7, 15].

Since pulsed radiofrequency (PRF) technology has been shown to be effective in the management of chronic pain, it is an interesting option for the invasive treatment of chronic pain and has a much lower rate of side effects compared to other techniques [1, 10, 18]. The temperature in the treated tissue does never rise above 42–43°C and there is thus no tissue destruction (Fig. 1).

Histochemical investigations have shown enzyme-like protein induction in PRF-treated nerve cells which is not observed in cells treated with continuous RF [6]. Moreover, histological analyses have not revealed any significant tissue damage to the treated nerve cells [3]. Maintaining a safety distance from the treated nerves is no longer necessary, on the contrary, distance diminishes the outcome.

Since only rigid electrodes and the thin electrodes (SMK-electrode) developed in the 1980s were available interventions had to be restricted to stimulating the nerves in or peripheral to the intervertebral foramina. A closer approach to the roots or treatment of (sacral or thoracic) ganglia in the spinal canal was only achievable by drilling burr holes, an intervention eschewed by many pain specialists [19].

In 2003, the flexible multifunctional electrode (PASHA-electrode®) was developed.

The multifunctional electrode is a flexible probe which allows us to apply PRF without restriction to almost any-target. This flexible electrode is a combination of a catheter with two electrodes located at the tip.

The rationale underlying this approach is that the dorsal horn plays a central role in modulating all nociceptive inputs on their way to the central nervous system.

O. Omar-Pasha MD
Interventional Pain Treatment, Hand and Foot Surgery, Am Anger 1, 53424 Remagen, Germany
e-mail: pain@omar-pasha.de

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Acta Neurochirurgica Supplementum 108, DOI 10.1007/978-3-211-99370-5_13,

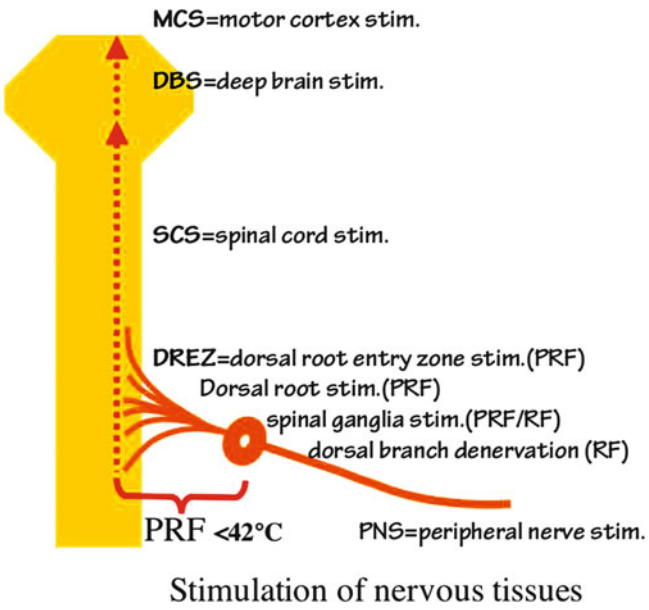

Fig. 1 Targets for neuromodulation. *PNS* peripher nerve stimulation; *PRF* pulsed radiofrequency stimulation of the DREZ region; *SCS* spinal cord stimulation; *DBS* deep brain stimulation

With this Device We Can Perform the Following Procedures

- Stimulate any nerve or spinal nerve root at any frequency, e.g. 80 Hz test stimulus for sensory stimulation, in order to determine the exact level
- Apply PRF at the dorsal root entry zone, the dorsal roots and conus medullaris peripheral nerves and any other structures
- Injection of medications and agents
- Online measurement of the temperature at the tip to avoid damage to surrounding tissues
- Accurate placement without the need for radiopaque contrast materials, due to the visibility of the device in radiography and test stimulations
- SCS trial stimulation
- The multifunction device can be left in place for repeated PRF or injections

This paper summarizes these results and presents technical conclusions. After the treatment of more than 2500 patients, new algorithms have been developed for the management of chronic pain patients.

The Multifunctional Electrode

The flexible multifunctional electrode is a combination of a catheter and two electrodes placed at its very soft distal end (each 3 mm long and 4 mm apart). The distal opening of the catheter is situated between the two electrodes. The catheter is 60 cm long and has a maximum outer diameter of 1.38 mm (4 F), the stylet diameter is 0.35 mm (Fig. 2).

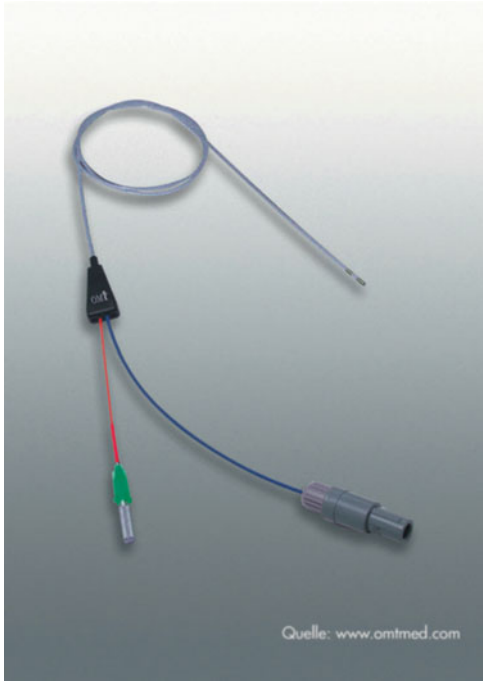

Fig. 2 Multifunctional electrode (PASHA-electrode)

Stimulation Parameters

The generator power output is in the 0,1–5 Watt range (in a few cases above 10 W). The conductivity of electrical current in epidural fat is very low (0.04 Ω^{-1} m^{-1}) compared to 1.4 Ω^{-1} m^{-1} in the CSF. The duration of the active phase is 20 ms and the pause between active phases lasts 480 ms, resulting in two active phases per second. The voltage usually is less than 45V (Fig. 3).

Practical Implementation

The epidural space is accessed using the loss-of-resistance technique. X-ray visualization is recommended. The narrowness of the epidural space should be considered and only small amounts of NaCl injected. In the cervico-thoracic region, the ligamentum flavum is thin and may even be non-existent, in which case the loss-of-resistance technique is inaccurate and even dangerous. For that reason, we prefer to penetrate the epidural space at the T3/4/5 level or even lower when treating the cervical spine (Fig. 4).

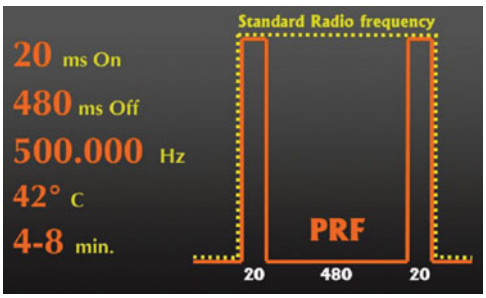

Fig. 3 PRF-stimulation parameters

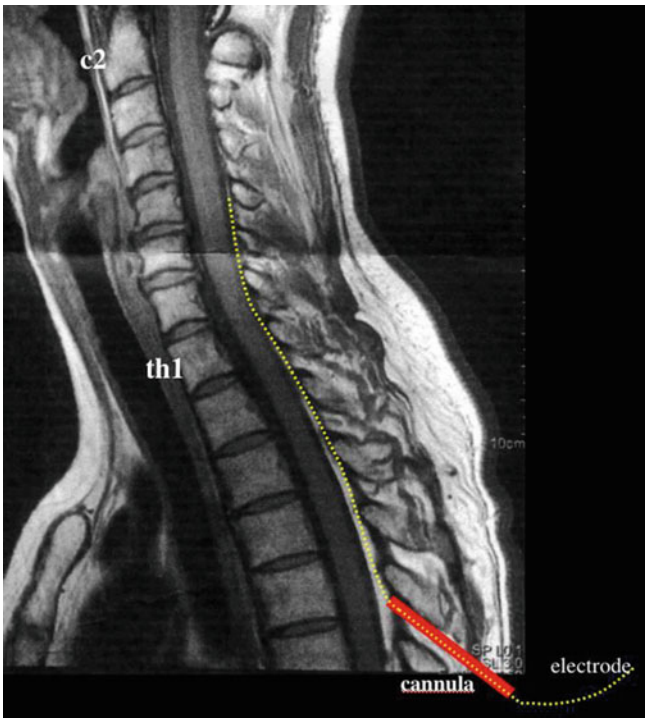

Fig. 4 The paramedian access from the contra-lateral side

Our standard approach for lumbar, sacral and radicular pain in the legs is the paramedian access L3/4 from the contra-lateral side. We use introducing cannulae familiar to us from introducing spinal cord stimulation (SCS) electrodes [13, 14]. The introducer should not be less than 14 G to avoid difficulties in handling the electrode or prevent damage to the multifunctional electrode (Fig. 5).

Approximately 1.5 cm proximal to the tip, we bend the electrode slightly to make navigation easier (approximately 20–30°). This curvature must not be excessive as this would complicate the reinsertion of the mandrins (Figs. 5–8). We do not place the multifunctional electrode over the dorsal column as in SCS. When treating the lumbar and sacral area, our target is the dorso-lateral parts of the spinal cord (Fig. 9).

Fig. 5 14G Introducer

Targets When Treating the Spinal Cord and Its Nerve Roots

- By introducing the electrode using a paramedian approach and entering the epidural space between the third and fourth lumbar intervertebral space, we can treat all the lumbar roots and the upper sacral roots (Figs. 9–12).

Using this approach we are also able to treat the conus.
The electrode can be advanced, if required, to the thoracic and even cervical parts of the spinal cord. Usually, if our target is the thoracic region, we prefer to enter between the second and third vertebra. When treating the cervical spine, we usually introduce the electrode between the third and fourth thoracic vertebra.

- Treating the DREZ region at the conus medullaris or at the levels of the lower thoracic spine appears to have a similar outcome as treating the nerve roots directly. The specific indications for the different targets in the future will have to be determined by further research (Fig. 13).
- The electrode can be introduced via the sacral hiatussacral hiatus. This method was adapted from our experience in performing adhesiolysis. The primary indication for this method is treatment of the sacral nerves, which are difficult to approach in the lumbar spine because they are concealed ventral to the lumbar roots. For the management of mononeuropathy, e.g. affecting the pudendal or obturator nerves, we chose the sacral approach. Treating

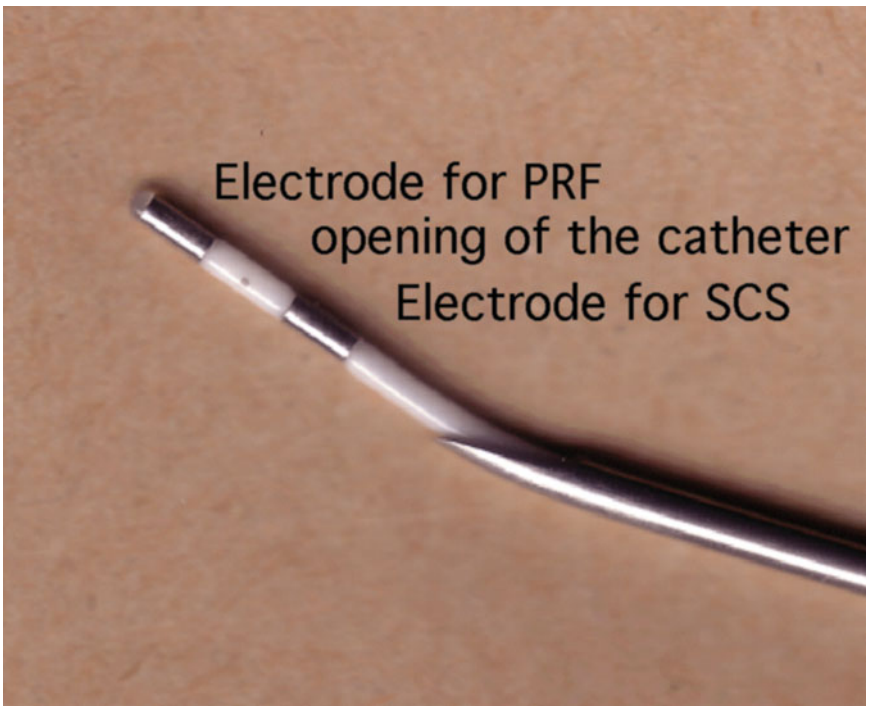

Fig. 6 Tip of the electrode. Notice the slight bending of the tip

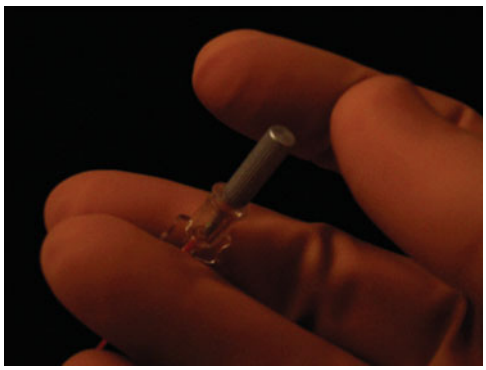

Fig. 7 Fixing the end of the electrode by the third and fourth digit

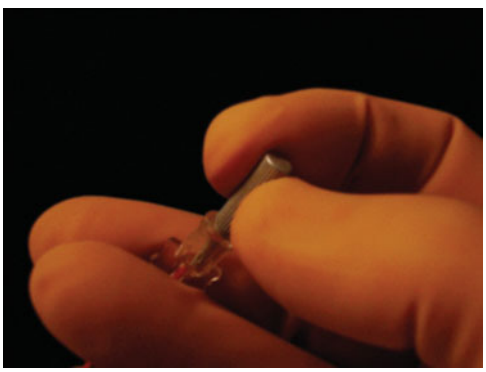

Fig. 8 Steering the mandrin by forefinger and thumb

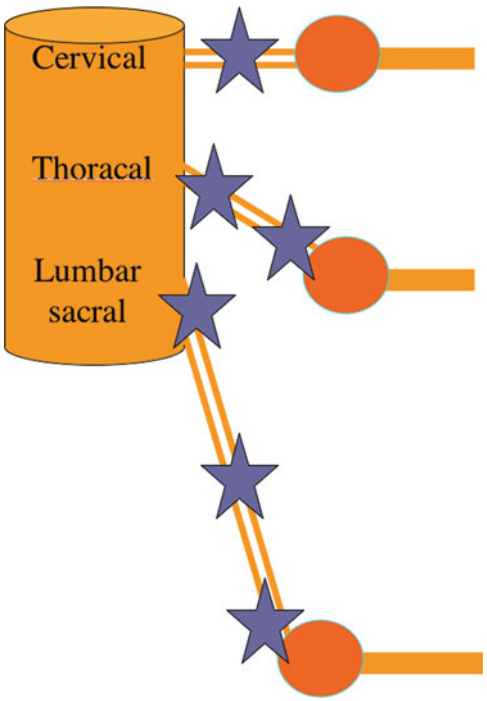

Fig. 9 Possible targets for PRF-stimulation at different spinal cord levels

the distal parts of the sacral roots therefore modulates the dorsal root entry zone (Fig. 14).

If the requirement is to treat an oligo or monoradiculopathy or use the technique for "educational" purposes, it is

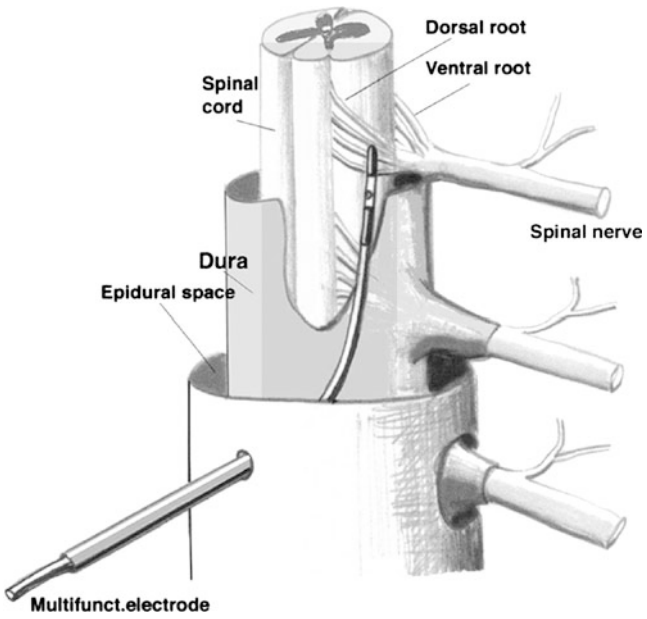

Fig. 10 View of the lumbar spine showing the position of the multifunctional electrode

preferable to stimulate the dorsal nerve roots directly. The technique can best be demonstrated in this region. Clearly, stimulating the roots one by one is the most time consuming of all techniques. For the patients, however, this technique is the most impressive because it allows them to identify each root exactly, thereby making it easier to distinguish the different painful areas. This can be psychologically significant.

The patient is placed in the prone position with a cushion under the abdomen to reduce the lordosis.

The return electrode (ground plate) is positioned cranially to the area we intend to modulate or ventrally over the abdomen.

Local anaesthesia is administered which already provides important information about the tissue to be passed. If the intervertebral space is too bony, the approach can be changed at this stage.

A small incision is made and the introducing cannula is advanced to the intervertebral ligaments.

The epidural space is accessed using the loss-of-resistance technique. Since many patients suffering from chronic pain have already undergone several operations, the procedure is sometimes not easy. If the dura is uninten-

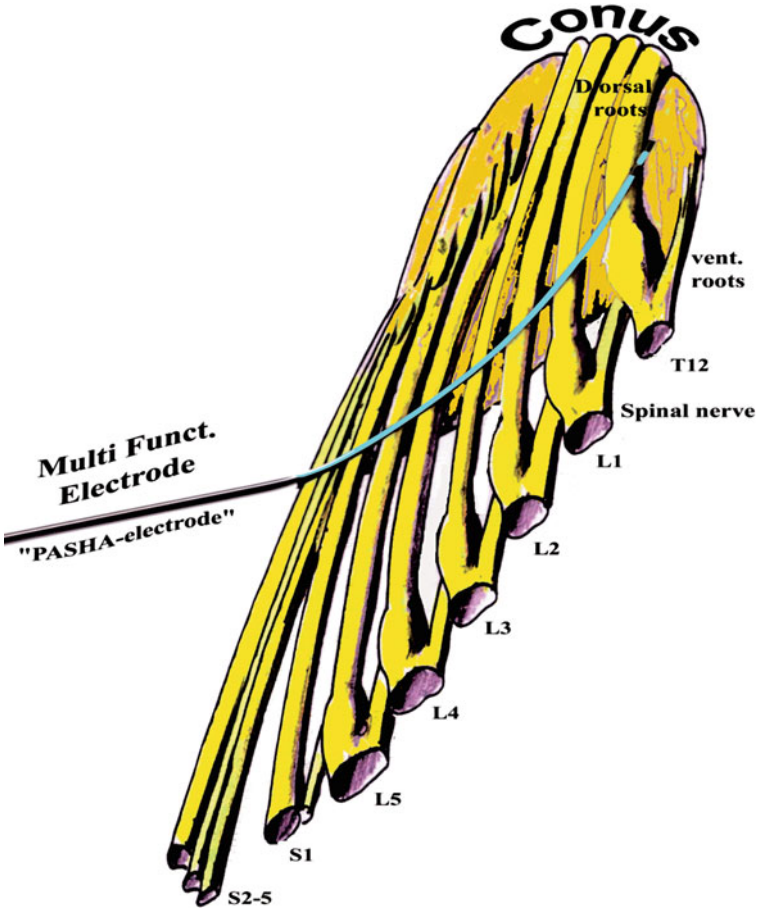

Fig. 11 PRF stimulation of the conus medullaris and dorsal roots

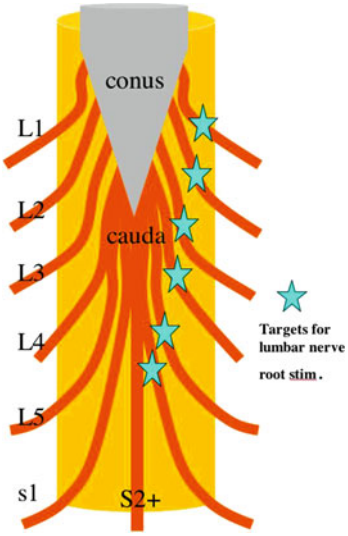

Fig. 12 PRF stimulation of the lumbar spinal roots

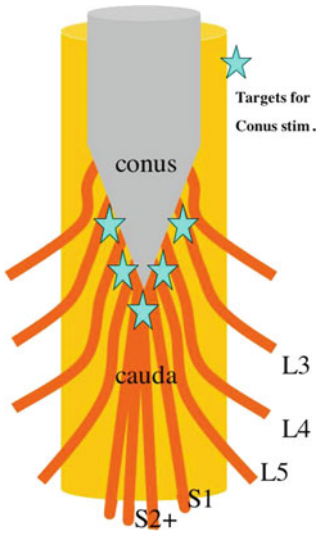

Fig. 13 PRF stimulation of the conus medullaris

tionally punctured, the introducer is not retracted, and the procedure is continued. The following steps are even easier if performed intrathecally and PRF appears to be even more effective. The intrathecal approach is not the preferred method because of the likelihood of dural headache and other possible – if rare – complications.

The electrode is introduced through the cannula and advanced smoothly towards craniolateral. The soft curved tip acts as a guiding mechanism facilitating advancement to the levels above the area to be treated.

It should be attempted to produce perceptible stimulation in the patient with voltages <0.8 V to ensure that the tip of the electrode is close enough to the nerve roots, which considerably enhances the effect of the PRF. If the electrode

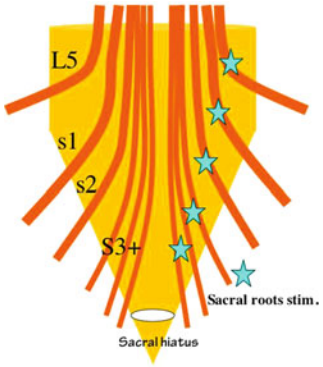

Fig. 14 PRF stimulation of the sacral and lumbar roots via hiatus sacralis

is accidentally or intentionally positioned intraspinally, the stimulation is perceived at considerably lower currents – sometimes as low as 0.1 V. However, the currents required vary depending on where the electrode is positioned in the spinal canal. If the dura is thick or calcified, higher currents may be required. If there is severe nerve root damage and deafferentation, the patient often has no sensation. In this case, it is necessary to rely on the fluoroscopic position of the electrode.

In this way the roots can be located and treated in succession.

The duration of the active phase is 20 ms and the pause between active phases lasts 480 ms, resulting in two active phases per second.

Each nerve root is stimulated for 240 s. The temperature at the electrode tip measured online does not exceed 42°C.

The goal is to achieve the closest possible proximity to nervous structures.

The dorsal roots are stimulated with 70 Hz and the electrode tip is moved until the stimulation is sensed by the patient at its lowest voltage threshold.

The identified nerve roots are then treated with PRF. The electrode is gently withdrawn applying continuous stimulation until the following caudal root is localized, which is identified in the same manner by test stimulation and treated with PRF.

Results

Pain Reduction

95 of the first 101 treated patients, post-treatment pain ratings were obtained after 3 months
Mean age 59.7 years (maximum 94, minimum 32).
Females 71, males 27
88 patients lumbar pain – 1 patient thoracic pain – 11 patients cervical pain.
75 patients had back pain – 55 patients leg pain – 15-patients had neuropathic pain.

The mean VAS score before treatment was 8.5±1.3 U with a minimum 5 U and a maximum 10 U, indicating severe pain.

The mean post treatment pain score was 4.3±2.8 U, with a minimum 0 U and a maximum 10 U, indicating that some patients did not benefit from the treatment. Nevertheless, the pain reduction in the pre-post comparison is highly significant ($p<0.0001$). Mean pain reduction was 48.3%.

Dividing the group according to the duration of PRF stimulation (60, 120, and 240 s), the pre-post comparison for pain reduction in each subgroup is still highly significant (60 s, $N=21$, $p=0.0002$; 120 s, $N=28$, $p<0.0001$; 240 s, $N=46$, $p<0.0001$). Pain reduction in the subgroup with a 240-s stimulation period was mean 54.7±33.0%.

Besides the mean pain reduction, it was to be ascertained how many patients benefited substantially (more than 70% pain reduction) from the treatment. With a stimulation period of 60 s, 3 of 21 patients (14.3%) had a pain reduction of more than 70%. With a stimulation period of 120 s, 9 of 28 patients (32.1%) experienced this degree of pain reduction and with a stimulation period of 240 s, 22 of 46 patients (47.8%) experienced 70% pain reduction. These differences in frequency distribution were statistically significant (chi-square=7.29, $p=0.0262$) (Fig. 15).

PRF treatment of 101 patients was found to provide definite pain reducing effects without evidence of neuronal lesions. The only side effects were headache in four patients due to accidental intrathecal puncture.

With a stimulation period of 60 s, which is also used in RFTC, 3 of 21 patients (14.3%) had a pain reduction of more than 70%, and when the stimulation period was increased to 240 s, 22 of 46 patients (47.8%) responded with a pain reduction of more than 70% (Figs. 16–18).

The analysis showed a highly significant treatment effect. Using a 240 s stimulation period, 47.8% of the patients experienced a pain reduction of 70%.

The main parameter influencing the pain reducing effect was the stimulation period.

Long-Term Follow-Up

Post-treatment pain ratings were obtained of the first 101 treated patients after 3 years. Sixty-four patients answered the questionnaire:
The mean VAS score before treatment was 8.85. The mean VAS score after >3 years was 3.12.
The comparison for pain reduction: Post-operative pain reduction after 4 weeks was 80.71%. After >3 years the pain reduction was still 64.79%.
The team of V.Vadokas in Heilbronn had the following results $N=44$. The mean VAS score before treatment was 9.55.

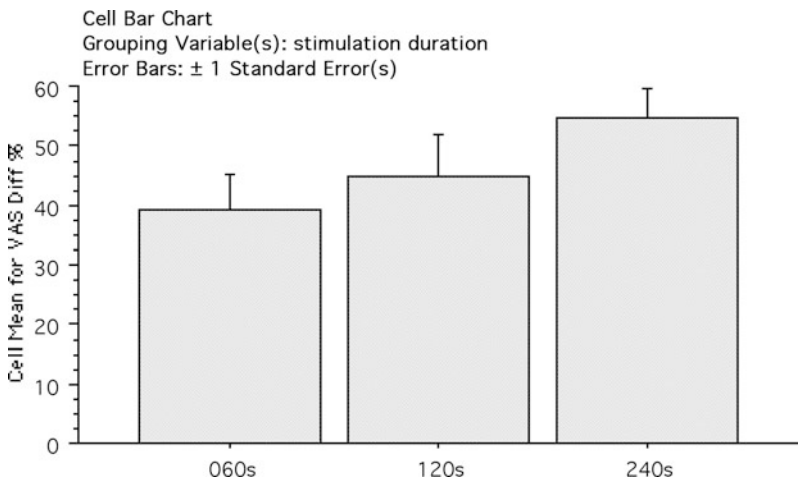

Fig. 15 Percent of pain reduction depending on stimulation period (60, 120, and 240 s). The longest stimulation period shows the best effect. Differences between 60, 120, and 240 s were statistically significant ($p=0.0462$)

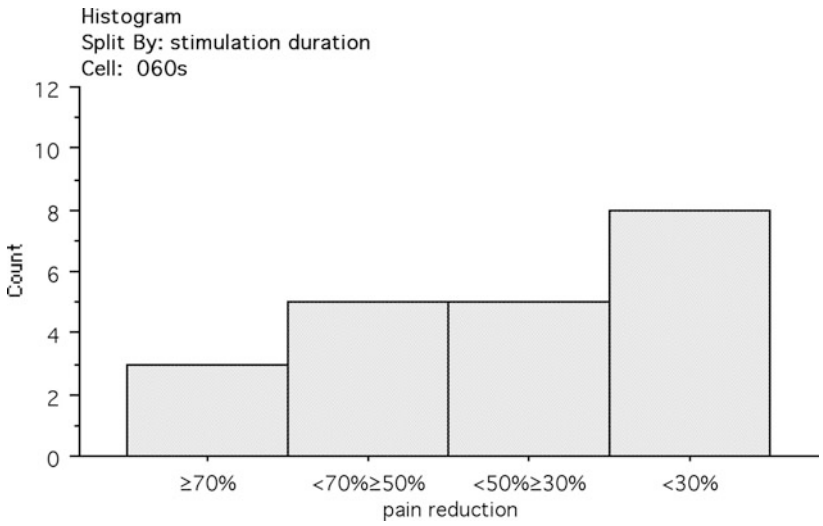

Fig. 16 Stimulation duration 60 s. Number of patients with a pain reduction of 70, <70 to 50, <50 to 30 and <30% respectively. The differences in frequency distribution are statistically significant (chi-square=7.29, p=0.0262)

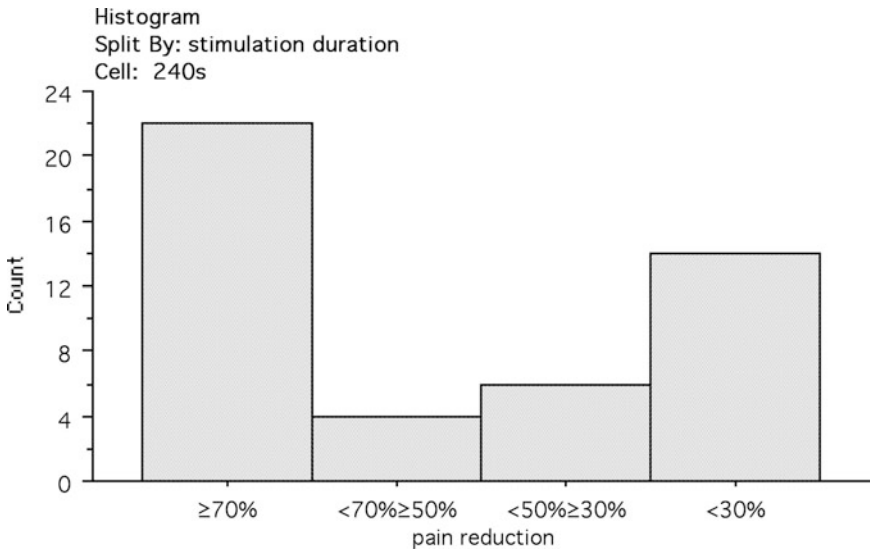

Fig. 17 Stimulation duration 120 s

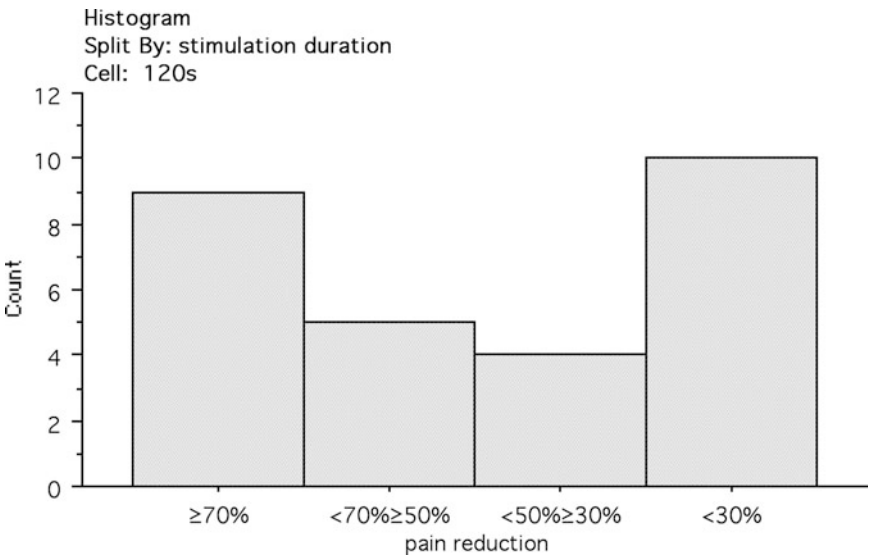

Fig. 18 Stimulation duration 240 s

Post-operative pain reduction after 4 weeks was 77.95%. After 12 months the pain reduction was 70.30% (personal information 2007).

Indications

The indications established to date for pulse radiofrequency (PRF) treatment and/or infiltration by means of the multifunction electrode are:

- Neuropathic pain
- CRPS 1 and CRPS 2
- "Failed back surgery syndrome"
- Cervical and thoracic spinal pain syndromes. Here this approach is safer and avoids the complications of the conventional needle puncture techniques
- Mixed pain: back and radicular pain
- All indications suitable for facet joint denervation (specifically thoracic and cervical)
- Multi-level spinal stenosis
- Restless leg syndrome
- Cervicogenic headache
- Visceral pain?

The varying origin of chronic pain sometimes makes it necessary to combine different procedures and apply them successively. The multifunction electrode allows multiple procedures to be completed in a single step, minimizing possible complications, treatment time and costs.

The new approach is not intended to replace SCS, but is merely a step in the therapeutic algorithm, and may help patients without implanting expensive devices or attempting other invasive techniques.

In addition to the benefits described above, there is no longer any need for all the test infiltrations usually performed to identify pain pathways. The levels can be mapped more accurately with the electrode – and with fewer complications.

In fact, there are no complications except those also observed with any other catheter or electrode.

Since we are treating the transmission and translation of pain and are modulating the dorsal horn entry zone, the origin of the nociceptive input is not a primary consideration.

Causal treatment should self-evidently be the goal of every treatment, but where it fails, multifunctional electrode PRF can be used to modulate the input of the spinal cord at the dorsal root entry zone before considering the use of destructive techniques, SCS, intrathecal drugs or even initiating the use of morphine.

Topics of Interest for Future Research

- The optimal stimulation parameters have to be determined. It is not known whether a stimulation period longer than 240 s might provide even more effective pain relief.
- The long-term effect of the procedure also has to be evaluated. Good results have been reported in 2-year follow-up studies for radiofrequency thermocoagulation [9, 12, 15], but not yet for the relatively novel pulsed radiofrequency technology.
- In addition to stimulation of the spinal nerves, blockades of sympathetic ganglions are a common approach to treatment of chronic pain. Koenig et al [7] reported the effect of radiofrequency thermocoagulation on the superior cervical sympathetic ganglion in non-traumatic neck pain. Applying PRF to sympathetic structures can yield comparable results [11].
- We used PRF stimulation of the dorsal roots in patients with neuropathic bladder dysfunction with extremely promising results. However, it is still too early to draw statistically significant conclusions.

It is not yet possible to predict the treatment outcome. There still is a lack of knowledge as to how the pain processing system functions and what physical and psychological parameters may alter the effect of the treatment. But is there an understanding of how spinal cord stimulation works, even though this procedure has been performed for decades?

Discussion and Outlook

An important factor in the pathogenesis of chronic pain appears to be the conditioning of central nervous structures by persisting sensory input of A-delta- and c-fibres of the peripheral nerve [14, 23]. The use of radiofrequency currents to interrupt this sensory input (radiofrequency thermocoagulation, RFTC) is effective in treating patients with chronic back pain syndrome [5, 25], although the idea that noxious heat is the main effect is doubted [16, 20]. Especially when using the radiofrequency current in pulsed mode (pulsed radiofrequency, PRF) the temperature in the tissue surrounding the electrode tip does not exceed 42°C, so that the electric field itself is thought to be effective in modulating

the sensory input to the spinal cord [10, 11, 16, 18, 20]. The main advantage of the PRF technology is thus the low risk of damaging the neuronal structures and causing sensory or motor impairment [2, 10].

In the treatment of 101 patients with PRF reported above, clear-cut pain reducing effects were observed without evidence of neuronal lesions. The only side effect was headache in four patients due to accidental intrathecal puncture. The main parameter influencing the pain reducing effect was the stimulation period. With a stimulation period of 60 s, which is often used in RFTC [15], 3 of 21 patients (14.3%) had a pain reduction of more than 70%, and when the stimulation period was increased to 240 s, 22 of 46 patients (47.8%) responded with a pain reduction of more than 70%. These results are very promising compared to those of RFTC technology [4, 12, 24].

Although PRF treatment shows good efficacy and is very safe, its use continues to present technical challenges. As mentioned above, PRF treatment produces the best results when the patient feels the sensation in the same area as the pain during diagnostic low frequency stimulation. This requires a search procedure to find the optimal stimulation position in the area of the dorsal root entry zone (DREZ).

With relatively rigid equipment like SMK-electrodes, this search procedure often requires multiple punctures at different sites. This can damage blood vessels or spinal nerve roots and can be very unpleasant for the patient. Especially in the cervical region, there is the risk of injuring the vertebral artery. In the thoracic region, the conventional needle approach can result in pleural puncture. The thoracic and sacral ganglia cannot even be treated without drilling holes.

The multifunctional electrode solves many of the technical problems associated with the use of PRF. The technique is comparable to that of an SCS electrode or an epidural catheter. The electrode can replace periradicular and paravertebral injections as well as facet joint denervations, since these interventions can be completed in a single-step procedure.

Conclusions

The new multifunctional electrode presented in this article, together with the associated procedure described above, considerably extends the range of therapeutic options for the management of chronic pain. In addition to the definite therapeutic effect, the lower rate of complications and side effects also make this new procedure and device appear an attractive diagnostic and therapeutic modality.

The 2,500 patients we have treated so far had undergone several other treatments that failed, meaning that a selection effect for "untreatable cases" may have been present. Very promising results were achieved in this sample and the outcome may be even better in "standard" chronic pain patients.

It is planned to modify the technique, optimize the parameters and define the indications and outcomes with greater accuracy in the future. PRF application to the dorsal horn entry zone and the dorsal roots could play a major role in the management of pain.

Conflicts of Interest Statement We declare that we have no conflict of interest.

Since this procedure has only minimal side effects (if any), its use can be considered where conservative treatments have failed and before performing ablative procedures or surgery, or even before considering long term opiate medication.

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Automated Nucleotomy and Nucleolysis with Ozone

Marcos G. Baabor, Pedro F. Vázquez, and José A. Soriano Sánchez

Abstract Lumbar and radicular pain due to HNP has been described since 1934. It is thought that the pain is caused by compression and by other local chemical mediators that are present in the area of interaction between the root and the disc.

With the objective of treating patients suffering from this syndrome and with a percutaneous minimally invasive approach, we designed a mixed technique: percutaneous automated nucleotomy plus nucleolysis and periradicular infiltration with ozone.

A retrospective study of 105 patients was conducted, including 60 men and 45 women with an average age of 43 years. All patients were treated with that technique between November 2006 and August 2008. Clinical follow-up of 15.2 months was provided by telephone, utilizing a modified Mac Nab scale. The results were as follows: 60% excellent, 22.8% good (82.8% success), 9.6% acceptable, 7.6% poor. From the eight patients that reported poor results, five were considered to have recurrent symptoms (4.8%), because they had initially shown a period of significant improvement post operatively. Morbidity was manifested by transient pain and muscle spasms in the post operative area (2.8%).

We conclude that this new mixed technique, compared to automated percutaneous nucleotomy alone, may be more widely utilized by broadening the indications, with acceptable results.

M.G. Baabor (✉) and P.F. Vázquez
Hospital Clínico Universidad de Chile, 11 de Septiembre 1363 of. 1502 Providencia, Santiago de Chile, Chile
e-mail: marcosbaabor@yahoo.com; pvazquezs@yahoo.es

J.A.S. Sánchez
Avda. Carlos Gráez Fernández 154 of. 106 Plaxala Santa Fe Cuajinualta, México DF 05300, Mexico
e-mail: neurojass1@hotmail.com

Keywords Blocks · Hernia · Nucleolysis · Nucleotomy · Nucleus pulposus · Ozone · Percutaneous · Radicular pain

Introduction

Lumbar and radicular pain, associated with a herniated nucleus pulposus (HNP), is a pathological entity which was described by Mixter and Barr [1] and which has been accepted by the medical community ever since. The pain appears to be precipitated by compression and by biochemical mediators originated from the rupture of the disc and/or by the inflammatory process generated by this interaction [2]. It is only in the 1950s that surgical treatment emerged as an option in the treatment of this entity, with microsurgery of the disc becoming the gold standard [3].

While searching for a minimally invasive solution to the treatment of unrelenting and disabling lumbar and radicular pain, we reviewed our personal experience and what was reported in the literature on automated percutaneous nucleotomy (APN) [4]. We also looked at the results of nucleolysis and periradicular infiltration with medical ozone (O_3) (mixture of oxygen and ozone) [5–8] and decided to design a mixed surgical technique. We utilized Kambin's lateral approach [9, 10] for access and infiltration.

The literature suggests that surgical removal of the HNP does not change long-term outcomes [3]. For that reason, we proposed a mixed technique as a new form of treatment, not only because it addresses the compression but also because it targets the inflammatory component. First, we achieve extraction and dehydration of the nucleus pulposus to be treated (APN + nucleolysis) and then, we infiltrate the periradicular area with O_3 Through a system of cutting and aspirating, APN allows the extraction of 1–2 cc of nucleus pulposus with the purpose of decreasing intradiscal pressure [4]. On the other hand, O_3 produces an intense oxidation and

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dehydration of the nucleus. At a periradicular level, O_3 also has a potent analgesic and anti-inflammatory effect because of the induction and release of antioxidant enzymes that are capable of neutralizing the effect of acidic radicals [5–8].

Our objective is to describe this new surgical technique, its indications and to show our short, medium and long-term results.

Materials and Methods

We performed a retrospective analysis of 105 patients, 60 men and 45 women with an average age of 43 years (range from 23 to 78). The operated discs were, in order of frequency: L4–L5=58, L5–S1=35, L3–L4=18, L2–L3=10 and L1–L2=2. It is important to note that 14 patients had 2 discs which were operated on and that 2 patients had 3 discs which were operated simultaneously. This makes a total of 123 operated discs. The average duration of the preoperative symptoms was 10.3 weeks (range of 4–24 weeks). The hospitalization time was 24 h because the procedures can be performed in an ambulatory setting. This allowed an evaluation without sedation postoperatively. All patients suffered from a HNP and from lumbar and radicular pain and were diagnosed clinically and by MRI studies. All patients had undergone APN + nucleolysis and periradicular infiltration with O_3 between November 2006 and August 2008.

Inclusion Criteria

(a) Clinical

- Lumbar and radicular pain not responsive to conservative treatment for at least 4 weeks.
- Lumbar and radicular pain with a dynamic component. It is worsened by certain positions and exercises and improves partially with rest.
- Recurrent lumbar and radicular pain shortly after some improvement with medical treatment.

(b) Imaging (MRI)

- Herniated disc towards the canal, recess and/or foramen.
- Disc with loss of maximum height of 40% compared to a healthy disc.
- HNP's afeccting less than 50% of the canal.
- Preserved or not preserved annulus.

Exclusion Criteria

(a) Clinical

- Lumbar and radicular pain with severe motor deficit or cauda equina syndrome.
- Lumbar and radicular pain which does not improve with rest.
- Pregnancy, infections, medical contraindications to surgical intervention, poor patient cooperation.

(b) Imaging (MRI)

- Migrated disc fragment.
- Canal, recess or foraminal stenosis of significance with respect to the HNP.
- Calcified HNP.
- Spondylolisthesis grade II or greater.

Surgical Technique

This is a minimally invasive procedure that is performed under local anesthesia (Lidocaine 1%) and sedation, which allows continuing and permanent monitoring of the spinal root during surgery. The patient is placed in the lateral decubitus position, and the disc approached by the symptomatic side. We utilize AP and lateral fluoroscopy during surgery (Fig. 1). One gram of cefazoline is given intravenously for prophylaxis. The site of puncture is marked between 8 and 10 cm from the midline towards the painful side.

The nucleotome is introduced. This consists of a system of cutting and automated aspiration as described by Gary Onik [4] in 1984. We utilized Kambin's lateral approach [9, 10] for access and infiltration as well as a system of dilating tubes. Once the tip of the nucleotome reaches the center of the disc, we perform an automated nucleotomy for approximately 10–20 min extracting 1–2 cc of nucleus pulposus which is then sent to the pathology laboratory.

Later, through the same nucleotome, we inject O_3 on two different occasions at a concentration of 30 ug/cc of oxygen, 10–15 cc each time with an interval of 1–2 min (Fig. 2).

The nucleotome is then placed in the foramen during removal and we inject another 5–10 cc of O_3 with a concentration of 15 µg/cc of oxygen at a periradicular level, with the purpose of taking advantage of its analgesics and anti-inflammatory properties. In addition, 40 mg of methylprednisolone are injected as a radicular block [11, 12].

Finally the nucleotome is removed and adhesive tape is placed at the site of the puncture (Fig. 3).

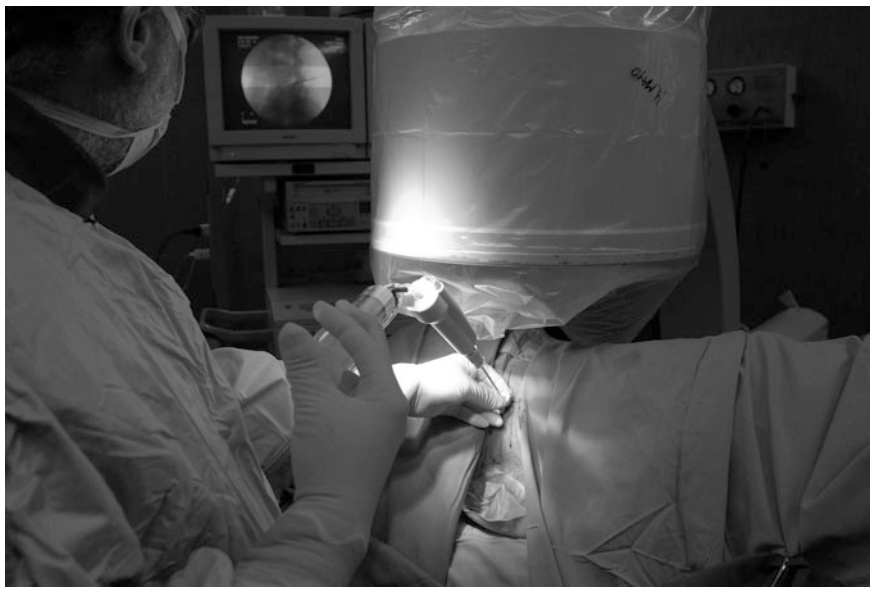

Fig. 1 Patient during procedure, lateral decubitus position under fluoroscopy with nucleotome in situ

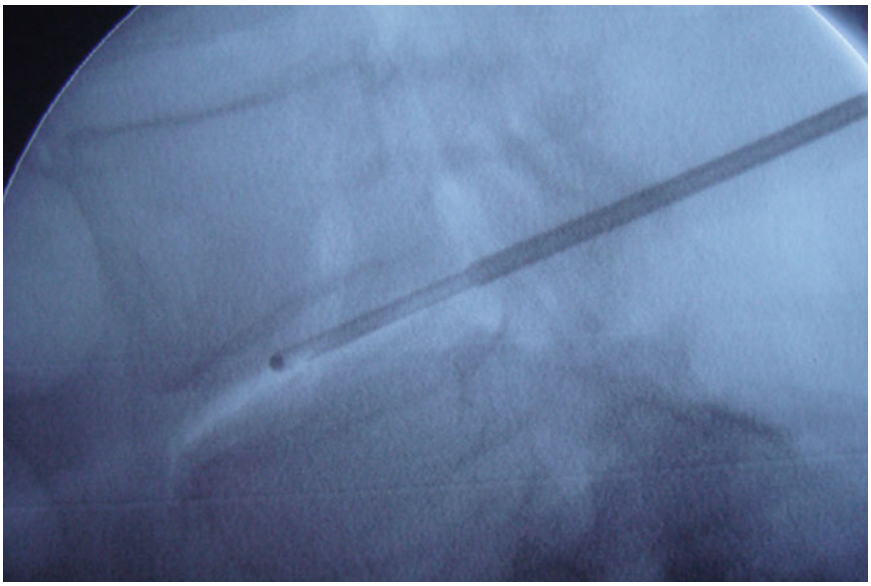

Fig. 2 O_3 being injected through nucleotome. Notice nucleus contrast

Clinical Follow-Up

We recorded immediate clinical improvement (post operative and at 24 h) as reported by the examining physician and again at 1 month and after 3 months. The last evaluation is performed through a telephone interview by a third party not involved in the previous care of the patient to try to achieve more objectivity. Modified Mac Nab criteria is utilized as follows: excellent, good, acceptable and poor results. Recurrent symptoms are felt to have occurred whenever there is a recurrence of pain after an initial period of clear improvement. If the patient presents again with radicular pain, then microsurgery of the disc is offered as an alternative.

Results

During the preoperative period all patients were severely incapacitated, unable to work, suffering from unrelenting pain that averaged 7.9 on the visual analogue scale (VAS) with a range of 4–9. Immediately after surgery, all patients experienced significant improvement of their pain with

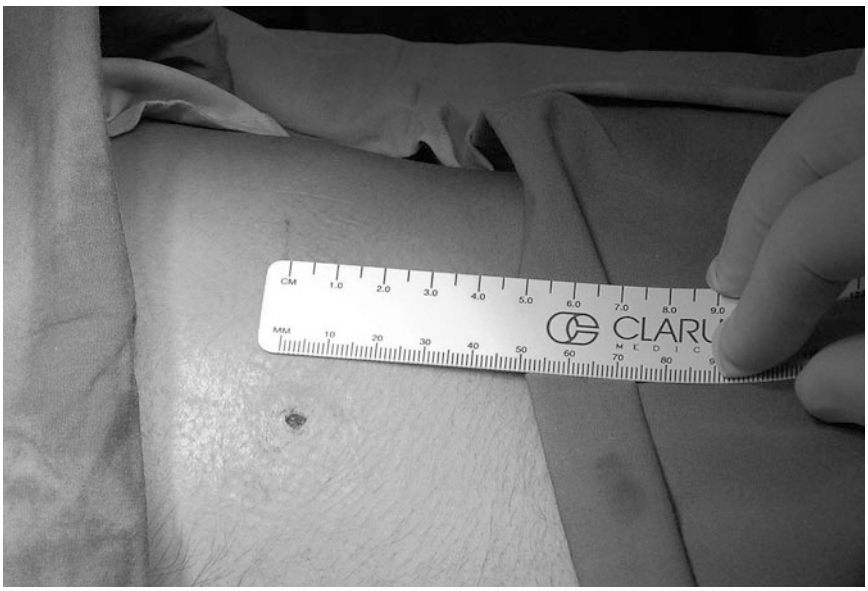

Fig. 3 End of surgery, minimally invasive technique

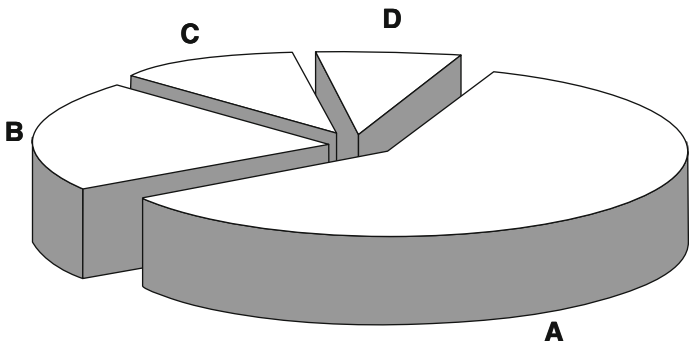

Fig. 4 Results: (**A**) Excellent (60%), (**B**) Good (22.8%), (**C**) Acceptable (9.6%), (**D**) Poor (7.6%)

a decrease in the VAS to 0.7 on average and with a range of 0–2. At 1 month, and after completing ten sessions of physiotherapy, the results showed an average pain level of 1.6 (range 0–4). Ninety-one patients returned to their pre-pain activity level between 3 and 30 days postoperatively and only 14 maintained some degree of inactivity. Intraoperative morbidity was minimal and transient (less than a month): 3 patients (2.8%) presented with some degree of post operative pain due to muscle spasms that resolved after a few days of analgesics and physiotherapy. Telephone interviews, made after 3 months with an average follow-up of 15.2 months (range 3–32 months) revealed: 63 patients excellent (60%), 24 patients good (22.8%), 10 patients acceptable (9.6%), and 8 patients poor (7.6%). If we consider a successful outcome those results that were excellent and good, then the success rate was of 82.8% (Fig. 4).

From the eight patients that had poor results, five were considered recurrent because they fulfilled the specific criteria previously described while three never showed any improvement postoperatively.

From the group of five (4.8%), three had then microsurgery and from the group of three (2.8%), two had microsurgery as well. This represented a total of five patients that had to have another surgery (4.8%) with two of them improving considerably and the remaining three only partially.

Discussion

From the author's experience with APN [13], we conclude that this is an excellent technique with excellent results, where excellent + good total 95.9% but only in very carefully selected patients with HNP, protrusions with preserved annulus, young age, and with a short pre operative course. This makes the number of patients for which this technique is appropriate somewhat proportionally small. If we broaden the indications, we notice that the positive results decrease dramatically [14–16]. The results in that context vary from a 40 to a 70% success.

With the purpose of improving the long-term outcomes and indications of this minimally invasive technique, we propose to add to the APN, nucleolysis and periradicular infiltration with O_3 [1, 7, 17, 18], which already by itself demonstrates a significant success rate (70–80%).

This mixed technique allowed broadening of the inclusion criteria for a minimally invasive approach with all the advantages that this implies. Some of these advantages are decrease of epidural fibrosis, dural leaks, infections, vascular lesions, and post surgical instability while we still remain aware of the risks involved in APN [19]. In addition, the fact that the procedure is performed under local anesthesia eliminates potential contraindications for older patients and patients that have a greater risk under general anesthesia.

If we compare the results of the mixed technique with those of APN alone, it appears that the former is less effective (86% vs. 96%). However, these results were somewhat expected because the discs operated with the mixed technique were in worse shape than those that underwent APN alone.

As far as post-operative morbidity is concerned, we noticed that it decreased from 8.1 to 2.8% due to the lack of radicular irritation and discitis [11]. The only complaints of pain occurred at the surgical site, and most likely they are minimized by the anti-inflammatory effect of ozone, which owing to its antiseptic properties also prevents the development of infection.

If we look at the results obtained by the author using APN alone and the current work, the number of patients per month that are treated by the new mixed technique has increased by almost 100%: 68 patients in 40 months vs. 105 patients in 32 months.

Conclusion

Based on our experience, we conclude that APN plus nucleolysis and periradicular infiltration with ozone, is a minimally invasive technique that can be used to effectively treat lumbar and radicular pain caused by HNP. This mixed technique carries a low risk and morbidity. In addition, it allows us to increase the number of potential patients that may benefit from this type of surgical intervention as long as they are carefully selected.

Conflict of interest statement We declare that we have no conflict of interest.

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Treatment of Discogenic Low Back Pain with Intradiscal Electrothermal Therapy (IDET): 24 Months Follow-Up in 50 Consecutive Patients

Roberto Assietti, Mario Morosi, Giovanni Migliaccio, Luigi Meani, and Jon E. Block

Abstract *Background:* Degeneration of the intervertebral disc can be the source of severe low back pain. Intradiscal electrothermal therapy (IDET) is a minimally invasive treatment option for patients with symptomatic internal disc disruption nonresponsive to conservative medical care.

Methods: Using MRI and discographic findings, 50 patients with lumbar discogenic pain were identified, underwent IDET treatment and were followed for 24 months. Outcomes included assessments of back pain severity by an 11-point numeric scale and back function by the Oswestry disability index (ODI).

Findings: There was an average 68 and 66% improvement in pain and ODI, respectively, between pre-treatment and 24 months ($p<0.0001$ for both comparisons). The global clinical success rate was 78% (39 of 50). Clinical success was associated with discographic concordance ($p<0.0001$), HIZ ($p=0.003$), Pfirrmann grade ($p=0.0002$), and percent annulus coverage ($p<0.0001$).

Conclusions: The findings of this study suggest that durable clinical improvements can be realized after IDET in highly selected patients with mild disc degeneration, confirmatory imaging evidence of annular disruption and concordant pain provocation by low pressure discography.

Keywords Back pain · Disc disruption · IDET · Intradiscal electrothermal therapy

R. Assietti, M. Morosi, G. Migliaccio, and L. Meani
Department of Neurosurgery Ospedale Fatebenefratelli E Oftalmico, Milano, Italy

J.E. Block (✉)
2210 Jackson Street Suite 401, San Francisco, CA 94115, USA
e-mail: jonblock@jonblockphd.com

Introduction

Experimental and clinical evidence has established that the intervertebral disc can be a pain generator and the primary source of refractory low back pain and diminished quality of life for millions of patients worldwide [5, 7, 11, 15, 16]. Pathologic internal disc disruption is characterized by definitive annular tears or ruptures, and is distinct from asymptomatic degenerative disc disease [13, 15].

Most patients with imaging evidence of degenerated discs or internal disruption and severe back symptoms that persist beyond 3 months do not have a good prognosis for recovery with conservative management alone [12]. These symptomatic annular tears can be treated percutaneously with a minimally invasive technique known as intradiscal electrothermal therapy (IDET), and in properly selected patients this can provide symptomatic relief.

Using MRI and discographic findings, a carefully selected group of 50 consecutive patients with lumbar discogenic pain were identified, underwent IDET treatment and were followed prospectively for 24 months.

Methods

Patients

This study prospectively evaluated the effectiveness of the IDET procedure in 50 consecutive adult patients with chronic low back pain and impaired physical function that were refractory to comprehensive conservative medical management, including physical therapy, of at least 6 months' duration. Eligible patients had severe low back pain increased in hyperflexion, single level internal disc disruption demonstrated on MRI, provocative discography at the affected level, and $\geq 60\%$ preserved disc height. The degree of disc

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degeneration was graded using the Pfirrmann scale and the presence of a high intensity zone (HIZ) on MRI was noted.

Interventions

All patients had concordant pain reproduction by low pressure (<50 psi) discography at the affected level, without pain reproduction or with discordant pain at adjacent unaffected levels. Discograms were performed independently and pain provocation was rated as concordant or highly concordant.

The IDET procedure was applied to the affected disc level using methods previously described [14]. In all cases, the IDET navigable intradiscal thermal resistive coil (SpineCATH®, NeuroTherm, Wilmington, MA USA) (Fig. 1) was used and the percentage of coverage by the catheter across the posterior annulus was estimated.

Outcomes

Patient outcome measures were evaluated pre-treatment as well as at 12 and 24 months after the IDET procedure. Lumbar back pain severity was assessed using a standard 11-point numeric scale [6] and back function was evaluated using the Oswestry disability index (ODI) [3].

Statistical Methods

Baseline values for pain and functional outcomes were compared with the final follow-up values using the matched pair t-test, two-tailed. Global clinical success was defined as no reoperations at the affected level, a ≥2-point improvement in pain severity and a ≥15-point improvement in the ODI [4, 10].

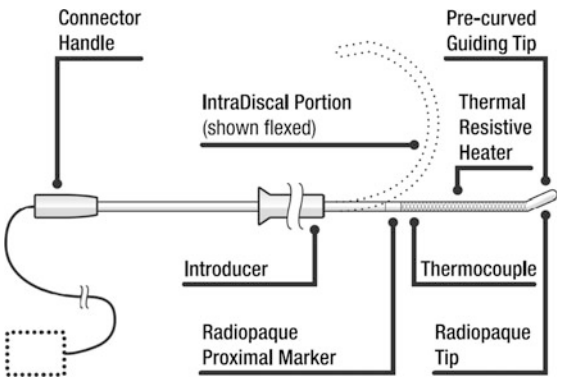

Fig. 1 Graphical illustration of the SpineCATH® intradiscal catheter (NeuroTherm, Wilmington, MA USA)

Results

There was an average 68% improvement, from 7.6±1.1 to 2.4±1.5, in back pain severity between pre-treatment and 24 months ($p<0.0001$) (Fig. 2). Likewise, there was an average 66% improvement, from 59.0±7.6% to 20.1±11.3%, in the ODI between pre-treatment and 24 months ($p<0.0001$) (Fig. 3).

Due to persistently severe back symptoms at 6 months post-IDET, nine patients had surgical treatment at the affected level (four spinal fusion, five total disc replacement). Additionally, one patient failed to achieve a ≥2-point pain improvement and one patient failed to achieve a ≥15-point ODI improvement by 24 months. Thus, the global clinical success rate was 78% (39 of 50).

There were strong and notable associations between clinical success and discographic concordance ($p<0.0001$), HIZ ($p=0.003$), Pfirrmann grade ($p=0.0002$), and percent annulus coverage ($p<0.0001$).

No complications occurred during the IDET procedure and no post-procedural adverse events such as infections or neurological sequelae were reported.

Conclusion

It is generally accepted that internal disc disruption (IDD) can lead to chronic, intractable low back pain. IDET offers an intermediate step in the continuum of care of patients

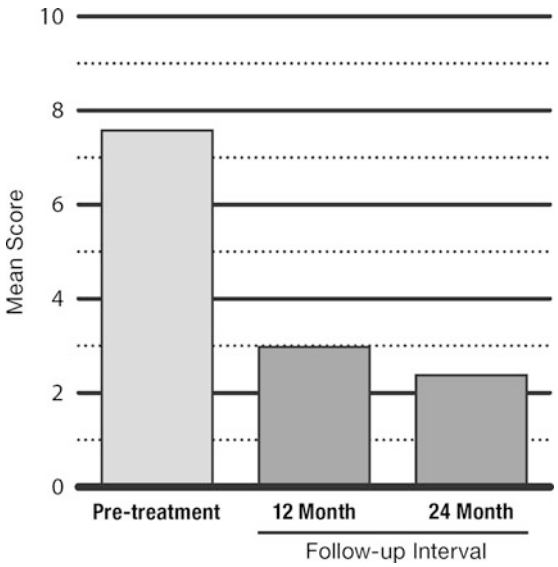

Fig. 2 Mean values for pain severity scores at baseline (7.6±1.1), 12 months (3.0±1.4) and 24 months (2.4±1.5). There was an approximate 68% overall average improvement between pre-treatment and 24 month back pain levels ($p<0.0001$)

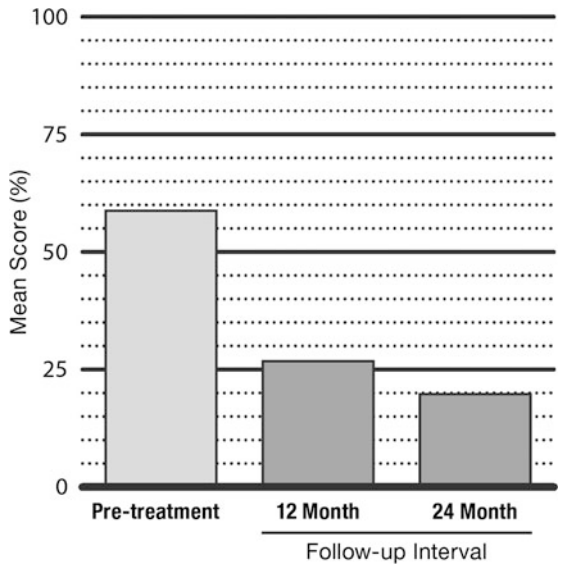

Fig. 3 Mean values for ODI scores at baseline (59.0±7.6%), 12 months (27.0±9.8%) and 24 months (20.1±11.3%). There was an approximate 66% overall average improvement between pre-treatment and 24 month back function levels ($p<0.0001$)

with symptomatic annular tears and has the advantage of preserving the native disc structure. Comprehensive systematic reviews and meta-analyses of IDET have concluded that the procedure is safe and effective for carefully-selected patients with discogenic low back pain, non-responsive to conservative care with definitive imaging and discographic evidence of internal disc disruption [1, 2].

The average pain and functional improvements and the 78% success rate achieved in the current study compare favorably with clinical results reported in other recently published studies of IDET using similar patient selection criteria [8, 9]. Thus, IDET offers a minimally invasive treatment alternative for these patients with durable, long-term clinical improvement.

Conflict of interest statement We declare that we have no conflict of interest.

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Percutaneous Coblation Nucleoplasty in Patients with Contained Lumbar Disc Prolapse: 1 Year Follow-Up in a Prospective Case Series

Tariq Sinan, Mehraj Sheikh, Josip Buric, Khalida Dashti, and Ali Al-Mukhaimi

Abstract *Background*: Nucleoplasty appears a successful minimally-invasive treatment for symptomatic contained disc herniation (protrusion). The purpose of this prospective study was to assess the effectiveness of nucleoplasty for alleviating pain and dysfunction in our patients.

Method: All patients who presented with established low back and/or leg pain of at least 3 months' duration were clinically followed for 1 year following the nucleoplasty procedure. Self-reported grading of pain using the Visual Analogue Scale (VAS) and the Roland Morris Disability Questionnaire (RMDQ), and subjective global rating of overall satisfaction were recorded and analysed.

Results: Eighty-three patients, aged between 20 and 65 years who were treated with nucleoplasty were included in the study. No complications were noted. At the 12-month-follow-up, the median VAS and RMDQ scores were significantly reduced in the patients who were considered successful (VAS by 6–7 points, RMDQ by 8 points) compared to the patients who were considered failed showing much less reduction. (P=0.000 in both cases; Mann-Whitney U test.) There was no significant difference in the baseline VAS and RMDQ scores in the two groups. Patients who were considered to have failed the procedure tended to be older. Multilevel disc decompression did not appear to be a risk factor for failure.

Conclusions: This disc decompression procedure was a safe and effective treatment option for carefully selected patients affected by low back and leg pain due to contained disc herniation.

Keywords Disc herniation · Low back pain · Minimally invasive · Nucleoplasty · Radio frequency

Introduction

The success rates reported of lumbar discectomy for lumbar disc herniation are fairly consistent, between 76 and 93% with approximately 10% of patients reported to undergo surgical revisions [8–10, 18, 19, 30]. In a substantial proportion of patients with gradually increasing symptoms after primary successful surgical treatment, epidural scar formation with tension on neural tissue appears to play an important role. Patients with extensive epidural scars are three times or more likely to experience recurrent radicular pain than those with less extensive epidural scarring [21]. A number of minimally invasive percutaneous techniques have been developed over the years, with the common tenet being the ability to act directly on the disc content without violating the spinal canal and increasing subsequent risk of scarring.

Electrosurgical technology has been developed for use in the spine and possesses few, if any, of the drawbacks of the other percutaneous disc decompression techniques. Plasma-mediated radiofrequency-based excision allows precise etching of tissue [20] and when used for tissue ablation (excision) in the disc excises target material without gross thermal or structural damage to adjacent tissue [6]. The NUCLEOPLASTY® (ArthroCare Corporation, Sunnyvale, CA) procedure is performed using a plasma-mediated radiofrequency-based device, which uses radiofrequency to excite the electrolytes in a conductive medium, such as saline solution, to create a precisely focused plasma. The energized particles in the plasma have sufficient energy to break molecular bonds, excising or dissolving soft tissue at relatively

T. Sinan (✉)
Department of Radiology, Kuwait University, PO Box 24923, Safat, 13110, Kuwait
e-mail: drtariq999@yahoo.com

M. Sheikh and K. Dashti
Department of Radiology, Mubarak Al Kabeer Hospital, Kuwait City, Kuwait

J. Buric
Functional Unit for Spine Surgery, Florence, Italy

A. Al-Mukhaimi
Department of Orthopedics, Al Adan Hospital, Kuwait

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low temperatures [23, 24, 27]. The purpose of this longitudinal prospective case series was to evaluate effectiveness of the NUCLEOPLASTY discectomy procedure for alleviating pain and dysfunction over the 12-month postoperative period in patients treated for symptomatic small contained disc protrusion.

Methods

Selection Criteria and Significant History

Beginning in February 06, patients who presented with symptoms and signs of contained disc protrusion were considered as candidates for receiving the NUCLEOPLASTY discectomy and only those patients who were followed up for at least 1 year were included in the study. No patient had a history of previous back surgery and all presented with a classical non-traumatic initiation of symptoms. Patients had chronic low back or/and leg pain lasting for at least 3 months, which had not responded to conservative treatment. Duration of symptoms ranged from 3 to 13 months. Patients had received at least 15 days of NSAID pharmacological treatment as well as some steroid treatment; none had taken opioids. Twenty eight patients complained of pure lumbar pain, 14 patients had low back pain radiating into the crural-gic region, and 41 patients had low back pain radiating into sciatalgic territory.

Significant Physical Exam and Imaging

In all cases, provocative discography was positive for pain provocation, positive for annular integrity, and negative for annular disruption. The level of disc protrusion corresponded to the level of symptoms. Evidence of slight sensitive and/or motor disturbance was demonstrated by 41 patients (13 patients in L4 territory, by 20 patients in L5 territory, and by 8 patients in both L4 and L5 territory). Forty two patients demonstrated no clinical sign of sensory or motor palsy.

In all cases, magnetic resonance (MR) imaging showed positive evidence of contained disc protrusion; the outer diameter of the protrusion was never larger than 3 mm. Any patient who demonstrated severe motor palsy (Fisher <4), "black disc" morphology, severe narrowing of disc space (<50%), annular disruption, any other spinal pathology such as tumours, lyses, fractures, deformities, stenosis, or instability, had previous spinal surgery or history of other diseases that may correlate with the symptoms or, eventually, aggravate them (diabetes, hypertension, thyroid problems, polyneuropathies, use of narcotics or history of mental diseases) were not considered for this treatment.

All viable treatment alternatives, along with detailed explanation about the various procedures and the probabilities of success as well as the risk factors were discussed with each patient. All patients accepted the treatment by signing informed consent.

The NUCLEOPLASTY Disc Decompression

The procedure was performed in the interventional suite of the radiology department with the patient under moderate sedation. No preventive antibiotic therapy was given. The patient was prepared by the anaesthesiologist with pharmacological sedation half an hour before the procedure and then brought to the room and positioned in lateral decubitus leaving the affected side upward with the legs folded. The table was folded too, as to assume an upward convex shape. This allowed the interventional radiologist to have an easier access to the lower discal space (L5–S1), even in the patients with a high iliac crest or important spondilo-arthrosic deformities. The Crawford introduction catheter was introduced by the standard postero-lateral, extra-articular percutaneous approach. The entire procedure was performed under continuous fluoroscopic control.

Once in place, the position of the Crawford catheter was confirmed by laterolateral, oblique and antero-posterior imaging. Discography was performed as usual. Only those patients who presented with evidence of an intact annulus and a positive pain response to low and medium pressure discography were selected to undergo this procedure. The Perc-DLE device (ArthroCare Inc., Sunnyvale, CA) was introduced into the disc space under fluoroscopic imaging. The discectomy was performed using the technique recommended by the manufacturer of the device. Six to twelve channels were ablated into the nucleus pulposus, in a clockwise direction. The ablation portion of the procedure takes about 2 min. After the procedure was completed, the patient was brought to the recovery room and allowed to recover for approximately 3 h, before being discharged on the same day.

For the first 3 days, the patient received instructions not to sit although walking was encouraged. These instructions were given on the presumption that the discectomy may alter consistency of the disc and by assuming postures that may implicate flexed or extended positions may cause an inadequate pressure distribution inside the disc space. In the first 3 weeks, prolonged sitting, weight lifting, and driving vehicles for longer periods of time were prohibited. The patients were instructed to take care during the first two post-procedure months.

Postoperative Follow-Up

Preceding a disc decompression procedure, patients were asked to quantify pain using a numeric pain scale (visual analogue scale [VAS]) from 0 to 10, 0 signifying no pain and 10 signifying severe incapacitating pain or that requiring admission to the hospital. At the time of discharge each patient was given a VAS scoring chart to rate their pain score daily for a week following the procedure. The charts were then handed over at the time of the first follow-up examination at 1 week. Each patient was also asked to complete the Roland-Morris Disability Questionnaire (RMDQ). The RMDQ used was formally approved and validated for use in the Arabic language. The pain rating scale on the RMDQ questionnaire was not used.

The patients were followed-up prospectively as it is standard for patients receiving a disc decompression procedure in our department. All patients returned for physical exam at 1 week, 1, 3, 6, 9 and at 12 months. At each visit the patients were asked to rate pain using the VAS, and at 12 months' follow-up the patients in addition to the VAS score were also asked to complete the RMDQ and to rate overall satisfaction with the disc decompression treatment. Overall satisfaction rating was conducted where the patient was asked to indicate the percent of his/her general sense of satisfaction with the treatment. Using the 12-month clinical outcomes information as a reference, we examined whether any baseline characteristics emerged as potential predictors of a successful or failed outcome. Patients classified as failed were those who (1) had undergone secondary surgery (2), were lost to follow-up, and (3) were less than 50% satisfied with postoperative outcome.

Statistical Methods

Median VAS and RMDQ scores were compared between successful and unsuccessful patients using Mann-Whitney U test at various time points after the procedure. Significance was $p < 0.05$. All analysis was done according to SPSS version 16 (Chicago IL).

Results

Eighty-three patients (53 males and 30 females), aged between 20 and 76 years were treated during the study period. Sixty-two patients (74%) had one-level discectomy (one at L3–L4, 39 at L4–L5, and 20 at L5–S1) and 21 patients (26%) had adjacent two-level discectomy (one at L3–L4 and L4–L5, and 20 at L4–L5 and L5–S1). Prior to the disc decompression procedure, baseline median (IQR) VAS for pain was 9 (7–9) points and for the RMDQ was 9 (8.75–9) points.

In the peri-operative phase following the procedure, two patients developed numbness in both legs which lasted for about 3 months, in two patients the pain became worse which resolved uneventfully within 10 days after symptomatic treatment and one patient developed discitis who was treated with surgical fusion. No events or complications associated with muscular or epidural hemorrhage, meningitis or nerve root damage were observed. The vast majority of the patients reported reduction in pain in the period varying form 1 week to 1 month post-procedure; two patients who initially experienced worsening pain required more time, showing improvement between 2 and 3 months after the procedure.

Table 1 demonstrates a similar median pain and RMDQ score at baseline in both groups. In the successful group the scores were markedly better than in the unsuccessful group by 1 month post therapy, and this difference was maintained thereafter in the successful group. The change in VAS was of a magnitude of 6–7 points out of 10 and was maintained at 1, 6 and 12 months in the successful patients.

Assessment regarding satisfaction level revealed: 59 patients (71%) reported 80–100% satisfaction, 4 patients (5%) were moderately satisfied, and 20 (24%) patients (9 of which underwent open disc surgery) were less than 50% satisfied.

The failed patients tended to be older but with no significant difference in the pre-operative VAS or the RMDQ score. Of patients who were >50 years of age (18/83), 45% ($n=8$) were considered failed at 12 months. In contrast, in the subset aged <50 years (70/83), only 14% ($n=10$) patients were considered failed. A multi-level disc decompression procedure did not appear to be a risk factor for failure; out of the 21 patients who received a two-level discectomy, 17 were considered a success at 12 months.

Discussion

Contained disc bulging and protrusions are seldom indications for open surgery. The main treatment for patients affected by this pathology is a conservative pathway, such as medical and/or physical therapy. If these treatments are unsuccessful over the long term, then a fusion or open discectomy procedure is generally considered. For properly selected patients, percutaneous discectomy is a less invasive measure, which may provide an alternative to an open procedure or extend the time until surgery may be required. Nucleoplasty is increasingly emerging as a method of treatment

Table 1 Clinical measures of postoperative exam in patients classified as successful or "failed" 12 months after percutaneous disc decompression

		Clinical outcome for 1, 6, and 12 months after disc decompression		
		Successful (n=63)Age=39.3±11.7M/F 39/24 Median (IQR)	Failed (n=20)Age=44.6±12.9M/F 14/6 Median (IQR)	P value[a]
VAS for pain	Pre (baseline)	9 (7–9)	8 (7–9)	0.71
	1 month	2 (0–4)	5 (2–7)	0.001
	6 months	1 (0–2)	7 (5–8)	<0.001
	12 months	2 (1–3)	7.5 (6–9)	<0.001
Change in VAS	1 month	−6 (−8 to −4)	−4 (−5 to −2)	0.001
	6 months	−7 (−8 to −6)	−2 (−4 to 1)	<0.001
	12 months	−6 (−7 to −5)	0 (−3 to 1)	<0.001
RMDQ	Pre	9 (8.75–9)	9 (6.75–9)	0.74
	Post	1 (0–3)	9 (4–9)	<0.001

[a]Mann–Whitney U test

for contained herniated disc and has been approved by FDA for the treatment of such conditions. The procedure adopts coablation technology with a non heat driven ablation process, it produces minimal damage, minimal thermal penetration and localized effect [2, 6]. This technique has therefore minimized the invasive nature of surgery and helped avoid complications such as fibrosis and infection linked to open surgery [2]. The advantages of this procedure are percutaneous approach, outpatient procedure, local anesthesia and very short procedure time. Most of our patients reported substantial pain relief within 1 month following the NUCLEOPLASTY discectomy, with the majority of them reporting minimal or no pain or disability and satisfaction with results after 1 year.

Patients with contained disc protrusion are thought to have a less superior response to open surgical microdiscectomy [4, 15]. Carragee et al. found that 38% of patients identified as having "No Fragment-Contained" herniation had recurrent or persistent sciatica postoperatively; this was compared to a success rate of 1–27% for other types of disc herniation [4]. A retrospective 16-year review from one center indicated that patients with contained disc protrusion were three times more likely to undergo revision surgery following lumbar discectomy than patients treated for extruded or sequestrated discs [18]. Mayer and Brock reported that a higher proportion of patients with contained disc herniation (i.e. outer border of the annulus was intact), who received percutaneous endoscopic discectomy had successful outcome compared to patients treated using open microdiscectomy [15]. Depending on the measure, the success rate with microdiscectomy was 65–69%, whereas success with percutaneous procedure ranged between 80 and 92%; the number of successful subjects in this cohort receiving percutaneous discectomy was double or triple that of microdiscectomy. Our success rate at 1 year not only compares favorably with these past studies on these various percutaneous procedures but also compares favorably with other prospective [1, 12, 14, 16, 22] as well as retrospective [28] studies on nucleoplasty, all reporting reduction of symptoms by at least 50% and, like in our study, more than 65% of the patients being satisfied with the procedure. Variables like age, BMI, smoking status and pain duration are shown to be independent of the outcome of the procedure [1].

Our encouraging results, like others [16], are due to the strict selection criteria adopted for the procedure which included classical symptoms and signs of contained disc protrusion, including extended duration of symptoms showing no response to active conservative care and provocative discography positive for pain provocation, positive for annular integrity, and negative for annular disruption. In a study by Cohen et al. [6] only one patient out of seven reported >50% reduction in pain score. They adopted less strict selection criteria and attributed such high failure to annular tears and large disc herniations extending more than 5 mm. They suggested, as we also believe, that nucleoplasty should be done only in patients with small (not larger than 6 mm) contained disc herniations and annular integrity. Confirming annular integrity of the affected disc(s) using discography is essential. Our failed patients tended to be older who may have had other undetected pathology or psychosocial risk factors. In a previous study it was reported that in patients with low back pain undergoing aggressive conservative care, non-recovery was significantly affected by age >45 years, having two or more neurological signs, and specific psychosocial factors [10]. This suggests the additional requirement of reconciling symptoms and physical findings, particularly in the older patient.

Two main effects were reported as possibly being at the basis of effect with percutaneous disc decompression. Mechanical decompression of the nucleus pulposus with partial emptying of the disc space with consequent pressure lowering inside the disc space is considered as a mechanical explanation of the procedure [5, 26]. The other mechanism that has been hypothesized is a chemical disruption of degenerative metabolic processes inside the disc space which (1) many induce changes in disc metabolism related to

inflammation and/or (2) initiate an autoimmune response in surrounding tissue to affect pain symptomatology [11–13]. These mechanisms remain under study and any headway in these investigations should provide guidance for enhancing treatment algorithms.

This prospective case series carried out over 1 year adds support that plasma-mediated radiofrequency-based disc decompression may be a good alternative for patients with symptomatic contained disc bulging or protrusions before opting for open surgery. The next step of course, is to evaluate this approach in a carefully designed controlled study. It is well known that the majority of patients suffering lumboradicular symptoms from a disc disease will get better spontaneously and, if present, the symptomatic herniation will resolve without any treatment [3, 21, 25]. A previous study suggested that 76% of patients who present (to a primary care clinician) with low back pain and who are treated conservatively may be expected to recover in 4 weeks [5], emphasizing again the necessity of a careful and precise treatment algorithm.

Conclusion

The present study reveals that NUCLEOPLASTY discectomy; a minimally invasive technique, must be considered as a valid alternative to surgery when evaluating possible treatment options in patients affected by contained lumbar disc herniations. A careful patient selection and strict inclusion criteria are essential. It appears particularly indicated for patients who have exhausted conservative treatment modalities, but have not yet reached clear-cut indications for open surgical treatment, and in such patients it could be safe to undergo a trial of nucleoplasty treatment. An extended follow-up is recommended to assess long-term effectiveness of the procedure.

Conflict of interest statement We declare that we have no conflict of interest.

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Plasma-Mediated Disc Decompression for Contained Cervical Disc Herniation: Results Through 5 Years

Alessandro Cesaroni and Pier Vittorio Nardi

Abstract Conventional treatment for cervical disc herniations often defaults to open cervical discectomy, potentially supplemented by intervertebral fusion. Newer treatment strategies focus on percutaneous, minimally invasive procedures which are capable of resolving herniation pathology while offering decreased morbidity and convalescence time when compared to fusion. In cases where patients complain of radicular and neck pain symptoms related to a contained herniated disc, plasma disc decompression may be used as a minimally invasive treatment option on the cervical intervertebral discs.

Three hundred and forty-nine patients who presented with a contained herniated cervical disc or focal protrusion causing pain associated with cervical nerve root compression were treated between January 2003 and May 2007. This case series study was conducted to evaluate clinical results through 1 year postoperatively.

Keywords Cervical · Coblation · Disc · Herniation · Minimally invasive · PDD · Percutaneous · Plasma-mediated

Introduction

Cervical disc herniations are traditionally treated using protracted conservative care regimes or open cervical discectomy with or without intervertebral fusion. Conservative care treatments may have limited success in resolving herniation pain symptoms, and surgery can be indicated if severe radicular pain continues for more than 6–12 weeks [15, 23]. Open discectomies with fusion are associated with significant risks and potential side effects [2, 9–11, 26, 33], and fusionless procedures carry the possibility of disc space collapse, resulting in cervical kyphosis and the potential to compromise the neural foramina [14]. Plasma-mediated disc decompression (PDD) serves as a third alternative: a minimally invasive percutaneous technique for the treatment of cervical contained disc herniations.

During PDD, radiofrequency energy is applied in an electrically conductive fluid, most often a saline solution, to produce a plasma field, about 75 mm thick comprised of highly ionized particles. These particles dissolve organic molecular bonds, breaking tissues into elementary small molecules and low molecular weight gases. The same technology has been used successfully in a wide range of applications, including arthroscopy, otolaryngology, laparoscopy, and malignant vertebral tumor removal. Though the use of PDD in the lumbar region has been well-documented [3, 17, 22, 29], it has been studied less frequently in the cervical spine [12, 19, 20, 27, 30, 34], and there is relatively little data on longer-term follow-ups.

Materials and Methods

From January 2003 to December 2007, 349 patients with contained herniated cervical disc or focal protrusion causing pain associated with cervical nerve root compression underwent PDD.

All patients reported persistent cervical or unilateral arm pain for a minimum of 3 months, and had failed previous conservative treatment. Patients had a cervical disc protrusion or contained herniated disc not larger than 3 mm and not compromising more than 1/5 of the central spinal canal, demonstrated on magnetic resonance imaging (MRI). Patients affected by spinal fractures, acquired stenosis, tumors, advanced spondylosis resulting in osseous foraminal stenosis or disc space collapse, or previous spinal surgery on the same level were excluded from this procedure. Presence

A. Cesaroni (✉) and P.V. Nardi
U.O.C. Neurochirurgia, Policlinico Casilino, Via Sicilia 15 Monterotondo, 00015, Roma, Italy
e-mail: acesaro@tin.it

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of a radicular deficit, such as hypoesthesia or objective motor deficits or hyporeflexia, indicated candidates for an open procedure excluding PDD. Paresthesias were frequently associated with pain.

The PDD procedure was always performed under intravenous sedation (Fentanyl and Propofol) with a facial mask (oxygen 40%, air 60%, sevorane MAC 0.81%). The patient was placed in a supine position with the head slightly hyperextended. The intervertebral space was detected under a fluoroscopic LL view. The surgeon held the sternocleidomastoid muscle laterally and the trachea medially. The introducer needle (19-gauge, 7.6 cm) was then inserted medially to the SCM and vessels through an anterior lateral approach, and stopped only when the annulus/nucleus junction was reached (Fig. 1). The tip of the needle stylet was aimed for the center of the nucleus in both the coronal and sagittal planes. X-ray monitoring (both AP and LL) confirmed the precise positioning of the needle within the annulus (Fig. 2).

The stylet was withdrawn from the introducer needle and replaced with the Perc-DC SpineWand (ArthroCare Corp., Sunnyvale, CA, USA). The wand was advanced until its tip extended approximately 5 mm beyond the tip of the needle, in order to ensure that the active portion of the wand was deployed in the annulus when activated. A short initial coagulation (<0.5 s) was performed upon wand insertion to ensure correct placement; if stimulation or movement was detected, the wand was repositioned. As the wand was drawn back out through the disc, three ablation cycles of approximately 8 s each were performed, rotating the wand tip 180° each time to form three consecutive channels within the disc (Fig. 3).

Patients were immediately mobilized following the procedure. They were discharged 24 h after surgery; antibiotic prophylaxis with a common cephalosporin was given in all cases. They were placed on a standard rehabilitation program as routine following interventional spinal procedures. Clinical status was assessed immediately postoperatively, at 3 months, and then every year.

Results

The C3–C4 disc level was treated in 4% of cases, C4–C5 in 13%, C5–C6 in 42%, C6–C7 in 40%, and others (C2–C3 and C7–T1) in 1%. Patient population available for VAS follow-up was 302 at 1 year, 190 at 2 years, 170 at 3 years, 124 at 4 years, and 69 at 5 years. At all time points, 50–60% of patients had good results, 30–40% of patients had satisfactory results, and 5–10% showed no change in condition (Table 1). In 349 cases, only one complication associated with the procedure was observed (0.29%). At 15 days following the procedure, one patient presented with discitis, which was treated successfully with antibiotics and immobilization with a brace for 2 months.

Conclusion

During PDD, plasma-mediated ablation creates small channels in the disc's nuclear material that relieve hydrostatic pressure while removing minimal tissue volume [5]. The

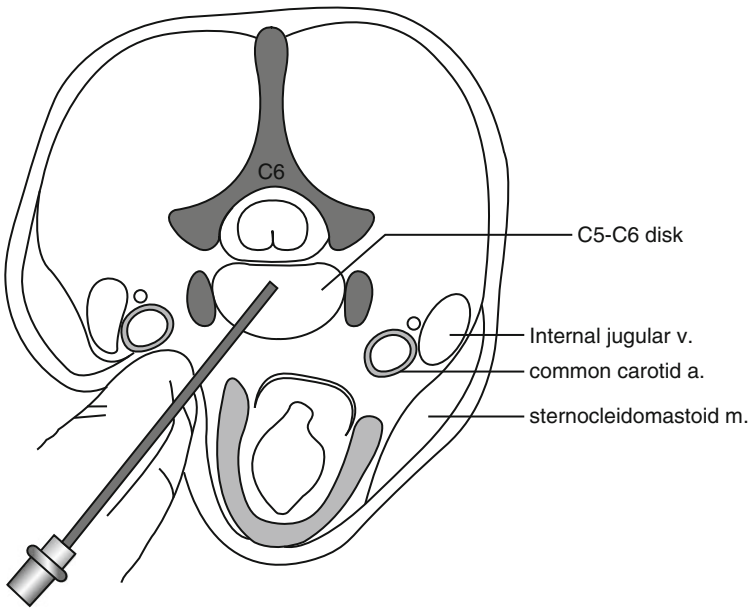

Fig. 1 Needle approach to the herniated disc

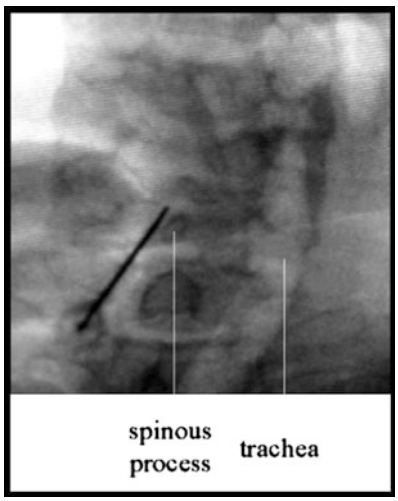

Fig. 2 X-ray monitoring to confirm proper positioning of the needle within the annulus

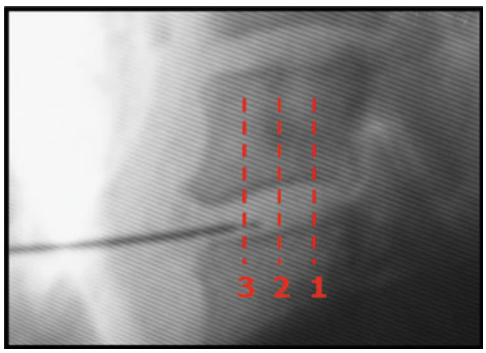

Fig. 3 Ablation channels formed by wand rotation

Table 1 Post-operative results

	3 Months (%)	1 Year (%)	2 Years (%)	3 Years (%)	4 Years (%)	5 Years (%)
Good	59.8	56.9	56.9	56.7	62.1	60.8
Satisfactory	35.6	35.5	38.4	38.6	31.4	30.6
No change	4.6	4.6	4.7	4.7	6.5	8.6

resultant disc decompression theoretically reduces internal forces which irritate the neighboring nerve root [1, 6, 25, 28, 31], likely down-regulating local inflammatory mediators, reducing overall disc size, and initiating the healing process, all contributing to a reduction in discogenic pain [8].

Spontaneous regression of disc herniations is far less likely in cervical discs than in the lumbar region [16]. In a retrospective study by Mochida et al. which performed MR imaging over a mean interval of 42 weeks, cervical disc herniation regression and symptom resolution occurred in only 15/38 (40%) patients [21]. Plasma disc decompression also is only applied to contained disc herniations, in which the annulus remains intact. This may prevent the initiation of natural immune and vascular responses which would promote regression of the herniation. Annular tears expose nuclear material, which is treated as a foreign body and initiates phagocytosis via macrophages [4] and neovascularization [13]. The infiltration of nuclear material into the epidural space also incites autolysis of its proteoglycan chains, resulting in dehydration of the herniated disc and promoting its natural shrinkage and regression [4]. A CT study by Maigne et al., which displayed regression of cervical disc herniations with radiculopathy via conservative therapy, found that the largest herniations were the ones most likely to reduce in size; this was posited to be a result of annular rupture and entry of nuclear material into the epidural space [18]. In an MR study, Bush et al. [4] concluded that the sole cervical herniation which did not undergo regression was formed of primarily annular material.

PDD has met with encouraging and significant results when utilized to treat pain associated with contained cervical disc herniations [3, 17, 22, 29]. Most recently, Li et al. [17] reported a series of 126 consecutive contained cervical disc herniation patients who underwent plasma-mediated disc decompression. Mean VAS scores showed statistically significant improvement at all time points through 1 year (Pre-op: 7.25 ± 0.44, 12 months: 2.42 ± 0.72; P-value: 0.000), and Macnab standard results were excellent or good in 83.73% of cases [17].

Allowing a contained cervical disc herniation to persist without effective intervention may permit the progression of disc degeneration. Other authors have cited the 6–12 week window for conservative treatment of cervical disc herniations, beyond which non-responsive patients are generally indicated for surgery. Conservative treatment of cervical radiculopathy is largely regarded as a short-term measure with no lasting effect [35]. It is our opinion that a proactive approach should be taken with plasma disc decompression, employing it as an early-response measure to prevent further disc degeneration. This case series demonstrates PDD as a safe treatment which stabilizes the spine and provides robust and sustained improvement in local and radicular pain over a 5-year period. Emerging research into plasma-mediated RF electrosurgery has indicated that the technique may positively affect inflammatory mediators in and around the disc [24], and that it is projected to stimulate healing and angiogenesis while down-regulating nociceptors [7, 32]. These potential factors may explain the excellent success of PDD in resolving symptoms not only quickly and efficiently, but maintaining positive results over a longer timeline.

Conflict of interest statement We declare that we have no conflict of interest.

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Percutaneous Laser Discectomy: Experience and Long Term Follow-Up

P.P.M. Menchetti, G. Canero, and W. Bini

Abstract The classical microsurgical approach in the treatment of herniated nucleus pulposus (HNP) has been substituted over the years by endoscopical approach, in which it is possible to practice via endoscopy a laser thermodiscoplasty, and by percutaneous laser disc decompression and nucleotomy. Percutaneous laser disc decompression and nucleotomy have been performed worldwide in more than 40,000 cases of HNP. Because water is the major component of the intervertebral disc and in HNP pain is caused by disc protrusion pressing against the nerve root, a 980 nm Diode *(Biolitec AG-Germany)* laser introduced via a 21-G needle under X-ray or CT-scan guidance and local anesthesia, vaporizes a small amount of the nucleous pulposus shrinking the disc and relieving the pressure on the nerve root. A multicentric retrospective study with a mean follow-up of 6 years was performed on 900 patients suffering from relevant symptoms that had been therapy-resistant for 6 months on average before consulting our department. Evaluation included 585 (65%) males and 315 (35%) females. The average age of patients operated was 46 years (18–54). The success rate at a mean follow-up of 5 years (2–6 years) was about 70% with a very low complication rate.

Keywords Diode laser · Herniated nucleus pulposus · Laser discectomy · Percutaneous laser decompression

Introduction

Over the years several treatments have been performed in disc herniation. At present, in order to reduce complications, the gold standard seems to be all minimally invasive techniques, offering not only the best solution for the patient, but also a fast and effective postoperative recovery time. Percutaneous laser disc decompression and nucleotomy is based on a reduction of volume in a closed hydraulic space, resulting in a great fall of pressure. Because water is the major component of the intervertebral disc and in disc herniation pain is caused by the disc protrusion pressing against the nerve root, vaporizing and shrinking the nucleus pulposus leads to immediate decompression of the nerve root [1, 2].

Since its first application [3], several types of lasers (Nd:YAG 1,064 nm, 1.320 nm; KTP 532 nm; CO2 10.6 μm; Ho:YAG 2,100 nm, Diode 940 nm, 810 nm) have been employed over the years.

The authors believe that 980 nm is the optimal wavelength for laser disc decompression and nucleotomy because 980 nm is 10 times more absorbent than 810 nm and 5 times more absorbent than 1,064 nm, requiring less laser energy, which implies less heat diffusion in surrounding tissues and no undesirable side effects.

Materials and Methods

Inclusion Criteria

Nine hundred patients, 585 (65%) males and 315 (35%) females affected by contained disc herniation (magnetic resonance imaging –MRI- documented) *(protrusion, subannular extrusion),* were included in a multicentric retrospective study at a mean follow-up of 5 years (2–6 years). The average age of patients operated was 46 years (18–54), suffering from relevant symptoms that had been therapy-resistant for

P.P.M. Menchetti (✉)
Florence and Rome University, Via Jacopo Nardi, 15, 50132, Firenze, Italy
e-mail: menchetti@islass.org
G. Canero
San Feliciano Hospital, Rome, Italy
W. Bini
Spine Surgery Unit, Seligenstadt, Germany

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6 months on average before the laser procedure. The level of disc removal was L4/L5 in 409 cases (45%), L5/S1 in 377 cases (42%), L3/L4 in 78 cases (9%), L2/L3 in 22 cases (2.4%), L1/L2 6 cases (0.6%), T12/L1 4 cases (0.4%) and T11/T12 4 cases (0.4%).

Disc herniation had to be contained or at least in contact with the parent disc in order to permit a reduction of the pressure on the nerve root by laser energy. No free disc fragment *(sequestration)* was treated with this technique. Sequestration *was an absolute contraindication*.

Scar entrapment by previous microsurgical approach, because laser energy involves a fibrocartilage replacement in the disc from the inner layer of the annulus returning to normal after 3 months [4, 5], was another *absolute contraindication*. Other exclusion criteria included transannular extrusion, severe spinal stenosis, severe spondylosis with osteophytes and calcifications of the posterior spinal ligament.

The procedure consisted of a 21-G atraumatic tip chiba needle guided under C-arm, or CT-scan percutaneously inserted into a herniated disc under local anesthesia. Diode Laser 980 nm *(Biolitec AG-Germany)*, 1,200–1,500 J of total energy, was delivered through a disposable 360 μm Silica Fiber Optic; the power parameters were 12 W with exposure time 0.60 s in a pulsed wave, with 2 s pauses for heat dissipation. A smoke evacuation system specifically designed and worldwide patented (Menchetti's handpiece) connected to the needle permits to eliminate gas formation during the treatment by reducing postoperative muscle contracture (Fig. 1a–i).

Results

A retrospective multicentric evaluation with an average follow-up of 5 years (2–6 years) was performed doing MRI or CT scans at 3 months and 1 year. VAS (Visual Analogue Scale) and the Macnab's criteria (Table 1) were applied on a total of 900 patients.

The excellent/good results at mean 5 year follow-up according to Macnab were 68%, the fair results were 10%, and the poor results were 22%. The excellent/good results after mean 3 year follow-up were 78%, fair results were 11% and poor results were 9%. VAS decreased from a preoperative 8.5 to a postoperative 2.3 at 3 year f.u., up to 3.4 at 5 year f.u. MRI or CT scan showed a reduction of disc herniation at 3 months and 1 year in only 70% of excellent/good results, because a disc shrinkage of less than 1.5–2 ml is not detectable on MRI or CT scan [4, 6] (Fig. 2–4). No significant difference in outcome ($p > 0.05$) related to sex, age, disc level, and symptoms duration were found. Fair and poor results correlated ($p < 0.05$) with subannular extrusion, in which microsurgery was performed after 1–3 months in 40% of cases treated under C-arm.

In 72% of excellent/good results there was immediate pain relief with normal straight leg raising (SLR), in 12% after 72 h and in 16% after 3–7 days; improvement of neurological signs (motor weakness and reflex depression) was recorded at 1 month in 65% of cases, 3 months in 20% and 3–6 months in 15% of cases.

Complications

No complete disc herniation removal, 4 cases (0.8%) of spondylitis with good response to steroids, no septic or aseptic discitis was detected, no CSF fistula, no nerve root injury; eight patients (1.6%) advised headache post spinal lumbar puncture, in L5-S1 paramedian approach, returning to normal after 2–3 days bed rest.

Discussion

Percutaneous laser disc decompression and nucleotomy have been performed worldwide on more than 40,000 patients. The more used lasers were KTP 532 nm, Ho:YAG 2,100 nm, Nd: YAG 1,064 nm. Their combined success rate (excellent/good to fair) according to Macnab and Oswestry score were more than 80%, with a complication rate of less than 1.5% [5, 7, 8]. In order to obtain a good result it is very important not only to properly select patients, but also to carefully choose the laser used.

Regarding the use of the Diode 980 nm, we believe it to be the best and more advanced laser in the treatment of disc herniation with optimal water absorption. Because 980 nm is 10 times more absorbent than 810 nm and 5 times more absorbent than 1,064 nm, requiring less laser energy; it implies less heat diffusion in surrounding tissues and no undesirable side effects. A first introduction of Diode 940 nm in disc herniation treatment was performed in 1998 by Hellinger [9] in a prospective randomized study versus Nd: YAG 1,064 nm. The overall success rate (90%) confirmed the proper use of Diode in order to decompress the nerve root in disc herniation. Nakai et al. [10] also confirmed in an experimental study with a Diode 810 nm that Diode is less aggressive in the surrounding tissue, preserving the end plate and the vertebral body from any damage. No secondary changes on the intervertebral disc and adjacent vertebral body after Diode laser disc irradiation were detected.

Experimental studies performed both on human and specimen lumbar discs using the *Diode Laser 980 nm* showed an absorption of laser light of 90.27% in the disc and a retraction of about 55% (±1.7) on 2.7 mm of the tissue after laser treatment [11].

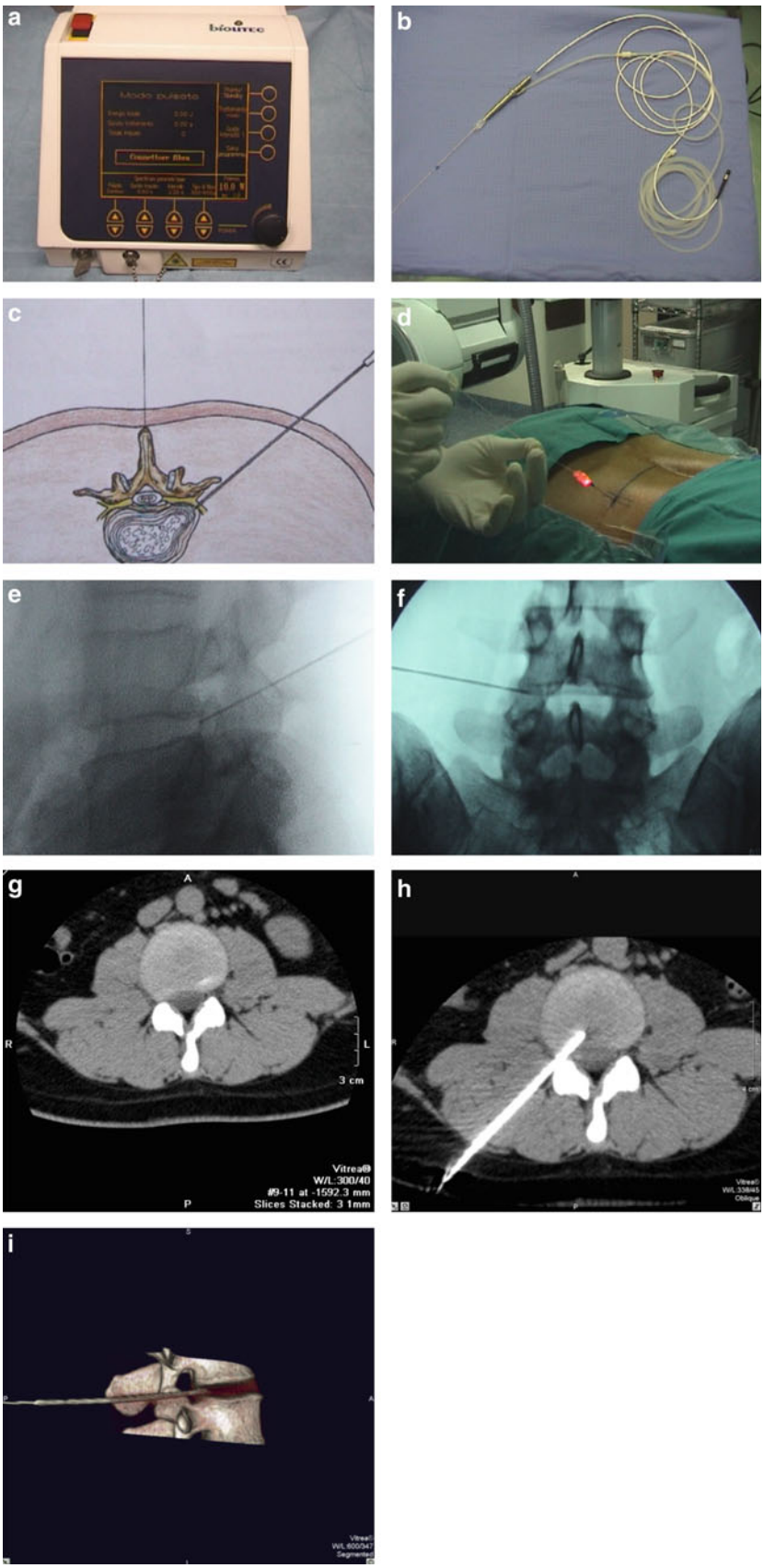

Fig. 1 (**a**) Diode 980 nm laser (Biolitec AG). (**b**) Disposable 360 µm silica fiber optic. (**c**) Access to foramen. (**d**) Optical fiber insertion. (**e**) C-arm guidance, LL view. (**f**) C-arm guidance AP view. (**g**) Foraminal disc herniation. (**h**) Laser discectomy under CT-Scan. (**i**) 3D reconstruction

Table 1 Macnab's criteria

Excellent/good	Resumed preop function, occasional backache, no objective signs of nerve root involvement
Fair	Intermittent episodes of mild lumbar pain and/or low back pain, no objective signs of nerve root involvement
Poor	Subjective no productivity, continued pain, inactive, objective signs of nerve root involvement

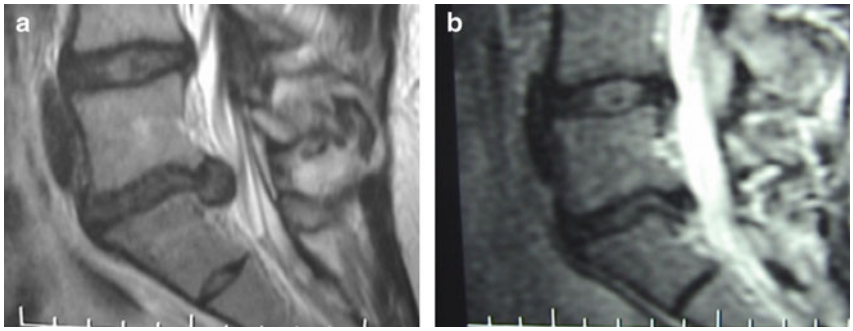

Fig. 2 (**a**) Twenty-seven year female L5-S1 HNP. (**b**) After Diode laser 980 nm

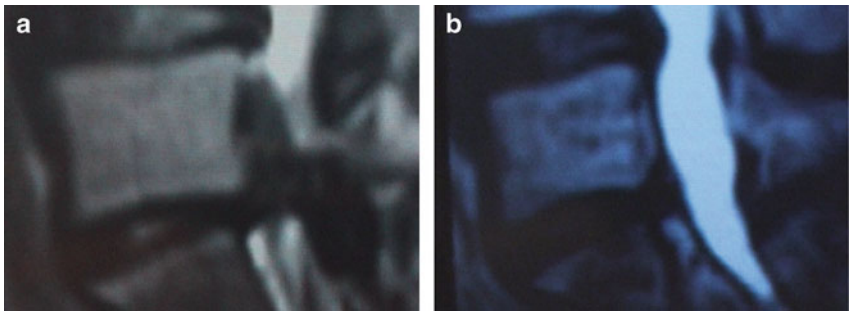

Fig. 3 (**a**) Thirty-eight year female L5-S1 transannular extrusion. (**b**) After Diode laser 980 nm

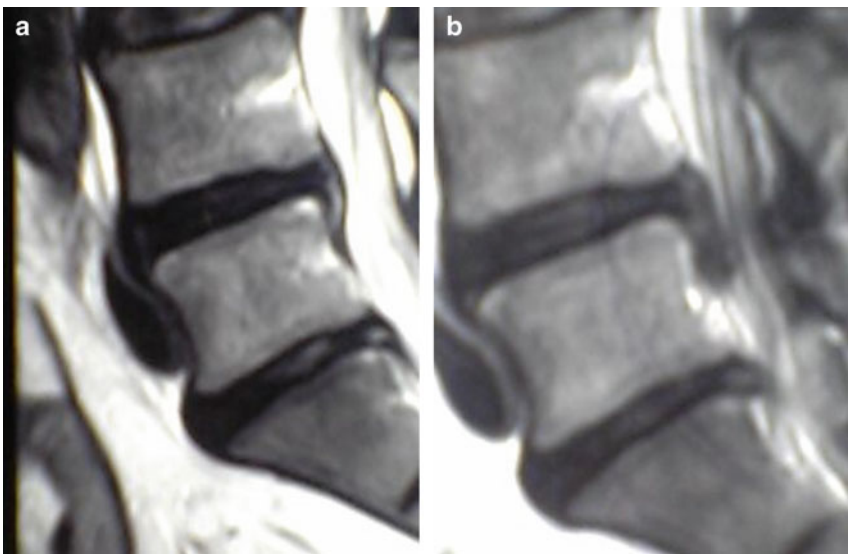

Fig. 4 (**a**) Forty-six year male L4-L5 HNP. (**b**) After Diode laser 980 nm

For these reasons the authors believe that using the specially designed and optimised Diode 980 nm Laser in the treatment of disc herniation is the method of choice, confirming the overall success rate of the literature [4, 5, 7, 8, 10] without any complications [12–14] related to heat diffusion in surrounding tissues (aseptic discitis and spondilytis, bladder injuries, vascular injuries to the abdominal cavity, abdomen injuries).

Conclusion

In conclusion, we strive for maximal use of this minimally invasive surgical technique that has proven to be safe and effective, is minimally invasive, is performed in outpatient setting, requires no general anesthesia, avoids skin incision (with reduced infection rate), no muscle damage (no post-operative pain), no bone removal (no vertebral instability), no peridural scar, and does not preclude microsurgery, if needed.

Conflict of interest statement I declare that I have no conflict of interest..

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Mechanism of Action of Oxygen Ozone Therapy in the Treatment of Disc Herniation and Low Back Pain

Emma Borrelli

Abstract In the low back syndrome the pain has a multifactorial origin and ozone can surprisingly display a number of beneficial effects ranging from the inhibition of inflammation, correction of ischemia and venous stasis, and finally inducing a reflex therapy effect by stimulating anti-nociceptor analgesic mechanisms. The intradiscal and intramuscular injection of oxygen–ozone is a successful approach comparable to other minimally invasive procedures, but the elucidation of the mechanisms of action remains elusive. This communication shortly reports the mechanisms of action of oxygen ozone therapy at the level of intervertebral disc and paravertebral muscles.

Keywords Low-back pain syndrome • Oxygen ozone injection • Mechanism of Action of Ozone Therapy

Introduction

Despite a large number of biochemical studies, the use of ozone in medicine still remains controversial. At present, ozone therapy is most commonly associated with the treatment of disc herniation and/or low back pain throughout the injection of an oxygen–ozone mixture in the vertebral disc or in the paravertebral muscles.

In the case of disc herniation, the clinical effects of ozone are reported to be related to the lysis and reduction of disc, and the success of the therapy is based on the possibility of statistically estimating in neuroradiological studies the reduction or disappearance of the anatomic protrusion.

Nevertheless, confusion persists concerning the amount of gas mixture, the concentration of ozone, the frequency of the therapy and the site of injection. The same efficacy has been reported with different methodologies such as paravertebral, intradiscal, intraforaminal or epidural ozone injections, and the variability of clinical responsiveness of patients in different studies with the same technical approach introduces further difficulties in the standardisation of the therapy.

Controlled and randomized clinical trials are urgently needed to prove the validity of ozone therapy.

This article briefly reports the biochemical mechanism of action of ozone in the field of neurosurgical disease.

Intradiscal Injection

In the case of gas injection directly into the nucleus pulposus, we have some evidence that ozone dissolves in the intradiscal water and reacts with the complex macromolecular components such as proteoglycans and glicosoaminoglycans. The reaction entails an oxidation of these substrates (galactose, glycuronic acid, glycine, 4-hydroxyprolin) and the breakdown of intra- and intermolecular chains leading to disintegration of the three-dimensional structure. Its collapse frees the entrapped water that, after reabsorption, allows a decrease of intradiscal pressure and possibly a disappearance of pain due to the reduced pressure on the nervous root. However, since ozone is very often released also along the injection path (i.e., intraforaminal) the final therapeutic effect is due to the combination of vasculomediated and biochemical effects (improved oxygenation, correction of local acidosis, disappearance of venous and lymphatic stasis). It seems important to postulate that in the intraforaminal space, the presence of lipids, an excellent substrate for ozone, may favour the release of oxidized phospholipids to be included among LOPs: surprisingly, during inflammation, these compounds can inhibit inflammation as it has been shown in mice undergoing a lethal endotoxic shock. Thus, ozone appears to display paradoxical and unexpected useful

E. Borrelli
Department of Surgery and Bioengineering, University of Siena, Siena, Italy
e-mail: borrelli@unisi.it

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effects such as inhibition of the release or inactivation of proteinases and likely enhancement of the release of immunosuppressive cytokines such as TGFβ or/and IL-10. Even more surprising is the recent evidence suggesting that ozone, by inhibiting COX-2, blocks the synthesis of proinflammatory prostaglandin E_2. Another important analgesic effect may be derived by the induction of antioxidant enzymes resulting in the adaptation to chronic oxidative stress. These novel and surprising aspects have allowed formulating the concept of the ozone-paradox.

Paravertebral Injection

The indirect approach consisting of the injection of 10–20 ml of gas in one to four sites of the paravertebral muscles in patients with back-ache, has become very popular in Italy, China, and Spain. This procedure is named "chemical acupuncture" because both the needle and oxygen–ozone must have a role in eliciting a complex series of chemical and neurological reactions, leading to the disappearance of pain in the majority (70–80% of good response) of patients with low back-pain. It has been clearly established that the ozone concentration must be neither below 18–20 mcg/ml, nor higher than 25–28 mcg/ml. If it is too low, it is hardly effective but higher than 20 mcg/ml can be, especially during the initial treatments, too painful and may even cause lipothymia and a risky vasovagal reflex. On the other hand, it has been often observed that, after five to seven treatments, the pain threshold raises and therefore we can carefully increase the ozone concentration.

What happens to ozone injected into the paravertebral muscle? Ozone dissolves mostly into the interstitial water and reacts immediately with antioxidants and PUFA generating hydrogen peroxide and LOPs, as it has been amply described. These compounds stimulate local C-nociceptors and cause a transitory but usually tolerable pain that is an essential requirement for achieving the final therapeutic effect.

Moreover, another overlooked effect is caused by the mechanical factor induced by injecting oxygen that is about 98% of the gas volume. This certainly is another stimulus causing a feeling of tension and pressure on the muscle and it is, at least in part, responsible of the final therapeutic effect. Unfortunately, in spite of several formal requests, only once the effect of oxygen alone was systematically ascertained when, unintentionally, it was injected into the lumbar muscles of 30 patients against 66 experimental (ozone: 20 mcg/ml). Interestingly, albeit slightly less even control patients improved. All other reported studies have NO CONTROL and this, from a scientific point of view, is a pitfall. This serious drawback has been recently emphasized by an American scientist, who has specified that the FDA will not approve the use of ozone unless a randomized and controlled study is performed. A sham injection with normal saline has been proposed, but this is not correct and should be substituted by the injection of oxygen that represents the bulk of the gas mixture.

The stimulation of nociceptors is able to elicit the elevation of pain threshold and an antalgic response via the well-known descending antinociceptive system. As it occurs during a cutaneous stimulation, or acupuncture, albeit at a far lower level, the introduction of the needle, reinforced by the pressure of the gas plus the generated chemicals, induces a sort of prolonged stunning of nociceptors. It is known that an algic stimulation of the skin and muscles can reduce pain through the mechanism of diffuse noxious inhibitory control (DNIC). Recently it has been shown that even minimal acupuncture that is the superficial needling of NON-acupuncture points, has a similar benefit as real acupuncture on patients with tension-type headache. Thus, although it is known that the placebo effect is important, it is important to ascertain its relevance.

Conclusion

In conclusion, the probable mechanisms playing a role are as follows:

(a) Activation of the descending antinociceptive system.
(b) Release of endorphins blocks transmission of the noxious signal to the thalamus and cortex.
(c) Hypostimulation (elevation of the activation threshold) linked to the oxidative degeneration of C-nociceptors.
(d) Simultaneous psychogenic stimulation of the central analgesic system induced by the gas injection, somehow due to a placebo effect.
(e) The localized oxygenation and analgesia are most important because they permit muscle relaxation and vasodilation, thus a reactivation of the muscle metabolism, by favouring oxidation of lactate, neutralization of acidosis, enhanced synthesis of ATP, Ca^{2+} reuptake and edema reabsorption.

In conclusion, we have seen that pain has a multifactorial origin and that ozone can surprisingly display a number of beneficial effects ranging from the inhibition of inflammation, correction of ischemia and venous stasis and finally inducing a reflex therapy effect by stimulating anti-nociceptor analgesic mechanisms.

The intradiscal and intramuscular injection of oxygen–ozone is a successful approach comparable to other minimally invasive procedures but a standardization of procedure and controlled randomized studies are needed.

Conflicts of Interest Statement I declare that I have no conflict of interest.

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Treatment of Symptomatic Lumbar Spinal Degenerative Pathologies by Means of Combined Conservative Biochemical Treatments

A. Alexandre, L. Corò, R. Paradiso, R. Dall'Aglio, A.M. Alexandre, F. Fraschini, and P.G. Spaggiari

Abstract Research in spine surgery has proposed new soft and less invasive techniques. These are the results of our experience with oxygen-ozone therapy, which we could experiment within the Italian National Health System over 3 years. A total of 1,920 patients were admitted on the basis of unselected enrolment because of lumbosciatic pain. Patients were divided into three groups: (A) Patients with degenerative disc disease and arthropathy: 509 (26.5%), (B) Patients with failed back surgery syndrome (FBSS): 1,027 (53.489%), and (C) Patients with pure herniated lumbar disc: 384 (20%). The rationale of the treatment for all these different pathologies we have taken into consideration is the biochemical mechanism by which they can engender pain and dysfunction. Treatment for group A: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days)+ endoscopic neurolysis. Treatment for group B: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days)+endoscopic neurolysis with intradiscal procedure (named percutaneous peridurodiscolysis). Treatment for group C: paravertebral injection (two cycles of 6 sessions, one each 3 days)+percutaneous discolysis.

The perceived quality of result for this minimally invasive procedure makes oxygen-ozone therapy an interesting weapon in the hands of doctors. Furthermore, if the technique loses its clinical effectiveness, it can be repeated without harm for the patient, and costs for the health organization are notably very low, above all if compared to surgical procedures.

We underline the need that this treatment should be performed in protected structures, in operative rooms, under anesthesiologic control, and in the hands of specialists.

Keywords Conservative biochemical treatments • Degenerative disc disease • Discolysis • Discoradicular conflict • FBSS • Herniated lumbar disc • Oxygen–ozone injections • Ozone • Periduroscopy • Spinal degenerative pathologies

Introduction

Problems, connected with pain and dysfunction due to discoradicular conflict in the lumbar or cervical area are nowadays well documented. Open surgery represents an option that is indispensable at times, but may cause a number of complications or adverse effects, which are not clearly defined because case records are generally confined to short-term follow-up, while complete reviews and metanalysis are lacking. The fact that in the long run a high percentage of patients will suffer recurrence and complications is evident. The frequency of the problem is so high that it is recognized and defined as a complete syndrome: the Failed Back Surgery Syndrome. Epidural scarring is a natural consequence of the bleeding caused by surgery, but it is not clear why at times this will provoke adhesion and compression on the nervous structures. Furthermore, instrumentation has contributed severely to an increase in this syndrome rather than helping to correct the problem [12, 32].

These are some of the reasons for the great increase of interest in minimallyinvasive techniques, which aim to act directly on the disc without entering the spinal canal.

Several substances have been injected into the disc in the last few decades and each substance has enjoyed a period of

A. Alexandre (✉), L. Corò, R. Paradiso, and R. Dall'Aglio
European Neurosurgical Institute (EU.N.I.), Via Ghirada 2, 31100, Treviso, Italy
e-mail: alexandre@eunionline.com

A.M. Alexandre
Department of Bioimaging and Radiological Sciences, Catholic University Sacred Heart Policlinico "A. Gemelli", Rome, Italy

F. Fraschini
Pharmacology Institute of Milan University School of Medicine, Milan, Italy

P.G. Spaggiari
General Direction and Administration, Cremona Hospital, Cremona, Italy

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popularity, some adverse effects, criticism, rejection or reduced application.

Research in spine surgery has proposed new soft and less invasive techniques. Some of them are readily available and have been practiced for years. Among these are oxygen-ozone injections, which we could experiment within the Italian National Health System over 3 years.

The objective of the treatment is to avoid any possible negative aspect of conventional surgery: general anesthesia, days of hospitalization and long-lasting postoperative limitations, spinal instability as well as the consequences of epidural scarring.

Recently critical reviews of the etiopathogenetic mechanisms underlying these manifestations of pain (that is, not just the mechanical conflict between the degenerated disc and the nerve roots or other algogenic structures, but also chemical irritation) have on the one hand suggested decreasing the use of conventional surgery for disc pathologies and on the other pointed towards more conservative minimally invasive surgical techniques that respect the anatomy and obtain a good response to the clinical problem.

Such techniques do not replace conventional surgery which, in carefully selected cases, remains first choice. Minimally invasive surgical techniques represent a midway stage between simple physiotherapy and open surgery. A high percentage of patients are thus spared open surgery, which is instead used on those who have no other choice.

Nowadays the aim is to give the person the sensation of wellbeing and not of being "ill" due to these pathologies, which are not life threatening but spoil the quality of life dreadfully.

It has been fully understood that even if there is no hope of a "full recovery" in the sense of eliminating the problem, patients can be offered a good quality of life despite the structural alteration.

This is done using simple methods aiming mainly at the biochemical correction of nerve dysfunction and hyschemia. These techniques have no significant side effects and can be repeated over years if needed; they can always be performed as 1 day procedures, and do not necessitate confinement to bed.

Patients and Methods

Patients

In the period September 05–December 07, 1,920 patients with lumbosciatic pain received biochemical treatments, mostly based on oxygen-ozone therapy, according to the Experimental Protocol code 119 of the observational studies of the Lombardy Region, Italy, under the supervision of the Pharmacology Institute of Milan University School of Medicine (Prof. F. Fraschini).

Patients were admitted to evaluation on the basis of unselected enrolment because of lumbosciatic pain, in the Division of Neuropathic Pain Treatment at Sant'Angelo Hospital, Lodi (supervisor Prof. P.G. Spaggiari).

Upon enrolment all the patients underwent evaluation and scoring according to the Roland Morris international disability scale and the International Pain Visual Analog Scale (VAS).

The same evaluation was performed upon clinical controls during the follow-up.

Further to clinical diagnosis, patients were studied by neuroradiological and EMG investigations. On this basis they were divided into three groups:

(a) Patients with degenerative disc disease and arthropathy: 509 (26.5% of the series)
(b) Patients with FBSS 1,027: (53.489%)
(c) Patients with pure herniated lumbar disc: 384 (20%)

Methods: Rationale for the Treatment

All these different pathologies we have taken into consideration have a biochemical mechanism by which they can engender pain and dysfunction. This is the general basis to argue that a biochemical treatment might be useful for controlling symptoms and allowing a better quality of life, avoiding open surgery.

(a) The process of disc degeneration is an aberrant, cell-mediated response to progressive structural failure. A degenerated disc is one with structural failure combined with accelerated or advanced signs of aging. The term "Degenerative Disc Disease" should be applied to a degenerated disc that is also painful. Cell-mediated responses to structural failure can be regarded as the final common pathway of the disease process [10]. Although mechanical loading precipitates degeneration, the most important cause of degeneration could be the various processes that weaken a disc before disruption, or that impair its healing response. The combined effects of an unfavorable inheritance, middle age, inadequate metabolite transport, and loading history appear to weaken some discs to such an extent that physical disruption follows some minor incident. An extensive review of nomenclature made clear distinctions between pathologic and age-related changes in discs, and included major structural changes such as radial fissures and disc narrowing in the former category [27]. Physical and biologic mechanisms produce structural failure

progresses and, therefore, this is a suitable marker for a degenerative process. Damage to one part of a disc increases load-bearing by adjacent tissue, so the damage is likely to spread to adjacent articular and ligamentous structures. Referring to tendon degeneration, Riley et al. [26] suggest an active, cell-mediated process that may result from a failure to regulate specific MMP activities in response to repeated injury or mechanical strain. There is a growing consensus that degeneration involves aberrant cell-mediated responses to progressively deteriorating circumstances in their surrounding matrix.

(b) Failed Back Surgery Syndrome is a definition bespeaking the clinical effect of biochemical nerve structure dysfunction. This dysfunction may be provoked by peridural scarring, by local ischemia because of reduced blood flow and/or of reduced CSF perfusion on the nerve roots and ganglia. Several reports have shown that surgical reintervention and physical decompression may not be a solution [11, 19, 28].

(c) Pure herniated lumbar disc with no other concomitant factors. Herniated intervertebral disc tissue has been shown to produce a large number of proinflammatory mediators and cytokines [7]. Several studies have identified inflammatory mediators (phospholipaseA2, prostaglandin Ez, leukotrienes, nitric oxide, immunoglobulins, proinflammatory cytokines such as interleukin [IL]-I~, IL-11~, IL-6, and tumor necrosis factor alpha (TNFM) and autoimmune reaction (macrophages expressing IL-11~, intercellular adhesion molecules) in disk herniation. An appealing hypothesis is that the leakage of these agents may produce an excitation of the nociceptors, a direct neural injury, a nerve inflammation, or an enhancement of sensitization to other pain-producing substances (such as bradykinin), leading to the nerve root pain [7, 8, 15, 19, 21, 28, 29]. With the exception of those cases in which the severity of the motor deficit or of intractable pain perfectly fitting with neuroradiological investigations made surgery the only correct indication, patients were offered the possibility of resolving their clinical problem without open surgery and with reduced amounts of drugs. In cases where dexamethasone was being administered, it was progressively stopped at the beginning of ozone treatment. Non-steroid anti-inflammatory drugs were administered occasionally as needed.

Methods: Specific Procedures

1. *Intradiscal treatment, so-called discolysis* entails a mixture of oxygen and ozone in concentrations of 35 μg/mL being injected directly into the disc.

The action of the ozone consists of dehydrating the amorphous matrix of the nucleus by breaking the mucopolysaccharide structure and thereby releasing water.

There is ample literature in various fields of medicine showing that in tissues with normal blood supply ozone activates antioxidant metabolism mechanisms, has an important anti-edema effect and a very powerful anti-inflammatory effect. It also helps oxygenation of the tissues and has a positive hemorheologic effect [5].

A mixture of oxygen and ozone has been used in medicine since the thirties for treating pain and dysfunction in patients with thrombotic and ischemic illnesses. Empirical observation of the long-lasting and potent effect of an injection of this mixture into the paravertebral muscles, to treat radicular dysfunction and pain caused by the disco-radicular conflict, has led to in-depth studies on the subject. Although working in different fields, researchers surprisingly noted that a short and calculated oxidative stress, obtained by administering ozone, can correct a persistent imbalance, caused by an excessive or chronic oxidative trauma or stress. It is by now clear that repeated small injections of ozone increase superoxide dismutase, catalase and gluthatione-peroxidase activity, inducing a state of adaptation to the oxidative stress with consequent important therapeutic implications [5]. In 1982 Jacobs [13] reported the absence of side effects in more than five million sessions of ozone therapy for various pathologies. Intramuscular treatment brings about pain relief in most patients together with decongestion, re-absorption of the edema and improved motility. All this led to the idea of injecting the oxygen-ozone mixture into the intervertebral disc and into the conjugate foramen in order to obtain a powerful effect directly on the pathogenetic mechanism [2, 9, 16].

Many studies have been carried out on various aspects of disc pathology and possible solutions to the problem. Studies on pain originating from this pathology show that it can be the consequence of biochemical mechanisms of acid intoxication of the nerve, which to some extent may have nothing to do with the mechanical problem, but may depend on an autoimmune reaction that triggers a chronic inflammatory response, engendering an acid environment or ischemia [20, 23, 30]. In 1990 attention was drawn to phospholipase A2 as the cause of radicular pain. Saal et al. [29] showed that phospholipase A2 is the cause of radicular pain irrespective of the immunological response or a direct inflammatory process. Phospholipase A2 is responsible for freeing arachidonic acid and therefore prostaglandins. High levels of phospholipase A2 have been found in herniated discs. These problems can be resolved with a biochemical approach, thereby reducing the need for surgery [6, 8, 15, 29]. Ozone injected into the disc and the epidural space of the conjugate foramen and along the posterior longitudinal ligament acts as a powerful stimulus in activating the antioxidant defence

mechanism, helping normalize the oxidation-reduction balance with neutralization of acidosis, increase in ATP synthesis, uptake of calcium-ions and re-absorption of the edema [6, 18, 23, 30]. On the other hand the mechanism of endplate sclerosis and the spontaneous elimination of herniated fragments have been meticulously studied over the years and it has been shown that an autoimmune response develops against "non-self" material with a chronic inflammatory reaction [30]. Experimental models suggest that the material of the nucleus pulposus subject to degeneration can act as a chemical or immunological irritant and that these mechanisms can produce an inflammatory response [7, 19, 28]. Until now studies have presumed that the injection of such a powerful oxidant as ozone induces an excess production of antioxidant enzymes, which neutralize the chain formation of unstable reactive oxygen species (ROS) [6]. Ozone seems to reactivate the immunity system response. After intradiscal injection ozone can accelerate proteoglycan degradation in the nucleus pulposus that is degenerating, leading to its re-absorption and dehydration with consequent reduction of the hernia volume causing compression of the nerves [14, 17, 22, 24].

The intradiscal injection follows the posterolateral, extra-articular route. A fully equipped aseptic operating theatre is required with the necessary anesthesiologic assistance. Fluoroscopic apparatus allows direct control of placement. The procedure includes discography.

After an anesthesiologic assessment and before entering the operating theatre the patient is sedated with Valium 25 gtt × os and with i.m. analgesic.

At the moment of disc puncture and immediately prior to the intradiscal injection, the anesthetist sedates the patient preferably with Diprivan, an i.v. hypnotic anesthetic.

The median line and the parallel line along the lateral margin of the paravertebral muscles on the side of the pathology are drawn on the skin of the back in preparation and then the edge of the iliac crest. The skin is then disinfected and the sterile field prepared.

A 22 G 8 Chiba type, TW, 72 mm × 20.32 cm needle is used in such a way as to compose the hypotenuse of a triangle in which the other two lines are: (a) the distance along the median line between the skin and the disc (approximately 9 cm), and (b) the distance between the median line and the marginal parallel line of the paravertebral muscles (approximately 9 cm). The puncture is then made along the paravertebral line with an inclination of approximately 45′ towards the median plane in a craniocaudal direction so as to be as parallel as possible to the disc plates. A fluoroscopic check is made. Presuming a possible inter-reaction between the gas and the iodide ion we avoided the radiopaque contrast. We have instead exploited the possibility of seeing and photographing the same type of information regarding disc conditions through a minimal volume of oxygen injected.

The purpose of discography is:

(a) To confirm correct needle placement.
(b) To exclude communication with vascular or subarachnoid spaces.
(c) To show the extent of disc degeneration.
(d) To provide documentation of the procedure.

The mixture concentration is 35 μg ozone/mL, but higher dosages have been used in cases of smaller or intraforaminal herniation or in young patients.

The injected quantity varies according to disc conditions. A fissured and degenerated disc allows 20–30 mL of gas to be introduced, since it will also spread into the surrounding tissues, thereby automatically creating an epidural and periradicular distribution. A solid taut disc on the contrary allows only 2–4 mL of mixture at the most to be injected under great pressure.

After the procedure the patient should be made to rest in a supine position for at least 2 h so that the gases are not immediately dislodged by the orthostatic load.

2. *Endoscopic epidurolysis* is another technique which fits the characteristics of minimal invasiveness. It aims at "freeing" the nerve roots from adhesions that could have formed as a consequence of the conventional microdiscectomy operation. Apart from the Failed Back Surgery Syndrome, endoscopic epidurolysis is indicated in stenosis of the vertebral canal due to arthrosis, which causes the classic neurogenic claudication.

The epidurolysis procedure consists of penetrating the spinal canal through the sacral jatus with an endoscope containing an optic fiber 0.9 mm in diameter, a flushing and suction channel, and a metallic guidance system.

The endoscope goes up in the vertebral column as far as the first lumbar vertebra.

The procedure is carried out under local anesthesia with a very low iatrogenic risk [1, 25].

3. *Outpatient treatment*: In outpatients the purpose of the treatment was the nutrition of the nervous structure, against its actual situation of sub-ischemia, as well as the correction of the acid balance. This was done by a series of outpatient procedures, carried out in the pre- and post-operative phases.

Oxygen-ozone gas mixture has been administered locally to the site, in and through the paravertebral muscles (with a periganglionic or periradicular target), thereby greatly reducing the need for corticosteroids while having a fast, continual effect on the pain. The doses were 10 mL gas mixture, at 15 μg ozone concentration per ml, injected on each side paravertebral at the level of the pathology, through a 20-G needle 5 cm long. After the injection the patient is left 5 min resting lying down.

Patients often felt an instant benefit as if an anesthetic had been injected, thanks to the strong anti-edema and anti-inflammatory effect.

One of the authors, a general medicine professional (R.d.A.) could add ozone into 300 mL venous blood drawn off into a transfusional bag, at the dose of 50 mL 0203 gas mixture at 30 μg/mL ozone concentration, performing the so-called autohaemotherapy [3, 4].

All these procedures have greatly reduced the need for conventional anti-inflammatory drugs and cortisone, all to the benefit of suppressing the incidence of side effects [31].

Based on these methods, this is the protocol of treatment for each pathological situation:

Treatment for group A: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days)+ endoscopic neurolysis.

Treatment for group B: paravertebral injection and phleboclysis (two cycles of 6 sessions, one each 3 days)+ endoscopic neurolysis with intradiscal procedure (named percutaneous peridurodiscolysis).

Treatment for group C: paravertebral injection (two cycles of 6 sessions, one each 3 days)+percutaneous discolysis.

Results

As mentioned we treated 1,920 patients, 43.5% of whom were men and 56.4% women.
In the table the age distribution is shown:

Age of patients	Total (%)	Women	Men
20–35	n.538=28.02	247 (45.9%)	291 (54.09%)
36–45	n.774=40.31	453 (58.52%)	321 (41.47%)
46–88	n.608=31.66	383 (62.9%)	225 (37%)

Patient Group A with Degenerative Disc Arthropathy

Five hundred and nine patients, 26.5% of the entire series. These were persons suffering from problems involving multiple vertebral and disc levels with degenerative and arthrosic factors that make "conventional" surgery either impracticable or very invasive, probably involving stabilization with multi-level instrumentation, i.e. vertebral arthrodesis with metal implants.

Results were calculated according to the Roland Morris international disability scale and the International Pain Visual Analog Scale (VAS).

These patients underwent outpatient treatment with the prospect of passing on to the percutaneous operation of endoscopic neurolysis. In the outpatient phase.

9 p. (1.76%) showed no clinical result whatsoever during those applications, so treatment was suspended and they were removed from classification.

225 p. (44.2%) showed a moderate result and were passed on to percutaneous endoscopic neurolysis.

122 p. (23.9%) showed a good clinical result and were passed on to the percutaneous endoscopic neurolysis.

153p. (30.05%) showed an excellent result and the cure was considered sufficient and was ended.

We consequently assessed the results obtained after percutaneous endoscopic neurolysis and compared these to the situation scored at the end of outpatient therapy.

The 225 patients with moderate result changed as follows:

43 out of 225 (19.11%) passed to a situation of excellent result
57 out of 225 (25.33%) passed to a situation of good result
121 out of 225 (53.77%) remained with a situation of moderate result
4 out of 225 (1.77%) passed to a situation of poorer result

The 122 patients with good result changed as follows:

65 out of 122 (53.27%) passed to a situation of excellent result
55 out of 122 (45.08%) remained with a situation of good result
2 out of 122 (1.63%) passed to a situation of moderate result

After outpatient treatment and minimally invasive percutaneous endoscopic neurolysis in patients with multi-level degenerative disc arthropathy of the lumbar column the *result was*:

Excellent in 153+65+43=261 cases out of 509 (51.27%)
Good in 55+57=112 cases out of 509 (22%)
Moderate in 121+2=123 cases out of 509 (24.16%)
Poor in 4=4 cases out of 509 (0.78%)
It was impossible to treat 9 cases out of 509 (1.76%)

Adding together excellent±good means 373 cases out of 509=73.28%

Patient Group B: Failed Back Surgery Syndrome FBSS

Thousand twenty seven people came to us because of persistent pain in the vertebral column having the characteristics of pain-dysfunctional suffering typical of the failed back surgery syndrome: lumbar pain, abnormal gait and fatigability, diffuse reduction in the strength of the lower limbs and frequently persistent pain also during the night.

As already mentioned, in this group the treatment was: paravertebral injection and phleboclysis (two cycles of

6 sessions, one each 3 days)+endoscopic neurolysis with intradiscal procedure (named percutaneous peridurodiscolysis).

With regard to outpatient treatment the results after two cycles of 6 sessions were:

2 p. (0.194%) treatment not tolerated and stopped immediately – eliminated from the study group
30p. (2.92%) no useful clinical result
256 p. (24.9%) moderate result
441 p. (42.94%) good result
298 p. (29.01%) excellent result
Total 1,027

Minimally invasive percutaneous peridurodiscolysis was then carried out with the following results:

Out of the 30 p. with no result from the outpatient treatments:

10 poor result, insufficient
15 moderate improvement
5 good improvement

The 256 patients with moderate outcome changed as follows:

20 out of 256 (7.8%) passed to a situation of excellent result
64 out of 256 (25%) passed to a situation of good result
172 out of 256 (67.18%) remained with a situation of moderate result

The 441 patients with good outcome changed as follows:

105 out of 441 (23.8%) passed to a situation of excellent result
314 out of 441 (71.2%) remained with a situation of good result
22 out of 441 (4.9%) passed to a situation of moderate result

The 298 patients with excellent outcome changed as follows:

35 p. decided to suspend the cure, not feeling any need for further therapy (11.74% out of 298 patients).

Two hundred and sixty three underwent percutaneous epidural-discolysis:

258 out of 263 (98%) remained with a situation of excellent result.
5 out of 263 (1.9%) had a reduction in the quality of the clinical result, which became moderate.

After outpatient treatment and minimally invasive percutaneous peridurodiscolysis in patients with failed back surgery syndrome, the *result is:*

Excellent in 20+105+35+258=418 cases out of 1,027 (40.7%)
Good in 5+64+314=383 cases out of 1,027 (37.29%)
Moderate in 172+22+5+15=214 cases out of 1,027 (20.83%)
Poor in 10=10 cases out of 1,027 (0.97%)
It was impossible to treat 2 cases out of 1,027 (0.19%)
Total 1,027

Adding together excellent±good means 801 cases out of 1,027=77.99%

Treatment Group C: Patients with Herniated Lumbar Disc and No Other Concomitant Factors

Treatment for this group was paravertebral injection (two cycles of 6 sessions, one each 3 days)+percutaneous discolysis. In some cases of very painful clinical situation, the intradiscal injection of 0203 (percutaneous discolysis) was performed simultaneously to the outpatient treatment, not after it.

Out of 384 patients, 78 (20.3%) benefited greatly from the outpatient treatment to the extent that they did not wish to be admitted for intradiscal injection of the 02/03 mixture. They therefore finished the cure of just paravertebral therapy with a result considered

Good in 49 (12.76%)
Excellent in 29 (7.55%)

Another six patients were not admitted for the intradiscal injection procedure of the 0203 mixture due to existing anticoagulant therapy [27] or existing cardiologic problems. They therefore finished the cure of just paravertebral therapy with a result considered

Good in 4 (1.0%)
Excellent in 2 (0.52%)

The remaining 300 patients were treated with an intradiscal injection of the 0203 mixture after the outpatient treatment: *discolysis*

In order to obtain a very careful evaluation, the result of the percutaneous treatment for these patients was compared with a similar series of *300 patients treated by the same group of professionals over the last 3 years, by the conventional open microsurgical removal procedure: microdiscectomy*. The case record trend is as follows:

Level of Lumbar Hernia

	Microdiscectomies		Percutaneous discolysis	
L1-L2	1	(0.33%)	3	(1%)
L2-L3	4	(1.33%)	3	(1%)
L3-L4	28	(9.33%)	36	(12%)
L4-L5	159	(53%)	165	(55%)
L5-S1	108	(36%)	93	(31%)

Type of Lumbar Hernia

	Microdiscectomies	Percutaneous discolysis
Contained	197 (65.6%)	200 (66.6%)
Extruded	93 (31%)	82 (27.3%)
Migrated	10 (3.3%)	8 (6%)

(a) Regression of pain at check-ups (VAS Regression $\geq$ 4 points)

Check-ups	Microdiscectomies	Percutaneous discolysis
4–6 months	292/300 (97.3%)	280 (93.3%)
1 year	275 (91.6%)	276 (92 %)
18 months	250 (83.3%)	262 (87.3%)

(b) Regression of pain/level, after 1 year (VAS Regression $\geq$ 4 points)

	Microdiscectomies	Percutaneous discolysis
L1-L2	1 (100%)	3 (100%)
L2-L3	3 (50%)	3 (100%)
L3-L4	24 (82.1%)	33 (91.6%)
L4-L5	143/159 (89.9%)	150/165 (90.90%)
L5-S1	104/108 (96.2%)	88/93 (94.6%)

(c) Regression of pain/type of hernia (VAS Regression $\geq$ 4 points)

Hernia	Microdiscectomies	Percutaneous discolysis
Contained	163/197 (82.74%)	172/200 (86%)
Extruded	85/93 (91.39%)	76/82 (92.6%)
Migrated	9/10 (90%)	15/18 (83.33%)

(d) Regression of pain/intraforaminal localization of the hernia (VAS Regression $\geq$ 4 points)

Microdiscectomies	Percutaneous discolysis
22 (91.6%)	22 (84 6%)

(e) Regression of sensorial dysfunction at 18 months

	Microdiscectomies (%)	Percutaneous discolysis (%)
Complete	82.5	83.2
Partial	12.4	9.4
Insignificant	5.1	2.4

(f) Regression of motor deficit at 18 months

	Microdiscectomies (%)	Percutaneous discolysis (%)
Complete	86.6	85.7
Partial	9.8	8.3
Insignificant	3.6	6

(g) Regression of initial severe motor deficit at 18 months

	Microdiscectomies (%)	Percutaneous discolysis (%)
Complete	44.4	40
Partial	22.2	20
Insignificant	33.3	40

(h) Complications observed in the two series of case records related to the procedure:

Microdiscectomies	Percutaneous discolysis
4 fistulas of cerebrospinal fluid	2 chemical discitis
1 bacterial discitis	

Conclusion

We have mentioned patients for whom results were insignificant and who abandoned the cure, but we must call attention to the two patients who could not tolerate the treatment applied for FBSS (treatment group B), which was immediately stopped. They both showed reactions of intolerance to ozone with consequent sudden changes in systemic arterial pressure, hypertension and hypotension respectively, which were well controlled and managed and promptly resolved by the appropriated emergency care treatment. This made it impossible to re-propose the treatment to these patients. Such reactions were studied, and are explained to be very likely due to enzymatic changes in the hyperoxidation control mechanisms, which could in turn be due to existing latent clinical situations such as forms of favism in which certain anti-hyperoxidation control enzymatic chains are missing.

Patient Group A with Degenerative Disco-Arthropathy

At the end of paravertebral outpatient treatment, 122 patients (23.9% of the group) showed a good clinical result and 153 (30.05%) showed an excellent result. Summing together these two groups, we have a total positive effect of oxygen-oxone gas mixture administration in the paravertebral area of 53.95%. The remaining 225 (44.2%) patients showed a moderate result, which was anyway considered by them positive. The perceived quality of result, in consideration of the minimal invasiveness of the procedure, made several of these patients doubtful on the need of the further peri- and intradiscal treatment which we had suggested in order to make the result more consistent and stable. After having performed peri- and endoscopic neurolysis, 100 patients with moderate result passed to excellent or good result. Thus the total result adding together excellent + good results means 373 cases out of 509, that is 73.28%.

Patient Group B: Failed Back Surgery Syndrome FBSS

After outpatient treatment and the minimally invasive percutaneous peridurodiscolysis, for patients with failed back surgery syndrome, the result is positive in 801 cases out of 1,027 = 77.99%.

This result should be compared with overall results averaging 40% for open revision surgery and an average of 65–70% for rigid vertebral stabilization techniques (arthrodesis) with metal implants.

Leaving aside the sizeable difference in clinical results and also considering that there is a natural tendency for the quality of the result to diminish after many months in both procedures (minimally invasive as described here and conventional open surgery), three essential reflections remain:

1. The minimally invasive technique involves the patient in nothing more than outpatient treatment during some days of life, which remains normal. The single admission to hospital for one or two nights is reserved to treatment without disabling consequences or limiting the patient's active life, neither in the short nor the medium term;
2. When the minimally invasive techniques have lost their clinical effectiveness, they can be repeated without harm for the patient at an interval of 1 or 2 years. (We are talking of patients currently considered either as untreatable or as needing an invasive major surgical procedure);
3. Costs for health organizations are notably very high for surgical revisions and even more for instrumented rigid stabilizations, while the costs for minimally invasive techniques are extremely limited.

Treatment Group C: Patients with Herniated Lumbar Discs

As observed in previous papers [20] there were no statistically significant differences in the outcome for microdiscectomy and oxygen-ozone injection at 18 months after treatment. There is, however, the absolute difference in invasiveness of approach, the percutaneous procedure being closed and without general anesthesia, using just pharmacological sedation under anesthesiologic control.

Microdiscectomy is indispensable in situations of particularly high pain levels and when there is acute and severe motor deficit. The morbidity and mortality rates of the microdiscectomy procedure are well known, as are the possible consequence of FBSS.

Discolysis is a procedure that is practically free from short- and long-term complications and can be applied even when general health is poor. It should be noted that in the event of unsuccessful results with discolysis the situation is not worsened by difficulties for future treatment due to post-surgical scar or weakening of the bone structure, as is the case with open surgery.

General Comment

As a general consideration we must comment that the adverse effects that have been observed during oxygen-ozone treatment underline the need that this treatment should be performed in protected structures, in operative rooms, under anesthesiologic control, and in the hands of specialists. Anyway, the incidence of such adverse effects is extremely low as compared to any other kind of medical treatment for these diseases.

The results obtained by this therapy are clinical results; there is nowhere the idea that this therapy will solve the problem. Pain and dysfunction coming from degenerative pathologies of the spine have no way a complete definitive solution: these are problems which cannot be cured, since they represent the clinical expression of morphological alterations which are in the physiological range rather than "diseases". This should be clearly explained to all the patients, irrespective of the kind of therapy that is undertaken.

Ozone therapy is useful in the terms in which it avoids major surgery and allows a better quality of life despite structural degeneration. Recurrence can be treated in the same manner with irrelevant risk.

Disclosure of competing interest: no competing interests.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Oxygen–Ozone Therapy for Degenerative Spine Disease in the Elderly: A Prospective Study

Matteo Bonetti, Alessandro Fontana, Francesco Martinelli, and Cosma Andreula

Abstract We describe our experience of oxygen–ozone therapy to treat degenerative spine disease in the elderly. From April 2004 to March 2008 we selected 129 patients with CT and/or MR evidence of spondyloarthrosis and disc degeneration of the lumbar spine. All patients enrolled in the study had contraindications to the administration of commonly used analgesic and anti-inflammatory drugs.

Oxygen–ozone therapy was given by CT-guided intraforaminal injection as the first treatment followed by 4 weekly paralumbar infiltrations on an outpatient basis. The full treatment lasted a month. Clinical outcome was assessed 3 months and 1 year after treatment. The good results obtained indicate that oxygen–ozone therapy is an ideal treatment with no side-effects in elderly patients with degenerative spine disease.

Keywords Elderly · Intraforaminal infiltration · Medical ozone · Oxygen–ozone therapy · Spondyloarthrosis

Introduction

Gains in the average life span have been flanked by an exponential increase in degenerative spine disease in the elderly. In particular, spine disease other than disc degeneration (osteophytosis, pseudo-spondylolisthesis, canal stenosis, facet joint syndrome) is increasingly responsible for disability in people who already have other age-related conditions (e.g., endarteritis obliterans of the lower limbs, diabetes, cerebrovascular failure, etc.) [11, 17].

Concomitant disease is often a factor limiting the administration of analgesic and anti-inflammatory drugs to relieve the pain caused by degenerative spine disease and hence improve patients' quality of life. We studied 129 patients aged between 65 and 92 years to assess the therapeutic efficacy of intraforminal infiltration of an oxygen–ozone gas mixture (O_2–O_3) completed by outpatient paravertebral infiltrations in patients with contraindications to commonly used analgesic and anti-inflammatory drugs. Clinical outcome was evaluated 3 months and 1 year after the end of treatment.

Materials and Methods

After reading and signing an informed consent form, 129 patients (57 men and 72 women aged between 65 and 93 years, average age 76 years) with chronic low back pain underwent CT-guided infiltration of an O_2–O_3 gas mixture. Patients were treated between April 2004 and March 2008. A clinical record was prepared for each patient on enrolment noting age, date of birth, date of enrolment, date of treatment, and clinical information on the type of pain, pain irradiation, presence of paresthesias, Lasègue's sign, degree of sensitivity, lower limb reflexes, plantar and dorsal extension of the foot and dorsal extension of the great toe. All patients had CT or MR evidence of advanced zygo-apophyseal degenerative arthrosis, multiple levels of lumbar disc disease, segmental canal stenosis, pseudo-spondylolisthesis and severe scoliosis. The patients enrolled in the study had chronic unilateral or bilateral low back pain irradiating along the regions innervating the lumbosacral plexus.

Patients with electromyographic evidence of neurogenic injury (diabetic neuropathy) and those with concomitant

M. Bonetti (✉)
Servizio di Neuroradiologia, Istituto Clinico Città di Brescia, Via Gualla 15, 25123 Brescia, Italy
e-mail: matbon@numerica.it

A. Fontana
Department of Neuroradiology, Istituto Clinico Città di Brescia, Brescia, Italy

F. Martinelli
University of Florence, Florence, Italy

C. Andreula
Department of Neuroradiology, Anthea Hospital, Bari, Italy

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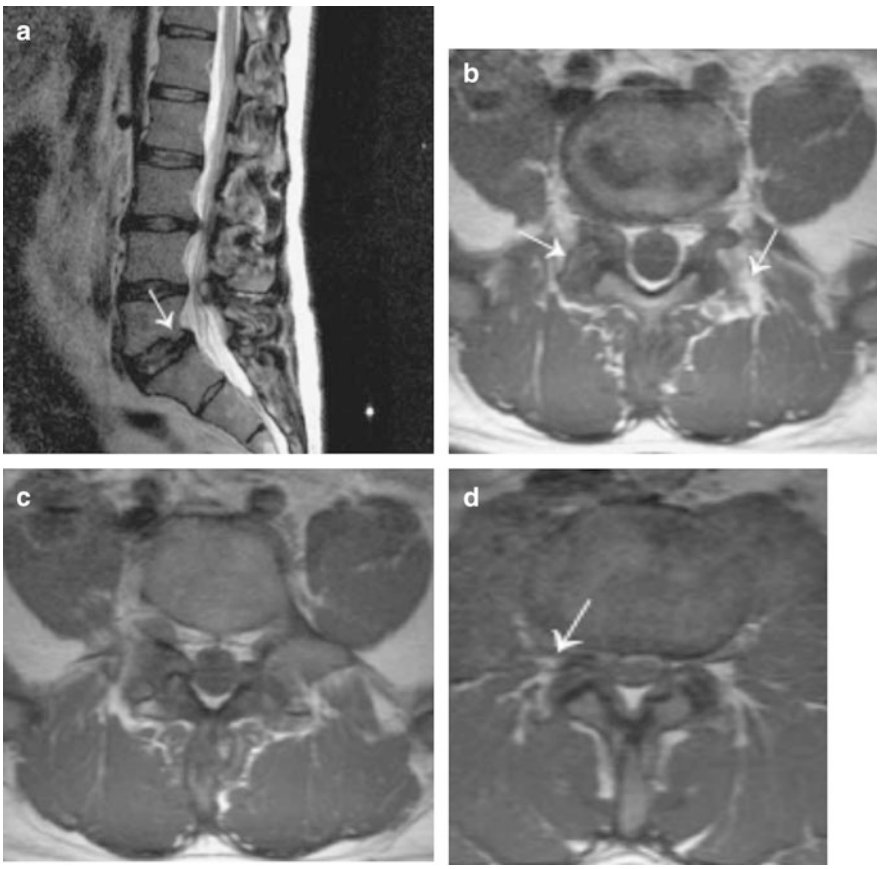

Fig. 1 A 66-year-old man with chronic low back pain complicated by right sciatic nerve pain. MR scan (**a**–**c**) depicts spondylolisthesis of L5 over S1 (*arrows*) associated with degenerative arthrosis of the facet joints (**d**). Circumferential protrusion of the L3–L4 disc is also present mainly in the right intra-extraforaminal region (*arrows*). The patient underwent O_2–O_3 treatment with CT-guided intraforaminal infiltration into both L3–L4 (right monolateral) and L5–S1 (bilateral) followed by four outpatient treatments with paravertebral intramuscular injections into the two levels. At 1 year follow-up the patient referred an excellent resolution of clinical symptoms (assessed by our modified McNab method)

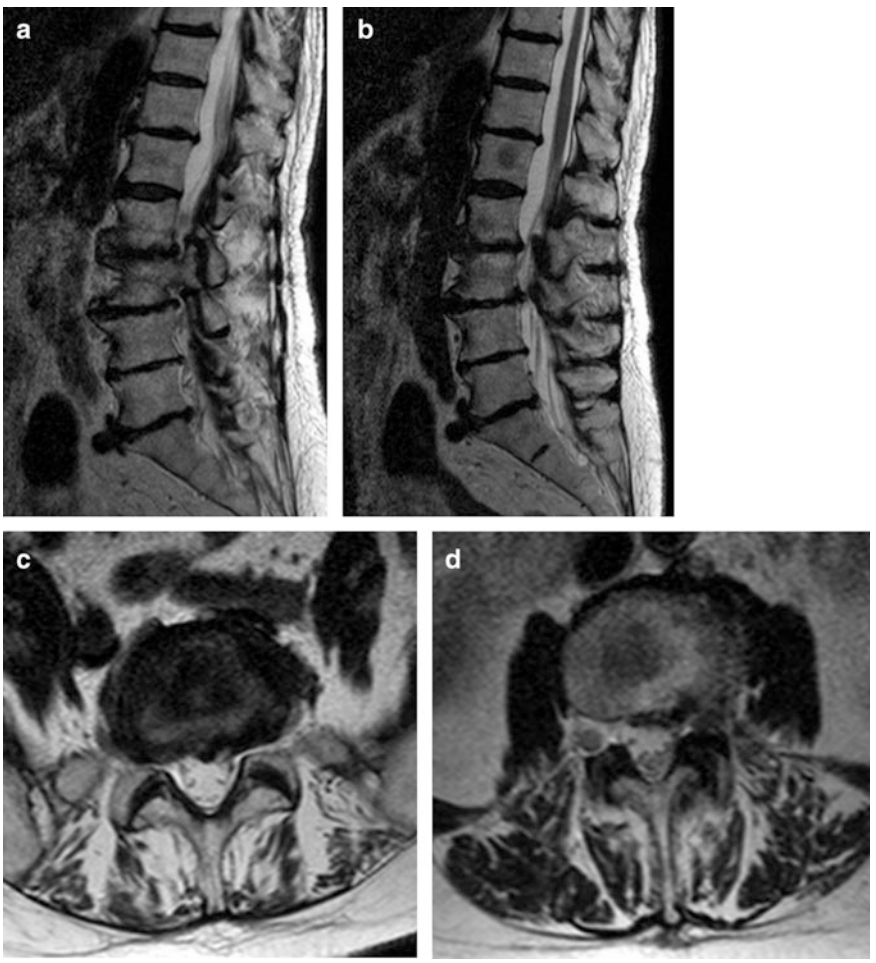

Fig. 2 (**a**–**d**) A 74-year-old woman with chronic low back pain. MR scan (**a**–**b**) depicts advanced lumbar spondyloarthrosis with multiple levels of disc degeneration: the discs are thinned and present a hypointense signal in T2, mainly in L5–S1 (**c**) and L3–L4 with associated disc protrusion showing a left intraforaminal focus (**d**). She was treated by a three-level approach first with intraforaminal O_2–O_3 infiltration (L2–L3, L3–L4 and L5–S1) followed by four paravertebral intramuscular injections. Clinical outcome was deemed excellent at 1 year follow-up

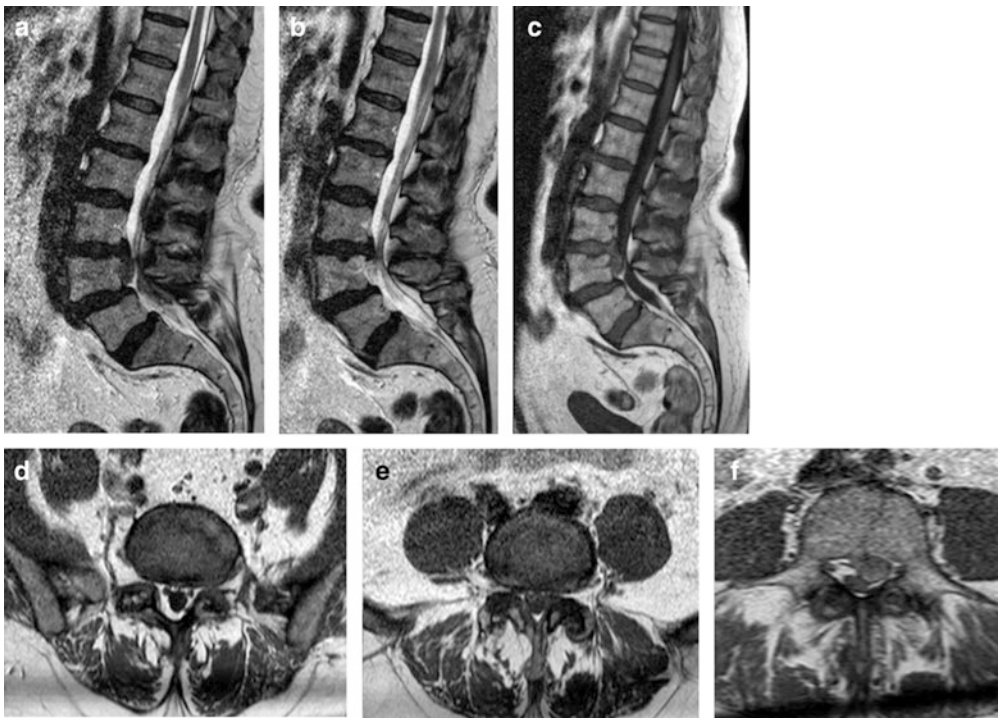

Fig. 3 A 74-year-old woman with low back pain complicated by a 1 month history of severe left sciatic nerve pain irradiating along the region innervating the left L4, treated with O_2–O_3 administration with a poor clinical outcome. (**a**–**c**) Sagittal MR scans show first degree listhesis of L4 over L5 according to Meyerding (*arrows*) and a large extruded L3–L4 disc (*arrowheads*). (**d**) The L5–S1 disc also shows severe zygo-apophyseal degeneration (*arrows*). (**e**) The axial scan at the L4–L5 passage documents the reduced canal diameter caused by the listhesis. (**f**) Large extruded left L3–L4 herniation (*arrow*)

endarteritis obliterans of the lower limbs with grade II and IV intermittent claudication were excluded from the study.

Before treatment the skin area was disinfected and local anaesthesia administered by ethyl chloride spray in all patients. Infiltrations were performed by specialist neuroradiologists at the Neuroradiology Service at Istituto Clinico Città di Brescia. A CT scan was done to identify the point of infiltration and marked on the skin, then, the distance from this point to the spinal root canal was measured. A 22G Terumo needle was positioned 2–3 mm from the foraminal region close to the ganglion of the nerve root to be treated. We usually used a 9 cm needle but a longer needle was used in some cases depending on the patient's size.

Another CT scan was then performed to check accurate needle placement. The O_2–O_3 mixture was injected into the joints in patients with facet joint syndrome or immediately around the joint capsule when it was not possible to reach the intervertebral space (osteophytosis, asymmetric facet joints and particular shape of the joint aperture). Up to three periganglionic infiltrations were made in patients with multiple levels of disease. Infiltration involved injection of 3 cc of the O_2–O_3 gas mixture at 25 μg/ml; then, the needle was retracted a few millimetres injecting another 5 cc of the mixture to involve the region surrounding the facet joint. CT scans were done in all patients to check the correct distribution of the gas mixture in the root canal and facet joint. All treatments were performed using equipment fitted with a photometric detector, monitoring the concentration of ozone in the gas mixture.

The treatment cycle was completed with four paravertebral infiltrations given weekly on an outpatient basis.

These infiltrations were done by injecting 10 cc of the O_2–O_3 gas mixture at 25 μg/ml into each infiltration point, using 23G Terumo needles and a medical ozone device (Alnitec Futura 2), fitted with a photometric detector monitoring the concentration of ozone in the gas mixture. The infiltration point was kept constant at 2 cm from the spinous apophysis of the diseased space. Multiple level treatments were usually performed. All patients had follow-up checks at 3 months and 1 year after treatment.

We used a modified version of McNab's method to define clinical outcome as follows:

(a) *Excellent*: resolution of pain and a return to normal daily activities performed before the onset of pain.
(b) *Good or satisfactory*: more than 50% reduction of pain.
(c) *Mediocre or poor*: partial reduction of pain less than 70%.

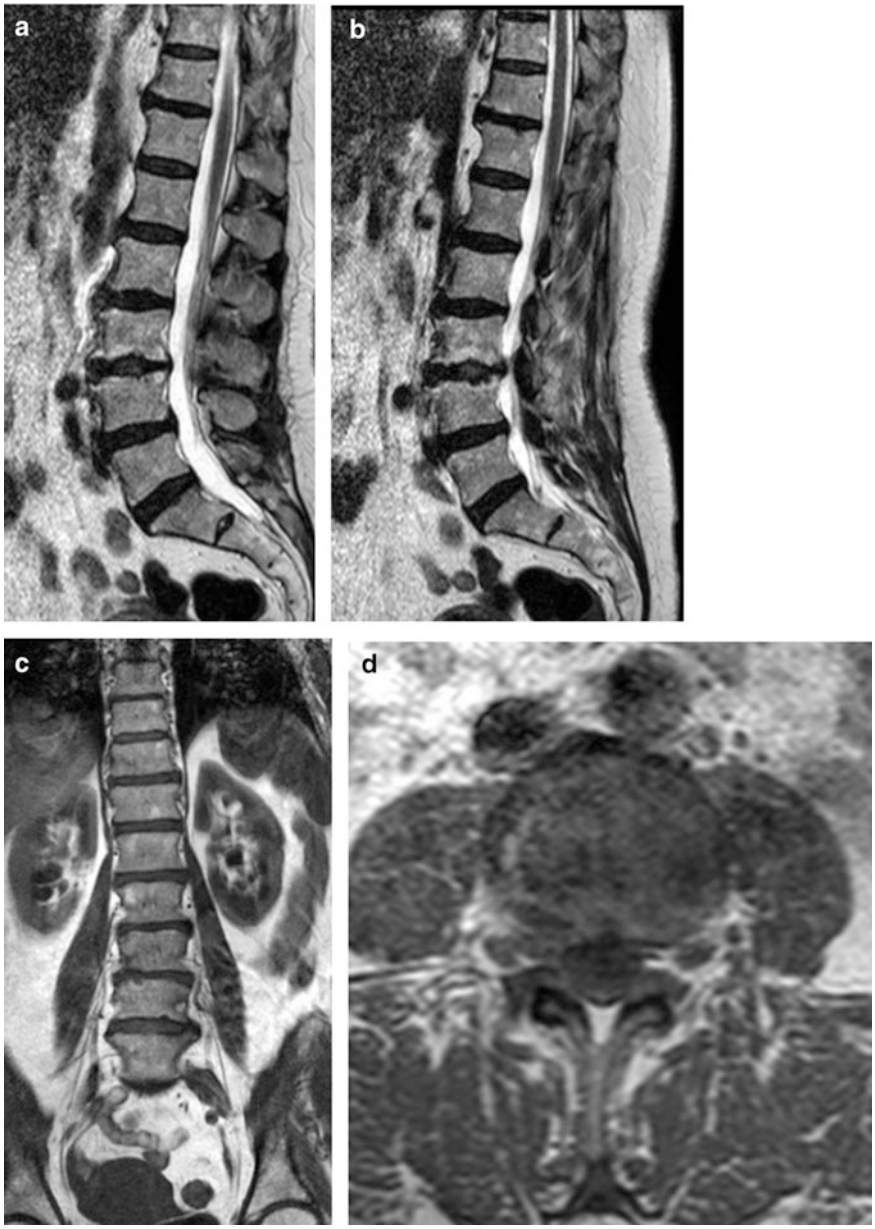

Fig. 4 A 67-year-old man with low back pain lasting several months sometimes complicated by right sciatic nerve pain, treated by O_2–O_3 administration with an excellent clinical outcome. (**a**, **b**) Sagittal MR scan shows L3–L4 disc degeneration with associated osteochondrosis of the opposite end plates (*arrows*). (**c**) Coronal MR scan shows an initial scoliosis secondary to the degenerative spondyloarthrosis. (**d**) The L3–L4 disc protrusion is focused in the right preforaminal region (*arrows*)

Results

At 3 months follow-up 74 (57.3%) patients referred a marked improvement in clinical symptoms with almost complete disappearance of low back pain, whereas 32 (24.8%) were satisfied with the treatment but had only a partial reduction of pain. The treatment produced little or no benefit in 23 (17.9%) of patients. One year follow-up was done in 127 patients as two had died from natural causes in the meantime. Of these, 43 (33.9%) had maintained an excellent quality of life with an almost complete disappearance of low back pain. The number of patients with good or satisfactory benefit after treatment had increased to 34 (26.7%): pain had returned but was decidedly less severe than before treatment. Treatment was deemed mediocre or poor in 50 (39.4%) patients.

Discussion

At 1 year follow-up after O_2–O_3 treatment 33.9% (43/127) of our patients reported a clear-cut improvement in quality of life following a resolution of pain and a return to normal daily activities previously abandoned (Fig. 1). Ten patients no longer required walking aids (crutches and corsets) (Fig. 2). After a partial resolution of pain, 34 out of the 127 patients treated (26.7%) experienced a recurrence of

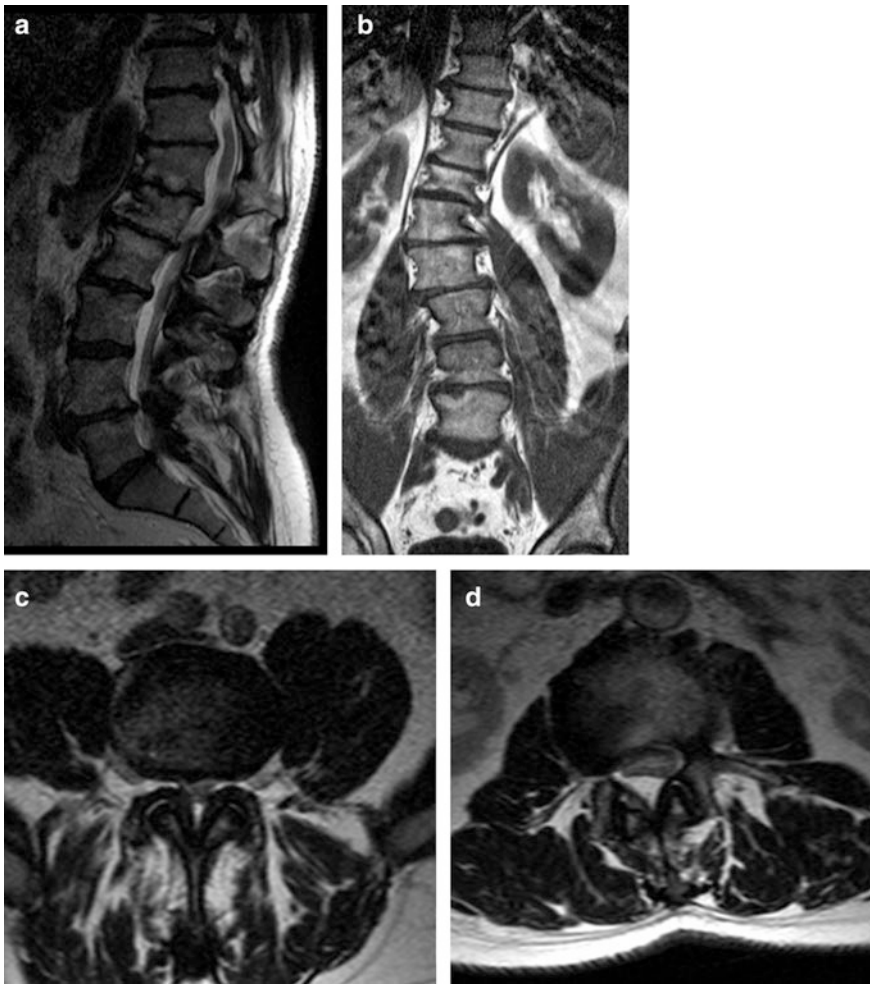

Fig. 5 A 71-year-old man with chronic low back pain treated by O_2–O_3 administration with a good clinical outcome. (**a**) Sagittal MR scan shows severe degenerative arthrosis at the dorsolumbar and lumbosacral passage (*arrows*). (**b**) Coronal MR scan shows dorsolumbar scoliosis secondary to the degenerative spondyloarthrosis. (**c**) The L4–L5 disc shows severe degeneration as do the facet joints (*arrows*). (**d**) Scoliotic L1 vertebral body tending to rotate anti-clockwise

symptoms but pain was judged to be much milder than before O_2–O_3 treatment and almost all patients requested another cycle of treatment (Fig. 5). Of the 50 patients with a poor outcome at 1 year follow-up (39.4%) only one patient with multiple levels of segmental canal stenosis opted for surgical decompression. The good treatment outcome obtained at 3 months follow-up is due to the capacity of O_2–O_3 injection into the ganglionic region to normalize the level of cytochines and prostaglandins, increase superoxide dismutase (SOD) and minimize reactive oxygen species (ROS) thereby enhancing local periganglionic circulation with a eutrophic effect on the nerve root [9, 10, 12, 14, 15, 16, 17, 18, 19]. This effect, however, appears to subside in the long-term, especially when the morphostructural changes to the spine result in continuous pain stimulation. The patients most refractory to treatment proved to be those with canal stenosis resulting in mechanical nerve root compression by bony structures which prevented long-lasting pain relief due to the continuous recurrence of the nociceptive stimulus caused by mechanical stress (Fig. 3). Of the 34 patients with satisfactory outcome 29 requested a second cycle of treatment and of the 50 patients who failed to benefit from treatment 22 opted for a new cycle of O_2–O_3 infiltrations.

O_2–O_3 administration proved an effective treatment for root pain caused by spondylolysis thanks to its well-known pain relieving properties [7, 8, 16] (Fig. 4). Treatment is a valid alternative to many drugs like corticosteroids which have non negligible adverse effects (e.g., sensory impairment, bowel/bladder dysfunction) especially problematic in the elderly [6, 13].

By contrast, several studies have demonstrated the lack of side-effects linked to short and long term O_2–O_3 administration [20].

Conclusions

Conservative O_2–O_3 treatment is effective in relieving chronic low back pain and can offer significantly long improvements in quality of life in patients like the elderly with contraindications

to drug management or concomitant age-related diseases [1, 2, 3, 4, 5]. The lack of side-effects means that O_2–O_3 treatment can be repeated at 6 month to 1 year intervals to guarantee pain-free cover and avoid recourse to surgery.

Conflict of interest statement We declare that we have no conflict of interest.

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Ozone the One and Only Drug

Pepa Osvaldo Alberto

Abstract Experience based on evidence shows the use of one drug over time.

Ozone has great therapeutic properties. Nowadays, hardly anyone questions its effectiveness.

We treated 270 patients with discal hernia of one or multiple levels in a minimally invasive way and under fluoroscopic control in real time, between 1 and 7 ml intradiscal and 3 ml periganglionic, in a concentration of 30 mg/ml of a mixture of oxygen and ozone as the one and only drug.

A second group was created, out of which 120 patients were treated with physiatric and kinetic treatment (magnetotherapy) prior to any other type of treatment, whether surgical or minimally invasive.

The time period was 3 months. All the patients were followed up from April 2004 to July 2008 with the MacNab, VAS and Owestry scales. We obtained 86% of excellent results, 12% satisfactory results, and 2% poor results.

To sum up, we can say that ozone therapy has opened up a new future in the medical field.

Discussions go on. New effects, new concentrations and the combination with bioenergetic therapies are the future in the treatment for backaches.

Keywords Disc herniation · Fluoroscopy · Intradiscal technique · Minimally invasive · Ozone therapy

Introduction

Disc herniation is defined as the protrusion of the nucleus pulposus through a tear in the annulus fibrosus towards the vertebral or root canals.

P.O. Alberto
Instituto Central de Medicina, 43 n 581 (1900), La Plata, Buenos Aires, Argentina
e-mail: oapepa@yahoo.com.ar

Nowadays, the number of patients with disc herniation is rising constantly alongside the increase in the average age of the population. Recent epidemiological findings show that disc disease is also on the increase among the young.

Car travels, extreme sports, long hours standing up and other factors contribute to back problems. Eighty per cent of the population will experience an episode of the low back with or without sciatica at least once in their lives [2].

In this study, we only consider a group of patients with disc herniation causing back pain, leaving aside the degenerative pathology of the posterior osteomuscular ligament complex, because their dynamic works as constant modulator of the function of vertebral segments. The subsequent stress is evaluated and treated. In order to keep the dynamics of the back, we must evaluate the orientation of the facet joints, curvature alterations, and the special involvement of the following anatomic structures: ligamentum flavum, interspinal ligament, supraspinal ligament and paravertebral muscles.

These anatomic structures are particularly evaluated from the morphostructural and dynamic point of view.

In order to evaluate the inflammatory and dysfunctional manifestations of the segment, studies of RM T2 FAT SAT and T1 FAT SAT are used, since they express the segmental microinstability as a result of the mechanical stress that the spine receives as a sign of backache [5] (Fig. 1).

In cases of lumbar radicular dysfunction due to discal-radicular conflict, the classical surgical treatment by open surgery entails a high percentage of complications or failure.

A lot of minimally invasive techniques have been developed, which also help alter the peridural space.

A mixture of oxygen and ozone gases has been employed in medicine since the thirties to treat pain and dysfunction in patients with thrombotic and ischemic diseases. The empirical observation of the powerful long–lasting effect of injection of this gas mixture into the intradiscal and periganglionic spaces to treat pain and radicular dysfunction because of disco-radicular conflict, has led to detailed studies on the subject. Working in different fields, researchers have surprisingly noted that the

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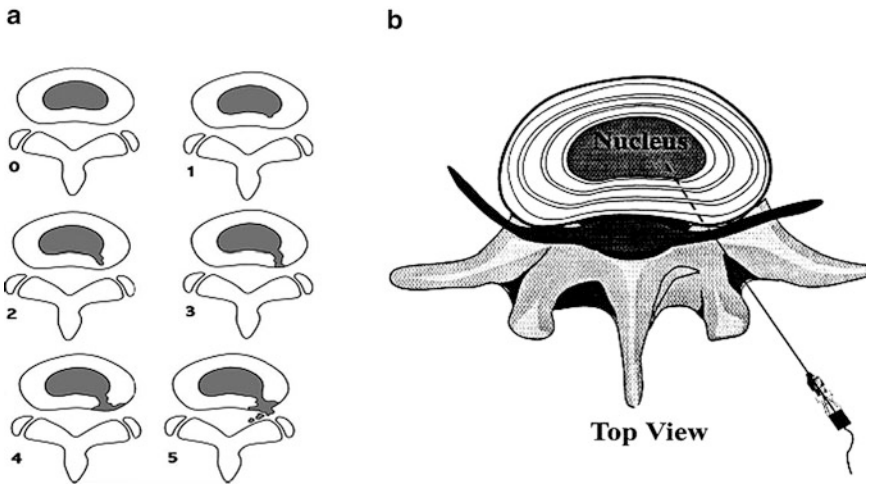

Fig. 1 Discography: is a provocated test which tries to reproduce the original pain in the patient, through the injection into the disc causing an intradiscal pressure increment (**a**). Discolysis with O_2-O_3, (**b**) intraspinous stabilization

short, calculated oxidative stress achieved by ozone administration may correct permanent imbalance caused by excessive or chronic oxidative injury, and it is becoming clear that modest, repeated ozone treatment increases the activity of super-oxide dismutase, catalase, and glutathione peroxidase, inducing a state of oxidative stress adaptation with major therapeutic implications.

At least 80% of the Western adult population suffers from backache at any given moment of their lives, and 55% suffer from radiculopathy [4].

Due to its great mobility and vulnerability to serious or minor injuries, disc herniation is the second most treated pathology.

Mild and single herniations are not very frequent. Most of them are multiple and hard, with degenerative processes.

Materials and Methods

Two groups of patients with herniated disc of one or multiple levels were studied and treated. The first group of 270 patients had subligament herniation and were treated with a mixture of oxygen and ozone. The second group of 120 patients received physiatric and kinetic treatment.

We followed up all the patients from April 2004 to July 2008 with the MacNab, VAS and Owestry scales. Before the patients were treated, they were clinically studied with RMT2 FAT SAT and T1 FAT SAT. The first group received diagnostic discography and treatment with a mixture of oxygen and ozone (Fig. 2).

Inclusion Criteria

Subligamentary discal herniation; patients who failed clinical treatment after 90 days.

Exclusion Criteria

Neurological failure; expulsed disc herniation; hyperthyroidism; anemia; pregnancy; degenerative disease; previous surgeries; narrow canal.

Intradiscal Technique

Under direct fluoroscopy, a mixture of oxygen and ozone of 7 cc was applied in the lumbar disc and 3 cc in the cervical disc in one session. The patients belonging to the second group completed 30 sessions of magnetotherapy and kinesiology as their only treatment.

Results

Of the 270 patients treated with oxygen-ozone mixture, 83% did not have any recurrence of their symptoms, of the other 17% 18 patients received another therapy in addition to ozone therapy to solve their problems [3], i.e. pulsed radiofrequency and endoscopic discectomy, 28 patients did not receive any other treatment.

Patients in the second group, before undergoing ozone therapy; they first had to take 30 sessions of kinetics and magnetotherapy as a regular procedure. From those 120 patients with subligament herniation, 90 of them had a session with intradiscal ozone therapy because they had no modification in their rating points (Oswestry, VAS, MacNab). The other 30 patients did not need any other treatment and only one patient had complete remission of symptoms and on MRI image.

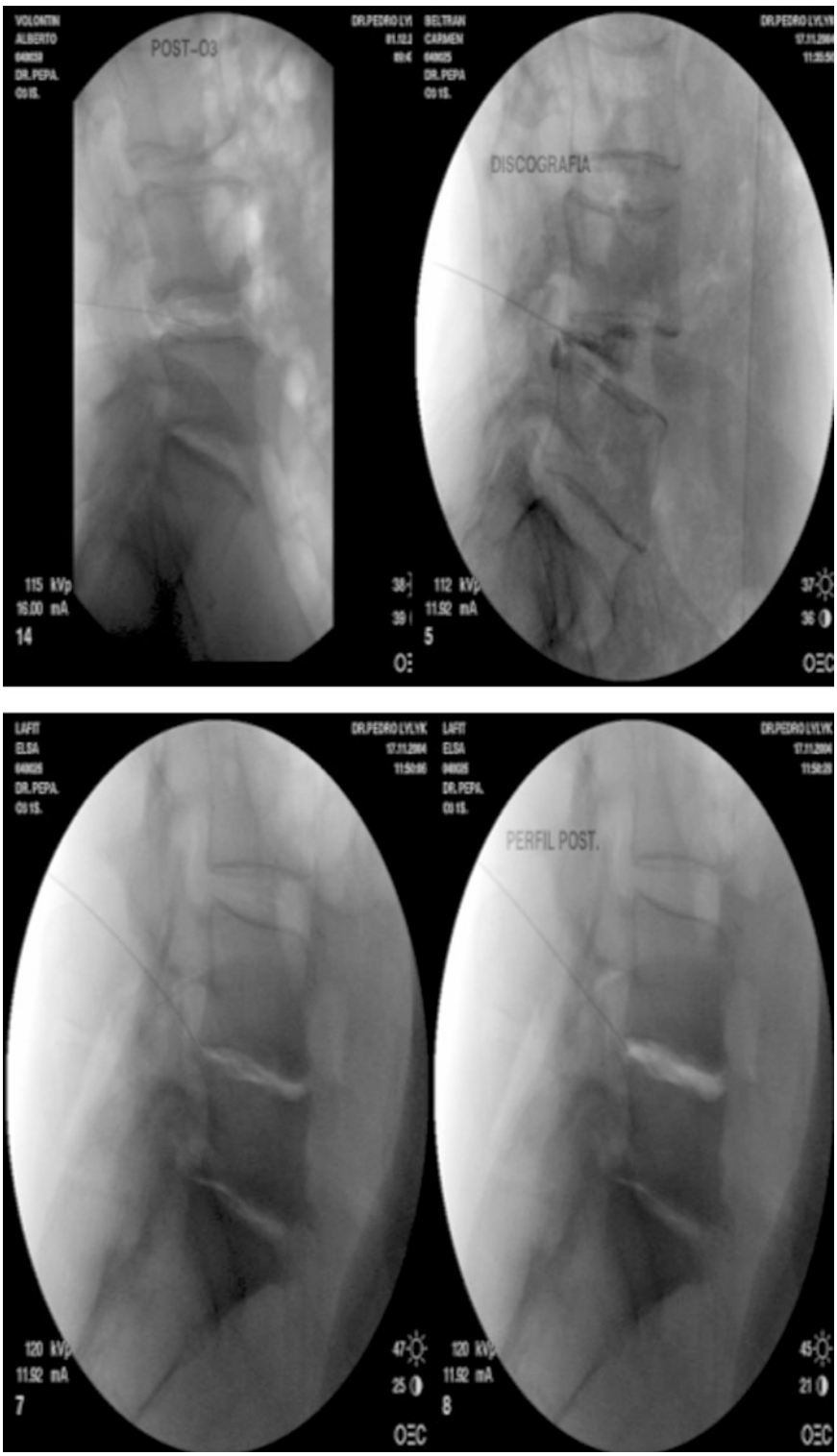

Fig. 2 Diagnostic and therapeutic discography

At 6-month follow up after treatment with ozone, the VAS scale in the first group demonstrated that 224 patients from a maximum of nine and a minimum of six at the beginning of treatment had a score of two at the end of treatment.

The Oswestry scale showed a reduction of 15% after the first week of treatment; the MacNab scale after 18 months showed excellent to good results that allowed the patients to get back to their occupational activities.

Conclusion

We know that the inflammatory and immune factors are determinants in the evolution of herniations, producing the symptomatology and pain that cause the disability in the affected person. We could demonstrate that ozone therapy, as the only one drug administrated [1], clinically and radiologically not only improved the life of the patient but can also modify and rebuild the histoarchitecture of the affected spine segment.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Vertebral Augmentation: 7 Years Experience

Giovanni Carlo Anselmetti, Giuseppe Bonaldi, Paolo Carpeggiani, Luigi Manfrè, Salvatore Masala, and Mario Muto

Abstract Percutaneous vertebroplasty and kyphoplasty are procedures used to treat pain associated with vertebral compression fractures. Controversies are still open regarding indications, efficacy and safety of the procedures, and regarding the potential benefits, advantages and shortcomings of PV versus KP.

Aim of this article is to report 7 years' experience in vertebral augmentation of the E.VE.RES.T. (European VErtebroplasty RESearch Team) group. The main topics are the treatments of hemangioma and malignant lesions, technically challenging cases such as vertebra plana, multifragmented fractures, multilevel treatments, refracture of augmented vertebra, and treatment of cervical junction and sacrum.

Keywords Bone cement · Kyphoplasty · Spinal interventional radiology · Vertebral fracture · Vertebroplasty

Introduction

Percutaneous vertebroplasty (PV) is a radiologic procedure for treatment of pain associated with vertebral compression fractures. First performed in France in 1984 [1], PV was introduced in the United States in 1994 and has become widely available worldwide since 1997 as a treatment for pain associated mostly with compression fractures due to osteoporosis, but also with bone cancer or bone metastasis, aggressive hemangiomas, or trauma. The procedure traditionally entails percutaneous injection, under imaging guidance (fluoroscopy or CT), of a biomaterial, usually methyl-methacrylate (PMMA) into a lesion of a vertebral body, with the aim to stabilize the collapsed vertebra, thus reducing or eliminating pain [2]. Kyphoplasty (KP) is a similar procedure, entailing the use of intrasomatic inflation of non-compliant balloon tamps prior to cement injection, to restore body height, reduce kyphotic deformity and likelihood of cement leakage [3]. Despite many completed or still ongoing trials, controversies are still open regarding indications, efficacy and safety of the procedures, and regarding the potential benefits, advantages and shortcomings of PV versus KP. However, both procedures are becoming more and more popular among patients, who often ask for the treatment because of its very good renown. In fact, it is common experience that in skilled hands and with proper indications, PV or KP dramatically improves back pain within hours of the procedure, provides long-term pain relief and has a low complication rate, as demonstrated in multiple studies, and can prevent further collapse of the vertebra, thereby preventing the height loss and spine curvature commonly seen as a result of osteoporosis. This good renown and the consequent refusal of patients to be randomized in trials is one of the reasons limiting recruitment and thus progression of a real medical evidence in the field. Another consequence of the wider and wider diffusion of the procedure is that many different surgical communities do it, frequently surmising to be the only one entitled to: radiologists, neuroradiologists (who invented the procedure, and who had been the only ones to perform it for many years), orthopaedic surgeons, neurosurgeons, and other "improvised" specialists (anaesthesiologists, pain specialists, rheumatologists and so on). It is our strong opinion that a previous, thorough experience in performing vertebral percutaneous X-ray guided interventions (such as biopsies, discectomies etc.) should be mandatory

G.C. Anselmetti
Department of Radiology, IRCC Candiolo, Torino, Italy
G. Bonaldi
Department of Neuroradiology, Ospedali Riuniti, Bergamo, Italy
P. Carpeggiani (✉)
Department of Neuroradiology, NOCSE, Modena, Italy
e-mail: p.carpeggiani@ausl.mo.it
L. Manfrè
Department of Neuroradiology, AO "Cannizzaro", Catania, Italy
S. Masala
Department of Radiology, Ospedale Tor Vergata, Rome, Italy
M. Muto
Department Of Neuroradiology, AORN Cardarelli, Naples, Italy

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before doing PV. This condition would limit the procedure to really skilled physicians, thus dramatically reducing the complications, while at the same time improving both safety and clinical results. Of course the decision to perform PV should be made by a multidisciplinary team, because the choice between PV, surgery, radiation therapy, conservative and/or medical treatment, or a combination thereof depends on a huge number of factors. This article refers to the experience of the E.VE.RES.T. (European VErtebroplasty RESearch Team) group, constituted of radiologists and neuroradiologists, who, for 7 years now, have been sharing their clinical and technical experience in the field. The number of patients treated so far by the group by means of both PV and KP is, joining the single case series, not less than 7,221 patients, with no major complication (i.e., death or neurologic deficit lasting more than hours or a few days after the procedure). Of course, in years experienced operators tend to widen indications, and such attitude is based not only on the clinical results, but also on the possibilities offered by improved technical skills, availability of new devices and materials, better use of imaging equipment and so on. A continuous feedback from the patients' clinical and radiological follow-up, constantly shared and discussed within the group, must help us remaining within the limits of an ethical, safe and efficient surgical practice, while at the same time allowing treatment of more difficult cases. Aim of this article is to share with everyone doing PV and/or KP our "tips and tricks of the trade", the availability of new technologies, the technical advances we could develop in our long and common experience. Obviously – a warning to us all – the golden rule for every operator in every field of surgery must remain to very gradually increase the difficulties faced in every intervention and never perform one without being definitely certain to be perfectly trained and prepared to.

Hemangioma

Asymptomatic vertebral hemangiomas (VH) are relatively common accessory findings in radiological studies (12%) performed for unrelated reasons. They remain stable over time and do not need treatment in most cases [4]. A very low percentage, 0.9–1.2%, of all VH is symptomatic. Symptoms may vary from simple vertebral pain (approximately half of cases), to progressive neurological deficit due to an overcome vertebral fracture or spinal cord and roots compression. VH can be radiologically distinguished as being *nonaggressive*, when they have prevalent fatty stroma and are confined to the vertebral body, or *aggressive* when the cortical bone appears interrupted, the posterior arch is involved and the angiomatous tissue invades the epidural or paravertebral space. Radiologic diagnostic work-up is aimed to typify the lesion and to exclude other causes of pain. Perivertebral and epidural soft tissue extension is best identified on T1W enhanced MRI. Typical structural bone rearrangement and osteolysis are best seen on CT. Surgery or radiotherapy has been the treatment of choice for several years. Surgery is the gold standard for aggressive VH with neurological symptoms (75% efficacy, 20–30% recurrence) and is generally performed after arterial embolization to reduce intra- and postoperative haemorrhagic complications [5]. Risk of myelopathy is the main drawback of radiotherapy. PV was first introduced as "alternative" treatment for VH [1]. The aim is to fill directly the angiomatous network, obtaining an irreversible sclerosis of the venous pool, and contemporarily to augment the vertebral body, stabilizing the trabecular micro fractures which are responsible for the pain. A bilateral approach is worth in lumbar vertebra, a monolateral approach is usually sufficient in dorsal level. Generally the cement easily permeates through the entire lesion, filling all the vascular spaces. The filling is better achieved if the needle tip is positioned in the far anterior part of the vertebral body and the injection is performed progressively retrieving the needle. In this way, also the pedicles and even the posterior arch may be packed (Fig. 1). In case of aggressive hemangioma the perivertebral and epidural component of the lesion could progressively become occluded even if it is not directly involved in the cement injection because of thrombization following the cementification of the main vascular bed [6]. Treatment of the epidural extension can be obtained also with the complementary use of "glue" or ethanol [7] (Fig. 2). If surgery is planned, vertebroplasty can precede it, avoiding the need of corpectomy and

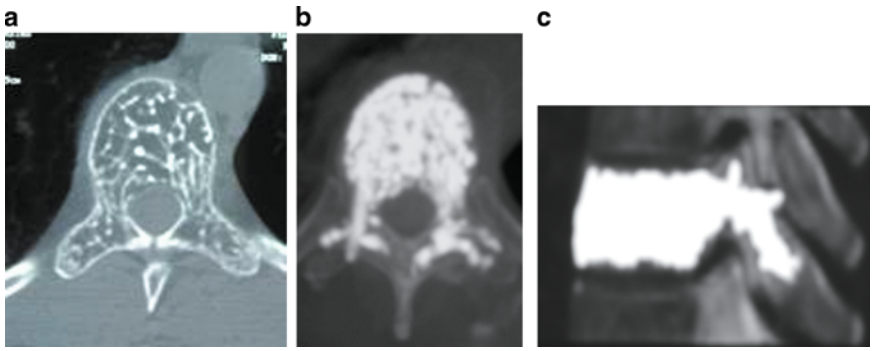

Fig. 1 Painful hemangioma completely involving the body and the neural arch (**a**), fully packed by bilateral injection performed retrieving the needles (**b**, **c**)

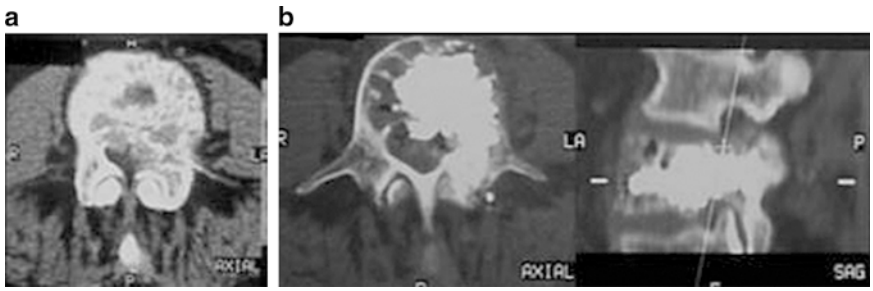

Fig. 2 Painful aggressive hemangioma (**a**) treated with cement injection into the vertebral body-left pedicle component, and completed with cyanoacrylate injection into the articular pillar (**b**)

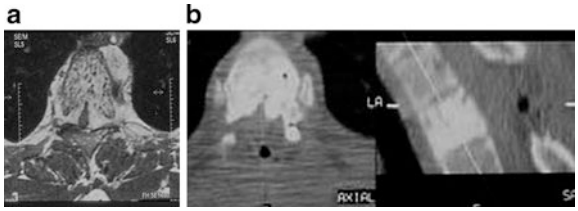

Fig. 3 Pre-surgical vertebroplasty in aggressive hemangioma (**a**). Post surgical control (**b**)

reducing the bleeding (Fig. 3). The risk of leakage and pulmonary embolism is the main concern due to the presence of wide high flow blood venous drainage. For this reason venography is useful to identify the main venous collectors. It is also essential to inject very dense cement, carefully verifying its progressive distribution by continuous fluoroscopy (Fig. 3). In E.VE.RES.T. series 52 VH were treated. Our results confirm that up to 90% of nonaggressive painful symptomatic VH can be definitely cured with PV alone [8]. No neurological, hemorrhagic or embolic complications were noted.

Malignant Lesions

PV is now commonly applied also for malignant lesions to obtain pain control and vertebral stabilization [9]. Its use, in any case, is compatible with all the other types of treatment (medical, surgical, radiotherapy) thus widening the therapeutic opportunities that can be applied. In the E.VE.RES.T. group, 1,422 patients (1,160 metastatic and 262 myeloma) were treated with PV. Indications were painful metastasis or myeloma involving the vertebral body not responding to conventional therapy such as radiotherapy, chemotherapy or conservative medical management. PV was not performed if neurological symptoms due to spinal cord compression were present. In metastatic disease the procedure is technically more challenging because the extension of osteolysis and/or the presence of osteosclerotic reaction make the spreading of cement more irregular and quite unpredictable, increasing the possibility of cement leakage from the vertebra. Consequently, there is a higher risk of complications compared to osteoporotic fractures. For this reason, especially if the bone landmarks are obscured, needle positioning is highly facilitated using Computed Tomography (CT) guidance. Nevertheless, digital fluoroscopy is mandatory to monitor the PMMA injection. To treat huge osteolytic lesions involving the posterior vertebral wall the use of very dense high viscosity cement reduces the risk of the leakage (Fig. 4). Analgesic efficiency seems to be not directly proportional to the degree of vertebra filling and can be obtained also with low filling percentages, even of 25%. Good clinical results were achieved: an average VAS score before PV of 8.3 ± 1.3 significantly changed to 2.1 ± 2.2 after PV and most of the treated patients could suspend opioid medical therapy and brace support with a significant improvement in the quality of life. Unfortunately the follow-up is generally short in these patients because of their poor general conditions. In fact PV has been commonly proposed when all other therapies have failed and the tumour is widely spread. Better results probably could be obtained in the future knowing the more appropriate timing to perform PV, alone or in combination with other therapy (Fig. 5) and ablative technique (see below), before clinical conditions had become so poor. Notably superior results, up to 90% of pain control, can be achieved in myeloma, where vertebral compression fractures may be the consequence either of direct osteolysis or of secondary osteoporosis. Often the entire axial skeleton is involved and multilevel treatment is necessary.

Vertebral Fractures with Cleft

A cleft is a cavity or slit within a fractured vertebra. Vertebral osteoporotic fractures with cleft occur primarily at the thoracolumbar junction and need special attention. Two types of clefts are radiologically identifiable depending on their content. Vacuum clefts contain gas (so called Kummell's sign) are well recognized by standard X-ray or better by CT scan [10]. Fluid filled clefts are more frequent, occur in up to 40% of benign osteoporotic fractures and are best seen by T2 MRI [11]. Both may coexist and a shift from one

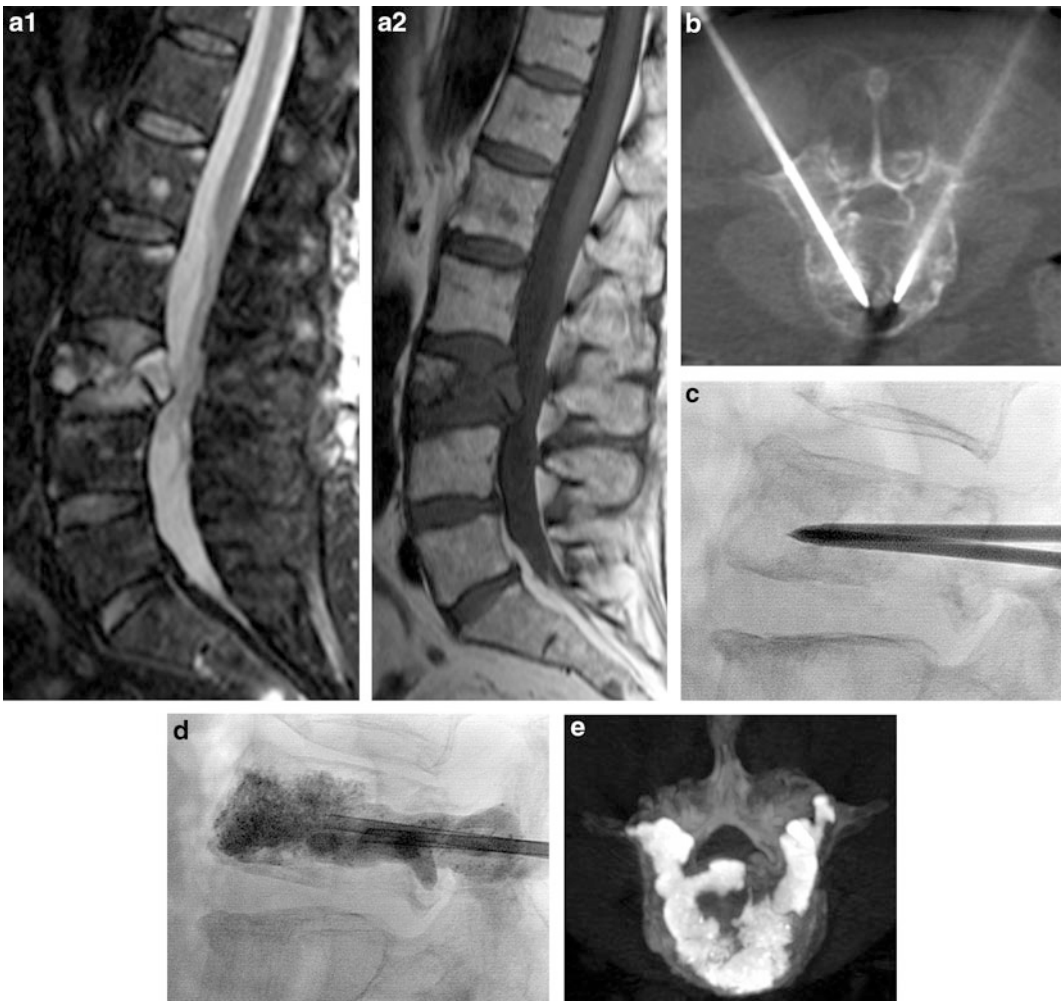

Fig. 4 Bladder carcinoma metastasis involving the body and the pedicles of L3 with collapsed vertebral body protruding into the spinal canal (**a1**, **a2**). Bilateral transpedicular approach with combined CT (**b**) and fluoroscopy (**c**) control of correct needles positioning within the collapsed vertebral body. By means of a high-viscosity PMMA fluoroscopy checked injection no leakages and good cement perfusion of the vertebral body and the pediclesis is achieved (**d**). Correct PMMA distribution verified by post-procedural CT

to the other has been observed [12]. Generally clefts indicate a benign osteoporotic fracture, but rarely are they associated with neoplastic fracture or osteomyelitis. There are evidences that clefts are the result of avascular osteonecrosis [13, 14]. Liquid clefts seem to occur in the early stage as the consequence of fluid formation into osteonecrotic cavitation. Vacuum clefts are probably the resulting end stage of fracture non-union, outcoming in pseudoarthrosis and chronic instability with persistent pain. The degree of vertebral body collapse is generally more severe with a vacuum cleft than with fluid cleft. Extension radiograph can demonstrate fracture mobility and may reveal the vacuum sign itself, underestimated on standing radiograph [15]. Only a few reports have evaluated vertebroplasty in the setting of intraosseous cleft and no systematic studies have been done, nevertheless many aspects can be outlined. PV efficacy in fractures with cleft is similar to that in fractures without cleft, but there is a tendency to better results with liquid cleft [13]. If clefts are a sign of non-union and evolution in pseudoarthrosis, they should be considered a stronger indication to early percutaneous treatment instead of conservative treatment. According to our experience, the sero-hematic content can be syringed out through the needle positioned inside a liquid cleft; then the cavity may be filled with air, becoming more appreciable on fluoroscopy. Cement injection into the cleft cavity gives a characteristic dense well shaped filling, which is different from the diffuse filling of the spongiosa. Bone sclerosis around the cleft may create a compartment within the vertebral body. If the needle is positioned in the spongiosa outside the cleft the injected cement may not penetrate into the cavity and vice versa. In such a case the needle must be repositioned to obtain a complete vertebral body filling. If the cleft is recognized in advance a bilateral approach may be chosen to accurately insert one needle in the cleft and the

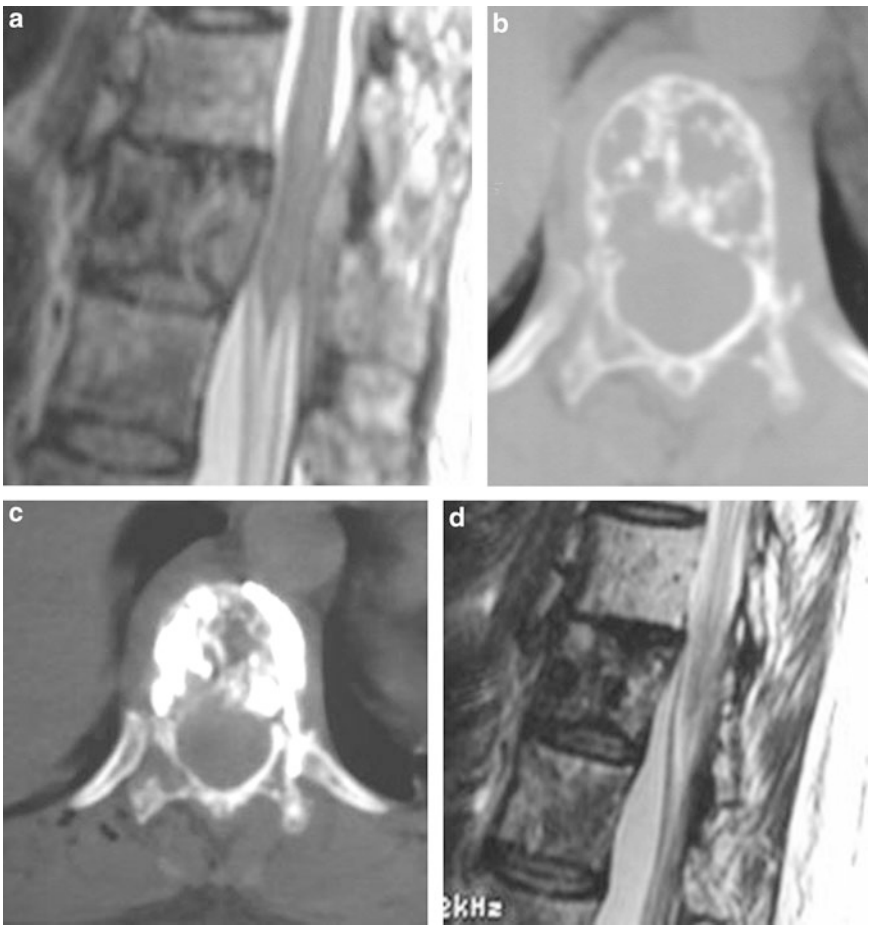

Fig. 5 (**a**–**d**) Breast carcinoma metastasis extending into the spinal canal (**a**, **b**). Vertebroplasty was performed before radiotherapy to gain immediate pain control and to prevent body collapse (**c**). Follow-up at 6 months shows regression of epidural extension and maintained vertebral body thickness

other in the remnant body part (Fig. 6). Due to fracture instability PV performed with forced hyperextension can obtain a substantial recovery of the vertebral body height and reduction of local kyphosis angle [16, 17]. Leakage in the adjacent disk is more frequent and there is a higher risk of subsequent fracture of the adjacent vertebra both in untreated and treated cleft [18]. Prophylactic PV at adjacent levels may be considered [19].

Vertebra Plana

Very severe vertebral compression fractures, or vertebra plana (VP), refers to vertebral body collapse to less than one-third of its original height [5]. VP can be caused by various pathological conditions including eosinophilic granuloma (Calvè's diseases), giant cell tumour, aneurysmal bone cysts (ABCs) trauma and metastases, but myeloma and severe osteoporotic compression fractures are the most frequent in adults. Differential diagnosis can be achieved by radiological work-up but biopsy may be necessary. In case of osteoporotic fracture MRI and CT can differentiate chronic stable fracture from not healed unstable fracture, on the basis of increased signal corresponding to bone marrow oedema and bony abnormality on T2-weighted and STIR, and the identification of smallest vacuum sign. Fragmentation and retropulsion of the posterior wall must be evaluated. Usually patients have restricted mobility, severe mechanical back pain, requiring narcotic analgesics, and are refractory to conventional medical treatment for a long time. Surgery is usually not an option, unless neurological signs are present, and PV offers immediate pain relief and strengthening of the fractured vertebra. Initially VP was considered a relative contraindication to PV, unless for very expert operators, because of technical difficulties and risk of complications. Actually with increasing operator experience and developing technique PV is currently performed safely and effectively, with no major complications [20, 21]. In this setting the procedure is not more difficult, although more caution is required and some technical tricks are useful. If the central part of the vertebral body is completely depressed a bilateral approach is recommended, placing the needles more laterally to the side of the vertebral body to decrease the chance of inserting the tip into the disc space [22]. If a tiny cleft is detectable, the needle tip must be put into it [4]. In this way a

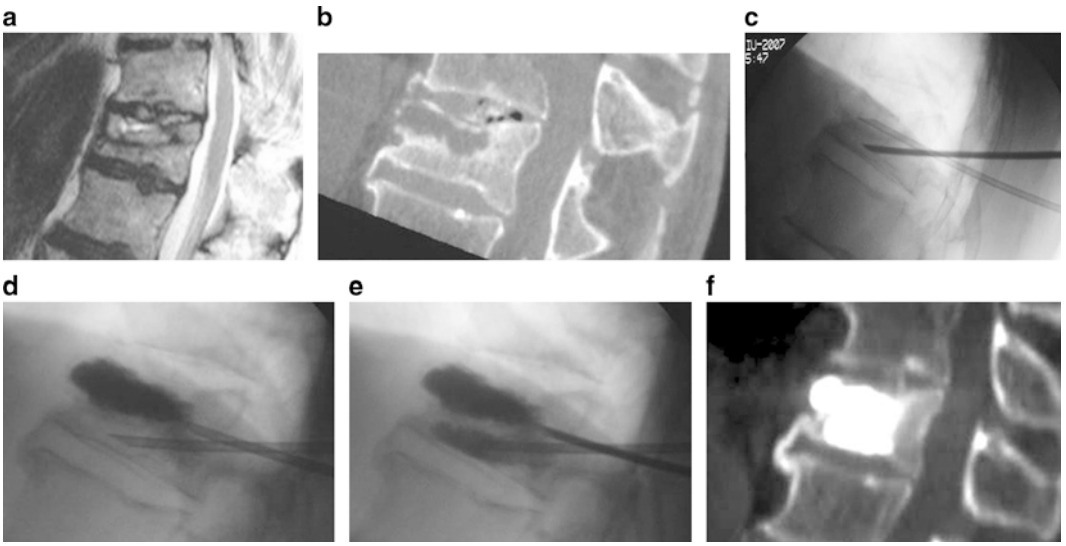

Fig. 6 Osteoporotic fracture with liquid cleft showed by MRI (**a**). The cavity is surrounded by sclerotic bone reaction demonstrated by CT, dividing the vertebral body in two compartments (**b**). One needle is inserted superiorly into the cleft and the other inferiorly into the remnant body part to achieve complete body filling (**c**–**f**). The different appearance of the injected cement into the cleft (dense, well shaped) and in the remaining spongiosa (more diffuse) may be appreciated

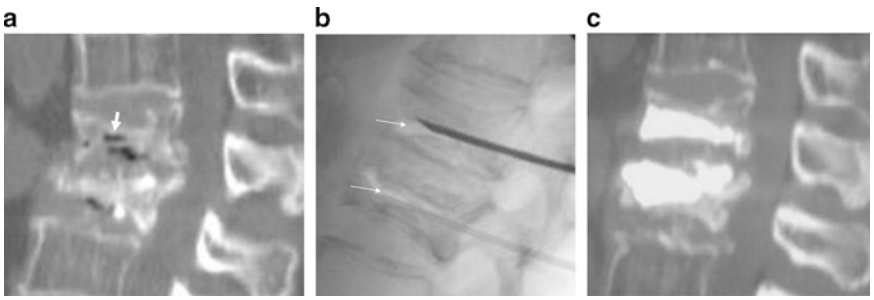

Fig. 7 L1 and L2 osteoporotic fracture with severe body collapse (vertebra plana) (**a**). A fine vacuum cleft is visible only in L1 (*white arrow*). L2 is apparently completely collapsed. 15G needle is inserted into each vertebral body. The injection of a few cc of air shows the appearance of thin radiolucent lines, demonstrating the presence of a virtual cavity in both L1 and L2 (*white arrows*, **b**). Post procedural CT shows the very good vertebral body filling with partial thickness recovery and kyphosis reduction

good bilateral filling can be achieved also using a monolateral approach, even if the needle is away from the central part of the vertebral body. Fine needles (15G or even 16G) more easily enter into the very thin residual bone space. The injection of some cc of air through the cannula may make visible a slit where the needle can be advanced farther to reach the anterior portion of the vertebra. In many cases partial thickness recovery can be achieved (Fig. 7).

Multifragmented Fractures

Performing PV, injection of the cement is relatively straightforward, the latter remaining contained inside the vertebral body by the relatively undamaged cortical bone and endplates. Such condition usually occurs when treating the classical osteoporotic collapse (subsidence of the cancellous bone with cortical integrity), but also injecting hemangiomas, myelomas and most neoplastic litic situations. On the contrary, in cases of traumatic lesions, either in osteoporotic patients or not, the vertebral body may be fractured in many different fragments, with presence of fragment dislodgement and numerous fissures interrupting cortical bone and endplates (compression fractures with burst or split vertebral bodies, type A according to Magerl's classification, one or two-column involvement according to Denis). In such situations, the injected cement does not remain contained to the cells of the cancellous bone, but immediately leaks through the fractures outside the limits of the vertebral body. In these cases the use of intrasomatic balloon tamps prior to cement injection (KP) represents the ideal solution for a few reasons.

First, inflation of the tamps, which in such cases always occurs at very low pressures, makes a void inside the body, void in which the cement remains without leakage. Also, in such voids injection of very viscous cement (less prone to leakage) is allowed. Moreover, pressures of the balloons tend to compact the dislodged fragments and, stretching the ligaments when undamaged (kind of ligamentotaxis), can reduce the fracture itself, the impingement of the spinal canal, the kyphotic angle and at least partially restore body height. From a technical point of view, we note that the random morphology of the fractures could favour an asymmetric inflation of the tamps, and consequently, also of the cement deposition; to obviate this, we always use a curette before tamp inflation, to make room for the tamp in the desired direction. Usually we use a bilateral approach, and with curettage we favour kissing of the balloons on the midline after inflation. One might argue about lack of stabilization after a treatment by means of KP alone. However, judgement about instability is still controversial. All spinal structures contribute to stability, all lesions result in certain instability, but complete instability is rare. This is particularly true in Magerl type A fractures, among which usually type A3.2 and A3.3 are considered the more unstable. Classically these fractures are treated by means of a two-session surgery, first posterior fixation (with canal decompression when needed), second surgery to stabilize the anterior spine and restore stress resistance. In our experience, a single KP session is sufficient, when there is no need of canal decompression, and we treated such patients by KP alone, with good clinical result and no complications. In any case, KP would allow skipping the second surgery and could be carried out at the same time as the posterior fixation, thus reducing the overall surgical aggressiveness toward these, often fragile, patients (Fig. 8).

Multilevel Vertebroplasty

Some authors and published guidelines on PV [23–26] consider as safe practice not to perform more than three levels in a single session to avoid major complications. This is a golden rule especially if the operators have not a huge experience of PV. But there are some particular cases, such as multiple myeloma, secondary osteoporosis and metastases where the patients have more than three painful vertebral

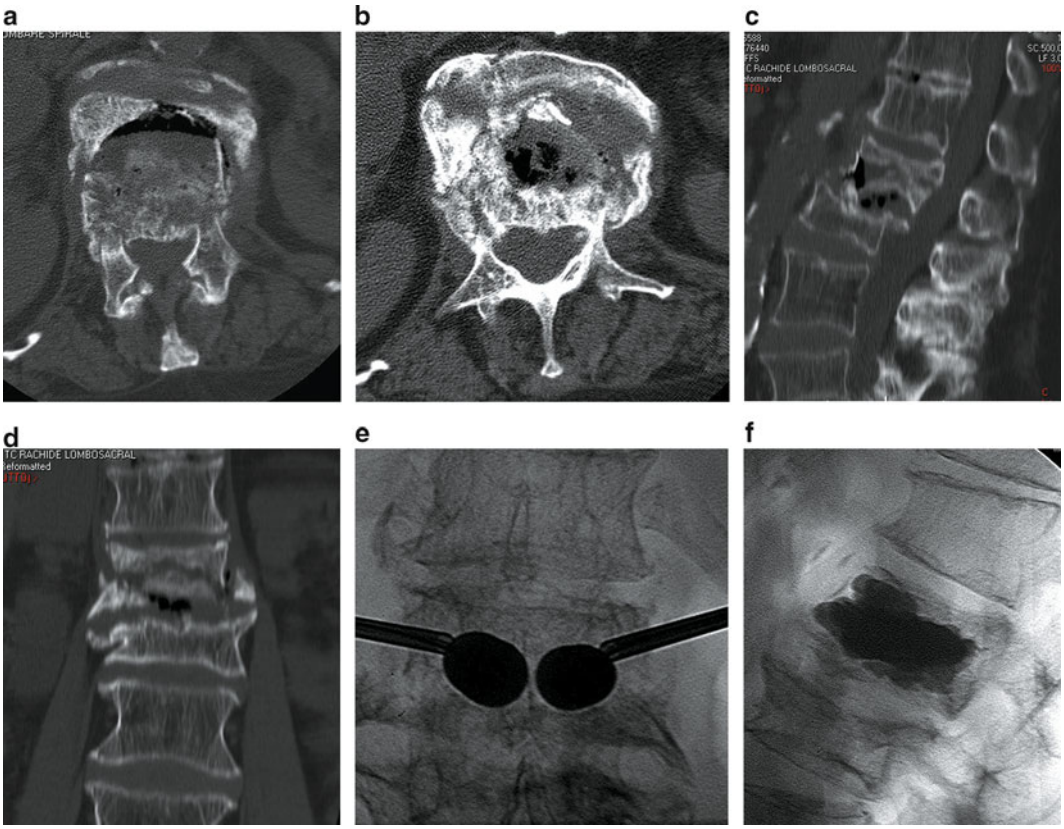

Fig. 8 Axial (**a**, **b**), sagittal (**c**) and coronal (**d**) CT images of an L1 traumatic A3.3 burst fracture in an osteoporotic patient. An old asymptomatic L2 fracture is also present. Patient unable to stand and walk, pain present also during bed rest. (**f**) Tamps kissing on the midline during inflation. (**e**) Final result. Patient is able to walk without pain the same day and is discharged the following day without bracing

collapses, and a multilevel treatment is needed to achieve back-pain regression and quality of life improvement. In these cases, if a mini-invasive technique is employed by a skilled operator, multilevel vertebroplasty could be feasible, safe and successful. Multilevel PV can be performed by means of monolateral approach with a thin (13–15G needle) and low volume bone cement injection in each vertebra (Fig. 9) considering that pain regression is not dependent on the volume of the cement injected within the vertebral body and that patients with multilevel vertebral collapses usually need a minimal vertebral augmentation to improve. In the experience of the E.VE.RES.T group 802 patients (631 females and 171 males, mean age 69.2 years; 678 osteoporotic, 124 malignant) underwent multilevel PV. In the same session we treated from 4 up to 13 levels with monolateral approach, local anesthesia, injecting from 1.5 to 3 ml (mean 2.5 ml) of polymethylmethacrylate (PMMA) each level. ECG, blood pressure and oxygen saturation were monitored during and after procedure for 6 h. In all patients PV was completed without any major complications and with an overall good clinical outcome (average VAS score before PV of 8.1 ± 1.5 significantly dropped to 1.4 ± 1.7 after PV). To compare complications and back-pain regression with a control group (1,068 patients where 1–3 levels where performed in the same session), the Fisher's exact test and unpaired *t*-test with Welch correction were performed; no significant difference in complications ($p = 1.000$) and back-pain regression ($p = 0.7185$) was noted.

Refracture of Augmented Vertebra

PV is a remarkably successful procedure. According to the E.VE.RES.T. group data, there is no pain relief in just 3% of cases. Much attention has been focused on the increased risk of new adjacent vertebral fractures as a cause of recurrent pain. Refracture of an already treated vertebra seem a rare event but may occur [27] and repeated PV has been reported in some cases. Asymptomatic progressive height loss after successful PV has been described [28]. On follow-up we observed 12 out of a group of 610 patients treated with percutaneous augmentation, who presented recurrent pain related to new fractures of the treated vertebral body [29]. The underlying pathology was osteoporosis in 11 cases and myeloma in one case. Eleven patients had been treated with PV and one with kyphoplasty. Noteworthy, a cleft was present at the time of treatment and osteonecrosis was histologically documented in ten cases treated by PV and in the single case treated by kyphoplasty. Refracture was most frequent at the dorso-lumbar junction. All 12 patients reported pain relief after first treatment but intense pain returned to the original location very soon after 2–5 days in seven patients and later after 1–7 months in the remaining four patients. Only in one case the pain restarted after a trauma. In the others it began spontaneously. Radiological work-up was performed with CT and MRI and revealed additional vertebral height loss in 7 patients and true fracture with bone or cement fragmentation in four patients. In two

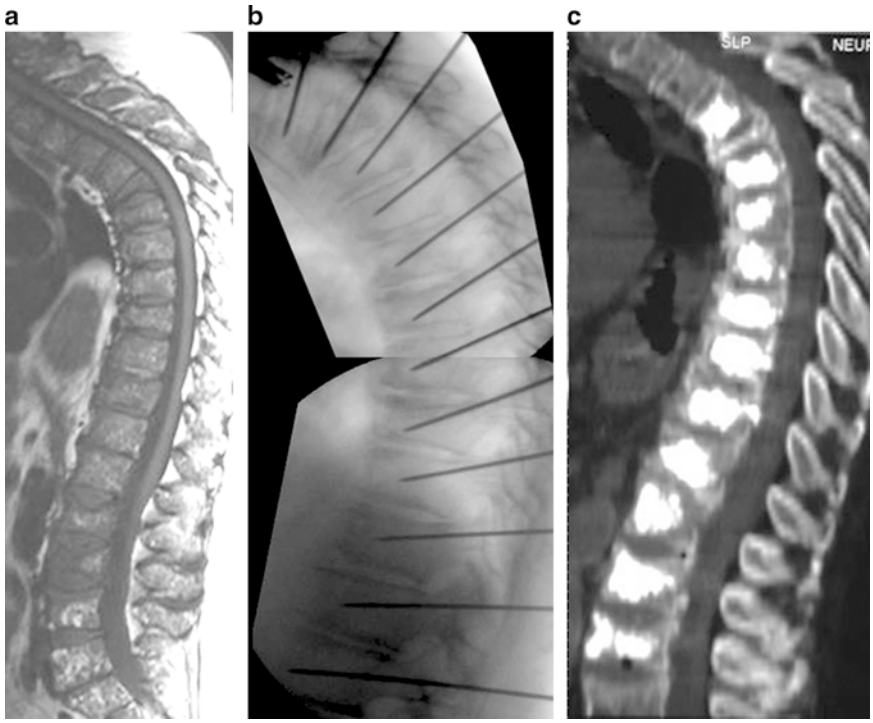

Fig. 9 Diffuse Multiple Myeloma spinal involvement with severe, not localizable pain (**a**). All the 15G needles have been placed before starting the injection (**b**). Low volume filling is obtained, mainly in the central part of the vertebral body, from the upper to the lower end-plate, to ensure enough strength restoration. CT control after the procedure shows the cement within the vertebral bodies (from T4 to L3 – 12 levels) (**c**). The procedure was performed in local anaesthesia, without sedation

patients a thin liquid collection around the cement was noted. In all cases other vertebral fractures or different causes of pain at other levels were excluded. The post treatment control CT of all patients was reviewed and insufficient volume of injected cement was judged in seven cases, as the filling was limited to a part of the vertebral body and did not extend from the upper to the lower end plate. Eight patients were treated conservatively with brace and analgesic drugs, obtaining pain remission within 3 months. In four cases PV was repeated to obtain complete filling of remnant vertebral body, with successful pain relief. Only one patient required surgery due to spine instability. Figure 10 illustrates an example of following height loss occurred in a L1 fracture already treated with vertebroplasty. The cement filling was limited to the large cleft cavity. After immediate relief, progressive pain increasingly recurred 2 days later. A control CT performed after 2 weeks documented further height loss. The patient was treated conservatively and was pain free within 3 months. An example of L1 refracture 1 month after treatment is reported in Fig. 11. There is anterior dislocation of the cement mass and widening of cement-bone interface filled with liquid, as shown by MRI. This should not be confused with simple edema. Treatment was performed with repeated PV. Figure 12 shows bone reabsorption around bone-cement interface, documented 7 months after vertebroplasty of a compression fracture of L4. The vertebral height is paradoxically slightly increased. The empty space around the cement, which is well depicted by air injected through the cannula, was completely refilled with cement. Our experience confirms that refracture of the augmented vertebra is a rare but possible event that must be considered as a cause of PV failure and back pain recurrence. We think that insufficient cement filling, osteonecrosis with large cleft and dorsal-lumbar junction location are possible risk factors. Likewise aseptic loosening of cemented arthroplasty [30], fluid collection around the cement could be a multifactor consequence of bone remodelling or osteonecrosis, disjunction of bone-cement interface and cement failure [31, 32]. Repeated PV may be performed with success. Even if the ideal volume of cement to be injected is still a matter of debate, at least upper to lower endplate filling should be obtained to achieve fracture stability and restore the biomechanical vertebral properties [33, 34]. For the same reason in case of cleft, both the cavity and the remaining vertebral body must be filled to prevent further collapse. Also when performing kyphoplasty, injection should not be limited to fill only the created cavity but also be extended to the surrounding spongiosa to achieve complete bone-cement penetration.

Cervical Junction

The lesions of the first two cervical vertebrae such as malignancy or trauma are not so uncommon, in these cases conservative treatment with Halo vest and Minerva or surgery (in trauma) or radiotherapy and chemotherapy (in malignancy) usually leads to healing of fracture or bone consolidation.

Fig. 10 Osteoporotic fracture of L1with osteonecrotic cleft (**a**). Cement filling limited to the large cleft cavity (**b**). Pain relapse after 2 days. Control CT performed after 2 weeks shows further height loss (**c**)

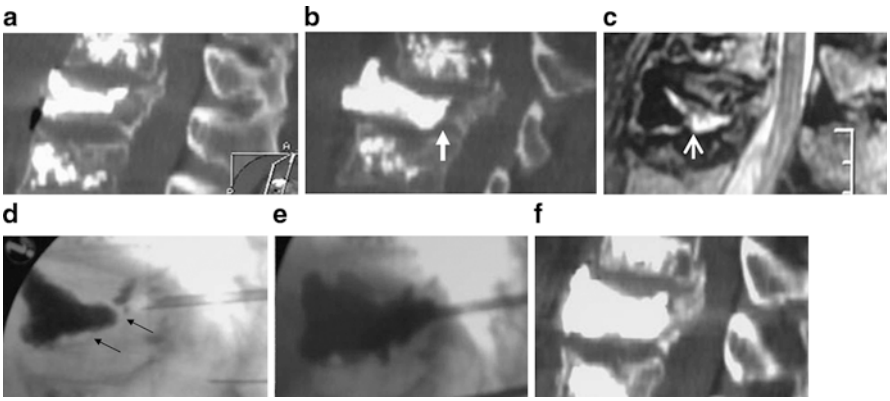

Fig. 11 Already treated L1 (**a**) shows a refracture with anterior dislocation of the cement mass and widening of cement-bone interface (*white arrow*, **b**). The space around the cement is filled with liquid (*white arrow*, **c**). Vertebroplasty was repeated (**d**). After aspiration of the liquid a radiolucent line is visible around the cement mass (*black arrows*). The space is completely refilled with new cement (**e**, **f**)

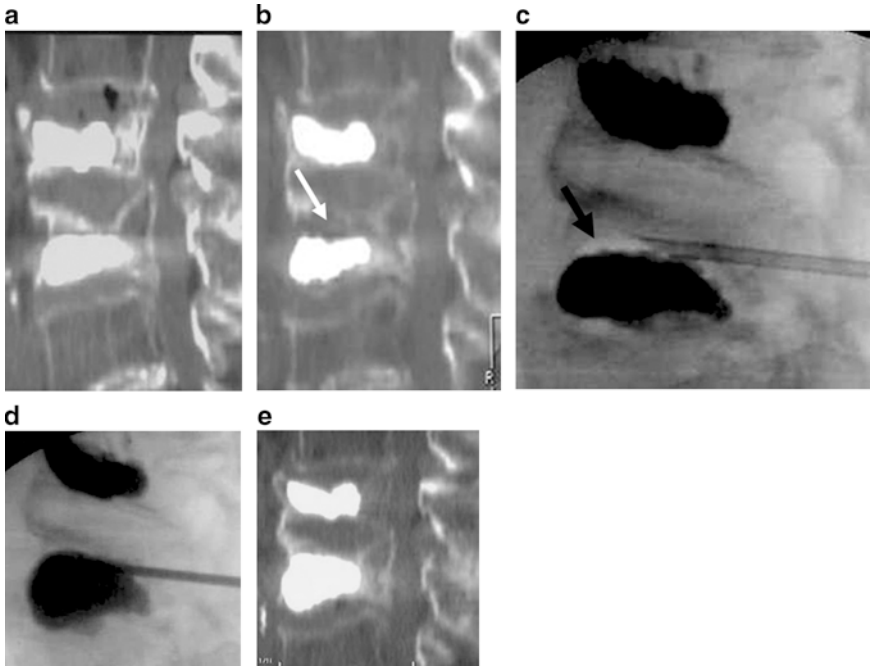

Fig. 12 Pain relapse after 7 months of treatment of L3 and L4 (**a**). Bone reabsorption around the cement is documented with paradoxically increase of vertebral body height (*white arrow*, **b**). The empty space is depicted by air injected through the cannula (*black arrow*, **c**), and then completely packed (**d**, **e**)

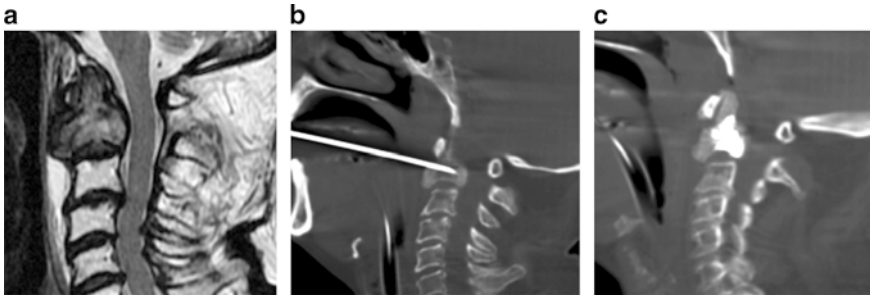

Fig. 13 MR demonstrating a huge painful breast cancer metastasis of C2 (**a**). CT control during the procedure allowed correct transoral needle placement within the lesion (**b**). Postprocedural CT showing consolidation of C2 and the absence of leakage (**c**)

If this kind of lesion occurs in the elderly patient, conservative treatment is frequently unsuccessful due to co-morbidity (concomitant osteoporosis and poor clinical conditions) and surgery is at risk due to the complication rate [35, 36]. In the older patient the quality of life is very poor as he or she is obliged to wear a Halo vest and to stay in bed with lower healing rate due to concomitant osteoporosis. In these cases physicians, if feasible, may propose minimally invasive treatment such as PV as the first published case of PV in 1987 [1] was performed on the second cervical vertebra (C2). PV on the atlas (C1) or on C2 is challenging but possible if the correct technique is respected; usually a combined CT and fluoroscopy guidance is needed to achieve correct placement of the PV needle and to avoid puncture of the anatomical structure (artery, spinal cord) surrounding the lesion. For the treatment of C2, in our experience (21 cases), the best approach is the transoral route as the vertebral body is located immediately under the oral mucosa and puncture of the arteries and spinal cord can easily be avoided. An example of huge painful breast cancer metastasis not responding to conventional treatment is shown in Fig. 13. Successful treatment was obtained with transoral PV. This approach requires patient's general anesthesia (Propofol 200 mg and Fentanyl 0.1 mg) with placement of a flexible reinforced endotracheal tube and a self-retaining pharyngeal retractor to keep the tongue depressed and the mouth constantly open. The patients need to be premedicated with IV antibiotics (1 gm of vancomycin hydrochloride and 100 mg of gentamycin immediately before the procedure, then a 7-day course therapy of 150 mg of oral clindamycin every 6 h is usually prescribed prophylactically). Uncommon PV on the body of C1 was previously reported in only two cases (37, 38) and we have experienced only one. In these cases the preferable approach is from lateral under CT guidance using a thin needle, but in such an extremely rare case, material and methods need to be selected according to the lesion to be treated by a very skilled physician only. PV performed transorally on C2 and the only one performed on

C1 by the E.VE.RES.T. group were successful without any major complication, in only one case of C2 a posterior surgical consolidation was needed because of the large extension of metastases to pedicles also, but the patient could be spared the more complex surgical anterior approach.

Sacroplasty

Insufficiency fractures of the sacrum are a frequent pathological condition associated with severe primary osteoporosis, but even rheumatoid arthritis, chronic corticosteroid therapy, pelvic irradiation, fibrous dysplasia, Paget's disease, osteopetrosys and local osteomalacia can be responsible for sacral fracture [39]. Sacral insufficiency fractures should always be considered in elderly patients complaining about severe low back pain; it is frequently underestimated as conventional plain X-ray evaluation is generally almost normal. CT can sometimes depict sacral alae fractures parallel to the sacro-iliac joints, however only MRI and bone scanning showed to be very sensitive in demonstrating total or partial sacral insufficiency fracture. Neoplastic involvement of the sacrum can be part of secondary disease, being responsible for severe local pain, preventing the patient to sit or stand-up position. Recently sacral injection of PMMA has been proven to be very powerful in stabilizing the sacrum. Patients affected by sacral insufficiency fractures or sacral malignancies experience disappearing or significant reduction of low back pain when percutaneous sacroplasty treatment is performed, and clinical results remain stable even in the late follow-up [40–42]. A transiliac fluoroscopy guided approach can be used to introduce the needle into the sacrum body at S1–S2 (Fig. 14). However, fluoroscopy alone is insufficient to depict the sacral complex anatomy in order to safely introduce the needle and to control the diffusion of the cement, particularly in those patients with extensive sacral neoplastic destruction. The best way is to combine CT to fluoroscopy so that needle insertion can be easily oriented along the main sacrum axis avoiding sacral foramina (Fig. 15). Moreover, with manual PMMA microinjection by small syringes (i.e., 1.5–2 cc by time), one can precisely manage the cement progression, immediately stopping the injection as initial intraforaminal leakage is appreciated and moving the needle away from the foraminal area before restarting it. In case of sacral malignancy, needle approach is chosen according to the best way to reach the core of the osteolytic area. In patients with extensive osteolysis related to malignancies, the possibility to see immediately the real PMMA distribution inside the sacrum allows to perfectly consolidate the total area involved by the disease. Using CT control even the posterior arch of the sacral canal (laminoplasty) as well as massive sacral destruction can be treated safely (Fig. 16).

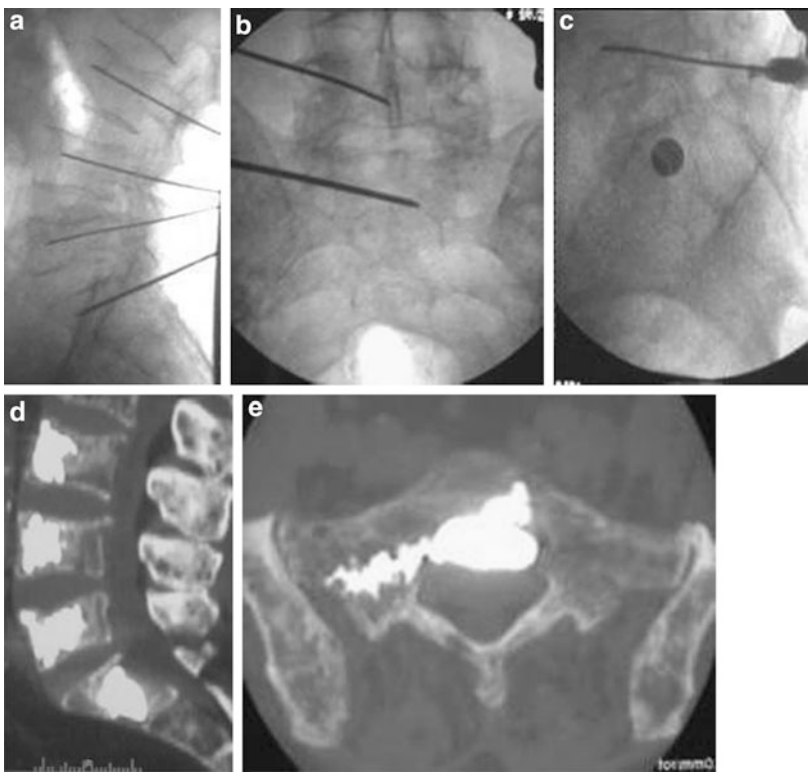

Fig. 14 L3, L4, L5 and S1 multilevel vertebroplasty. Needle positioning inside the body of S1 is performed through a transiliac approach under fluoroscopy guide. Lateral view (**a**), A–P view (**b**), oblique view (**c**). Postprocedural CT control (**d**, **e**)

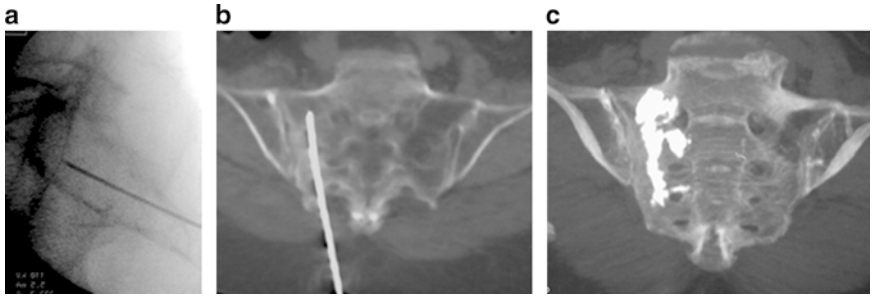

Fig. 15 Monolateral sacral insufficiency fracture. Combined CT and fluoroscopy control allows precise needle positioning along the main axis of the sacral wing avoiding sacral foramina (**a**, **b**). Postprocedural control CT (**c**)

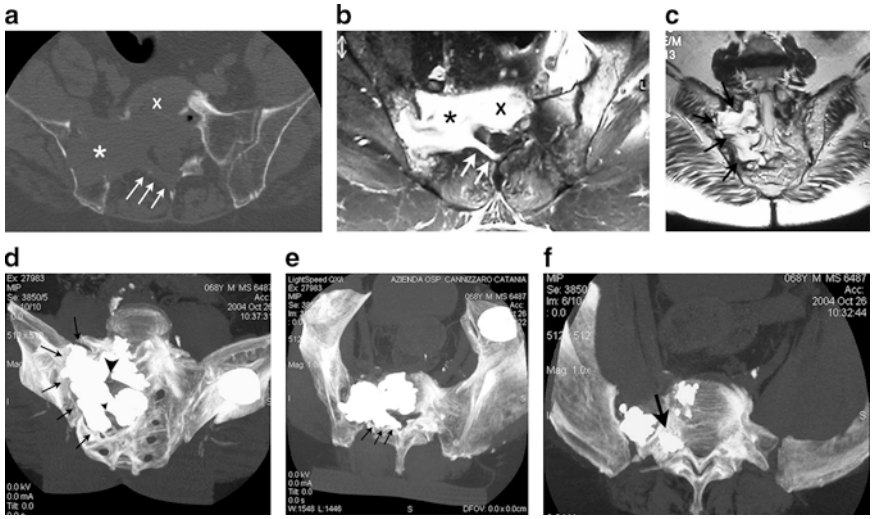

Fig. 16 Extensive erosion, related to massive myeloma infiltration, of the whole right wing (*asterisk*), the body (*x*), and the right posterior lamina (*arrows*) of the sacrum can be appreciated on axial CT (**a**), with high signal intensity on T2-weighted STIR axial (**b**) and coronal (**c**) scans. 2D coronal (**d**) and axial (**e**, **f**) reformatted CT demonstrate reconstruction of the sacral areas previously destroyed by the disease. Noteworthy is the remodelling of the I and II right sacral foramina (*arrowhead*) without any leakage inside

Combined Treatments in Malignant Lesions

In most cases PV alone is effective to achieve back-pain reduction caused by vertebral metastases, but when the malignant lesion extends beyond the vertebral wall, infiltrating the paravertebral space or compressing the spinal cord or nerves, bone consolidation is not sufficient. In these very selected cases a combined treatment, first to destroy the tumour mass and second to augment the bone, could be a solution [43, 44]. Many ablative techniques have been developed. The E.VE.RES.T. group experienced combined treatment such as radiofrequency thermoablation (RFA), cryotherapy and coblation (cavity) plus PV. RFA alone demonstrated to reduce pain in bone metastasis. The aim of combining RFA to PV is to achieve a large tumour tissue thermal destruction and thrombosis of paravertebral and intravertebral venous plexus, before cement injection. RFA causes immediate cell death due to coagulative necrosis but decompression effect cannot be expected. Because of the high temperature applied over a long time (generally 100°C for more than 20 min), RFA can cause permanent nerve injuries and damages to the nearby viscera. It is contraindicated if the lesion is very close to the spinal cord. Although RFA is pain effective, the more important limitations are: (a) the inability to precisely control the ablation margin with TC during the procedure; (b) the pain associated with the procedure that requires deep sedation and may increase during the immediate post treatment period; (c) the long latency before substantial pain reduction is achieved [45] (Fig. 17). Contrary to RFA, cryoablation (CA) utilizes alternate freeze/thaw cycles that result in formation of an "ice ball" within the lesion. At least a double freeze/thaw cycle is required to ensure cell destruction at high subzero temperatures, which must be −40°C. At this temperature 100% of cells are destroyed by extra- and intracellular ice formation, based on the cooling rate. The frozen tissue appears as a low-attenuating area with sharp rim, enabling real-time monitoring of the procedure performed under unenhanced CT control. After each freezing step a CT scan reveals the iceballs within the lesion, visualized as hypodense areas arising from the probe tips, enveloping the greater part of the lesion, and a small surrounding area, sparing the wall of the vertebral

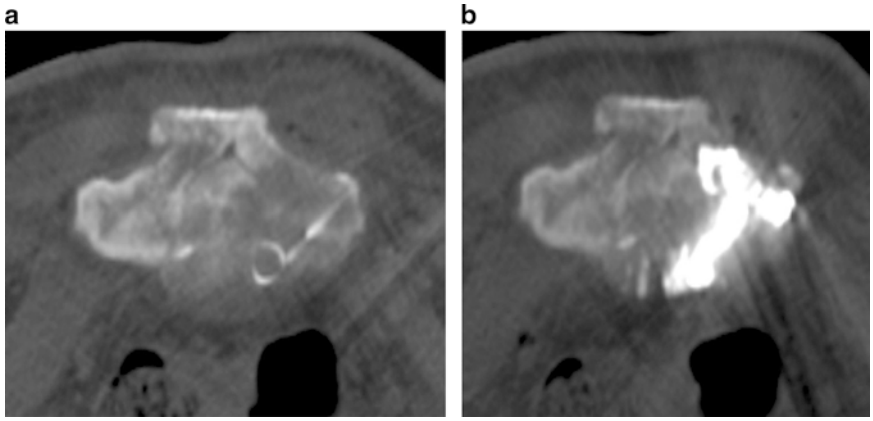

Fig. 17 Painful lesion at the coccyx treated with a single radiofrequency thermoablation needle (**a**); after the ablation, cement was injected in order to enhance the pain reducing effect and to make the coccyx stronger (**b**)

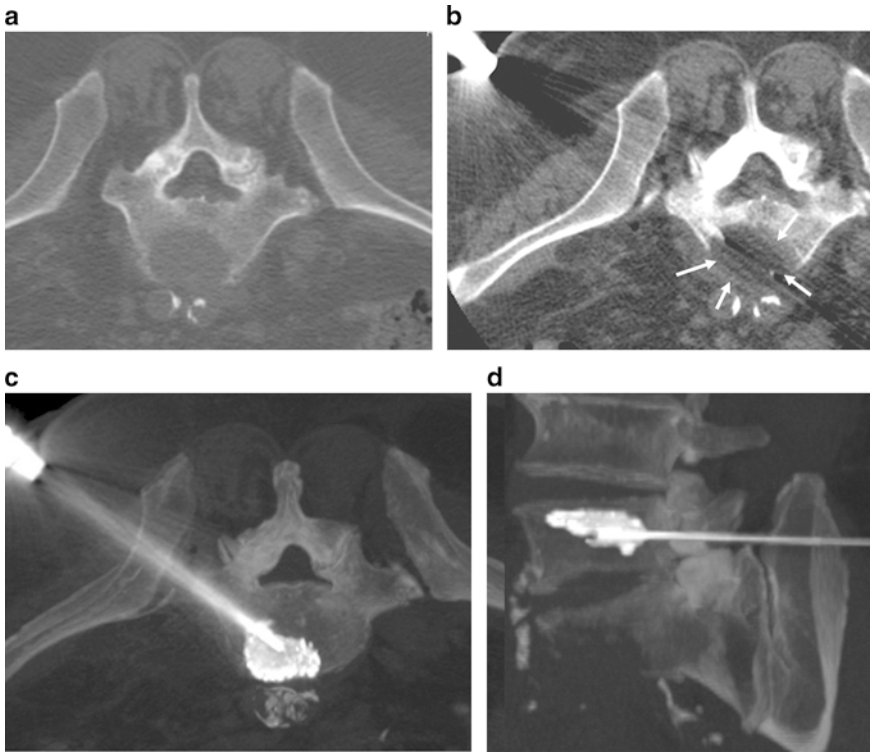

Fig. 18 Metastasis that destroys the most part of L5 vertebra is seen in (**a**); the cryoneedle has been inserted in the lesion using a transiliac approach, the iceball is visible in the middle of the lesion (*white arrows*, **b**); axial projection and MIP reconstruction of the lesion after the cement injection (**c**, **d**)

bone (Fig. 18). Freezing causes partial analgesia, reducing nociceptor activity and synaptic transmission, so that patients do not experience pain during the procedure. Compared to RFA the time of procedure is longer, but the risk of permanent thermal nerve injuries is less and cryoablation can be used also with lesions close to the spinal cord or to the nerves. Like RFA, cryoablation causes coagulative necrosis so decompression cannot be achieved [46]. Preliminary experiences using plasma-mediated radiofrequency ablation (Coblation) are promising [47]. This technique can create a cavity in soft tissue where to inject the cement, with low heat deposition, and could be useful in treating vertebral malignancy extending into the spinal canal when surgery is not feasible. The whole procedures of RFA, cryoablation and coblation, in combination with PV, are better performed under CT-fluoroscopy guidance, to allow precise positioning of needles and probes and have demonstrated to be feasible and safe. According to Medline review, new tendencies in minimally invasive therapies for spinal tumours are essentially directed toward developments of "hybrid" treatments, combining vertebral augmentation with other ablative procedures. Probably in the coming years we will observe their validation in large series and the development of other new procedures.

Conclusions

We presented an overview of our experience using minimally invasive techniques for vertebral augmentation. Their use, although widespread, remains controversial, however, in our experience they have proved very effective. Obviously it is essential to carefully select the patients clinically and radiologically. These procedures when performed by experienced operators are very safe. The continuous development of new materials and technologies can improve performance, extend the indications and reduce the risk of complications, however, deep knowledge of radiological anatomy, underlying pathology, technical aspects and a thorough experience in performing vertebral percutaneous X-ray guided procedures remain the key pillars for good practice and to get the best results.

Conflict of interest statement We declare that we have no conflict of interest.

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Kyphoplasty in the Treatment of Osteoporotic Vertebral Compression Fractures (VCF)

Procedure Description and Analysis of the Outcomes in 128 Patients

Guillermo Saul Fernandez Molina, A. Campero, R. Feito, and S. Pombo

Abstract In recent years, the advent of percutaneous techniques in the management of osteoporotic vertebral compression fractures has proven to be a great step forward in the evolution of patients suffering from this pathology.

Vertebroplasty, which was developed in 1984 by Galibert and Deramond, presents the disadvantage of leakage of the cementation material and the impossibility to restore spinal deformity. Kyphoplasty has shown to be almost a definite solution to these problems. The description of the technique, its indications, and the outcomes resulting from our series of 200 vertebral fractures in 128 patients are presented in this paper.

Keywords Kyphoplasty · Osteoporosis · Vertebral fractures

Introduction

Nowadays, osteoporotic fractures represent a severe problem for public health care all over the world. According to several reports carried out by the European Union, over 100 million people worldwide, and nearly 30 million in the United States, are a potential risk to develop fractures secondary to osteoporosis [2]. The risk of developing compression fractures increases with age: almost one fourth of women over the age of 50 are afflicted by osteoporotic bone fractures; in women 80–85 years of age, up to 40% suffer osteoporotic bone fractures. According to the figures shown in these research studies, the number of annual hospitalizations reached 100,000, with a hospital stay ranging from 10 to 30 days and very high costs in terms of pain medications, orthoses and physiotherapy [17], with a high rate of morbidity and mortality.

Percutaneous kyphoplasty has shown to be a significant development in the treatment of osteoporotic vertebral fractures. However, there are several factors to take into account when analysing the indications and the surgical technique, in order to improve results and patient evolution.

Anatomy

The anatomic unit of the spine is the vertebra and disc. Each vertebra has a body and six posterior elements: pedicle, superior facet, inferior facet, lamina, transverse process and spinous process. The part of the posterior elements that lies between the superior and inferior facet is named pars interarticularis, and it is best known as an isthmus of bone at the junction of the lamina and the pedicle [15].

The spinal canal is bounded anteriorly by the vertebral bodies and discs, laterally by the pedicles, and posteriorly by the lamina–facet joint complexes. Beneath each pedicle, the nerve root exits; the point of exit is known as the foramen.

The ligaments of the spine are: the anterior longitudinal ligament that runs the anterior aspect of the spine and is strongly attached to the anterior annular fibers of each disc; the posterior longitudinal ligament that runs the posterior aspect of the spine. It is flimsy in the lower lumbar spine [15]; the interspinous ligament, located between both spinous processes; the supraspinous process that runs over the tips of the spinous processes; and the yellow ligament, that bridges the interlaminar interval.

The neurologic structures in the spinal canal are: the spinal cord until L1–L2 level and cauda equine below that level, and bilaterally exiting nerve roots for each segment, all covered by the dural sheath. In the thoracic and lumbar spine, the exiting nerve root is numbered according to the pedicle beneath which it passes.

G.S. Fernandez Molina (✉), A. Campero, R. Feito, and S. Pombo
Instituto de Neurociencias, Columna Vertebral y Dolor, Calle 38-740, CP:1900, La Plata, Argentina
e-mail: guillermofmolina@ciudad.com.ar

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Pedicles/Nerve Roots Anatomy

The pedicle width of the thoracic segment decreases from T1 to T4 and then increases gradually to T12. The pedicle height of the thoracic segment increases gradually from T1 to T12 [12]. The pedicle width of the lumbar segment gradually increases from L1 to L5, and the pedicle height can be arranged from smallest to largest as follows: L2, L1, L3, L5, L4 [19]. Thus, according to "Lien et al." [12], pedicles are widest in L5 and narrowest in T4 in the transverse plane, and widest in T11 or T12 and narrowest in T1 in the sagittal plane. In individual pedicle, the ranges of the safe zone width and height are 3.4–7.7 and 8.6–13.7 mm, respectively, in T1–T10; and 7.2–17.8 and 13.9–16.7 mm, respectively, in T11–L5. The transverse angle of the pedicle decreases progressively from T1 to T12, then increase from L1 to L5. In sagittal angle, the largest angle located at T2 and the smallest at L5.

In the thoracic spine, no epidural space can be found between the dural sac and the pedicle. The average distances from the thoracic pedicle to the adjacent nerve roots superiorly or inferiorly at all levels range from 1.9 to 3.9 mm and from 1.7 to 2.8 mm, with a minimum of 1.3 mm, respectively [3]. Thus, Ebraheim et al [3] suggest that more care be taken into consideration when placing transpedicularly a needle or a trocar in the transverse plane than when placing a needle or a trocar in the sagittal plane in the thoracic spine.

In the lumbar spine, the mean distances from the lumbar pedicle to the dural sac medially and to the adjacent nerve roots superiorly and inferiorly for all levels are 1.5 mm, 5.3 mm, and 1.5 mm, respectively [4]. Thus, improper placement of the pedicle needle or a trocar medially or caudally in the lumbar spine should be avoided [4]. If the pedicle is considered to comprise four sections (superior, inferior, medial and lateral regions), the inferolateral portion is likely to be the safest zone for screw or trocar placement [8] (Fig. 1).

Physiopathology

Osteoporosis is the most common skeletal disorder. It can be defined as a progressive decrease in bone density, causing bones to become brittle, weakened, and with a high risk to develop compression fractures after minimal to no trauma.

Vertebral compression fractures are most commonly caused by osteoporosis; less frequently, they can be the result of trauma, but they generally have an osteopenic nature.

When a vertebral compression fracture occurs, it affects the vertebral body, frequently with an anterior wedging which moves the center of gravity forward resulting in a flexed posture which cannot be properly compensated by the muscles and ligaments.

The fracture of a vertebral body in an osteoporotic spine increases the risk of additional fractures since it alters the load-bearing capacity of an already injured spine (Fig. 2).

Symptomatology

Based on our biographical analysis and on 128 patients with VCF treated by our medical team, we can divide symptoms according to their clinical pattern as acute, subacute, chronic, or as a condition of reacuteness due to new fractures. The starting episode can spontaneously appear on an osteoporotic bone structure or caused by a sudden strain, bump or fall, generally not very significant.

Acute Pattern

It is characterized by the sudden appearance of dorsal or lumbar pain spontaneously or secondary to minimal trauma,

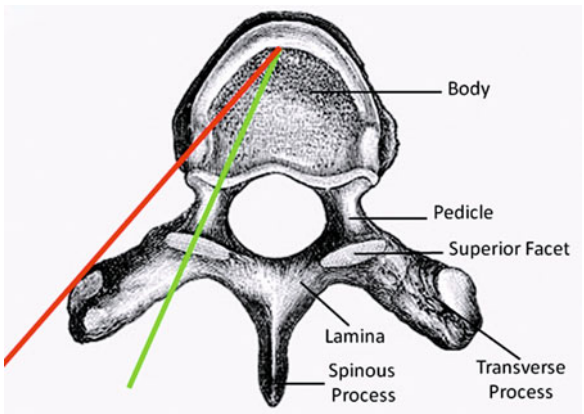

Fig. 1 Superior anatomical vision of a vertebra; the adecuate pedicular approach is shown in green while the extra-pedicular approach is in red

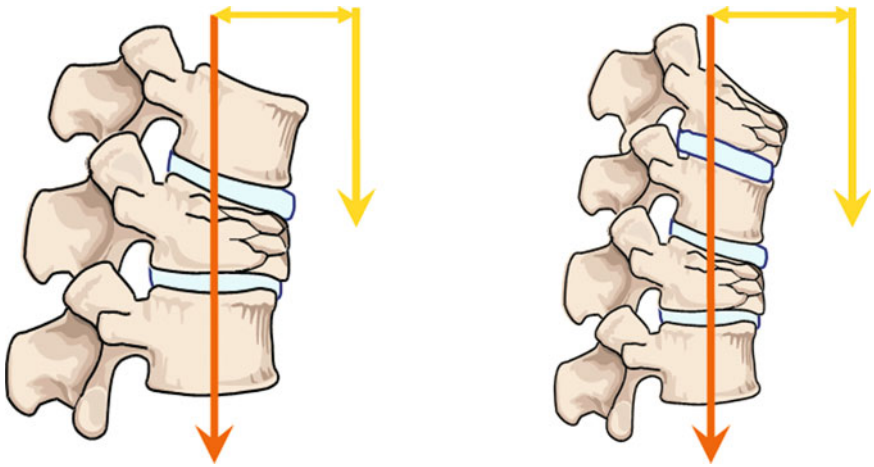

Fig. 2 Lateral image showing a vertebral compression fracture in which the center of gravity is moved forward, thus increasing the risk of additional fractures

with topography related to the location of the fracture. Pain worsens if carrying load, in standing position or when walking. It eases and may even disappear with bed rest.

Sometimes, pain is so severe that it forces the patient to be confined to bed, even when treated with narcotic analgesic medications.

Subacute Pattern

Progressively the patient's walking speed starts to decrease; there are alterations in balance and muscle fatigue at the risk of having falls and additional fractures. The risk of VCF increases 5 times after the first VCF [1].

Chronic Pattern

As time passes by, other symptoms appear such as weight loss, kyphotic deformity, protrusion of the abdomen, impaired pulmonary function, decreased appetite, sleep disorders, and depression.

The patient is in need of significant assistance of others [13] and there is an increase in the mortality rate [18] (Fig. 3).

In our series of 128 patients, we have found the following symptoms:

Dorsal – Lumbar Pain	128
Walking Speed Reduction	128
Depression – Astenia	128
Sleep Disorders	128
Balance Disorders	116
Weight Loss	97
Confinement to Bed	54
Impaired Pulmonary Function	35
Protrusion of the Abdomen	22

Diagnosis

A complete medical history is performed, it allows us to evaluate the risk factors for osteoporosis (age, gender, steroid use, sedentary lifestyle, etc), to rule out other etiologies, and to identify the level and the evolution of pain.

Fractures are assessed through X-rays, CT scans, and MRI scans. Bone gammagraphy can provide information regarding fracture age; although it might have negative effects in cases of acute pain.

Due to its high sensitivity, MRI scans can provide more and better information for our purposes. In the case of T2, we can diagnose acute fractures by an increase of signal at the starting point of the vertebral edema, but STIR sequence is the most sensitive for the identification of this type of lesions.

Kyphoplasty Treatment

It is of vital importance to perform an early diagnosis and treatment due to the disability caused by these types of lesions and also because they are frequently evolutive in relation to the severity of the fracture.

The main goals of the treatment of VCF are: pain relief, vertebral body height restoration and functional stability.

The treatment options described are:

- Conservative Non-surgical Treatment: it consists of bed rest (it worsens bone loss), pharmacological pain management (it can relieve pain but has the additional risks of the side effects caused by narcotic medications) and orthosis (it produces muscular atrophy and possibly does not represent any long-term functional improvement).
- Conventional Surgical Treatment: it may be suitable in cases of neurological deficit. It is an invasive procedure,

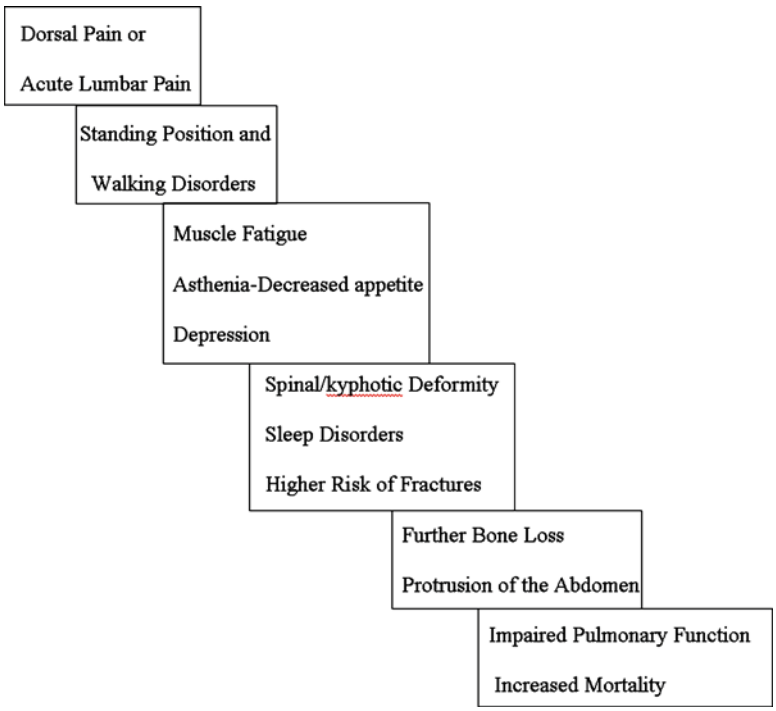

Fig. 3 Cascade of symtoms of osteoporosis

and it has inappropriate results in cases of osteopenic-osteoporotic bones.

– Vertebroplasty. This procedure was developed in France by Deramond and Galibert in 1984 [6]. It meant a great contribution until the advent of kyphoplasty. It is well tolerated and it eases pain in 80% of patients. Its main disadvantage is the high percentage of extravertebral cement leakages which may go into the spinal canal (with the risk of secondary neurological damage) or cause pulmonary embolisms [16]. On the other hand, by means of this technique it is not possible to restore vertebral height and therefore the spinal deformity cannot be corrected.

Balloon Kyphoplasty

Balloon kyphoplasty is a percutaneous technique where a balloon, which functions as an inflatable bone tamp, is inflated under high pressure to restore vertebral anatomy [7]. It was developed by Mark Reiley M.D., Berkeley, Calif. 1998 and it is currently the most popular procedure for the treatment of VCF. In recent years, other types of kyphoplasty without balloon have appeared, with similar therapeutic outcomes.

Our experience refers to balloon kyphoplasty; therefore we will exclusively discuss this procedure (Figs. 4 and 5).

Indications

It is of vital importance to establish the right indications and contraindications of kyphoplasty in accordance with the outcomes.

Kyphoplasty is indicated in cases of symptomatic osteoporotic and osteolytic vertebral compression fractures, either dorsal or lumbar ones, caused by:

– Primary Osteoporosis
– Secondary Osteoporosis
– Osteolytic Metastatic Tumors
– Traumatism

The main goals of the treatment of VCF are: pain relief, functional stability of the fracture, and vertebral body height restoration to avoid deformity [10] (Fig. 6).

Special care should be taken in cases of burst fracture with propulsion of bone fragments, and in patients under 40 years of age [11].

Contraindications

Contraindications are limited to fractures with propulsion of bone fragments into the spinal canal and neurological damage, coagulation disorders, osteomyelitis, pregnancy and technical constraints [5].

Fig. 4 Balloon inflated under high pressure for kyphoplasty

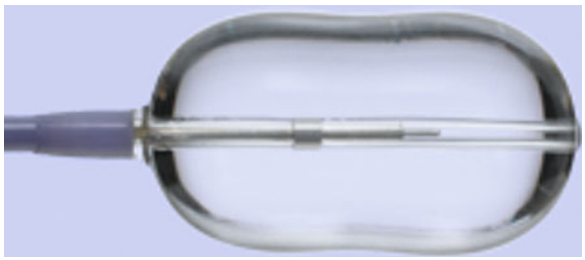

Fig. 5 The balloon functions as an inflatable bone tamp

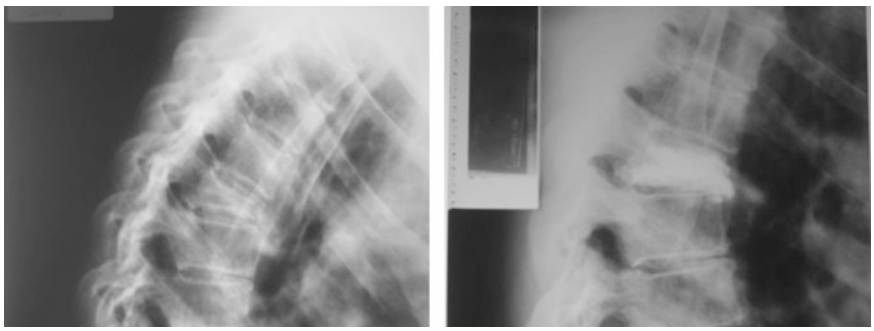

Fig. 6 Lateral view X-ray of the pre and post kyphoplasty T5 fractured in an 81-year-old woman

Surgical Technique

Patient Position

The patient is placed on a fluoroscope trolley in the decubitus ventral position, adequately standing out the thoracic region and pelvis in order to keep the normal function of the respiratory system and to avoid compression of abdominal organs. Positioning should promote extension of the thoracic and lumbar spine. A high resolution image intensifier is always used.

Anesthetic Considerations

On a series of 128 patients, we have used local anesthesia and neuroleptoanalgesia in 120 patients. General anesthesia was only used in eight patients due to their clinical conditions.

Localization of the Pedicle and Needle Pathway

The approach used was bilateral in all cases. Localization of the pedicle is of great importance in order to plan the needle pathway to follow [9]. We used an 11-gauge spinal needle. We performed an extra-pedicular approach for T5 and T10 fractures and a trans-pedicular approach in cases of T11 and L5 fractures; the diameter of the corresponding pedicles was taken into account.

Another vital point to consider when deciding on the needle direction is the type of fracture; if the fracture is a wedge compression fracture, the needle is guided back and forth, from the outside to the inside, and from top to bottom under fluoroscopic guidance at all times. If it is a biconcave fracture, the needle pathway is generally oriented along the horizontal plane, and if it is a fracture of the inferior endplate of the vertebral body, it will be oriented upwards (Fig. 7).

The topographic parameters to consider are the superior and inferior rims of the pedicle and the four rims of the vertebral bodies (superior, inferior, anterior and posterior).

If it is deemed appropriate, a biopsy sample is taken.

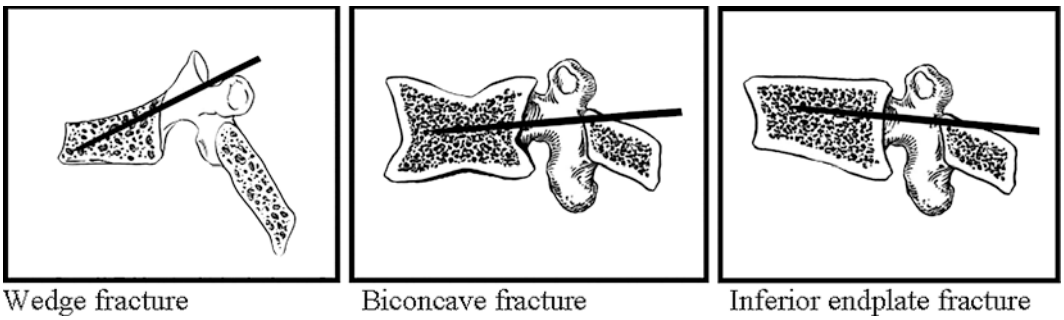

Fig. 7 Needle direction and the type of fracture

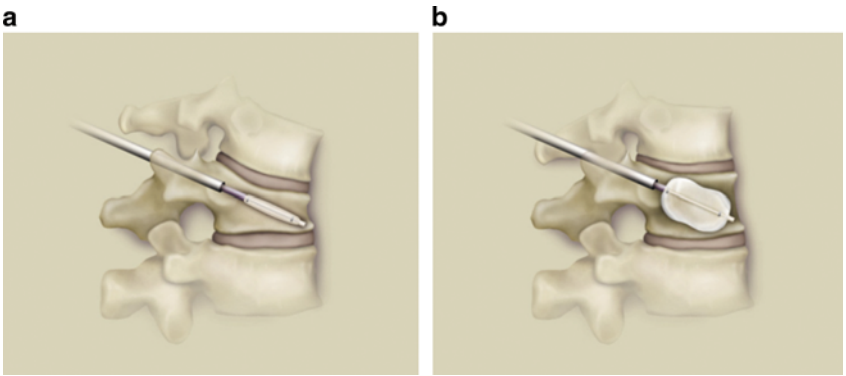

Fig. 8 (**a**) The balloon is placed through a cannula into the fractured vertebral body. (**b**) The balloon is inflated raising the fractured vertebral body endplate and therefore restoring its height

Balloon Placement and Inflation

The balloon size which corresponds to the exact dimensions of the fractured vertebra and the particular case is used.

Through a special cannula placed in position a few millimeters inside the vertebral body, a drill is put using manual control to enter the vertebral body just behind the anterior cortex. The drill is then removed. The catheter balloon is guided through the instrument into the vertebral body under fluoroscopic guidance, then the balloon is inflated using a radio opaque material, reaching a maximum of pressure of 300, in an attempt, if possible, to align the vertebral rims, and therefore, restoring vertebral height. If the balloon touches any of the walls of the vertebral body, the inflation step must be cancelled in order to avoid the risk of vertebral body fractures (Fig. 8).

Cementation

Once the vertebral body is in the correct position, the balloon is deflated and the catheter removed then, two cannulas are placed (one on each side) to fill the cavity (space) created by the balloon. The cavity is then filled with thick bone cement at low pressure in order to prevent any leakages. This last step also differentiates this technique from vertebroplasty (Fig. 9).

Case Series

Two-hundred osteoporotic vertebral body fractures in 128 patients were managed from July 2006 to June 2008. Medical history showed that the factor which triggered the fracture was related to a sort of traumatism in 77 patients (60%). The preoperative and postoperative clinical information was analysed, including the Oswentry and VAS scores, as well as the AO fracture classification. The minimum follow-up period was 6 months, mean 20 months. All patients were studied by means of X-rays and MRI scans. In our series, there were 96 dorsal fractures and 104 lumbar ones. 192 of the fractures occurred in women while only 8 occurred in men. 31 patients were treated in two levels, in 12 patients the

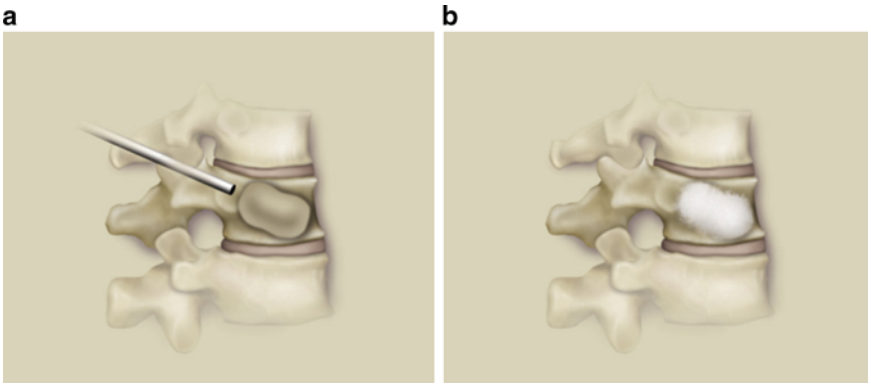

Fig. 9 (**a**) The balloon is deflated and removed creating a cavity (space) in the fractured vertebral body. (**b**) The cavity is filled with a surgical bone cement which forms an internal cast that holds the fractured vertebral body in place, and consequently the solidity sought is attained

procedure was carried out in three levels, 3 patients were treated in four levels, and in 2 patients the procedure was carried out in five levels. The mean age of the patient population was 77.8 years old, ranging from 62 to 86 years.

Results

All patients showed a significant relief in pain immediately after surgery. All patients were discharged from hospital within 24 h after the procedure. There was a minimum reduction of 6 points in VAS score and more than 25 points according to Oswentry score; there was at least a 6-month follow-up. Vertebral body height was attained (at different degrees) in all cases. No complications were reported.

Conclusions

The percutaneous treatment for vertebral restoration and cementation through kyphoplasty in cases of osteoporotic vertebral compression fractures has shown to be a safe and minimally invasive procedure [14]. It is carried out under local anesthesia and minimal sedation. It requires a very short hospital stay; it provides quick patient recovery and significant reduction in pain. In our series, there was immediate relief of pain in 93% of all patients. Stabilization of the fracture was reported in all cases and improvement of vertebral deformity in 83% patients.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Experience with Coflex Interspinous Implant

F. Villarejo, F. Carceller, A. Gómez de la Riva, and M. Budke

Abstract A first generation of Coflex implant for non-rigid stabilization of lumbar spine was presented by Samani (Study of a semi-rigid interspinous U fixation system. Spinal Surgery, Child Orthopaedics: 1707, 2000).

We started to treat patients with this Coflex device in 2004 and since then more than 600 patients have been operated in our Neurosurgical Department. We are reporting 156 patients treated between December 2004 and 2006 with complete follow-up. The clinical trials of this and other implants provide evidence that this interspinous non-rigid stabilization is useful against low-back pain due to degenerative instability and without serious complications.

Keywords Degenerative lumbar disc · Interspinous distractor · Interspinous implant · Low back pain · Lumbar spinal stenosis · Non-rigid fixation

Introduction

The Coflex interspinous implant is made of titanium having a U shaped form. It produces an interspinous and a discal distraction, dampening the antero-posterior forces and is compressible in extension, has some small reliefs that minimize expulsion, controls also rotation and spinal alignment.

This interspinous device is functionally dynamic: compressible in extension, allowing flexion and increase of rotational stability. Meanwhile the centre of rotation is close to the spinal canal. Coflex implant also protects the posterior elements performing stress reductions on facet joints with maintenance of foraminal height. Also it is easy to use because of the lesser invasiveness and tissue-sparing procedure.

Interspinous Coflex device stabilize intraoperative instability after decompression maneuver. Late instability may be prevented if projected. It is ideal in cases of facet arthrosis and all related decompressive procedures [1–10].

Material and Methods

From December 2004 to 2006, 156 patients with different lumbar problems were treated with a Coflex interspinous implant. These patients were controlled 6 months, 1 and 2 years after the operation.

The ethiologies of lumbar pathology were as follows:

Degenerative disc disease	42 cases	Fig. 1
Degenerative spondylolisthesis	9 cases	Fig. 2
Voluminous herniation	12 cases	Fig. 3
Vertebral instability	60 cases	Fig. 4
Recurrent disc herniation	6 cases	Fig. 5
Lumbar canal stenosis	27 cases	Fig. 6

The age of the patients in 9 cases were between 20 and 30 years old, 33 between 30 and 40, 36 between 40 and 50, 42 between 50 and 60, and 36 between 60 and 70 years old. Fifty-seven were male and 99 female.

Regarding the level, the Coflex was implanted in 26 patients at L_3–L_4 in 103 at L_4–L_5 and in 27 at L_5–S_1.

Degenerative disc disease (DDD) was diagnosed clinically when the patients had lumbar pain at least for 1 year and the MRI showed a decrease of disc height, loss due to hydration with image of black disk. Only in those cases we implanted the Coflex device. Degenerative spondylolisthesis was grade I, and in most cases patients were diagnosed with DDD. When there was a voluminous extrusion of the disc we also implanted a Coflex device since we only operated the fragment extruded without removing the rest of the disc, and we tried to avoid a

F. Villarejo (✉), F. Carceller, A.G. de la Riva, and M. Budke
Francisco Villarejo Ortega, Raimundo Fernandez Villaverde, 36, 28003 Madrid, Spain
Neurosurgery Unit of Luz Clinic, Hospital Niño Jesús, Madrid
e-mail: fvillarejo2@terra.es

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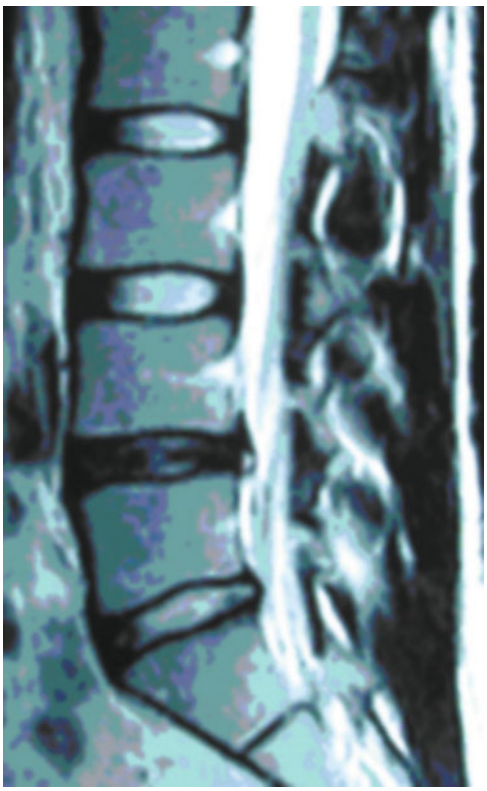

Fig. 1 MRI showing degenerative disc disease

recurrence of disc herniation. Vertebral instability is operated with Coflex when there is only one segment concerned to be clinically and radiologically confirmed. Recurrence of disc herniation is also treated with Coflex after removing the disc herniation, and lumbar canal stenosis is treated with foraminotomy, flavectomy and Coflex device.

Operative Technique

Under general anesthesia the patients were placed on a radiolucent table in decubitus prone position. After the operative level is confirmed through fluoroscopy, a middle sagittal incision of 4 cm is made over the spinous process of the level, paraspinal muscles are stripped off the laminae while preserving the facet capsules.

The interspinous ligament is sacrificed and any bony overgrowth of the spinous process that may interfere with insertion is resected. Ligamentum flavum is then also resected and microsurgical decompression is performed relieving all points of neural compression. Trials are utilized to define the appropriate implant size. Instruments are placed on trial to evaluate proper contact with the spinous process and the amount of interspinous distraction. Some bony resection of the spinous process may be needed to ensure proper contact of the implant. Distraction is considered to

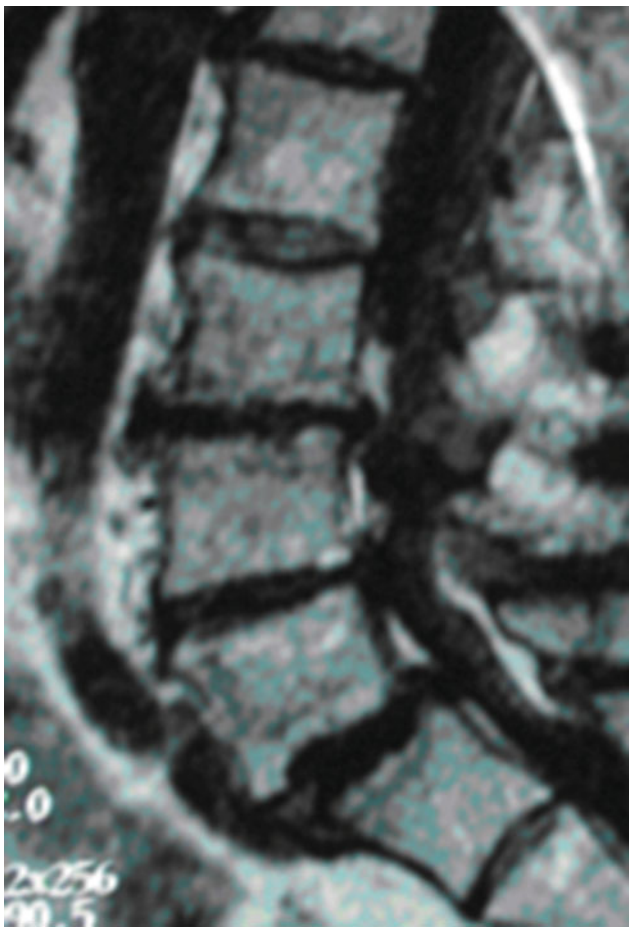

Fig. 2 MRI (T_1) showing degenerative spondylolisthesis

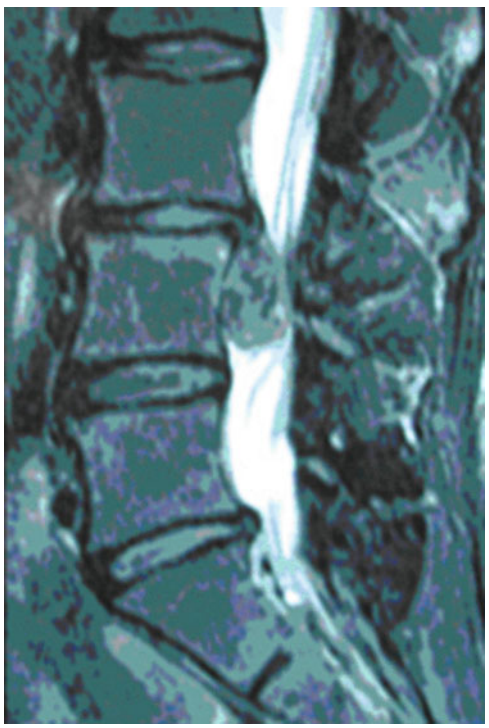

Fig. 3 MRI showing voluminous disc herniation

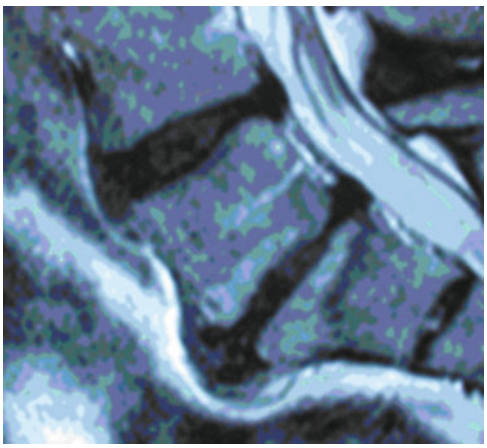

Fig. 4 MRI showing vertebral instability

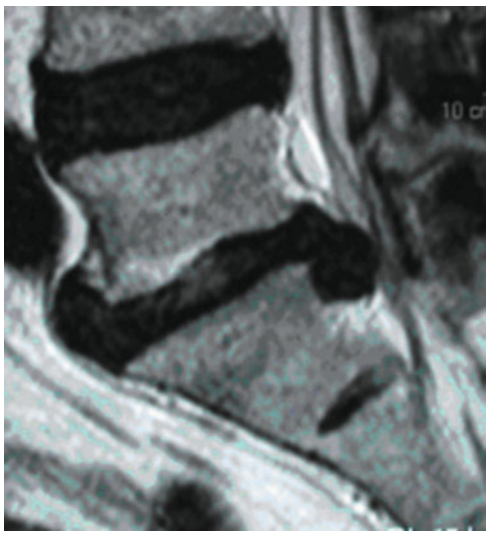

Fig. 5 MRI showing recurrence of disc herniation

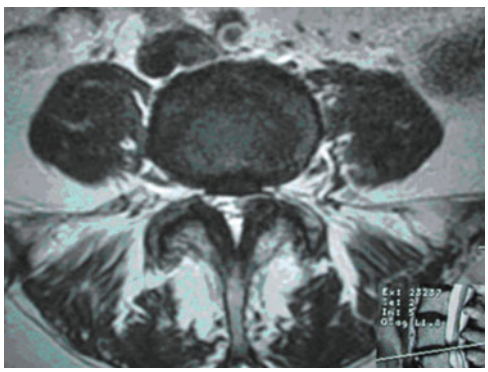

Fig. 6 MRI showing lumbar canal stenosis

be appropriate if it prevents any setting of the interspinous distance after successful decompression in cases of spinal stenosis. The wings of the device may need to be opened slightly using bending pliers at the mid portion of the wing to ensure appropriate depth of insertion. The implant is introduced via impaction. If the wings are not having sufficient bony contact additional stability can be achieved by slightly crimping the wings. The incision was closed and the patients were allowed to return home the next day after surgery.

Clinical Results

In our stadistic there are different clinical groups. We are going to differentiate the results in order to ethiology.

Regarding lumbar canal stenosis (42 cases) we followed the criteria that the patient must be older than 50 years, have mild to moderate stenotic symptoms, have pain that is relieved when flexed and aggravated when extended. We have excluded patients with unremitting pain in any position, fixed motor deficit, severe symptomatic lumbar spinal canal stenosis at three or more levels and spinal instability. We used to score these patients with the Swiss Spinal Stenosis (SSS) Questionnaire [11, 12]. The mean follow-up was 24 months after surgery. The patients were 19 male and 8 female, the age of patients were between 58 and 80 years.

Patient satisfaction of SSS demonstrated that 80% of patients were satisfied with the outcome of their surgery, 40% of patients had a significant change in symptom severity and 10% showed a significant improvement in physical function.

The mean dural sac changed from 74 mm^2 preoperatively to 90 mm^2 postoperatively. The intervertebral foramina was increased from 60 to 80 mm^2 and the interspinous distance increased from 4 to 9 mm.

We had 12 cases with voluminous disc herniation and recurrent disc herniation in six patients. Senegas [13] advises to treat cases of huge disc with removal of the extruded fragment plus interspinous spacer. The explanation for this is to avoid decrease of disc height and recurrence of disc herniation. In our 12 cases no recurrence of disc herniation happened and the disc height was similar as before the operation.

The recurrence of disc herniation was treated by removal of the fragment and insertion of the Coflex interspinous spacer. The goal was to avoid new surgery and also to avoid possible lumbar segmental instability, which, although they were a few cases, did not happen.

In the last group we could include altogether 42 cases of degenerative disc disease, nine cases of degenerative spondylolisthesis grade I, and 60 cases of single level segmental instability. They produce similar symptoms which are local lumbar pain when moving the lumbar region and decrease or disappearance of the pain when resting. Radiologically all of our nine cases of degenerative spondylolisthesis

grade I had local segmental instability and degenerative disc disease.

It must be stressed that the 60 cases of single level local segmental instability had also degenerative disc disease.

The 42 cases with degenerative disc disease had radiologically a black disc principally and local lumbar pain.

In the group of 111 cases (60 lumbar local instability, 42 DDD and nine degenerative spondylolisthesis) we verified the improvement in low back pain in 80% of cases and the Oswestry functional score changed from 60 preoperatively to 16 postoperatively.

Postoperative analysis of MR images showed marked improvement in bony lesions on both sides of the disc. There were cases when the U device could not be inserted due to extensive weakness of the spinous process during the surgical procedure. In these cases, patients were unable to benefit from this technique and conventional fusion with pedicular screws was performed.

There were no late neurological complications related to the U and no cases of U penetration inside the canal or infection.

Discussion

We have treated with Coflex interspinous spacer a heterogeneous group of patients with lumbar problems, but the final results after operation have been excellent. This non-rigid stabilization has solved the problem of low back pain due to degenerative instability, and in our cases of lumbar stenosis has avoided a more aggressive operation such as laminectomy with or without fusion. The current results demonstrate that the dural sac increases with the Coflex interspinous implant, as we usually also performed foraminotomy plus flavectomy, but not laminectomy. Inufusa et al. [14] reported findings with X-Stop interspinous implant, based on the computed tomography data that showed that flexion increased the size of the central canal by 24 mm^2 or 11% and extension decreased the size of the canal by 26 mm^2 or 11%. Shönstron et al. [15] reported that the cross-sectorial area of the spinal canal is reduced by 40 mm^2 and the mid-sagittal diameter of the canal is reduced by 2 mm when the lumbar spine moves from flexion to extension. Also the neural foramina dimensions were shown to be position dependent [16–20]. This technique is very favorable compared with laminectomy and fusion, since it is very easy and has no complications.

Regarding the other group of patients treated with the Coflex implant, they had significant resolution of low back pain. The functional improvement assessed using the Oswestry score was very clear.

Conclusion

In summary Coflex interspinous implant is a useful and easy technique in the management of some lumbar problems such as degenerative disc disease, lumbar segmental instability, grade I degenerative spondylolisthesis, mild lumbar canal stenosis and to prevent lumbar spinal instability after voluminous disc herniation or recurrent disc herniation.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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DIAM Device for Low Back Pain in Degenerative Disc Disease
24 Months Follow-Up

Josip Buric, Massimiliano Pulidori, Tariq Sinan, and Sheikh Mehraj

Abstract *Purpose*: To evaluate the usefulness of the DIAM device in patients affected by low back pain due to degenerative disc disease.

Background: Recently a number of interspinous devices for dynamic interspinous distraction-stabilization have entered the clinical practice in Europe. All of these devices have a common property of acting on the posterior part of the functional spinal unit by distracting the spinous processes and avoiding extension of the treated segment. Consequently, these systems seem to improve the cross-sectional area of the thecal sac and enlarge the diameter of the intervertebral foramina. What was found as a collateral observation after implantation of these devices was that those patients affected by low back pain, improved significantly in their pain level.

Methods and materials: Fifty-two consecutive patients were included in the study. There were 29 females and 23 males, aged between 29 and 77 years (mean 49.4 ± s.d. 12.4). The pre-operative symptom duration ranged from 6 to 84 months (mean 31.8 ± s.d. 20.2, median 24 months).The following diagnostic measures were performed in each patient: MRI, dynamic X-rays and provocative discography positive for pain reproduction.

The patients were followed for pain by VAS and for functional status by self-reported Roland-Morris Disability Questionnaire. The minimum follow-up was 24 months (24–36). The intermediate follow-up at 6, 12 and 18 months was tested for, too.

Results: To determine the number of improved patients we have arbitrarily selected a cut-off criteria based on a ≥30% of improvement as calculated on the Roland Morris Disability Questionnaire scale comparing the 24 months values to the baseline values. Forty-six patients (88%) were considered as success and 2 (4%) were considered as failure. No long-term complications were observed.

Conclusions: This preliminary report indicates that the DIAM device could possibly be useful in the treatment of LBP due to DDD. Further research with RCT is necessary to confirm these preliminary results.

Keywords Degenerative disc disease · Interspinous spacers · Low back pain · Spine instrumentation

Introduction

Low back pain is one of the leading problems of chronic disability and psychological distress and is one of the most frequent health problems for which medical help is searched. It was estimated that about 80% of Americans experience at least one episode of back pain during their lifetime while 15–20% of individuals tend to report this problem at least once a year [4].The European experience is not far away from the US data demonstrating life-time prevalence of pain of around 60% [17, 28]. Any of the innervated structures constituting the lumbar spine and surrounding areas may be a potential source of back pain. Ligaments, muscles, joints, bones and discs are the most frequent but other sources of back pain should not be forgotten e.g. pain reflex from internal organs, vascular pathologies, etc.

Being one symptom common to a variety of pathologies it is often difficult and, sometimes, impossible to demonstrate the source of back pain. However, it was reported that seemingly, about 40% of subjects presenting with this symptom do have a pain of discogenic origin [2]. A painful disc is thought to be the consequence of disc degeneration. Numerous nociceptors in the annulus and endplates are thought of being responsible for pain arousal although the question is

J. Buric (✉) and M. Pulidori
Functional Unit for Spinal Surgery, Cdc Villanova, Via di Careggi 38, 50139 Florence, Italy
e-mail: joburic@tin.it

T. Sinan
Department of Radiology, Kuwait University, PO Box 24923, Safat, 13110, Kuwait

S. Mehraj
Department of Radiology, Mubarak Al Kabeer Hospital, Kuwait City, Kuwait

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still open on what is the exact mechanism that triggers the pain symptomatology [5]. Degenerative disc disease may give rise to segmental instability due to reduction in the volume of the nucleus pulposus, loss of disc height and subsequent ligamentous laxity. This is characterized by small abnormal movements of the vertebrae out of the normal range of movements. This "wobbling" of the motion segment may be responsible for pain arousal [3]. Facet joints are thought to be another pain triggering structure possibly responsible for the low back pain although several clinical studies failed to demonstrate the validity of this theory [16, 22, 23].

The treatment of low back pain due to degenerative disc disease remains difficult and highly controversial. Physical treatment for low back pain showed to have some positive effect on acute pain. Specific back exercises and manual therapy showed best evidence among other physical treatment modalities [33]. Treatments for chronic low back pain like manual therapy, exercise therapy, multidisciplinary pain treatment and spa therapy showed strong evidence of being useful on a short term follow-up. However, there was no evidence that any of these measures is useful on the long term follow-up or as maintenance therapy [32].

Invasive treatment modalities for chronic low back pain are generally used after the conservative treatments fail to achieve results. Fusion and total disc arthroplasty are the most common surgical options to treat low back pain due to degenerative disc disease with or without segmental instability. Two main fusion approaches were conceived: instrumented and non-instrumented fusion. Fusion rates were greater when using instrumentation but there were no great differences in clinical outcome between the two procedures. Others have reported that there were no significant differences between surgical approaches: posterior, posterolateral, anterior, 270° or a complete, 360°, fusion. The clinical success of fusion varies widely (16–95%) and depends mainly on indication criteria being used [30, 31, 34]. Subjects who undergo spinal fusions or total disc replacement have higher rates of complications, longer hospital stays, and higher hospital charges than do subjects undergoing other types of back surgery.

Percutaneous intradiscal procedures were recently introduced in the treatment of low back pain due to degenerative disc disease. Their efficacy is still to be demonstrated in well-designed RCTs, however preliminary clinical series do show promising results [14, 27]. Recently, a number of interspinous non-fusion devices have entered the clinical practice in Europe. All of these devices have a common property of acting on the posterior part of the functional spinal unit by distracting the spinous processes and avoiding extension of the treated segment. These systems seem to improve the cross-sectional area of the thecal sac and enlarge the diameter of the intervertebral foramina [13]. Several authors have shown that patients receiving interspinous spacers for degenerative disc disease affected by degenerative disc disease improved significantly in terms of pain [21, 24, 25].

This longitudinal prospective case series study was conducted to verify the usefulness of the interspinous DIAM device surgery in the treatment of subjects affected by low back pain due to degenerative disc disease.

Materials and Methods

Study Design

This study is a report of 2-year follow-up of a consecutive series of 52 subjects treated for low back pain due to degenerative disc disease between December 2003 and December 2004.

Subject Population

All subjects presented with low back pain with 19 subjects complaining also of slight pain irradiating to buttocks and thigh. The pre-operative symptom duration ranged from 6 to 84 months (mean 31.8, SD 20.2, median 24). All subjects reported some type of conservative treatment modality performed in the past, mainly physical therapy and exercises addressed to their low back pain problem. Almost all subjects had occasionally and on need been taking NSIADs during the period of their sickness. Ten subjects had a history including discectomy without recurrence but later developed back pain. There were 29 females and 23 males, aged between 29 and 77 years (mean 49.4, SD 12.4). Twenty-five subjects were sedentary workers, 19 were heavy duty workers while the rest of subjects were on retirement.

Diagnostic work-up included collection of subject history, physical examination, Magnetic Resonance Imaging (MRI) of the lumbar spine, dynamic X-rays and provocative discography. Subject history was collected for description of the pain, its worsening and/or improvement on resting, sitting and loading of the spine. Physical examination searched for pain on palpation and pressure of spinous processes, straight leg rising test and sensitive or motor deficits. MRI was inspected for evidence of degenerative disc disease. Only subjects with Pfirmman type 3 and 4 disc degeneration and no more than Modic type 1 or 2 of vertebral body involvement were indicated for the treatment. Subjects with more severe disc degeneration, lysthesis and/or lysis, severe osteoporosis, signs of lumbar kyphosis, hypogenesis or agenesis of the spinous process, tumours, fractures, deformities

or history of other diseases that may correlate with the symptoms were not treated with DIAM. Similarly, subjects previously operated for disc herniation including laminectomy or hemilaminectomy were not indicated for surgery with DIAM.

Provocative discography was performed in a standard fashion with postero-lateral, extra-articular approach to disc and injection of 2 ml of non-ionic contrast dye inside the disc space under low to medium pressure (20–30 PSI). The concordance of evoked pain and memory pain was searched for during the procedure.

Dynamic X-rays were performed on all subjects and were reviewed for segmental instability. The spinal level was considered rotationally unstable if the intervertebral angle in flexion was greater than 5° or if flexion-extension range of motion was greater than 20° at L4–L5 or 19° at L3–L4 or L2–L3. Similarly, translational instability was defined if the translation from flexion to extension was greater than 10% of the anterior–posterior distance of the vertebral body [9, 15, 26].

All treatment alternatives, probabilities of success and risk factors were discussed with each subject and all subjects signed an informed consent.

Surgical Procedure

The surgery was performed under spinal anesthesia in knee-chest position. A C-arm control was always done for level identification and visualisation of the segment alignment. A midline skin incision was done between the superior and inferior spinous processes of the level/s involved. Fascia was cut on both sides and the paravertebral muscles were stripped from the spinous process until reaching the lamina on both sides. The interspinous ligament was removed while leaving the supraspinous ligament in place. Care was taken to leave no less than 0.5 cm of the supraspinous ligament width as to maintain its strength. The interspace between the two spinous processes was prepared diligently with complete removal of the intraspinous ligament and bony exposure of the spinous processes until the base and the most medial parts of the lamina. A distractor was positioned to separate the spinous processes. The interspinous space was measured by trials of different sizes. The surgeon selected the largest possible size that would not cause kyphosis. The device was placed from the side, under the supraspinous ligament. The positioning of the device was done as anteriorly as possible by pushing it deep inside until it made bilateral contact with the lamina. The device was anchored by passing the laces around the superior and inferior spinous processes. If the supraspinous ligament was found weak, a reconstruction with an artificial ligament was done. This event occurred in seven patients. The ligament was reconstructed by using the remnant part of the laces of the DIAM anchoring system and passing them through the superior and inferior spinous processes securing the lace ends by a knot. Intraoperative antibiotic was given to all subjects (Cephamezin 2 g) and the wound was closed in the standard fashion. No drainage was ever used. The operating time for the single level was between 15 and 35 min while for the double level was between 35 and 50 min. The subjects were made to rise from bed after 6–12 h and dismissed the next day. Subjects were not braced postoperatively.

Pre and Post-Operative Evaluation

Subjects reported their pain using a Visual Analog Scale (VAS). Dysfunction and disability were evaluated by self-administered Roland-Morris Disability Questionnaire (RMDQ). The subjects completed these questionnaires prospectively at 2, 6, 12 and 24 months.

Statistical Analysis

All statistical calculations were performed using Statistica Demonstration (Stat Plus, Tulsa, OK, USA). Questionnaire data were analyzed using a repeated measures analysis of variance with a within-subject effect of time (pre, 2, 6, 12 and 24 months) and the between-subject effects of the number of implanted levels (1 or 2) and history of previous discectomy (yes or no). Interactions and main effects were reviewed for statistical significance levels of $p < 0.05$. Additionally, subjects were divided into pass-fail criteria based upon improvement in RMDQ and freedom from reoperation. Thirty percent improvement in RMDQ has been proposed as a minimal clinically important difference in RMDQ [11]. Subjects with an improvement between 0 and 30% were considered possible successes and those with no improvement or worse scores were considered a failure.

Results

Both RMDQ and VAS scores showed a significant main effect of time ($p < 0.0001$). Subjects reported an improvement in both outcomes at 2 months and this benefit was maintained for 2 years. There were no significant effects or interactions associated with multiple levels or a history of previous discectomy; thus all clinical results are pooled over these variables. See Fig. 1 for clinical outcomes over time.

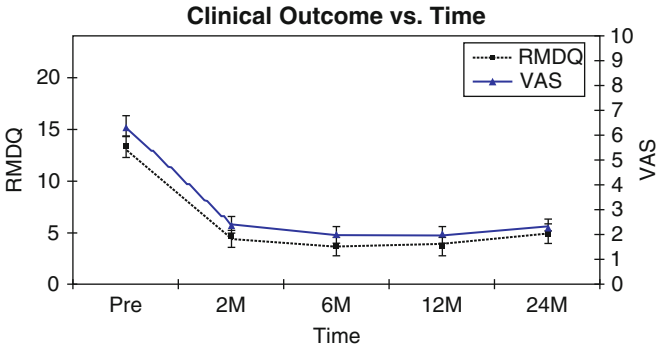

Fig. 1 Mean and standard errors for the RMDQ and VAS scores over time. There was a significant benefit from pre to 2M which was maintained through 24 months

Table 1 Success rates based upon RMDQ and freedom from reoperations

RMDQ	2M	6M	12M	24M
Success	44	47	46	46
Possible	7	3	3	4
Failure	1	2	3	2
Reoperation	2M	6M	12M	24M
Success	52	50	46	46
Fail	0	2	6	6
Combined	2M	6M	12M	24M
Success	44	46	43	42
No success	8	6	9	10

Based upon a 30% minimally important change in RMDQ, 46/52 (88%) subjects were considered a success and 2/52 (4%) were considered a failure at 2 years. Based upon freedom from reoperations, 46/52 (88%) of subjects were considered a success at 2 years. These reoperations included two cases of thermal ablation of the facet joints between 2 and 6 months post-operatively, three cases in which DIAM was implanted at an adjacent level (all between 6 and 12 months) and one fusion done at 12 months. One of the cases involving DIAM at an adjacent level was prompted by a fractured device due to fall. The device was reinserted at the same and at the adjacent level. Refer to Table 1 for a timecourse description of success based upon RMDQ, freedom from surgical interventions and the combined outcome.

Discussion

This study, even if lacking randomization and a control group, demonstrated that the DIAM interspinous device has a high percentage of positive clinical results up to 2 years post-operatively.

Low back pain may be triggered by any structure containing nociceptors and probably comprises signals from multiple structures simultaneously. Frequently, patients affected by low back pain describe improvement in pain when laying down and worsening when carrying heavy objects. Mechanical loading is an important triggering mechanism that stimulates many pain generators simultaneously.

Internal disc disruption and loss of water in the nucleus pulposus initiates a cascade of degenerative events including a loss of disc height. Morphological changes in the nucleus pulposus adversely affect its capacity to uniformly transmit loads to the vertebral endplates resulting in localized stress concentrations on the endplates [10, 18]. The narrowing of the intervertebral space induces loosening and buckling of the annulus fibrosus and posterior longitudinal ligament [1, 7, 25]. The annulus suffers stress tears which increase its sensitivity to altered pressures within the disc [19].

Malalignment of the facet joints contributes to pain due to inadequate contact between articular surfaces, causing arthritic changes, osteophytes and hypertrophy of the joints [6, 12]. Subsequently, sinuvertebral nerve impingement and segmental stenosis development is frequently observed.

Narrowing of the disc together with the hypertrophy of facet joints can induce neuroforaminal stenosis with partial obliteration of the nerve root passage and possible compression of both the neural as well as vascular elements. This may result in inflammatory and ischemic changes of nerve roots.

The disc degeneration is not a self-limited process. It affects indirectly the functioning of all the junctional elements between vertebrae by changing their mutual relationships and initiating long-term deformation of the structural parts of the vertebrae (endplate changes and osteophyte formations). Mechanically, the functional spinal unit loses its physiological properties and two distinct yet correlated pathophysiological events occur: reduction of regular movements between two adjacent vertebrae due to reduction of the intervertebral space available for the movement, and increase of anomalous movements (micro-instability) due to laxity of ligaments and annulus [8, 9]. Each one of these events may stimulate the known pain generators: mechanoreceptors in the endplates, nociceptors in the posterior part of the annulus, the posterior longitudinal ligament, the capsule of the facet joints, the dura mater as well as sinuvertebral nerves [5].

Therefore, even if its origin is not yet clearly established, low back pain is possibly not a consequence of stimulation of just one single structure, but more probably a sum of expression of various pain generators being triggered together at the level of the degenerating functional spinal unit.

Theoretically, helping the functional spinal unit during its degeneration by sustaining its height and limiting the narrowing of the intervertebral space, it should be possible to

regain more physiological conditions and, consequently, eliminate most of the pain.

Interspinous devices, as shown in cadaveric studies, distract the posterior part of the functional spinal unit, re-position and unload the facet joints and reduce the intervertebral pressure particularly in the posterior part of the endplates [20, 29]. As a consequence, these devices act on most of the known pain generators at the lumbar level. By repositioning the facet joints in a more physiological relationship, they unload the axial pressure on the articular surfaces and detend the joint capsule while limiting extension movements and the sinuvertebral nerve impingement. Distraction of spinous processes unloads the posterior part of the intervertebral disc, diminishes the axial load pressure across the endplates by transferring some of the load from the disc to posteriorly placed device and consequently unloads the endplate mechanoreceptors. Moreover, the distraction of the posterior part of the intervertebral space possibly stretches the annulus fibrosus and the posterior longitudinal ligament in a more natural position, improving their capacity in resisting the load stress from inside the disc space and, probably, reducing the solicitation of the pain receptors situated inside these structures. While producing beneficial effects at the level of treatment, biomechanical studies showed that the implantation of interspinous devices do not generate any negative effect on adjacent vertebral levels [20, 29].

Conclusion

Longer experience and controlled, randomized studies comparing these systems with other conservative and surgical means for the treatment will be necessary to prove definitely their usefulness in the treatment of low back pain due to degenerative disc diseases. However, these initial results are promising as a large proportion of the patients treated obtained satisfactory results with extremely low percent of complications.

Conflict of interest statement We declare that we have no conflict of interest.

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Percutaneous Surgical Treatment in Lumbar Spinal Stenosis with Aperius™–PercLID™: Indications, Surgical Technique and Results

P.P.M. Menchetti, F. Postacchini, W. Bini, and G. Canero

Abstract Interspinous spacers have recently been used in the treatment of lumbar spinal stenosis. In vitro studies have demonstrated a reduction in facet joint forces by 68% and annulus pressures by 63%. MRI studies have demonstrated increased canal and neural foraminal area after implantation of these devices. Previous studies by Zucherman et al. (Spine 30:1351–1358, 2005) demonstrated patient satisfaction rates of 71–73%.

We carried out a multicentric retrospective study to assess the clinical outcomes following percutaneous posterior decompression using an interspinous spacer device (Aperius™–PercLID™ System; Kyphon-Medtronic). A total of 70 patients were included in the study. All of them had evidence of radiologically and clinically proven lumbar stenosis. The average age was 63.5 years. Patients completed the Zurich Claudication Questionnaire (ZCQ) and recorded pain levels on a Visual Analogue Scale (VAS). Average stay in hospital was 2 days. The average improvement in ZCQ included both symptomatic pain disappearance and functional ambulatory recovery. The average VAS pain score improved from 8.2 to 3.6 (scale of 1 to 10). The overall patient satisfaction rate was 76%. No complications were detected at 6 months' follow-up.

Keywords Interspinous spacers · Lumbar stenosis · Stand alone decompression · Stenosis percutaneous treatment

P.P.M. Menchetti (✉)
Florence University, Via Jacopo Nardi, 15, 50132, Firenze, Italy
e-mail: menchetti@islass.org

F. Postacchini
Sapienza University, Rome, Italy

W. Bini
Neurosurgical Department, Dubrovnik, Croatia

G. Canero
San Feliciano Hospital, Rome, Italy

Introduction

Interspinous spacers have recently been used for cases of Degenerative Lumbar Spinal Stenosis (DLSS) and spinal claudication. In vitro studies have demonstrated a reduction in facet joint forces by 68% and annulus pressures by 63%. MRI studies have demonstrated increased canal and neural foraminal area after implantation of these devices. Few publications have been found since 1975 on the long-term results and efficacy of conservative treatment alone for DLSS. In a prospective 10-year study, Amundsen et al. [1] performed on 100 patients followed for 10 years, selecting 31 patients randomly for surgery vs. Non Surgical Management (NSM), surgical management patients with severe symptoms had better outcomes than NSM patients after 10 years. Atlas et al. [2] in a prospective study on 119 patients followed for 4 years, reported that surgery patients had significantly greater pain relief from the primary symptoms (leg/back pain) ($p=0.05$) than NSM patients after 4 years. Patient satisfaction was also significantly greater than in NSM patients after 4 years ($p=0.04$). Patients with mild to moderate symptoms treated surgically had significantly greater satisfaction and pain relief from primary symptoms ($p=0.001$ and $p=0.05$, respectively) than NSM patients.

Surgical treatment of DLSS over the years has employed several procedures (decompressive surgery without or with fusion). Performing a meta-analysis of the literature from 1975 to 1995, Niggemeyer et al. [5], in 1,668 cases, found that patients with symptoms <8 years had better results with decompressive surgery without fusion, patients with symptoms for 8–15 years had better results with decompressive surgery+fusion. Patients with interbody fusion fared better than with posterior lateral fusion. However, after 7–10 years' Outcome of Decompressive Surgery for DLSS, Katz et al. [3], found in 88 consecutive patients treated with surgical decompression that at 7–10 years follow-up, 23% of patients had a re-operation and 33% had severe back pain. Turner et al. [8] concluded that success of surgery varies

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substantially between publications (23–100% success). In the past 10 years interspinous spacers have been used in conjunction with decompression surgery providing for neurogenic intermittent claudication (NIC), limits in extension and normal flexion. In vitro studies showed several effects of interspinous spacers on spinal canal diameters. At implanted levels, interspinous spacers increase the dimensions of the spinal canal, reducing dural sac impingement, becoming a load-bearing structure in extension unloading and reloading the disc in a more physiological pattern (62.8% pressure on the posterior annulus), and reducing IVD (intervertebral disc) pressure; at adjacent levels there is no effect [4, 6, 7].

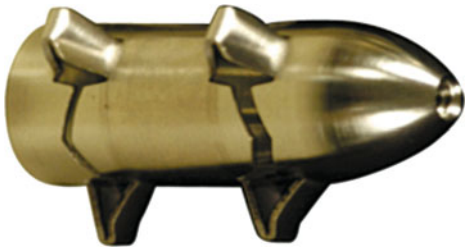

Fig. 1 Aperius™ PercLID™ System (Kyphon-Medtronic)

Materials and Methods

Percutaneous stand alone interpinous decompression in DLSS +/− NIC patients after failed conservative treatment (at least 6 months) in candidates for decompression surgery without fusion have been performed using the Aperius™ PercLID™ System (Fig. 1 – Medtronic). The device is indicated for patients suffering from symptomatic degenerative lumbar spinal stenosis with or without NIC exacerbated by prolonged standing or by activities in the upright posture and relieved by a flexed position of the lumbar spine in the space between levels L1–L5. Aperius™ PercLID™ System (Medtronic) contraindications included:

- Degenerative spondylolisthesis at the affected level greater than grade 1 (grading scale1–4)
- Significant radiological hypermobility
- Allergy to the materials used in the implant – titanium and titanium alloy
- Scoliotic deformity with a Cobb angle >25°
- Ankylosis at the affected level
- Kyphosis requiring surgical correction
- Fracture of the spinous process at the affected level
- Paget's disease
- Active infection and/or tumour of the spine

A total of 70 patients (46 males, 24 females) were included in the study. All of them had evidence of radiologically

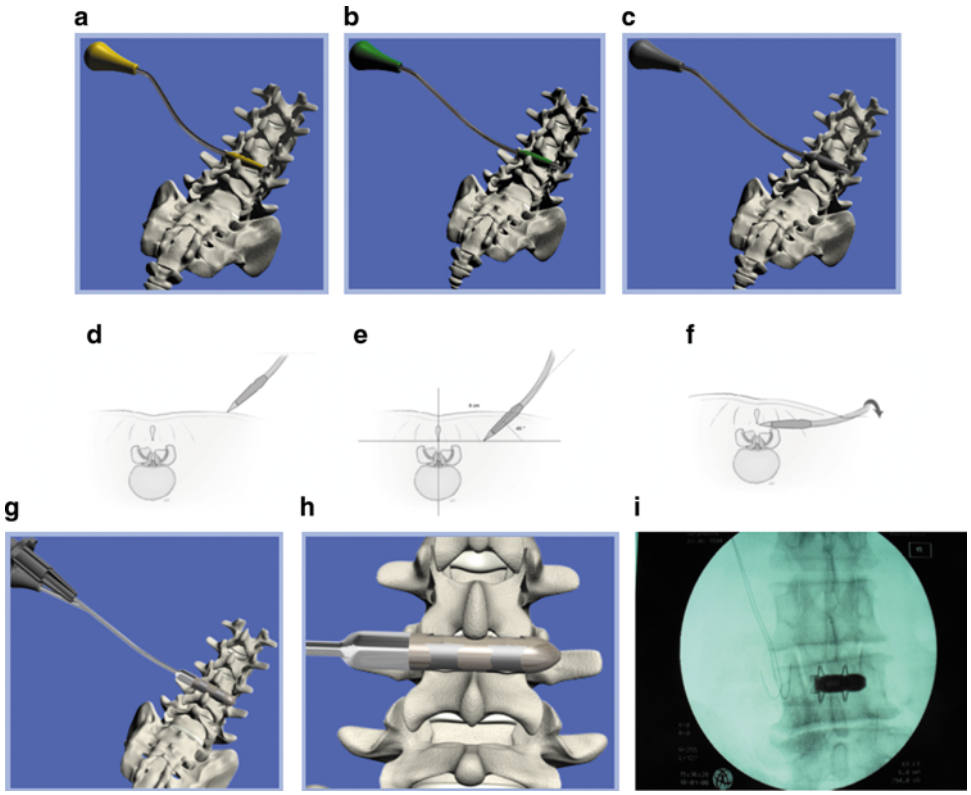

Fig. 2 (**a**–**i**) Aperius™ PercLID™ System, surgical steps implantation

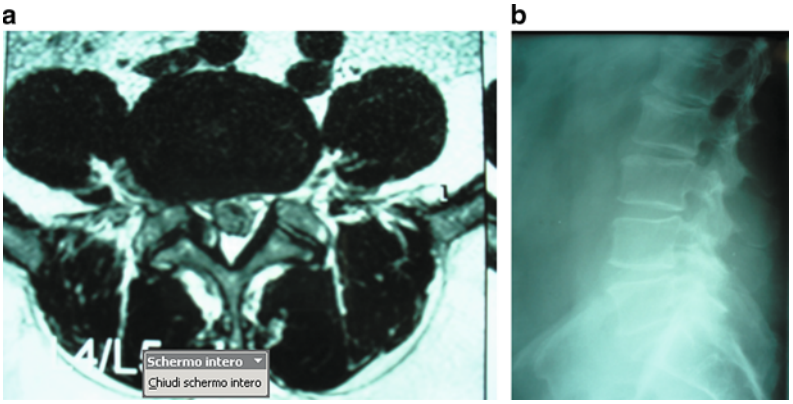

Fig. 3 (**a**–**b**) L4–L5 right foraminal stenosis

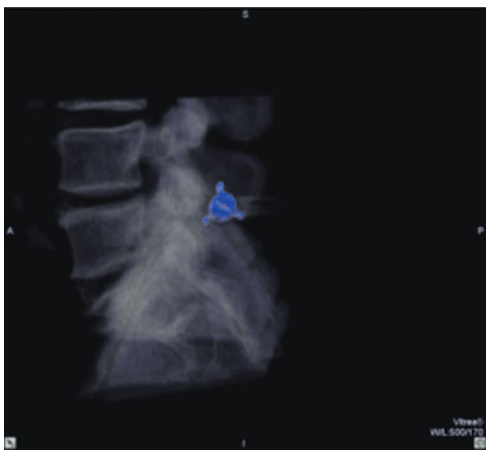

Fig. 4 Aperius

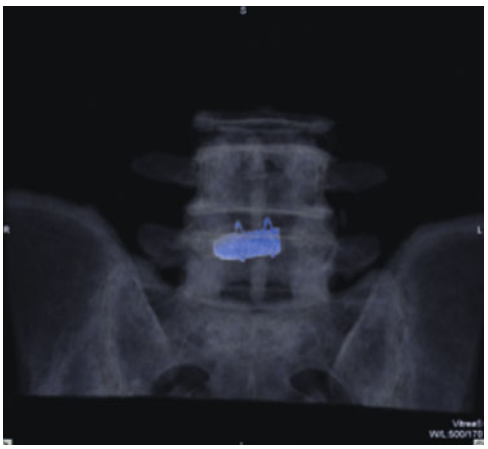

Fig. 5 Aperius PercLID

and clinically proven lumbar stenosis, with or without NIC exacerbated by prolonged standing or by activities in the upright posture and relieved by a flexed position of the lumbar spine in the space between levels L1–L5. The average age was 63.5 years. The level L4–L5 was treated in 40 cases, L3–L4 in 28 cases, L2–L3 in 2 cases. A retrospective multicentric study at 6 months' follow-up was performed on 40 cases. Patients completed the Zurich Claudication Questionnaire (ZCQ) and recorded pain levels on a Visual Analogue Scale (VAS). The ZCQ included symptoms severity (before and after surgery), physical function (before and after surgery) and patients' satisfaction. The ZCQ assigns an improvement in symptoms severity if there is an improvement >0.5, an improvement in physical function if there is an improvement >0.5 as compared to the preoperative parameters. The average stay in hospital was 2 days.

Through a unilateral percutaneous approach (1 cm skin incision 5–7 cm from the midline) under local anesthesia, respecting the thoracolumbar fascia and sovraspinous ligament, under C-arm A–P and L–L view, progressive interspinous trocar insertion permits to select the proper implant. The implant positioning and progressive wings deployment under C-arm enables percutaneous stand alone interspinous decompression (Fig. 2a–i).

Results

At 6 months' follow-up on 40 cases, VAS decreased from 8.2 to 3.6 postoperatively. Regarding the ZCQ, in 71% of cases, symptoms severity decreased, and in 72% of cases patients referred marked improvement in the physical function, with total patient satisfaction of more than 76% (Fig. 3a, b).

Conclusion

The percutaneous stand alone interpinous decompression in DLSS using the Aperius^{TM} PercLID^{TM} System (Medtronic) permits to avoid risks due to general anesthesiological

procedures (bleeding, infections, CSF leakage), with a reduction of operating time (10±5 min), reduction of risks and complications due to open surgery (bigger skin incision, bone removal, sovraspinous and interspinous ligament removal, muscle damage, postsurgical scar). It can be used even in spine deformities (scoliosis <25° Cobb angle), not precluding further open surgery (if needed). Furthermore in several cases many elderly patients could have important problems with most aggressive procedures (general anesthesia, bleeding), and for these reasons it is increasing the compliance. The surgical technique is relatively simple with very low complication rates and satisfactory results. It is a valuable addition to current treatment modalities. As compared to other interspinous devices, the Perc-LID™ System (Fig. 4, 5) presents the following advantages: (1) percutaneous procedure, through a 1 cm skin incision, (2) stand alone decompression system, (3) unilateral approach, (4) preserving the thoracolumbar fascia and thus the SSL, (5) avoiding open surgical approach, (6) permitting a fast return to daily activities.

Conflict of interest statement We declare that we have no conflict of interest.

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Six Level Cervico-Thoracic Circumferential Reconstruction: Report of the Second Case of the Literature

Visocchi Massimiliano, Md and Maira Giulio, Md

Abstract Anterior cervical corpectomy from C2 to T1 is being used to decompress the spinal cord and reconstruct the cervical spine. It is a well recognized treatment for degenerative, traumatic, tumoral, infectious cervical stenosis and/or instability. It has the advantage of allowing a thorough decompression and also improves fusion rates in cases in which multilevel decompression is needed.

In order to overcome the potential drawbacks of structural bone graft it is possible to use titanium plates and mesh cages with good results. The inconstant stability rate of the construct, with or without anterior plate, can justify supplementary posterior instrumentation in order to obtain circumferential reconstruction.

The author reports the successful outcome of a six-level-corpectomy across the spine with circumferential reconstruction in a patient with extensive chordoma of the cervical and upper thoracic spine. To the author's knowledge this is the second report of a corpectomy extending across six levels of the cervico-thoracic spine.

Keywords Corpectomy · Cervical spine · Circumferential fixation · Cervico · Thoracic reconstruction · Chordoma

Introduction

Anterior cervical corpectomy, along with grafting techniques from C2–T1, is being used to decompress the spinal cord and reconstruct the cervical spine in tumours; it is a well recognized treatment also for degenerative, traumatic, infectious diseases and for cervical stenosis and/or instability [1, 2]. Corpectomies of the cervical spine have the advantage of allowing a thorough decompression. They also improve fusion rates in cases in which multilevel decompression is needed and have been reported to extend across as many as four levels [1–4]. More extensive corpectomies have not been reported, perhaps because of concerns as to instrumentation failure and expected difficulty in obtaining adequate exposure of the anterior cervicothoracic spine [2, 4]. We present a successful six-level cervicothoracic corpectomy and circumferential reconstruction in a patient with extensive and recurrent aggressive chordoma.

V. Massimiliano, Md (✉) and M. Giulio, Md
Institute of Neurosurgery, Catholic University – Medical School, Rome, Policlinico Gemelli Largo Gemelli, 8 – 00168 Rome, Italy
e-mail: mvisocchi@hotmail.com

Case Report

History and Presentation

A 45-year-old female with a history of cervical chordoma who had already previously been operated, presented at our institution with progressive neck pain, dysphagia, and radiculomyelopathy. The patient had been operated in a different hospital on five occasions: (1) April 2005: C6 body chordoma removal; (2) March 2006: removal of C6 body recurrence; (3) April 2006: posterior interlaminar hook C6–C7 instrumentation; (4) September 2006: C5–C6–C7 somatectomy, with C4–T1 instrumentation with distractible titanium cages with incorporated distractible anterior plate; (5) October 2006: T1 somatectomy with distraction of the construct. Due to the aggressive clinical behaviour the patient underwent two cycles of radiotherapy (50 Gy+33 Gy), from June 2005 to March 2007.

Imaging Studies

Plain radiographs, computed tomography (CT) and magnetic resonance imaging (MR) showed extensive bony destruction

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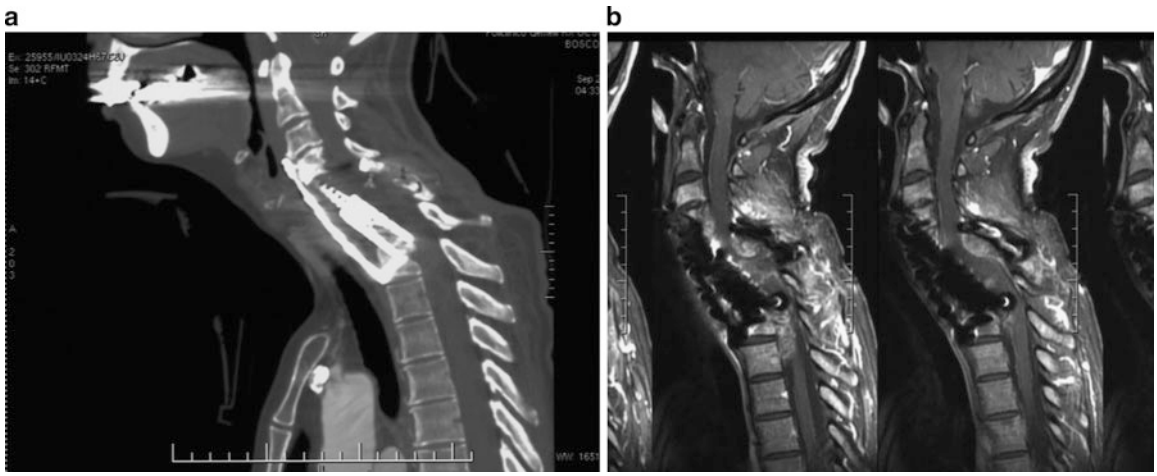

Fig. 1 (**a**) CT scan bone windows showing an extensive bony destruction and a marked kyphotic angulation of the cervicothoracic spine with subsidence and dislodgment of the construct C3–T1 with impingement of the cord. (**b**) MR Spin Echo T1 showing extensive prevertebral and epidural anterior and posterior enhancement surrounding the cervical and upper thoracic spinal cord, suggestive of chordoma recurrence and resulting in circumferential narrowing of the thecal sac C5–T2

and a marked kyphotic angulation of the cervicothoracic spine with subsidence and dislodgment of the construct. MR revealed extensive prevertebral and epidural anterior and posterior enhancement surrounding the cervical and upper thoracic spinal cord, suggestive of chordoma recurrence, resulting in circumferential narrowing of the thecal sac (Fig. 1a, b). Meticulous radiological planning of the epiaortic vessels area was performed by spiral angio-CT in order to confirm the choice of the trans-sternal approach.

Physical Examination

On physical examination, the patient was unable to extend her neck above the horizon and demonstrated 2+ out of 5 motor strength rates throughout all muscle groups related to upper extremities. Although 4+ out of 5 motor strength rates throughout all muscle groups related to lower extremities was evidenced, the patient was unable to deambulate. Moreover, the patient complained allodynia along with dysesthesia at the upper extremities where global hypoesthesia was present as well. Preoperative halo traction was not applied as the patient reported an intolerable amount of pain with any manipulation of her cervical spine.

Operation

A double staged anterior and posterior approach was planned in order to remove the hardware, to decompress as much tumour as possible, and to stabilize the cervico-thoracic spine. One staged surgery was refused by the patient.

An anterior approach to the cervical spine was performed first. The patient was positioned supine with traction on the Mayfield head holder in light extension in order to partially reduce the kyphotic deformity. Next, a longitudinal incision along the medial border of the left sternocleidomastoid muscle was made and connected to a median upper half sternotomy which was performed for exposure of the T1–T4 vertebral bodies. Wide exposure of the C4–T4 vertebral bodies was then carried out. The distractible titanium cages with incorporated distractible anterior plate was identified and removed. Leksell, Kerrison rongeurs and high speed drill were used to remove the tumour and bone remnants of C5, C6, C7, T1. De novo somatectomy and tumour debulking were performed at the T2 and T3 vertebral bodies down to the posterior longitudinal ligament. Next, an appropriately-sized lordotic titanium cage (De Puy Spine, Codman, Johnson & Johnson, USA) was impacted into position between C4–T4. An Aesculap ABC plate (Aesculap AG, Tuttlingen, Germany, and Aesculap Instrument Corp., South San Francisco, CA, USA) was then affixed to the spine with variable-angle screws into the C3–C4 and T4 bodies. After surgery the patient was fixed with Halo Vest. Total blood loss was 350 cc and the operating time was 5 h.

Twelve days later, after confirming radiological stability of the construct, the patient was turned prone; the halo head holder was secured to a Mayfield frame. The posterior spine was dissected out from C2 to T6. After the removal of hardware, T1 laminectomy and tumour debulking was performed. Under fluoroscopic control, lateral mass screws were placed bilaterally on C3–C4 along with pedicle screws from T3 to T5. Contoured rods were locked on the screws (Expidium

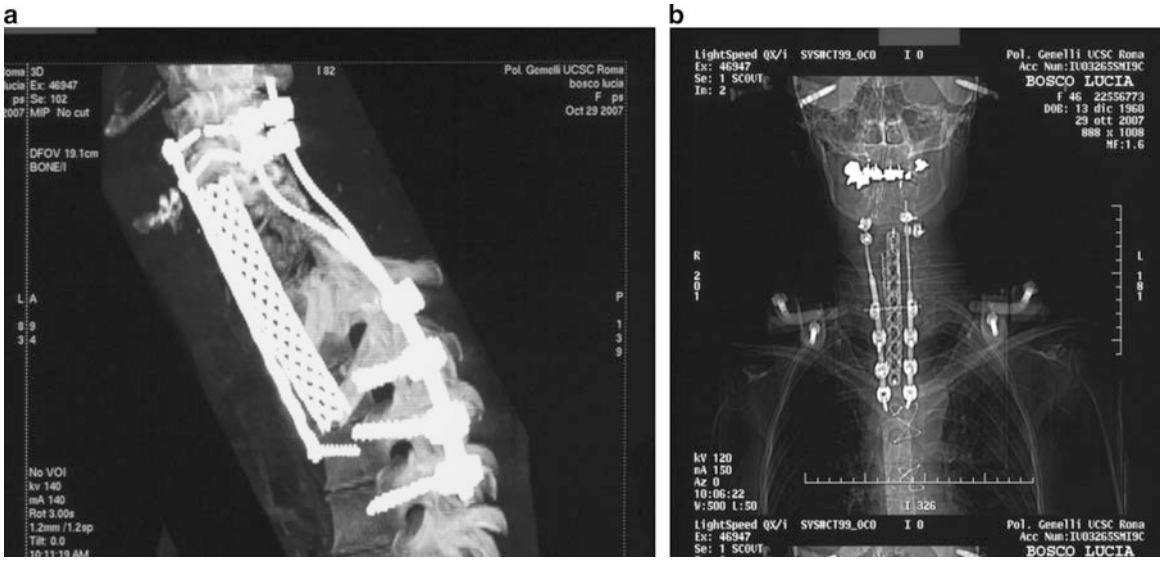

Fig. 2 (**a**) 3 D bone window CT scan showing the complex construct: (1) appropriately-sized lordotic titanium cage impacted into position between C4–T4 with anterior plate affixed to the spine with variable-angle screws into the C3–C4 and T4 bodies. (2) Posterior instrumentation with double contoured rods and lateral mass screws bilaterally on C3–C4 and pedicle screws from T3 to T5. (**b**) TC scan study with anterior scout view reconstruction showing the entire cervico–thoracic construct

– Vertex De Puy Spine, Codman, Johnson & Johnson, USA). A lateral radiograph was obtained before closure to confirm satisfactory graft and hardware placement. After removal from the Mayfield frame, the halo brace and vest were removed. Total blood loss was 325 cc and the operating time was 4 h. Pathological examination confirmed the diagnosis of chordoma, positive to cytokeratine, vymentine, and S 100 protein. Fifteen percent proliferating index (Ki 67) with 3–4% nuclear p53 storage was documented as well.

Postoperative Course

The patient began ambulating without physical therapy on the third postoperative day. She experienced improvement in all her neurological symptoms during hospitalization.

Postoperative AP and lateral plain radiographs and CT scans showed good hardware positioning with correction of the kyphotic deformity (Fig. 2a, b). The patient was braced with a Miami collar postoperatively.

Follow-up

Twenty days after the operation the Miami collar was removed. No evidence of hardware failure was shown soon after the operation, at discharge and at the maximum follow-up on neuroradiological examination.

At 6 months' follow-up, the patient's neurological examination was improved as opposed to admission and she demonstrated full strength throughout all muscle groups, normal sensation and resolution of the neck pain. She was able to ambulate without any assistance and denied any problems with breathing or swallowing. MR imaging showed chordoma local /recurrence and further cranio-caudal spinal diffusion. The construct was intact and in good position. At 7 months' follow-up the patient had died because of respiratory impairment.

Discussion

Chordomas are locally aggressive neoplasms with an extremely high propensity to recur locally following resection, despite adjuvant therapy. This biological behaviour has led most authors to conclude that, when possible, extensive resection provides the best chance for the patient's prolonged disease-free survival and possible cure [18]. Extensive anterior cervical fusion involving three or more levels, however, includes more complicated surgical exposure and has been associated with increased rates of graft-related complications, including bone graft or hardware dislodgment, spinal cord compression, and pseudoarthrosis [5–7]. Significant compressive forces on the anterior construct after extensive anterior cervical fusion have been confirmed in

biomechanical studies [3, 8]. The reported experience with anterior cervical fusion has been limited to four or fewer levels out of concern for these potential complications. Anterior column reconstruction after extensive anterior cervical fusion may be performed using strut grafts or titanium mesh cages [5, 9, 10]. Titanium mesh cages offer several advantages, including better correction of sagittal alignment (with pre-contoured cages), better endplate purchase, variable height and diameter options and the ability to be packed with auto- or allograft bone [11–13]. Sagittal alignment with the use of a lordotic titanium cage and anterior plate fixation after interbody grafting enhances the rigidity and stability of the construct and therefore lowers the risk of graft-related complications [1, 3, 7, 11, 17]. Finally supplementary posterolateral fixation after extensive anterior cervical fixation have been found to further decrease the rates of graft-related complications, deformity correction loss, and pseudoarthrosis rates [4, 7, 8, 14]. To the author's knowledge, the present case is the second report of a corpectomy extending across six levels of the cervico-thoracic spine, undergone with circumferential instrumentation, and the first case of such a technique in spinal chordoma surgery [15]. The anterior aspect of the cervicothoracic junction, particularly from the seventh cervical to the fourth thoracic vertebrae, is a difficult area to approach surgically, the thoracic duct needs to be identified and protected and the recurrent laryngeal nerve on the right side needs to be spared [16]. Moreover the right brachiocephalic artery and vein, and the innominate vein along with the left common carotid artery, must be retracted in order to control the anterior aspect of C4 and needs meticulous preoperative radiological assessment. Finally the author always recommends performing a spiral angio-CT scan of the epiaortic vessels preoperatively, in order to better plan the surgical strategy and to use the left side in order to avoid laryngeal nerve injuries. Nevertheless cardiothoracic surgeon involvement in the operating theatre is strongly advised.

Conclusions

A six-level corpectomy across the cervico-thoracic spine can be safely performed also in chordomas by combining a traditional longitudinal exposure of the cervical spine with a median sternotomy. Circumferential reconstruction with modern implants, such as an anterior contoured titanium cage-plate construct and posterior screw-rod fixation, is necessary to provide sufficient stability of the cervico-thoracic spine to allow for correction of sagittal alignment and to achieve bony fusion.

Conflict of interest statement We declare that I have no conflict of interest.

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Percutaneous Vertebral Augmentation: StabilitiT™ A New Delivery System for Vertebral Fractures

Scott C. Robertson MD, FACS

Abstract Percutaneous vertebral augmentation for compression fractures with bone cement has become an increasingly popular form of treatment. Various delivery techniques and bone cements have been developed. StabiliT Vertebral Augmentation System (DFINE Inc., San Jose, CA) is a unique radiofrequency (RF) based system which delivers an ultra-high viscosity bone cement. The patented StabiliT ER bone cement has an extended working time prior to RF warming. When delivered through this unique hydraulic system an on-demand ultra-high viscosity cement can be delivered into an osteotome created cavity resulting in a clinical procedure with the best qualities of both vertebroplasty and conventional balloon assisted kyphoplasty.

Keywords Percutaneous vertebroplasty • Bone cement • Osteoporosis • Vertebral fractures • Vertebral augmentation

Introduction

Osteoporosis afflicts over 300 million people worldwide. Vertebral compression fractures (VCF) are the most common complication of osteoporosis with over 1.5 million new vertebral fractures reported annually [3, 5]. VCFs may result in considerable pain and impair physical function and quality of life. Percutaneous vertebral augmentation with various bone cements has been developed to stabilize the fractures, reduce pain, and improve physical function. Galibert first reported vertebroplasty as a minimally invasive treatment for symptomatic vertebral hemangiomas [2]. This technique has been adapted for treatment of vertebral compression fractures causing intractable focal vertebral pain. Various delivery systems and cement combinations have been utilized over the years including convectional balloon assisted kyphoplasty introduced in 1998. Both, vertebroplasty and kyphoplasty techniques have reported complications associated with them including extravasation of cement outside of the vertebrae, adjacent vertebral fractures, and venous embolization. Vertebroplasties are quick procedures, which allow for greater filling of the vertebral body, but carry a higher rate of extravertebral extravasation and embolization of the low viscosity cement from the higher pressure delivery systems. Literature on conventional kyphoplasties (in which cement is delivered under lower pressure) report vertebral height restoration with few extravertebral complications, but take significantly longer and fill a smaller percentage of the vertebrae [3, 4]. High viscosity cements have been shown to reduce extravasation and embolization rates but found difficult to deliver through traditional vertebroplasty systems. We review a unique new hydraulic pressure delivery system, StabiliT Vertebral Augmentation System (DFINE, San Jose, CA), which combines the advantages of both vertebroplasty and conventional kyphoplasty.

StabiliT uses a unique ultra-high viscosity bone cement (Fig. 1) in conjunction with a radiofrequency (RF) delivery system (Fig. 2) that permits remote delivery of cement. The steady hydraulic pressure delivery of an ultra-high viscosity cement is capable of restoring vertebral height by simultaneously creating and filling a cavity within the fractured vertebrae. The extended working time of the bone cement prior to RF warming, enables the physician to work safely at multiple levels to help reduce procedure time and cost, while maintaining a very high level of safety and control with very little extravertebral complications. Additionally, the StabiliT System is controlled by a hand switch that enables the physician to stand as far as 10 ft from the radiation source during cement delivery.

S.C. Robertson MD, FACS
Bone and Joint Hospital, Oklahoma City, OK, USA
9060 Harmony Drive Suite E, Midwest City, OK 73130, USA
e-mail: www.scottrobertsonmd@hotmail.com

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Materials and Methods

Procedures can be performed under IV sedation or general anesthesia. The patient is placed in the prone position and the appropriate level(s) of the back are prepped and draped in the usual manner. The pedicle of the fractured vertebra is visualized with anterior posterior (AP) and lateral fluoroscopic images. The skin, subcutaneous tissues and periosteum are anesthetized using local anesthesia. A small skin puncture is made approximately 2.5 cm off of mid-line. An introducer (working cannula and stylet) is directed down the pedicle to the junction of the middle and anterior 1/3 of the vertebral body using the AP and lateral fluoroscopy (Fig. 3). Bilateral cannulas may be placed, but typically there is good filling across the vertebral body from a unipedicular approach. Once positioned, the introducer stylet is removed leaving the working cannula in place. Figure 4 shows the following steps. Under fluoroscopic guidance, a coring VertecoR Cement Staging Osteotome is advanced and through the working cannula to the anterior 1/3 of the vertebral body. The cement staging VertecoR osteotome is advanced, turned multiple times and repositioned as necessary to core and remove cancellous bone which creates a cavity in the vertebral body. The VertecoR cement staging osteotome is then removed and the introducer stylet reinserted. Bone removed during the cavity creation by the coring may be submitted for pathological analysis.

During the positioning of the working cannula the Activation Element (which contains the heating cartridge), delivery cables, and hydraulic assembly are connected to the Multiplex Controller (which contains both an RF generator and hydraulic controller) can be assembled and cement prepared. The radiopaque bone cement is mixed and the cement cartridge is filled and attached to the Activation Element and Multiplex Controller via the hydraulic assembly. After removal of the introducer stylet, the locking delivery cannula is attached to the Activation Element (cement heating cartridge component) of the StabiliT delivery system and is then inserted through the working cannula so that the end of the locking delivery cannula is in the cavity created in the anterior 1/3 of the vertebral body. The locking delivery cannula is locked into the working cannula to prevent displacement during the injection process of the ultra-high viscosity semi-solid cement.

The bone cement is converted to an ultra-high viscosity, semi-solid material as it is driven through the resistive heater (warmed by RF energy) within the Activation Element. The cement initially fills the cavity created by the osteotome at 1 cc/min. As the mass of ultra-high viscosity cement continues to grow in size it expands the cavity while simultaneously filling it. Cement delivery is monitored

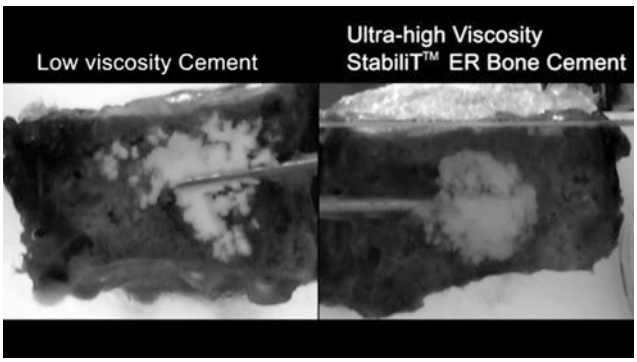

Fig. 1 Comparison of low viscosity cement (*left*) versus high viscosity StabiliT ER cement (*right*)

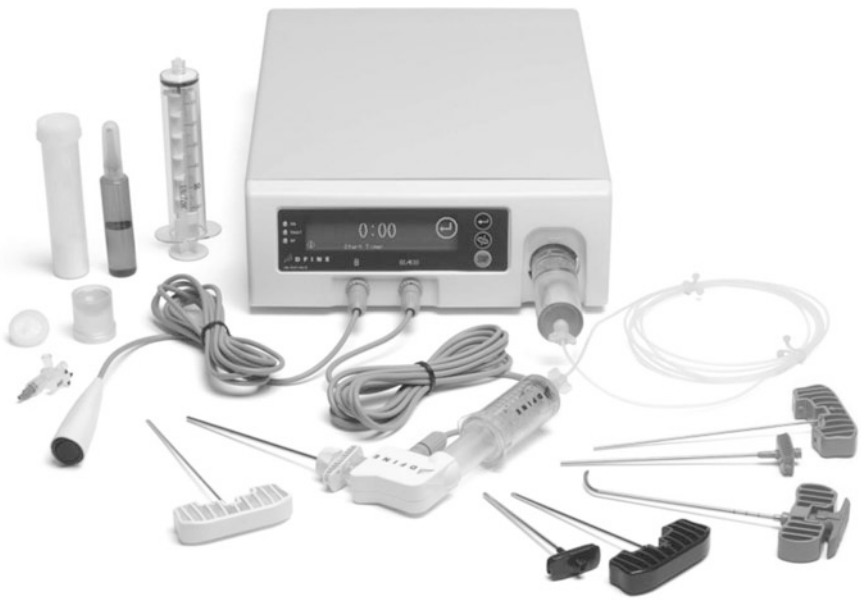

Fig. 2 StabiliT vertebral augmentation system includes hydraulic delivery system, cannulas, osteotomes, and bone cement

fluoroscopically. The remote hand switch allows the physician to move up to 10 ft away from the radiation source while maintaining on-demand control of the cement. The unique Multiplex Controller (which contains an RF generator and hydraulic delivery system) allow for a working time of over 20 min at 20°C using the specially formulated cement. If the cement is not being directed into the desired area or additional cement is required, the locking delivery cannula can be detached and the stylet replaced and the working cannula repositioned under fluoroscopic guidance before reinitiating cement delivery. The cement injection is terminated after the ultra-high viscosity cement adequately restores vertebral height or in the judgment of the treating physician, the vertebral body is safely filled (Fig. 5).

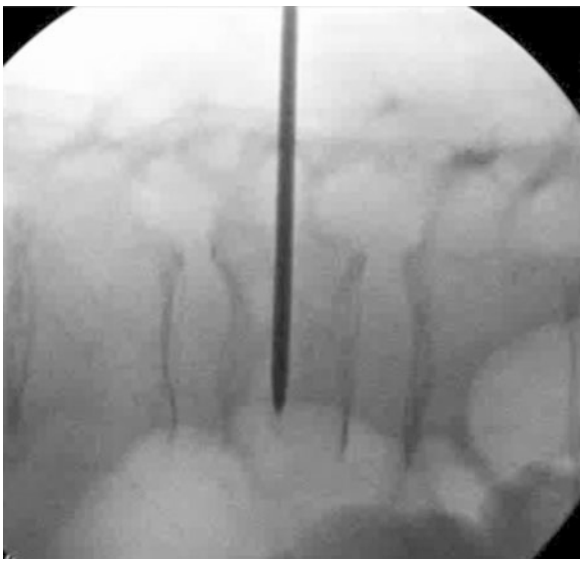

Fig. 3 Placement of the working cannula into the vertebral body

The entire process may be repeated on the contralateral side (if the cement did not adequately cross mid-line) using the same delivery cannula and cement, unlike other delivery systems. Multiple working cannulas can be placed at additional fractured vertebral levels or bipedicular prior to initiating cement delivery which allows sequential treatment and reduces time. Final intra-operative imaging is obtained to confirm alignment and fill. The stylet is replaced and the working cannula is removed and the incisions closed with skin glues and sterile dressing applied.

Results

In early clinical studies, over 300 levels have been treated in more than 250 patients using the StabiliT Vertebral Augmentation System without symptomatic extravasation of cement. Pain relief (measured by Visual Analogue Scale-VAS) and improved function (measured by Oswestry Disability Index – ODI) have been found to be equivalent if not superior to vertebroplasties and conventional balloon

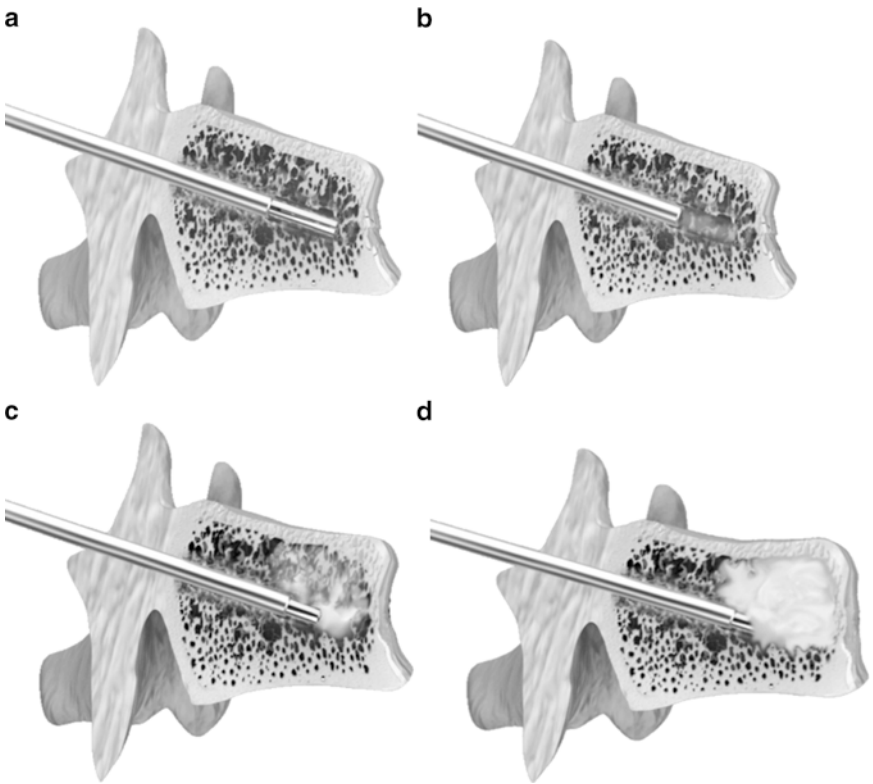

Fig. 4 (**a**) VectecoR cement staging osteotome, (**b**) vertebral cavity created by the osteotome, (**c**) placement of delivery cannula, (**d**) StabiliT ER cement delivery

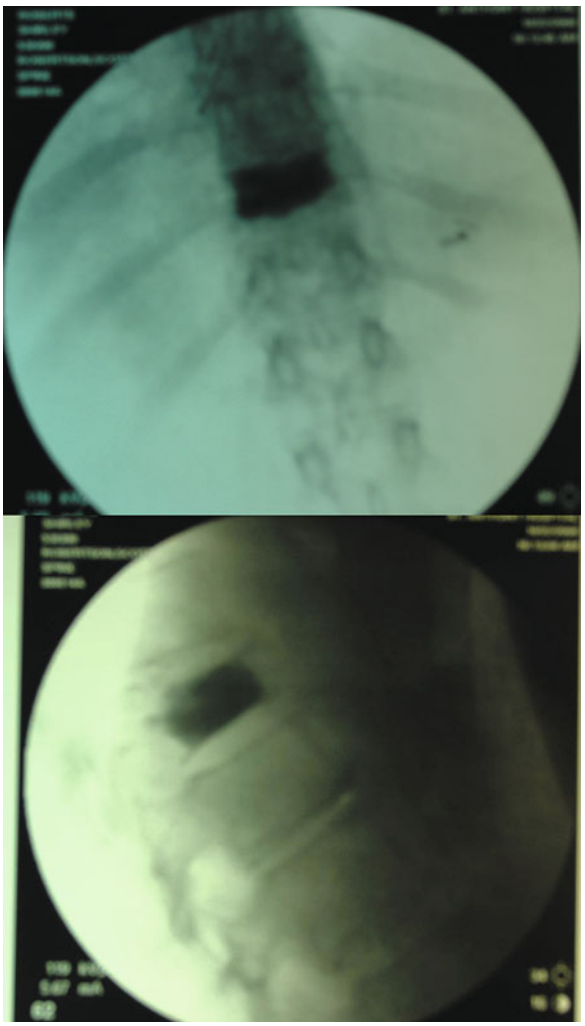

Fig. 5 StabiliT vertebral augmentation of a T11 osteoporotic fracture using a unipedicular approach AP (*top*) and lateral (*bottom*)

Table 1 Initial clinical trials involving 114 levels in 80 patients (Miko) [8]

Procedure	Visual analogue scale pain score (*n*)		Oswestry disability index Disability score (*n*)		
	Pre	3 months	Pre	1 month	3 months
Balloon kyphoplasty	6.2	2.8	46	30	ND
Vertebroplasty	7.5	3.5	75	ND	38.7
DFine VAS	7.2 (74)	2.5 (51)	55 (73)	33 (62)	26 (50)

assisted balloon kyphoplasty (Table 1) [4, 8]. Height restoration has been quantified in multiple cadaveric studies and found to be significantly better than vertebroplasties and equivalent to conventional kyphoplasty (Table 2) [4, 9–11]. Studies have shown the high viscosity cement can apply adequate force to vertebral structures to restore vertebral body height equivalent to balloon inflation [9, 11, 12].

Table 2 Initial clinical studies showing height restoration in cadaver spine model (Murphy) [9]

–	Vertebroplasty (%)	Balloon kyphoplasty (%)	Vertebral augmentation (%)
Height restoration	32.8±8.1	74.8±9.4	83.7±17.5
Specimens with extravasation	50	25	0

Conclusion

Clinical studies have supported the use of percutaneous vertebral augmentation for relief of pain and prompt functional recovery from osteoporotic compression fractures [1, 4, 5, 7]. Percutaneous vertebroplasty is a very quick and easily performed procedure but carries some risk of cement extravasation and venous embolization. Complications have been reported to be almost as high as 60% [1]. Conventional kyphoplasty has been reported to have fewer complications of cement extravasation, but increased surgical time due to drilling, balloon inflation, multiple 1 cc syringe delivery system and significant cost difference are drawbacks [4, 7]. The StabiliT Vertebral Augmentation System combines the benefits of both procedures with the added potential of reduced operator radiation exposure. The hydraulic pressure delivery system provides a consistent steady delivery of cement which can be stopped and started easily using a remote hand switch. Delivery cannulas are easily placed and the VertecoR cement staging osteotome creates a cavity without the risk of drilling and time consuming steps of multiple balloon inflations and deflations required when performing conventional assisted kyphoplasty. Multiple vertebral bodies can be injected with a single disposable kit reducing procedural time as well as cost. The ultra-high viscosity cement, which acts more as a flowable solid, significantly reduces the risk of extravasation or embolization. The StabiliT Vertebral Augmentation System is a unique delivery system for treatment of vertebral fractures. The proprietary StabiliT ER bone cement, which is not heated and converted to ultra-high viscosity cement until passing through the Activation Element, has an extremely long working time allowing for cannula adjustments, multiple intermittent cement deliveries and treatment of multiple levels. Current bone cements have a short working time of 5–10 min. The StabiliT ER bone cement has working times over 20 min.

Fluoroscopic radiation exposure to surgeons during vertebral augmentation procedures can be high as the vertebral filling is monitored. The remote hand switch allows reduced radiation exposure to the surgeon. Once the delivery cannula is secured to the working cannula the surgeon can be up to

10 ft away viewing the automated delivery of cement. The StabiliT Vertebral Augmentation System is priced at a 10% discount for a single level procedure and up to 30% discount on multiple procedures compared to conventional kyphoplasty.

Limitations of the system are similar to those noted in conventional kyphoplasty including highly compact or sclerotic bone may limit cement delivery and possible height restoration. In non-osteoporotic traumatic compression fractures the dense bone limits cross filling of the vertebral body and bi-pedicular injections may be required. Extravasation of cement may occur outside of the vertebral body if fissures occur in the cortical mantle of the vertebrae, but is usually very limited by the high viscosity of the cement.

Placement of spinal instrumentation in osteoporotic patients has been contraindicated in the past. However the development of new bone cements has increased interest in methods for augmentation of osteoporotic bone prior to instrumentation. Cement vertebral augmentation to enhance pedicle screw fixation in osteoporotic bone strength is being studied [6]. The long working time and ultra-high viscosity attributes of the StabiliT ER bone cement makes the StabiliT Vertebral Augmentation System a good method to enhance bone strength while allowing ample time for placement of hardware.

In concluding, StabiliT Vertebral Augmentation System appears to provide a unique, safe, and effective percutaneous treatment for vertebral compression fractures, using a cavity creating system and ultra-high viscosity cement, which appears clinically equivalent to conventional kyphoplasty with the potential for fewer complications. Additional clinical studies may prove it to be superior.

Conflict of interest statement We declare that we have no conflict of interest.

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Minimally Invasive Disc Preserving Surgery in Cervical Radiculopathies: The Posterior Microscopic and Endoscopic Approach

Angelo Franzini, Giuseppe Messina, Paolo Ferroli, and Giovanni Broggi

Abstract The aim of this paper is the report of the long-term results of a prospective study on spinal cervical lamino-foraminotomy via posterior route for the surgical treatment of cervical radiculopathies due to spondylodiscoarthrosis. The goal of the described surgical procedure is the bony decompression of the involved root leaving the intervertebral protruded or herniated discs intact. Indication, surgical technique, outcome and complications are discussed. Although anterior spinal cervical approach is the standard for centrally-located disc herniations with myelopathy, posterior foraminotomy appears to be a safe, minimally-invasive and effective treatment for postero-lateral radicular compression in the cervical spine. In our opinion, microscopic and/or endoscopic minimally invasive lamino-foraminotomy must be included within the surgical options for degenerative disc diseases of the cervical spine. This approach allowed us to reduce about 30% of the number of patients treated by the anterior approach, thus consistently reducing the need for intersomatic fixation.

Keywords Cervical lamino-foraminotomy · Cervical radicular compression · Posterior foraminotomy

Introduction

The posterior cervical approach to degenerative disc herniation was originally introduced by Scoville and Whitcomb in 1966 to treat cervical root compression due to disc fragments and/or foraminal stenosis at cervical levels [7]. Also Verbiest [9] described the antero-lateral approach aimed to obtain root decompression avoiding the risks of the anterior approach introduced by Smith and Robinson [5].

Nevertheless, the anterior approach, popularized by Cloward [2] became the gold standard for the treatment of intracanalar median or paramedian disc herniation.

In the era of minimally invasive surgery of the spine the posterior approach was revaluated either through microsurgery or through endoscopy to avoid in selected cases the risks of the anterior approach (such as vascular, visceral or neural lesions) and the need for anterior instrumentation [4]. We think that in cases, in which the cause of compression is not located centrally but instead posterolaterally, such as intraforaminal cervical herniated disc, the posterior foraminotomy has showed to be effective and safe [11].

In 1998 we designed a prospective study in which patients affected by lateral disc herniations were treated by posterior foraminotomy while patients affected from median disc herniation were treated by anterior approach and fusion. The prerequisite of such study considered also the clinical picture which consisted in radicular pain and deficits for the first group of patients and in the presence of spinal cord signs and changes in the second group. The indications for employing posterior foraminotomy included (1) clear clinical symptoms and signs of cervical radiculopathy confirmed by neurophysiological studies (2) neuroradiological evidence of compression of the clinically symptomatic cervical root such as a soft posterolateral herniated disc or foraminal stenosis, due to arthrosis of the structures delimiting the neural foramen (3) absence of myelopathy.

Contraindications to posterior cervical foraminotomy included (1) significative instability or kyphotic deformity at the involved level (in such cases removal of a relatively small amount of the posterior spinal elements can lead to a worsening of instability [1]); (2) local skin infection; (3) doubtful or absence of congruity between clinical and instrumental findings with regard to the spinal level affected and to be approached; (4) presence of clinical and radiological signs of spinal myelopathy.

A. Franzini (✉), G. Messina, P. Ferroli, and G. Broggi
Istituto Nazionale Neurologico "Carlo Besta", Milan, Italy
e-mail: angelo@angelofranzini.com

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The immediate and long-term results of such procedure on pain and neurological deficits in a considerable number of patients are reported along with complications.

Materials and Methods

From 1998 to 2008, 140 patients with cervical radiculopathy were treated with posterior cervical foraminotomy at the Istituto Nazionale Neurologico "C. Besta" in Milan. The mean age was 49 years (23–71 years); surgery was performed at one spinal level in 126 patients and at two levels in 14 patients. Three patients had already undergone previous anterior microdiscectomy and fusion at different spinal levels. Sixty-five patients were operated on at C5–C6 level, 40 patients at C6–C7 level, 15 patients at C4–C5 level, 15 patients at C7–D1 level and 5 patients at C3–C4 level.

All of the patients presented clear-cut clinical signs of a cervical radiculopathy, which was further confirmed by neurophysiological studies. CT and MRI were performed in all of them disclosing a soft disc herniation at the congruous level in 75% of patients and a foraminal stenosis in the remaining 25%. Clinical examination included assessment of motor strength, sensitivity and osteotendinous reflexes, along with research of Spurling's sign and evaluation of pallesthesia. An irritative radicular syndrome including pain and paresthesia at the affected dermatome was the most common finding in our series and was present in 95 % (n = 133) of patients. Light-touch hypoesthesia was the second most common finding, affecting 80% (n = 112) of our patients; osteotendinous hyporeflexia, upper limb motor strength deficit, and hypopallesthesia were present in 70% (n = 98), 40% (n = 56) and 30% (n = 42) of patients, respectively.

All of the patients had been complaining of the above-mentioned symptoms or signs for at least 2 months before admission to our Institute. Conservative treatments (including NSAIDs, corticosteroids, myorelaxant agents, with or without the use of cervical collar, at adequate dosages and therapy duration) revealed to be ineffective.

After admission all of the patients underwent pre-operative thin-slice spinal cervical CT or MRI scan to appropriately visualize the root involved and the structures (bony or ligamentous) responsible for compression. From 2004 we also used pre-operative three-dimensional images of CT-derived reconstructions of cervical spinal column to further asses the bony components of foraminal stenosis. In some cases we also use such image modality in the postoperative period in order to verify and better delineate the degree of decompression.

Surgery

The patient is positioned prone on the operating table; we do not use the sitting position for such intervention because of the increased risk of air embolism and vascular hypotension that such position entails.

A Mayfield three-point-fixation system is routinely used; we think it offers the double advantage of assuring a rigid position of the neck and avoiding eyeball compression, which could lead to retinal ischemia and subsequent amaurosis [8] with usage of horse-shoe head frames. The chin is slightly retropositioned to obtain a "martial" posture of the neck, which is very useful for stretching the posterior cervical skin. The minimal distance between the sternum and the chin should be of two fingers' breadth.

Superior thoracic and iliac crests' foam rolls are used after turning the patient into the prone position to avoid inappropriate abdominal compression during the intervention. The operating table is then set to a slight Trendelenburg's position to facilitate venous drainage from lower limbs. Compressive stockings are used to minimize the risk of deep venous thrombosis. Before incision a C-arm fluoroscope is employed for confirmation of the correct spinal cervical level and of adequate cervical spine's alignment; sometimes, and especially for lower cervical levels, it can be necessary to pull down the shoulders of the patients along the operating table with adhesive tapes for maximizing the radiographic visualization of the affected spinal levels.

We perform the preoperative control with a 16 gauge needle (either inserted perpendiculary to the long axis of cervical spine directly on the articular facets, or simply laid down along the cutaneous surface corresponding to the level to be approached).

For microendoscopic procedure, after adequate disinfection and draping of the operating field, a 2 cm-long paramedian skin incision is made. The muscular fascia is incised and insertion of the Kirschner needle pointing to the interarticular space is performed under fluoroscopic control. Sequential dilating METRx (Medtronic Sofamor Danek; Memphis, TN) rigid cannulas are then inserted along the guiding needle to the lateral mass of the affected level. The 18 mm working-channel, that is to say the definitive tubular rectractor, is lastly inserted and secured by fixing it to the operating table with the use of the appropriate self-retaining retraction's system.

At this point, an ad-hoc designed fixed endoscope can be connected to the tubular rectractor or, better in our opinion for the quality of images and operative flexibility, a hand-hold rigid 0° endoscope used by the assistant to visualize the operative space can be employed.

For open procedures, after a slightly longer skin incision (3 cm), the muscular fascia is largely opened to avoid an excessive muscle retraction and subsequent muscular ischemia and postoperative pain. Paravertebral muscles are

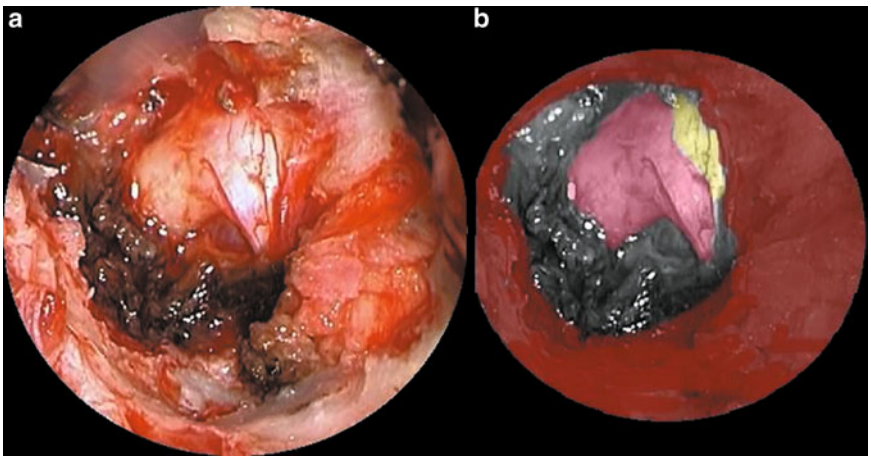

Fig. 1 (**a**) The nerve root is visualized after the bone drilling in microscopic view. (**b**) colour superimposition drawing of the same photo, where the root is in *pink*, bone is in *brown* and yellow ligament is in *yellow*

detached from the spinosus processes and the hemilamina and articular processes are skelotonized and exposed. A self-retaining Caspar retractor is then positioned. The operative microscope is brought into the operative field at this stage of the procedure.

Endoscopic and microscopic open procedures at this time point follow a similar course: a 4-mm diamond drill is used to remove the bone of the lateral part of the two adjacent hemilaminae, and the medial half of the corresponding articular facet. The yellow ligament is then removed by using a Kerrison rongeur thus exposing the lateral part of the dural sac. Bony removal usually begins at the junction between the medial portion of the articular facet and cervical lamina, and then carried on to the medial portion of the corresponding articular joint. Bone drilling then continues at the level of the articular facets until the dural sleeve of the root is evident and the root itself well decompressed. If an extruded and free disc fragment is present, it can be generally accessed enlarging a little bit the root exposure in the axillary region. At this stage, dural sac and emerging ipsilateral dural radicular pocket containing the motor and sensitive nerve roots should be visualized (Fig. 1).

To obtain an adequate visualization of the inferior vertebra's pedicle (where radicular pocket passes at the inferior margin of the neural foramen), further removal of the superior portion of the inferior lamina may be carried out.

The nerve root is inspected along its course from emergence off the spinal dural sac to its exit site at the neural foramina using a small nerve hook; such procedure allows for better clarifying the sites of more pronounced radicular compression. The nerve hook is used to elevate the axilla of the root, so as to expose ventral sites of compression of radicular pocket, such as intraforaminal disc herniation. If inferior vertebra's pedicle is identified as a significant cause of radicular compression, it can be partially removed in its superomedial portion [10] with careful trephination at this stage, taking into account the proximity of transverse cervical foramen (containing the vertebral artery and vertebral venous plexus), which is located just lateral to the pedicle. Removal of about 50% of articular facets (medial portion) is usually sufficient to obtain radicular decompression; anyway, when hypertrophy of this structure or extraforaminal disc herniation is clearly involved in radicular compression it could be entirely removed, taking into account the eventuality of posterior instability and prolonged postoperative pain. Anyway, in our experience such manoeuver has never been required. It has to be noticed that we always respect the disc, remove discal tissue and never pierce the annular ligament containing the disc soft tissue. We perform really a bony decompression of the radicular foramen leaving the disc intact.

Finally haemostatic agents such as Surgicel, Surgiflo (Johnson and Johnson New Brunswick, NJ Inc.) or Floseal (Baxter Inc) can be used to refine the haemostasis when an oozing bleeding from the peridural venous plexus is noticed. Surgical wound is closed in layers in a standard fashion. We do not routinely use postoperative subfascial drainage systems. Prophylactic antibiotics are only administered intraoperatively to reduce the risk of growth of multi-resistant bacterial lines; they are eventually continued in the postoperative period in cases of otherwise unexplained hyperpyrexia and after antibiogram confirmation of the most adequate therapeutic agents.

Results

Mean hospitalization post-operative time was 48 h.

Follow-up evaluations were carried out at hospital discharge, and then at 3 months, 6 months, 1 year and 3 years after the intervention. Three-year-follow-up is only available for 50 patients. In 98 patients (70% of total cases) radicular pain immediately disappeared on the first postoperative day; such benefit was maintained until the last

follow-up visits for all of them. In 40 patients (28.8%) radicular pain completely remitted within 1 month from surgery and, again, the clinical improvement was still present at the last clinical evaluation carried forward.

In patients also suffering from sensitive and/or motor signs, such findings disappeared within 2 months from surgery in all of them.

Persistence of radicular pain was observed in two patients (1.4% of total cases), as evaluated in the last follow-up examination.

Post-operative pain at the surgical site was present in 20% (n = 28) of our patients; anyway, it remitted within 1 week from surgery in all of them, with or without use of prolonged analgesic pharmacological therapy.

No infective, neurological or haematological complications (such as deep-venous thrombosis) were encountered in our series. As mentioned above, since 2004 we have employed (though not for all of the cases) three-dimensional CT reconstructions of the cervical spine (Figs. 2–3). We think such a tridimensional image reconstruction is a useful

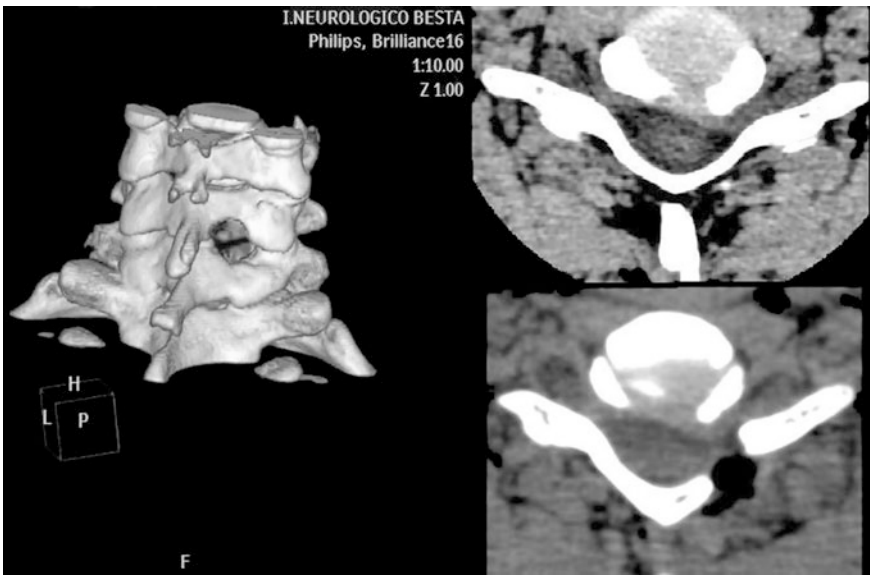

Fig. 2 *Left*: Postoperative three-dimensional CT image showing the site of foraminotomy. In this case bone removal was not extended to the medial facet joints. *Right upper/lower*: axial CT slices showing the level of nerve root compression, before (*upper*) and after (*lower*) surgery

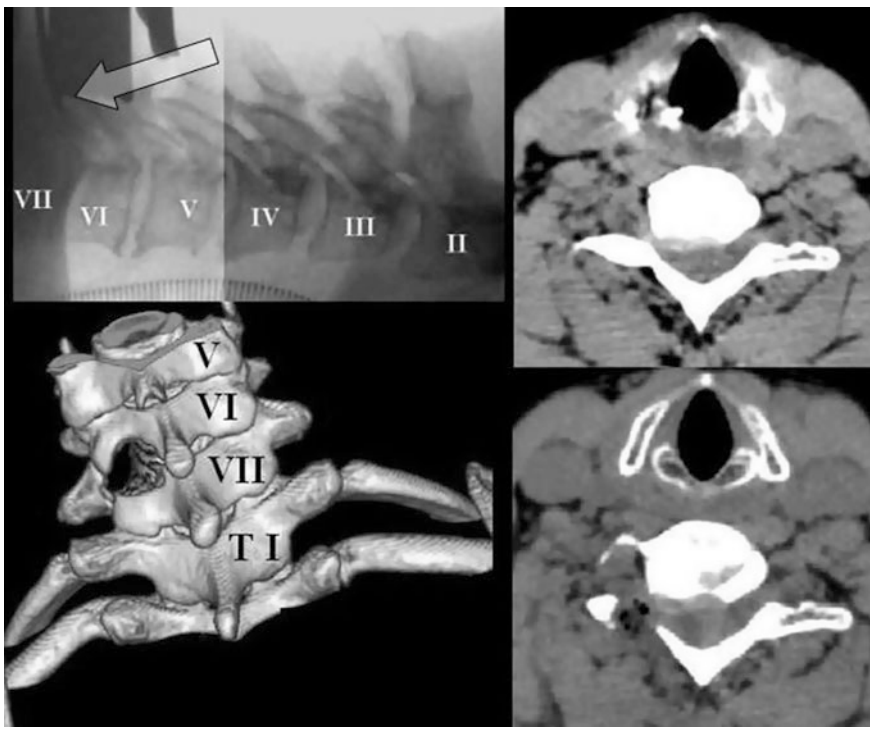

Fig. 3 *Upper left*: intraoperative X-rays control showing the Cobb's elevator used as a marker of the space. *Lower left*: Postoperative three-dimensional CT image showing a more laterally-extended foraminotomy with inclusion of the medial half of corresponding facets' joint into bone removal. *Right upper/lower*: axial CT slices showing the level of nerve root compression, before (*upper*) and after (*lower*) surgery

adjunct for a more detailed and accurate confirmation of adequate radicular decompression.

We did not find any substantial differences between the endoscopic and the open-procedure patients' groups in terms of amount of bone removal, clinical outcome, length of hospital stay or duration of post-operative neck pain, as advised by other authors [3].

Conclusion

The described "disc preserving" procedure in patients affected by cervical radiculopathies due to lateral disc herniation or foraminal stenosis had successful results in all but two of the treated patients.

Before this prospective study was started, those patients would have been treated with the anterior approach, which in our institution was currently utilized for all patients affected by herniated cervical disc.

The following remarks are stressed:

1. The selected cohort of patients was successfully treated without any kind of prothesis usually employed to stabilize the cervical spine or substitute the disc when the anterior approach is chosen.
2. The procedure was riskless and cost effective versus the anterior approach.
3. The long-term successful outcome and the recovery from radicular motor and sensory deficits was confirmed both in endoscopic and microsurgical procedures without any major difference regarding hospital stay and postoperative course.
4. The postoperative 3D reconstruction of CT slices is useful to check that the correct procedure was done.

So we stress the role of minimally invasive cervical foraminotomy in the management of degenerative disc disease of the cervical spine if a careful selection of patients is performed fulfilling the criteria of this reported study.

Finally it is important to stress that a correct indication to such a treatment cannot abstract from exclusion criteria, such as symptomatic posterior instability at the affected level (in which case conservative measures or spinal instrumentation could be valid and time-proved first-line treatments) and clear signs of myelopathy, when anterior approach is preferred.

In conclusion, posterior cervical foraminotomy, in our opinion, is a safe and effective modality for the surgical treatment of cervical radiculopathies where intraforaminal compression constitutes the main cause of pathology and when conservative treatments fail to relieve symptoms [6]. Congruity between clinic and neuroradiological findings is mandatory for choosing such an approach.

Conflict of interest statement We declare that we have no conflict of interest.

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The Fullendoscopic Anterior Cervical Fusion: A New Horizon for Selective Percutaneous Endoscopic Cervical Decompression

S. Hellinger

Abstract As a bridge between open and percutaneous therapy, endoscopy of the cervical spine started to be used at the beginning of the 1990s, following good experiences on the lumbar spine. The principle of microsurgery is combined with the minimally invasive principles by bringing the optical level to the forefront of pathology. Access morbidity has been significantly reduced by the percutaneous access technique. However, this procedure cannot be applied in patients with cervical disc herniation accompanied by segmental instability.

In further developing these endoscopic techniques, in view of the experiences with the classical "Cloward procedure", the aim was to do a bony fusion of the intervertebral space of the cervical spine by endoscopic access.

Material: A female patient with postraumatic instability of the cervical segments C4/5 underwent a fullendoscopic bony fusion. The technique will be described. The fusional process has been documented by CT and clinical assessment over 3 months.

Result: Having preoperative pain of VAS 8, it diminished to VAS 1 after surgery. The Ct-controls demonstrated a good placement of the bony dowel through the endoscopic sheath in the intervertebral space. After 3 months a bony fusion was documented by CT and in bending X-ray.

Conclusion: The result of this method displays that a fullendoscopic fusion of the cervical spine with a bone dowel is possible. The clinical result seems to be comparable to the classical Cloward procedure. To the best of my knowledge, this is the first report of a fullendoscopic osseous fusion on the cervical spine.

Keywords Cervical Pain · Cervical vertebrae · Intervertebral disc displacement · Spinal fusion · Surgical procedure, Endoscopic

S. Hellinger
ISAR Klinik, Windenmacher Str.2, Sonnenstr. 24-26, 80331, München, Germany
e-mail: hellinger@gmx.de

Introduction

There is a high incidence of cervical discogenic pain symptoms in the population. It is estimated that in Germany one person in five who visits an orthopedic surgeon presents with the symptoms of cervical disc syndrome. The treatment of cervical discogenic diseases makes high demands in terms of both diagnostics and therapy. Diagnostics have been made easier by improved imaging and the enhancement of neurological measuring methods. Consequently, there is now interdisciplinary consensus that the principal pathologic causes can be reliably identified.

The most common cause of cervical pain syndromes is a degenerative change in the intervertebral disc, where disc tissue is displaced, on the one hand, and damage occurs in the movement segment, on the other hand. Displacement of disc tissue to the epidural space may give rise to a biochemical lesion, vascular compression and mechanical compression of neural structures. This results in pain in the neck and head region, radiating into the arm, and also vegetative symptoms or even neurologic disorders [1]. Other causes of disc-related pain are to be found in the dorsal anulus fibrosus, the posterior spinal ligament and the periosteum of the vertebral bodies, where there are active pain receptors [2, 3].

With the aid of appropriate conservative therapy, approximately 80% of all cervical syndromes can be cured. Only once all the conservative and semi-invasive procedures have been exhausted should surgery be considered.

The development of surgical procedures for the treatment of intervertebral discs began in 1908 with the transdural removal of disc tissue with the aid of laminectomy by Oppenheimer and Krause. Extradural rectification of a herniated disc was prepared by Mixter and Barr in 1934. Later, Mixter and Barr also began looking at cervical intervertebral disc displacements [4]. The intervention was developed on the lumbar spine, progressing from laminectomy to hemilaminectomy, and then to fenestrotomy and finally endoscopy [5].

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The first operation on the cervical spine was performed by Elsberg in 1922, also transdurally. As from 1955, ventral methods of operation were introduced by Cloward, Smith and Robinson [6], and these are still standard procedures in the surgical treatment of discogenic diseases to this day. Both procedures have been combined with the fusion of the segment by a bone graft. This method continues to be accompanied by the problems of access morbidity (the incidence of recurrent laryngeal nerve lesions alone is put at 11–15%) [7]. The desire to reduce these problems led to continued development of the method. A discussion soon arose as to whether the fusion is necessary, and as early as 1960, Hirsch introduced the anterior cervical discectomy without fusion. In further studies, results comparable to fusion were obtained in many cases. The question regarding limited disc removal was also answered in favor of a selective procedure.

In recent years attempts have been made to preserve the physiologic mobility of the diseased movement segment by the use of intervertebral prostheses (artificial discs). This development will undoubtedly produce interesting results. The other focus of attention was on reducing surgical trauma and access morbidity. The first step was the introduction of the operating microscope by Hankinson and Wilson in 1966. Other innovations, such as high-speed burrs and bipolar electrocoagulation, produced a further reduction in surgical trauma.

With the aim of miniaturizing the treatment, non-endoscopic percutaneous procedures were soon being used on selected patients, and these also produced good results and a complication rate of less than 1% [8, 9]. Thus, chemonucleolysis, which was introduced by Smith in 1964, was performed on the cervical spine [10]. Similarly, automated discectomy [11], percutaneous laser disc decompression and nucleotomy [12–14] and the use of radiofrequency [15] broadened the percutaneous spectrum.

As a bridge between open and percutaneous therapy, *endoscopy of the cervical spine* started to be used at the beginning of the 1990s [16–20], following good experiences on the lumbar spine. The principle of microsurgery is combined with the minimally invasive principles by bringing the optical level to the forefront of pathology. Access morbidity [11] has been significantly reduced by the percutaneous access technique. Furthermore, a large proportion of the intervertebral disc, in particular most of the anulus fibrosus, is preserved. The pathology is only removed selectively in the area of the nucleus pulposus and on the dorsal fibrous ring. This preserves the remaining biomechanical function of the degenerated intervertebral disc. By means of tried and tested minimally invasive methods under vision, such as the use of a laser to ablate and shrink tissue, the risk of complications has been further reduced, at the same time as enhancing efficiency [21]. The advancement of the endoscopic technique with increased miniaturization of the endoscope and working options led to a restriction of use (e.g. LASE system [22]).

While our primary aim has been to save the motion segment by an endoscopic procedure as well as possible, we get sometimes patients with a severe instability of a cervical motion segment that requires fusion or prostheses. Here the logical consequence was to use the endoscopic experience to develop a fullendoscopic fusion procedure.

Case Report

We did the first *fullendoscopic fusion surgery* in March 2006. It was on a 50 year old female with neck and head pain of VAS 8. In addition there was a pain radiation into the left arm. The X-ray showed mild spondylosis and in functional pictures there was a movement between the vertebral bodies C4 and C5 to a quarter. On the MRI we found a disc extrusion left sided on this level. The preoperative evaluation and indication followed the recommendation by Lee [23], (Table 1).

The procedure was similar to the Selective Percutaneous Endoscopic Cervical Decompression. The level of the intervertebral disc to be operated on is marked using the C-arm. Then an approximately 5 mm skin incision is made at this level on the right side, medially to the sternocleidomastoid muscle, and the platysma is exposed without cutting. Following lateralization of the carotid artery and the jugular vein, and medialization of the larynx, trachea, esophagus and thyroid gland by applying pressure with the index finger and middle finger, the anterior surface of the cervical spine can be touched. Under fluoroscopy, an 18G spinal needle is then inserted into the intervertebral disc, preferably in the midline, via the skin incision. The position of the needle is checked in at least two planes with the C-arm.

Then a guidewire and various obturators can be placed on the intervertebral disc via the needle. A 6.5 mm working sleeve is inserted into the anterior fibrous ring via the last obturator. For this purpose, the dilation sleeve system has proved successful. The two narrow lips of the sleeve are tapped into the fibrous ring and, following removal of the fibrous ring inside the sleeve, the sleeve is rotated and the base plate and upper plate are spread apart. The working

Table 1 Preoperative conditions for endoscopic cervical fusion

Evaluation	Indication
CT and MRI	Disc extrusion
Dynamic X-ray	Angular instability
External fixation by brace	Pain alleviation
Symptoms	Axial pain like headacheNeck and shoulder painRadiculopathy

sleeve can now be advanced further into the disc space. The procedure is facilitated by using a trephine and a shaver. Under endoscopic vision, the intervertebral disc can be curetted in a wide channel as far as the posterior fibrous ring. The pathological region of the posterior fibrous ring, previously identified by imaging, determines the angle of entry into the intervertebral disc. This section of the disc is located and ablated together with the prolapsed disc tissue. When so doing, the working area can, if necessary, be extended as far as the uncovertebral joints by swiveling the endoscope. If required, the excision forceps can be used to carefully open the posterior spinal ligament and expose the epidural space. Similarly, relatively small osteophytes can be ablated under fluoroscopic vision using the ring curet. It is also possible, when working in the dorsal disc space, to change over to the gas medium. This gives a picture familiar from microscopy. A final check of the decompression is carried out with the palpation hook.

After the decompression we designed a bed for the bone graft in the midline with different burrs (Figs. 1 and 2). The bone graft has removed from the iliac crest with a special gauge to create a compressed spongeous cylinder of 6 mm diameter in the checked length. For safety we took more cylinder (Fig. 3). Then the graft in combination with osteoinductive proteins (Coloss®) was placed in the intervertebral bed through the working sleeve (Fig. 4) under endoscopic and fluoroscopic view with various pushers (Fig. 5). A last endoscopic view showed the correct position of the graft (Fig. 6). After removal of the scope the wound was closed like band aid surgery.

After the surgery the pain of the patient diminished to VAS 1. The arm pain disappeared. The postoperative CT scans and X-rays showed correct positioning of the bone dowel with good distraction (Figs. 7 and 8).

The following clinical controls showed further good clinical outcome with significantly diminished pain. There were no radicular symptoms. Only a moderate scapular pain occurred sometimes. After 3 months the CT-scan showed a bony fusion in the segment, the dynamic X-ray demonstrated no further instability.

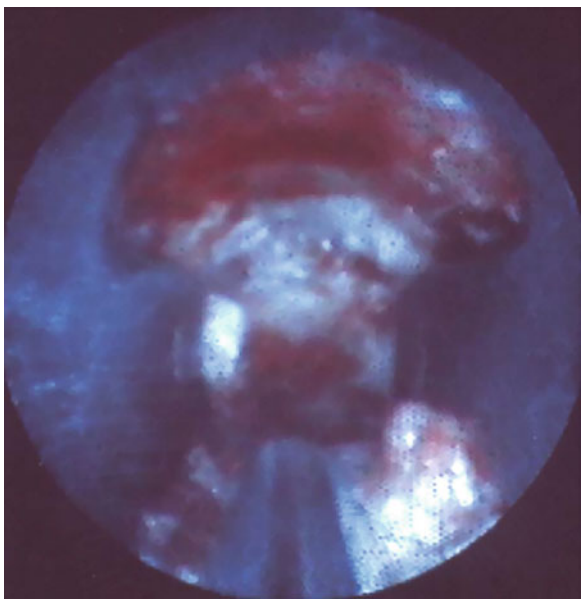

Fig. 2 Endoscopic view of the intervertebral space after preparation and control with a hook

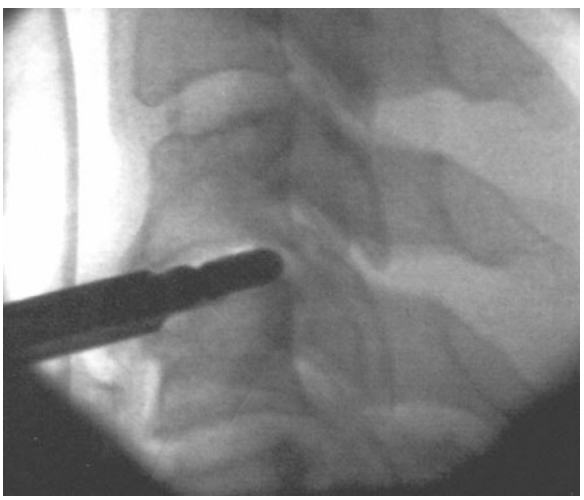

Fig. 1 Fluoroscopic control of the preparation of the endplates with a special burr

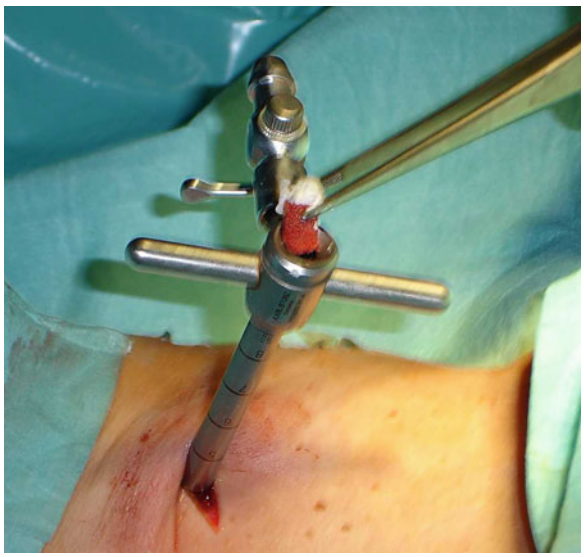

Fig. 3 Insertion of bone cylinder in the working sleeve

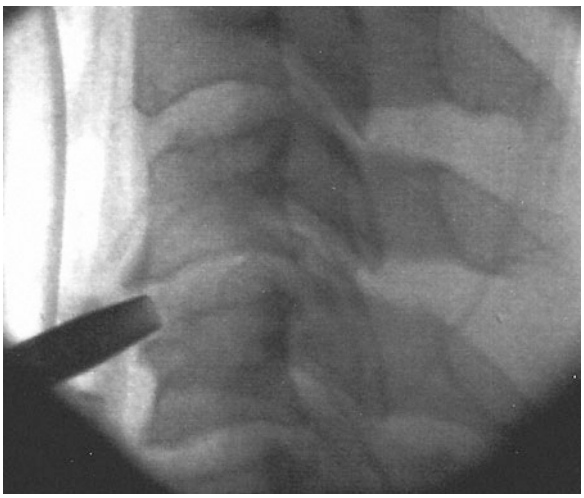

Fig. 4 Endoscopic intervertebral bone placement

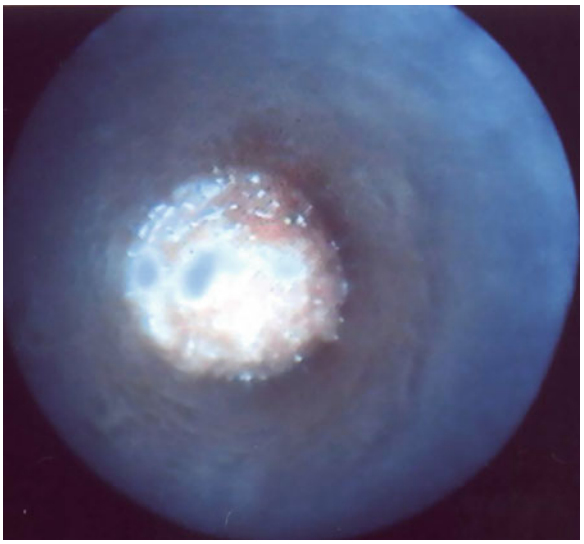

Fig. 5 Fluoroscopic view of the endoscopic placed bone craft

Fig. 6 Postoperative 3D CT-scan of the intervertebral bone dowel

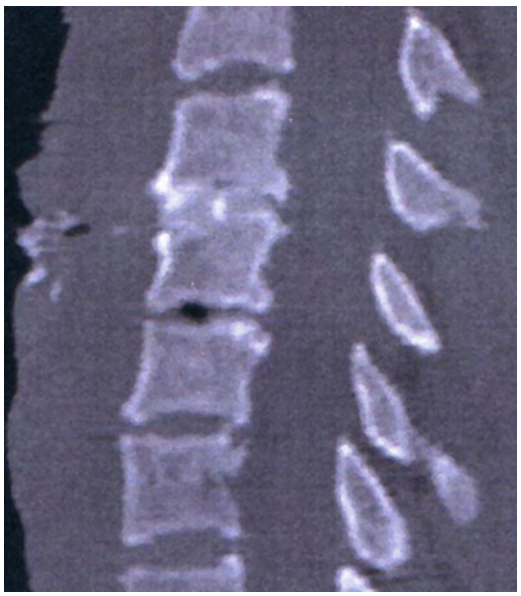

Fig. 7 Postoperative sagittal CT of the graft

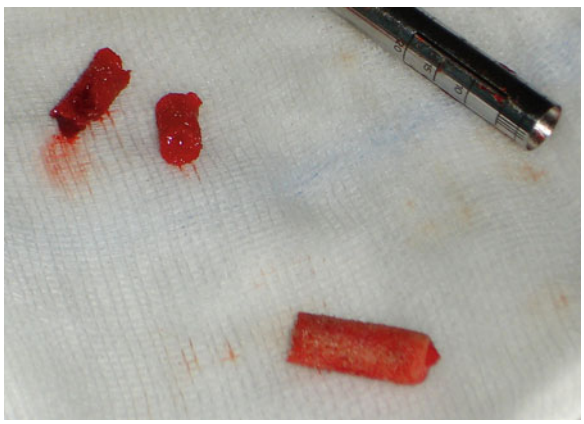

Fig. 8 Bone Dowel for intervertebral placement

Discussion

Our objective was to create an adequate working space in front of the endoscope while preserving the minimally invasive approach. This was achieved by the use of dilation sheaths, which force the base plate and upper plate of the vertebrae apart in the manner of a Cloward distractor, and permit a working field of 5 mm or 6 mm. Here the visualization is sufficient to expose the ventral epidural space. A swiveling maneuver of the endoscope enables the dorsal section of the intervertebral disc to be visualized from one uncovertebral joint to the other as necessary. Removal of disc material is limited to the pathologic part [24], in a way similar to arthroscopic meniscus surgery. Equally, the surgeon has to become accustomed to the fact that limited viewing fields are lined up, rather as in joint arthroscopy. An irrigation system is used to rinse the ablated disc material

out of the viewing field and to achieve partial hemostasis. Endoscopic cervical discectomy can also be performed using a gas medium. In this case, it is advisable to use a familiar view, such as through a microscope, to facilitate differentiation of the individual structures.

After the good experiences we got with our new endoscopic system in the treatment of cervical disc herniations with 85% success rate, comparable to the results of Chiu or Lee [21, 25], we tried to develop a system and a procedure to do a fusion through a working sleeve. Meanwhile Lee got good results in 2005 by using a WSHCervical B-Twin as a sole spacer in the cervical intervertebral space [23], we decided to modify the Cloward procedure for the endoscope. The intention has been by using a bone dowel to get an osseous fusion and to induce the resorption of spurs, like Cloward did.

The placement of the dowel and the following fusion process demonstrated the possibility of this surgical method. By the endoscopic approach damages of the anterior structures have been diminished. There were no complications. The special bone dowel, taken with a special instrument reduces also the donor side morbidity [26]. The procedure provides an excellent cosmetic effect and reduces the operating time and hospital stay.

Conclusion

The *result* of this method displays that fullendoscopic fusion of the cervical spine with a bone dowel is possible. The clinical result seems to be comparable to the classical Cloward procedure. But the approach by 6.5 mm avoids a lot of complications that are seen in open surgery. It entails less surgical trauma, and considerably reduces surgery-related stress for the patient, while also shortening the period of hospitalization.

To the best of my knowledge, this is the first report of a fullendoscopic osseous fusion on the cervical spine. Further investigations are necessary to determine the real outcome of this procedure. The future will show with further development of new instruments and implants what real minimally invasive spine surgery will enable on cervical spine.

Conflict of Interest Statement I declare that I have no conflict of interest.

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Leucocyte-Platelet Haemocomponents for Topical Use: Regenerative Potentiality

Gaetano Caloprisco and Alessio Borean

Abstract Wider and wider is the interest in different clinical ambits in the application of haemocomponents produced from peripheral blood for regenerative purposes. These are mainly made up of concentrated platelets capable of releasing locally growth factor (GF) that stimulates tissue regeneration. Our group has devised a method to produce a new leucocyte-platelet haemocomponent enriched in fibrinogen that integrates the GF stimulus with the presence of cells involved in the regenerative processes: monocytes and stem cells. The use of the cell separator to collect these haemocomponents from peripheral blood has allowed us to realize a safe standardized product, with good regenerative potentiality and reasonable costs. This is obtained by modifying some parameters of separation, and without cell manipulation.

Keywords Growth factor · Haemocomponents · Monocytes · Regeneration · Stem cell

Introduction

For some years, haemocomponents rich in platelets have been produced for regenerative purposes to be applied in different clinical sectors and on different tissue lesions; bony, cutaneous, tendinous [3–5, 12, 17, 18, 22, 23]. The rationale of the use of these haemocomponents is focused fundamentally on the production and local application of a platelet gel, given by activation with thrombin, and capable of releasing platelet growth factor (GF) [11, 24].

Recent scientific evidences have shown that besides the platelets, also resident and circulating monocytes/macrophageses and adult stem cells are very important in the processes of regeneration and tissue differentiation. Also the capacity of the platelet GF to stimulate mesenchymal stem cells expansion [1, 7, 14, 15, 25] has been emphasized. An important role in the regeneration is also played by the proteins of the extracellular matrix, such as fibrin and fibronectin, which constitute the scaffold for the cellular migration in the injured tissue [2, 8, 9, 13, 16].

Since the regeneration is tied up not only to the platelets but also to the monocytes/macrophageses and stem cells, our group has been devising for some years a system to get a leucocyte-platelet concentrate (CLP) enriched in fibrinogen where the major cellular components of regeneration were represented [4].

The purpose was to produce from peripheral blood and without cell manipulation a haemocomponent capable of integrating the effectiveness of the stimulus offering practicality of production, easy application, preservability and safety.

Our experience with these haemocomponents consists in about 400 treated patients, in various clinical ambits, for a total of over 6,000 applications. Bony, tendinous and cutaneous tissues have been particularly stimulated, with applications repeated over the time for cutaneous tissue. In the first clinical experiences we used haemocomponents for topical use as a source of platelet GF. Subsequently our attention was focused on the production and application of more complex haemocomponents with the purpose of looking for a synergy among platelet GF and mononuclear cells [4–6, 20].

Materials and Methods

Recently we have extended the application of autologous haemocomponents for topical use, in a setting of multidisciplinary collaboration, in minimally invasive surgery of the spine for reparation of the intervertebral disk. This has

G. Caloprisco (✉) and A. Borean
Dipartimento di Immunoematologia e Medicina Trasfusionale, Ospedale San Martino di Belluno, viale Europa 22, 32100, Belluno, Italy
e-mail: gaetano.caloprisco@ulss.belluno.it

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allowed us to verify some molecular and cellular parameters related to the effectiveness of the stimulus. Based on the haemocomponents used, derived primarily from collection with a cell separator, we measured the major GF involved in the regeneration (PDGF-AB, TGF-β1, IGF-I), we counted the platelets (PLT) and also the mononuclear cells and we verified their regenerative potentiality in cell culture [10, 19]. Fresh, preserved in lisate form (−40°C) and criopreserved in DMSO (−80°C), haemocomponents were appraised.

The haemocomponent we have obtained is a complex product that derives from mixing a leucocyte-platelet concentrate with cryoprecipitate, a source of fibrinogen and fibronectin.

By using a kit for collecting stem cells from peripheral blood (PBSC) and by modifying some parameters of the collection, by means of the cell separator Haemonetics MCS+ (Haemonetics Corp., Braintree, MA, USA) , a rich concentrate not only of platelets, but also of mononuclear cells, in particular of monocytes, is obtained. Results of the calculations on studied haemocomponents (45 procedures) show a concentration increase in all cellular typologies, with the higher factors of enrichment just in the mononuclear populations (Table 1).

The adopted procedure has allowed us to get a CLP very rich in PLT that correlates markedly with the concentration of the platelet growth factor (PDGF-AB, TGF-β1), after activation with thrombin [19]. This allows within certain limits, appraising the count of the PLT, to estimate the GF concentration expressed by the activated haemocomponents.

The underlined correlations (Table 1) between the concentrations of pre-collection cells and of the CLP allow evaluation of the concentration levels for single cellular population in every single patient/donor. This dependence shows that the configuration of adopted separation power can provide a haemocomponent of predictable composition, with the possibility to estimate what and how much is going to be applied on the injured tissue. This will improve the quality of therapy.

Characterization studies of CLP have allowed recognizing also a significant presence of CD34+ progenitors (81.3±26.7/μL), cells obtained without stimulating the patient/donor with haemopoietic GF and *covering a relatively lower part of the hematic volume (1,544±191 mL)*. The good correlation (r= 0.52) noticed in the CLP among mononuclear cells and CD34 + allows an easy evaluation of the concentration of CD34+ progenitors collected with the cell separator, confirming effectiveness and standardization of the separation procedure. The clonogenic assay effected on the CLP has shown that 87% of haemocomponents will give origin to colony forming units (CFU) showing that the CD34+ progenitors, involved in the formation of the CFU, *are functional in the CLP that have induced clonal growth*. Preliminary data of a Regional Sanitary Finalized study and of a study undergoing in the Policlinico Umberto I in Rome (Ferrazza et al.), confirm that a good share of the CD34+ collected possess also phenotype (CD133+) and culture's characteristic of the mesenchymal progenitors, and these data are confirmed by the literature [6, 21].

Results

In conclusion, it is possible to collect by cell separator at reasonable costs a haemocomponent where two cell populations important for processes of regeneration (PLT and monocytes) are well represented. Moreover, we must also consider the good CD34+ concentration obtained without stimulating the patient/donor and without any manipulation, but only applying a protocol of modified separation. The emergent interest in these haemocomponents consists in particular in the synergy between GF released after activation of the PLT and the mesenchymal progenitors that possess the specific GF-receptors.

To oversee, standardize and the quality control of these haemocomponents become main points for their effectiveness and safety. In the same context, transfusion medicine plays a leading role since it possesses all scientific, technical and legal competencies to include these haemocomponents in the routine processes. The general control during the whole productive cycle and intervention to safeguard the accuracy of their application in a joint effort with other

Table 1 Cell composition of the leucocyte-platelets concentrate (CLP), comparison and correlation with the pre-collection controls (n=45)

Cell count ($\times 10^3$/μL)	Pre-collection	CLP	Enrichment factor	Spearman's correlation coefficent (r)
PLT	274±64	4,454±1,239*	16.6±4.2	0.58**
WBC	6.37±1.7	80.9±24*	13±3.3	0.57**
NE	3.8±1.5	15.2±13.3*	3.9±2.8	0.53**
LY	1.75±0.4	45.7±12.5*	26.5±6	0.57**
MO	0.55±0.18	18.7±7.2*	35.6±12	0.52**
MN	2.3±0.5	64.4±15.2*	28.3±5.5	0.61**

PLT platelets; *WBC* white blood cells; *NE* neutrophil; *LY* lymphocytes; *MO* monocytes; *MN* mononuclear total cells
Data are represented as mean±SD. Comparison, *p <0.001 CLP vs. Pre-collection. Correlation coefficient, CLP/Pre-collection, **p <0.001. Level of significance p <0.05

specialised ambits assures the traceability and safety of the haemocomponents in a multidisciplinary vision of regenerative medicine.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Current Surgical Options for Articular Cartilage Repair

G.M. Peretti, A. Pozzi, R. Ballis, D. Deponti, and F. Pellacci

Abstract The articular cartilage lesions represent one of the major unsolved problems in the orthopaedic surgery. This is because articular cartilage has a limited capacity of self-repair following trauma. The aim of this study is to review the different surgical options for articular cartilage repair. They can be divided into three groups: techniques without transplant of cells or tissues; techniques based on the transplantation of tissues; the tissue engineering techniques.

The first group includes the joint debridement and the techniques based on the bone marrow-stimulation principle.

The second group includes the transplantation of periosteum and the transplantation of autologous or allogeneic osteochondral plugs. The tissue engineering techniques could be further divided as follows: methods based on the transplantation of cells either in solution, or in the form of microspheres, or carried on a biocompatible scaffold; the transplant of cartilage fragments; the cell-free techniques, based on the use of an acellular scaffold, able to entrap the reparative cells recruited from the host tissue and to guide their differentiation toward a chondral phenotype.

In this work we present various options for the treatment of chondral or osteochondral lesions. Today, however, due to the lack of comparative studies, it is not always possible to define the best treatment choice for the different cartilage pathologies.

G.M. Peretti
University of Milan, Milan, Italy
Department of Genetics and Cellular Biology, San Raffaele Scientific Institute, Milan, Italy

A. Pozzi and R. Ballis
Department of Genetics and Cellular Biology, San Raffaele Scientific Institute, Milan, Italy

D. Deponti
University of Milan, Milan, Italy

F. Pellacci (✉)
Orthopaedic Department, Villa Erbosa Clinic, Via dell'Arcoveggio 50/2, Bologna, Italy
e-mail: fpellacci@virgilio.it

Keywords Cartilage · Osteo-chondral defects · Scaffold · Tissue engineering

Introduction

The repair of chondral or osteochondral lesions still represents a big challenge for the orthopaedic surgeon. Many efforts have been made and are currently part of research and clinical programs to try to find the solution for this issue. Articular cartilage plays an important role in characterizing and maintaining the delicate balance of the joint. It is therefore easy to understand how a chondral lesion may trigger the development of pathological mechanisms able to alter the fragile articular balance, jeopardizing over time the joint function, causing pain and inducing the progression to the ultimate development of osteoarthritis [4].

When a cartilage lesion occurs, the human articular cartilage exhibits a poor or null regenerative potential, due to the inability of synthesizing a new tissue having the regular biochemical composition and biomechanical properties typical of the native cartilage tissue. Four reasons can be considered as explanation of this behavior: first, the articular cartilage is not vascularized and doesn't have a nerve supply; second, it has low cellularity; third, chondrocytes have low proliferative potential and are unable to produce a functional extracellular matrix following injury; finally, the chondrocytes capacity of responding to mechanical, chemical and pharmacological factors decreases with age.

The biological response of cartilage to injury varies in the different traumatic events. When a lesion is confined to the superficial layer, the repair process doesn't occur, as the inflammatory stimulus is too weak to stimulate the resident chondrocytes surrounding the lesion and, consequently, the defect persists [25]. However, when a full-thickness lesion occurs reaching the vessels of the sub-chondral bone, the inflammatory stimulus is more important, a bleeding from

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the bone marrow occurs allowing the access of growth factors and reparative cells in the lesion site. These cells are mainly fibroblasts and in a low percentage mesenchymal stem cells [24]. As a result, the newly formed reparative tissue differs from the normal hyaline cartilage in terms of morphology, biochemical composition and biomechanical properties. For these reasons it is called fibrocartilage.

Based on this, it is evident that a chondral or osteochondral defect requires a rapid treatment, in order to modify the natural evolution of these lesions, in the attempt of reducing the progression of the joint damage and the patient's symptoms, and to limit the development of early osteoarthritis [21]. The main goal should be the quick return to the normal physical activity for the young people and the prevention of the early implantation of joint prosthesis for the older patients, providing to all an improvement of the quality of life.

Surgical Techniques Which Do Not Require Cell or Tissue Transplant

In 1941 Magnuson [16] observed that the symptoms of patients with osteoarthritis were relieved by removing the bone spurs and regularizing the lesions' borders. This technique, named joint debridement, was originally performed by arthrotomy. Afterward, it was proposed by an arthroscopic approach and it is currently performed as palliative purpose mostly in old patients with severe osteoarthrosis.

It is well recognized that only an acute full-thickness lesion has the potential for self-repair by the formation of fibro-cartilaginous tissue. Based on this principle, several procedures were developed with the attempt of inducing bleeding from the bone marrow and, consequently, the migration of growth factors and stem cells into the lesion site. Chondro-abrasion was one of the original techniques. It consists in the removal of the calcified zone at the bottom of the defect in order to expose the underneath vessels. Afterward, Pridie in 1959 [10] suggested to use a drill in order to reach the bone marrow of the subchondral bone. In a second time, this technique was performed arthroscopically. Similar procedures are the spongialization and the microfracture. The first consists in the abrasion of the sub-chondral bone up to the exposure of the trabecular bone and its most important application is represented by the treatment of patellar lesions. The second is very similar to drilling, but microfractures are performed with a special tool instead of perforations. Today this procedure is largely utilized thanks especially to its fast execution.

These techniques are simple and are performed arthroscopically, but present the limit of generating fibro-cartilaginous tissue. This tissue presents inferior biomechanical properties with respect to the normal articular cartilage, and the beneficial early effects of surgery may quickly vanish.

Surgical Techniques Which Require Tissue Transplant

A different approach for the repair of a chondral lesion consists in the transplantation to the lesion site of a mature osteocartilaginous tissue. In this procedure, named O.A.T.S. (*Osteochondral Autograft Transfer System*), or mosaicplasty [2], healthy osteochondral cylinders are taken from low bearing areas of the joint and transplanted to the defect site. This procedure has the advantage of repairing a chondral or osteochondral defect by a mature and functional tissue. However, it presents some disadvantages: it cannot always be performed arthroscopically; it presents the technical difficulty of obtaining good-shaped cylinders from the donor site that perfectly fit and re-establish the cartilage surface of the lesion site; finally, the repairing of one defect requires the creation of one or more iatrogenic lesions having overall the same dimension of that to be repaired. This makes the defect size an important limit for the application of this approach.

For these reasons, other authors proposed the utilization of allogenic cylinders harvested from cadaver joints. This practice presents a certain morbidity risk and additionally may lead to a rejection of the transplant, with cellular necrosis and drastic reduction of the implant durability. Furthermore, the problem of the lack of donors should not be neglected.

The transplantation of periosteum represents another surgical technique for the repair of articular cartilage lesions. The periosteum is composed of two layers: the outer fibrous layer, which is a thick tissue that allows muscle insertion, and the inner cambium layer, also called osteogeneic, which is a thin tissue having an important role in bone formation and repair. Based on the fact that the pluripotent cells resident in the cambium layer turn into cells able to produce fibro-cartilaginous tissue once transplanted in the articular environment, the transplantation of the periosteum was employed as surgical option for cartilage repair. The technique consists in suturing a periosteal flap at the boundaries of the lesion's base by placing the fibrous layer facing the sub-chondral bone, and the cambial layer facing the articular space. The important limitation of this procedure is that it leads to the formation of fibro-cartilaginous tissue, similar to that obtained with the microfractures. For this reason, its current clinical application is significantly reduced [11].

Tissue Engineering Techniques for Chondral Regeneration

The techniques described above have two important limitations. In fact, both for the bone-marrow stimulation procedures and the periosteal graft the reparative tissue is made of biomechanically poor fibrocartilage; on the other hand, in the mosaicplasty, the availability of the adequate amount of osteochondral cylinders confines the application of this procedure to lesions of limited extension. In order to solve these problems, many efforts were made by the researchers in the last decades having the aim of finding new approaches for cartilage repair. The tissue engineering techniques and their application in clinical practice represent the principal answer to this question.

The common principle of all tissue engineering strategies is the aim of obtaining a newly formed mature tissue that presents superior qualities resembling those of the native cartilage. This can be attempted by different methods: by the direct cell transplantation into the lesion site; by the transplantation of cells, previously seeded onto a scaffold; by the implantation of acellular scaffolds that are capable of being repopulated by the cells at the implant site.

Therefore, the current tissue engineering techniques for chondral regeneration can be divided into three groups: first, the transplantation of chondrocytes or other cells in solution; second, the transplantation of cells previously seeded onto a scaffold; third, the implantation of acellular scaffold capable of the recruitment of nucleated mesenchymal stem cells from the bone marrow and the blood of the sub-chondral bone. Eventually, these scaffolds should also provide the proper stimuli for the correct differentiation of the reparative cells.

With the attempt of repairing an articular cartilage defect, from the 1990 many tissue engineering techniques were proposed, based on the transplantation of an adequate number of cells in the lesion site able to proliferate and maintain a chondral phenotype. The original technique was proposed by Brittberg in the 1994 [3] and was called A.C.I. (*Autologous Chondrocyte Implantation*). This procedure requires two surgical steps; during the first step, a cartilage biopsy is taken from an area of healthy cartilage and then transferred in a laboratory for cells' isolation and expansion. Cells are expanded in a monolayer culture until they reach the sufficient number to fill the defect. During the second step, the patient undergoes a second surgery; at this time, a periosteal flap is sutured at the boundaries of the lesion and the cells are injected in solution under the flap. Another technique very similar to the A.C.I. is called C.A.C.I. (*Collagen-covered Autologous Chondrocyte Implantation, Chondro-Gide-C*®, Geistlich); this is characterized by the use of a collagen membrane instead of the periosteal flap.

Fundamental requirements for indication of one of these techniques are isolated lesions, stable joint and young age of the patient [7]. In fact, only the cells from young patients are capable of a good in vitro proliferation [18]. The limits of A.C.I. and C.A.C.I. procedures are: the need of two surgical steps and the requirement of a high surgical skill, in those cases of lesions located in particular areas, like, for example, the posterior side of the femoral condyles. In addition, several other important risks should be taken into consideration like the cells mobilization immediately after surgery due to imperfect suture of the collagenic membrane or the periosteal flap [13]. Despite all these limits and risks, Brittberg obtained a good clinical outcome in 70% of the patients after 2 years follow-up, demonstrating the feasibility of the tissue engineering techniques for the repair of the articular cartilage lesions. Although this procedure is going to be slowly replaced by new techniques, it is still utilized (*Carticel*®, Genzyme; *Novocart*®, Tetec). Recently, new techniques became available having for instance the possibility of selecting, during the in vitro phase, the most active cells to be used in the implant time (*ChondroCelect*®, TiGenix). They may also allow for the application of A.C.I. even in old patients. Furthermore, some authors are investigating the possibility of using mesenchymal stem cells as repair elements [5].

In order to improve the integration of the newly formed tissue to the defect sides and to avoid the leakage of the cell solution out of the repair site in the early stage of the implantation surgery, some authors have proposed to seed the cells onto biocompatible scaffolds [22]. The materials employed as cell carriers are different. For example, in the M.A.C.I. technique (*Matrix-Induced Autologous Chondrocyte Implantation*, *MACI system*®, Genzyme) a bi-layered membrane (Fig. 1) made of type I and III collagen is utilized [6]. One side of the membrane is compact and it will be implanted facing the articular cavity. The other side of the

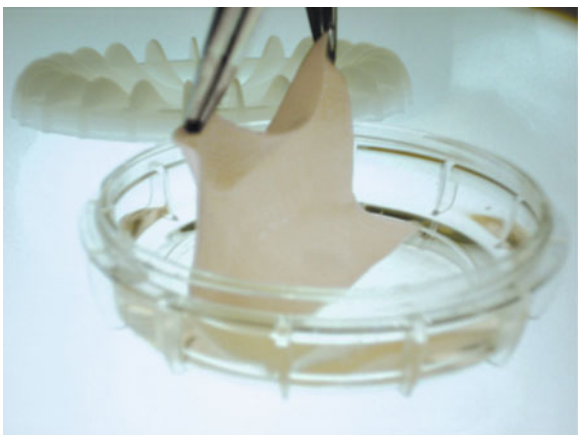

Fig. 1 Image of the membrane MACI system®, Genzyme (reproduced with permission of Genzyme that holds the copyright)

membrane is porous and will offer the environment where to seed the cells. This side will be implanted facing the bottom of the lesion. Few collagenic scaffolds are available (*Maix*®, Matricel), and some are also prepared together with chondroitin-sulphate (*Novocart 3D*®, Tetec), which would permit a better penetration of the cells into the membrane [20]. Another material is derived from hyaluronic acid (*Hyalograft-C*®, Fidia) that is one of the first materials employed as cell scaffold for cartilage repair in clinical practice [26] and that showed thus far encouraging results [14]. All these membranes are mostly entirely absorbable and have the advantage of being easy to be handled, making the surgery easier than the A.C.I. procedure and allowing a dramatic reduction of the surgical time. However, these techniques still require two surgical steps and the implantation of the membrane cannot be done earlier than 3 or 4 weeks from the day of the biopsy. Moreover, the biomechanical properties of these scaffolds are generally poor and require particular care by the surgeon during the implantation. Additionally, in some cases, these cell-scaffold composites lack the perfect integration with the sub-chondral bone and with the lesions' boundaries, thus jeopardizing the entire procedure. Finally, the cells seeded onto these biomaterials are often not equally distributed throughout the entire thickness of the membrane, but instead they appear concentrated in one side.

For these reasons, other new materials were developed, presenting a liquid phase that can solidify or jellify in a second time in the laboratory or even directly inside the joint. The benefit of this approach consists in the higher adaptability to the joint surface and to the lesion's shape and in the uniform distribution of the cells embedded inside the scaffold. In fact, they are not seeded onto the material, but remain "entrapped" into the scaffold when they jellify. These materials are called hydrogels.

Some hydrogels are entirely biological materials, such as the collagen gel *CaReS*®, Ars Arthro [1]; others are classified as biocompatible polymers, as for example alginate and agarose gels (*Cartipatch*®,TBF Tissue Engineering) [23] and poliglactin-polidioxanone gels that come together with fibrin glue (*Bioseed-C*®, BioTissue) [15]. For all the procedures performed using the hydrogels, a first surgical step is needed in order to collect the cartilage biopsy, from which isolate the reparative cells.

Photopolymerizable gels are currently studied by some investigators; this novel approach allows the execution of the procedure arthroscopically having the gel that jellifies directly into the joint by application of the light source, perfectly filling the lesion. This is the case of the polyethylene-glycol-diacrylate gel (PEGDA) (*ChonDux*®, Cartilix). Another technique consists in the transplantation of microspheres formed by polymers and cells directly into the joint (*Co-Don*®, AG). The microspheres are built in vitro and placed onto the lesion arthroscopically. Then they can adhere to the sub-chondral bone thanks to their intrinsic adhesive properties.

All these procedures employ autologous cells, obtained from a previous biopsy and, therefore, require two interventions. Recently, a new technique called C.A.I.S. (*Cartilage Autograft Implantation System*®, Mitek-DePuy) was proposed, consisting in the use of small cartilage fragments harvested from the patient, embedded in a glue gel and placed directly into the lesion. This is an example of a one-step procedure, as the cartilage fragments are prepared together with the scaffold setting, in the same single surgery.

Beside these techniques that involve the transplantation of cells, other approaches are currently used, based on the employment of non-seeded membrane. These products are based on the natural healing potential of full thickness acute lesions of the articular cartilage, as bone marrow-stimulation techniques do. One of these procedures is called A.M.I.C. (*Autologous Matrix Induced Chondrogenesis*) and consists in the use of a reabsorbable collagenic membrane. This membrane, placed over the area of the microfractures, can entrap the blood clot (that is rich of growth factors and cells) derived from bone marrow into its three-dimensional structure (*Chondrogide-C*®, Geistlich). Another similar procedure utilizes poly-ethylene-diacrylate, the photopolymerizable gel described above (*ChonDux*®, Cartilix).

Another important sector of the cell-free materials includes the bi-layered scaffolds, formed by an osteocompatible phase and by a cartilaginous phase. The great advantage of this method lies in the good integration into the subchondral bone granted by the osteocompatible phase. Some examples are the scaffold of Poly(D,L-lactide-co-glycolide) for the chondral phase and calcium sulfate for the bone phase (*Trufit*®, Smith&Nephew) (Fig. 2) [28]; also, a tri-layered

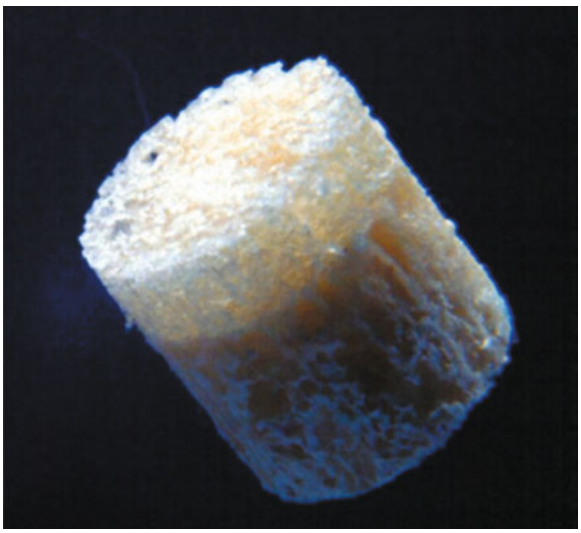

Fig. 2 Image of the osteochondral implant Trufit®, Smith&Nephew (reproduced with permission of Smith & Nephew that holds the copyright). The osteocompatible side is at the bottom

membrane built with collagen and hydroxyapathite fibres (*MaioRegen*®, Finceramica) (Fig. 3). For these procedures still remain to be demonstrated the higher quality of a newly formed tissue, especially in the comparison with the previously listed methods [17] (Table 1). The important advantage for all the cell-free procedures, however, is that only a single surgical step is required.

Fig. 3 Image of the osteochondral implant MaioRegen®, Finceramica (reproduced with permission of Finceramica that holds the copyright). The osteocompatible side is at the bottom

Conclusion

This work further demonstrates that the repair of chondral or osteochondral lesions represents one of the most difficult problems in the orthopaedic field. In the past years, a lot of efforts have been done by studying the lesions' biology and trying to improve the natural healing potential of the articular cartilage [19]. All the bone marrow-stimulation techniques are based on this principle, but have the limit of the low quality of the newly formed tissue.

In order to improve the biomechanical properties of the neo-tissue, many different procedures based on tissue engineering methodologies were proposed [12]. These can potentially reproduce a hyaline cartilage by more complex and expensive procedures, if compared to the "classical" techniques [9]. Unfortunately, comparative studies on the different approaches and on the diverse clinical situation are thus far still missing.

In the past years, the osteochondral scaffolds seem to have produced a particular attraction for many investigators and surgeons, due to the fact that they can provide a good integration between the newly formed tissue and the subchondral bone [27]. Other authors are focusing on the potential effects of the autologous growth factors such as the PRP

Table 1 Some of the main surgical procedures for articular cartilage repair

Procedure	One step vs. two steps	Technique/product	Producer
Surgical techniques which do not require cell or tissue transplant			
–	One step	Joint debridement	–
Bone marrow stimulation techniques	One step	Drilling	–
–	One step	Microfracture	–
–	One step	Chondroabrasion	–
–	One step	Spongialization	–
Surgical techniques which require tissue transplant			
–	One step	Periosteum transplantation	–
–	One step	Autologous mosaicplasty	–
–	One step	Allogeneic mosaicplasty	–
Tissue engineering techniques			
Chondrocytes' transplantation techniques	Two steps	*Carticel*®	Genzyme
–	Two steps	*Chondro-Gide*®	Geistlich
–	Two steps	*A.C.I. + ChondroCelect*®	TiGenix
–	Two steps	*Novocart*®	Tetec
Techniques of open matrix transplantation	Two steps	*M.A.C.I.*®	Genzyme
–	Two steps	*Novocart 3D*®	Tetec
–	Two steps	*Maix*®	Matricel
–	Two steps	*Hyalograft-C*®	Fidia
Techniques of hydrogel transplantation	Two steps	*CaReS*®	Ars Arthro
–	Two steps	*Cartipatch*®	TBF Tissue Engineering
–	Two steps	*Bioseed-C*®	BioTissue
Transplant of cartilage microspheres	Two steps	*Co-Don*®	AG
Transplant of cartilage fragments	One step	*C.A.I.S*®	Mitek-DePuy
–	One step	*Chondro-Gide-C*®	Geistlich
–	One step	*ChonDux*®	Cartilix
Techniques of biphasic cell-free scaffold implant	One step	*Trufit*®	Smith&Nephew
–	One step	*MaioRegen*®	Finceramica

(*Platelets Rich Plasma*) or some molecules of the BMP family (*Bone Morphogenetic Proteins*) as chondrogenic stimulus for the transplanted cells or the resident cells at the injured site.

The new generation of scaffolds will include growth factors incorporated in their structure, able to induce or maintain the cartilaginous phenotype of the reparative cells. Moreover, thanks to the evolution of research in material science and imaging, it will soon be possible to create a custom-made scaffold, based on the dimension and size of the patient's lesion [8].

In the future, embryological research will probably be largely involved in the healing and regeneration of the articular cartilage. In fact, a lot of molecules involved in the development of the joints may be crucial player in driving the reparative cells towards the correct cartilage formation. Moreover, other novel methodologies, such as gene therapy, will probably be playing a beneficial role for cartilage repair, allowing the release of reparative molecules or stimulating proteins at the defect site. These techniques cannot currently be used yet for this purpose, because of their low safety, restraining their applications only to life-threatening diseases.

In this work we have analyzed the current options for the treatment of cartilaginous defects; many efforts have been done in order to find an answer to this issue. Nowadays, none of the techniques described can completely and systematically restore the injured cartilaginous tissue. On the other hand, important steps can be considered being done so far at least in slowing down the typical progression of the osteoarthrosis that follows a cartilage injury. However, the problem of the treatment of osteochondral defects still remains a challenge for both surgeons and researchers.

Conflicts of Interest Statement We declare that we have no conflict of interest.

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Facial–Hypoglossal Nerve End-to-Side Neurorrhaphy: Anatomical Study in Rats

Liverana Lauretti, Manuela D'Ercole, Gilda Di Masi, Mariano Socolovsky, and Eduardo Fernandez

Abstract End-to-side neurorrhaphy (ESN) is presented as a sort of surgical technique for nerve repair that has the aim to obtain a good reinnervation of the recipient nerve and function preservation of the donor nerve. Several problems regarding this technique remain to be solved. Even if ESN could find some indications in particular cases of peripheral nerve surgery, we do not think that this technique can be first choice surgery for repairing a damaged facial nerve because of the complexity of the function of facial muscles and the necessity to offer an adequate number of motoneurons from the donor nerve for reinnervation of the recipient nerve.

So, despite some reports about the clinical use of facial–hypoglossal nerve ESN, we studied experimentally such technique in the rat, having as recipient the facial nerve and as donor the hypoglossus. The purpose was to establish the number of motoneurons with which the donor hypoglossal nerve innervates the recipient facial nerve, and to compare the result with that obtained after facial–hypoglossus end-to-end neurorrhaphy (EEN). Beside other interesting findings, the key point of the obtained results was that motoneuron contribution given from the donor hypoglossus to the innervation of the recipient facial nerve was limited in ESN as compared to the classic EEN.

Keywords Facial nerve · Neurorrhaphy · Number of motoneurons · Reinnervation

Introduction

End-to-side neurorrhaphy (ESN) has been proposed for nerve repair when the proximal stump of a transected nerve is unavailable so that the distal stump is connected to the side of an adjacent intact nerve. Already used in the late nineteenth century, ESN was abandoned with the advent of microsurgery when a direct end-to-end neurorrhaphy (EEN), even with direct fascicular repair, was preferred. In 1994, ESN was newly introduced by Viterbo et al. [16] and since then several experimental as well as clinical reports, often with contrasting results, have been published. From the surgical point of view, ESN consists of connecting the distal stump of a transected nerve (recipient nerve) to the side of an intact adjacent nerve (donor nerve) in correspondence of an epineurial window. The intent of this technique should be to obtain a good reinnervation of the recipient nerve without damaging the donor nerve. This purpose seems intriguing but the quality, quantity and mechanisms of reinnervation are not clear. Therefore, the clinical use of ESN remains questionable. The debate on ESN regards several unsolved questions related to the origin and type of reinnervating axons, the stimulus for axon sprouting, the penetrating power of axon sproutings across the thick perineurium and the endoneurium, and the real preservation of the donor nerve function. For instance, the primary supposed mechanism for reinnervation of the recipient nerve should be the axonal sprouting of the intact axons of the donor nerve, induced by the degenerative events into the recipient nerve and should also be positively influenced by some degree of axonal section in the donor nerve. Obviously, if some degree of axonal section in the donor nerve occurs unintentionally during surgery, instead of an ESN a partial EEN should be chosen, in which only a limited number of axons from the donor nerve are used to reinnervate the recipient nerve.

In order to improve the knowledge on the effectiveness of ESN in reinnervating an injured nerve, we performed an anatomical study in a rat model in which the recipient and

L. Lauretti, M. D'Ercole, and E. Fernandez (✉)
Department of Neurosurgery, Catholic University School of Medicine, Largo Agostino Gemelli, 8, 00168, Rome, Italy
e-mail: e.fernandez@rm.unicatt.it

G. Di Masi and M. Socolovsky
Department of Neurosurgery, University of Buenos Aires School of Medicine, Buenos Aires, Argentina

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the donor nerve were the facial and the hypoglossus, respectively. The anatomical results were compared with those obtained after EEN between the same nerves.

Materials and Methods

Nineteen male Wistar rats weighing 150–160 g were used. The animals were divided into three experimental groups: intact control Group rats (n=3), ESN Group rats (n=8), EEN Group rats (n=8).

Surgery: After deep anesthesia (Diazepam 2 mg/100 g intraperitoneally followed by intramuscular Ketamine hydrochloride 4 mg/100 g), microsurgical procedures were performed under aseptic conditions. Through a right curvilinear retroauricular skin incision, the facial and hypoglossal nerves were reached.

The facial nerve, exposed at the stylomastoid foramen, was cut and the distal stump was mobilized and directed downward to reach the hypoglossus isolated deep to the jaw angle. In the ESN Group of rats, a small epineurial window was created onto the side of the hypoglossus to receive the distal facial nerve stump that was secured by three epi-epineurial sutures using 10-0 monofilament nylon stitches. In the EEN Group of rats, the hypoglossus was cut and its proximal stump was connected end-to-end with the distal stump of the facial nerve with one or two epi-epineurial sutures using 10-0 monofilament nylon stitches.

Three months later, all the operated animals and three intact control rats were anesthetized. Under magnification, the orbicularis oculi and the orbicularis oris muscles of the right side were injected each with 0.4 µl of an 8% solution of wheat germ agglutinin-horseradish peroxidase (HRP) (Sigma Chemical Co., St Louis, MO). The injections were performed manually with a Hamilton microsyringe and slowly during a 5-min period. Two days later, the rats were deeply anesthetized and perfused with cardiac injection of saline water followed by 2.5% buffered glutaraldehyde. Then, the brainstem was harvested, transferred to 30% sucrose buffer and cut in the coronal plane into 40-µm sections on a freezing microtome. The sections from the brain stem were tested for HRP using tetramethylbenzidine; alternate sections were counterstained with cresyl-violet. Labeled motoneurons in both the right hypoglossal and facial nucleus were counted at the optic microscope.

After reopening the skin wound, the site of neurorrhaphy was searched. Then, a 10 mm-long segment of the facial nerve was harvested. In the intact control rats a corresponding segment of the facial nerve was picked up. The nerve segments were immersed for 4 h at 4°C in 1% glutaraldehyde and 4% formaldehyde in 0.1 M phosphate buffer (pH 7.2). The samples were soaked overnight in 0.1 M phosphate buffer, postfixed in 1% osmium tetroxide, dehydrated with ethanol, embedded in Epon 812, and cut with glass knives on an ultramicrotome. Transverse semi-thin sections (1–2 µm thick) were stained with toluidine blue. Sections of reinnervated and normal facial nerves were compared from a qualitative point of view under the optic microscope and the morphological differences reported.

The results were reported as mean ± standard error of the mean. The difference between two means was examined for significance, using the Student's *t* test. A probability of $P < 0.05$ was considered to be significant.

Results

The facial nerve function recovered in both groups of operated rats: the blink reflex was restored as well as the symmetry of the vibrissae pads.

The number of labelled motoneurons after HRP-injection into the orbicularis oculi and orbicularis oris for each Group of rats is cited below and summarized in Table 1.

1. Intact control Group rats with intact facial nerve: the number of labelled motoneurons in the facial nucleus was 228.6 ± 42.7 ($P < 0.05$ vs. ESN Group rats and EEN Group rats).
2. ESN Group rats: the number of labelled motoneurons in the hypoglossal nucleus (Fig. 1) was 56.0 ± 10.5 ($P < 0.05$ vs. EEN Group rats). The number of labelled motoneurons in the facial nucleus (Fig. 2) was 134.3 ± 19.8 ($P < 0.05$ vs. EEN Group rats).
3. EEN Group rats: the number of labelled motoneurons in the hypoglossal nucleus (Fig. 3) was 324.6 ± 53.1. The number of labelled motoneurons in the facial nucleus was (Fig. 4) 35.8 ± 17.7.

The results related to the facial nerve sections obtained from the different Groups of rats (Fig. 5) can be summarized as follows:

Table 1 Brainstem labelled motoneurons in the different groups of animals

	Normal Intact Group	ESN group	EEN group
FN nucleus	228.6±42.7 (p<0.05 vs. ESN and EEN)	134.3±19.8 (p<0.05 vs. EEN)	35.8±17.7
HN nucleus		56.0±10.5 (p<0.05 vs. EEN)	324.6±53.1
Total labelled motoneurons	228.6±42.7 (p<0.05 vs. ESN and EEN)	190.3±15.1	360.4±35.9

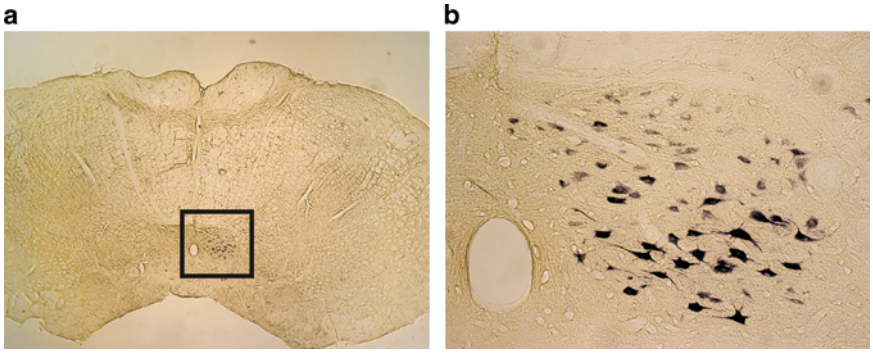

Fig. 1 ESN Group rat. Transverse section through the brain-stem: HRP labeled motoneurons in the hypoglossus nucleus. (**a**) ×2.5; (**b**) ×20

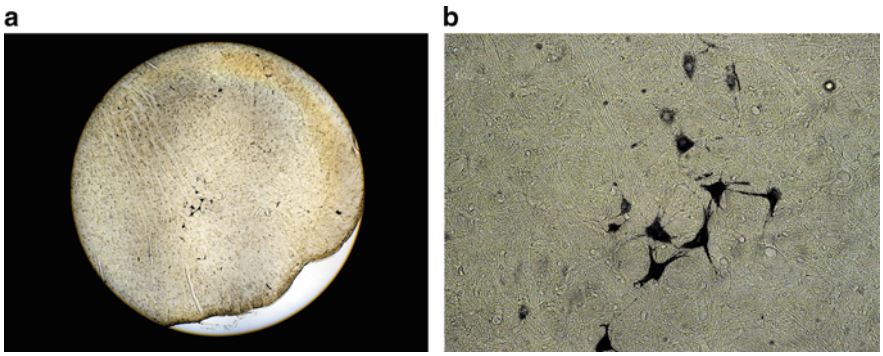

Fig. 2 ESN Group rat. Transverse section through the brain-stem: HRP labeled motoneurons in the facial nucleus. (**a**) ×2.5; (**b**) ×20

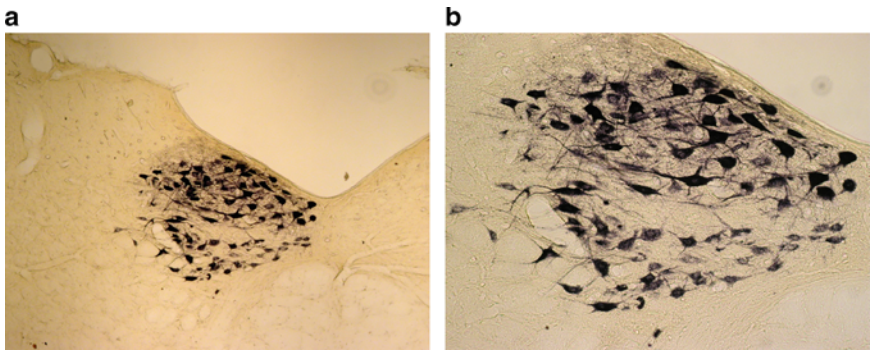

Fig. 3 EEN Group rat. Transverse section through the brain-stem: HRP labeled motoneurons in the hypoglossus nucleus. (**a**) ×2.5; (**b**) ×20

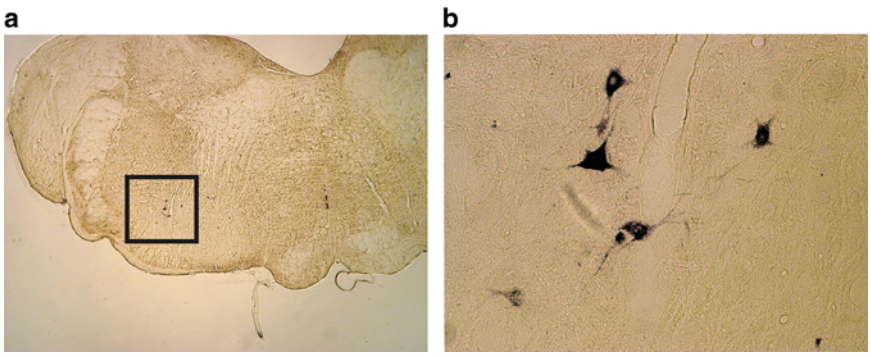

Fig. 4 EEN Group rat. Transverse section through the brain-stem of: HRP labeled motoneurons in the facial nucleus. (**a**) ×2.5; (**b**) ×20

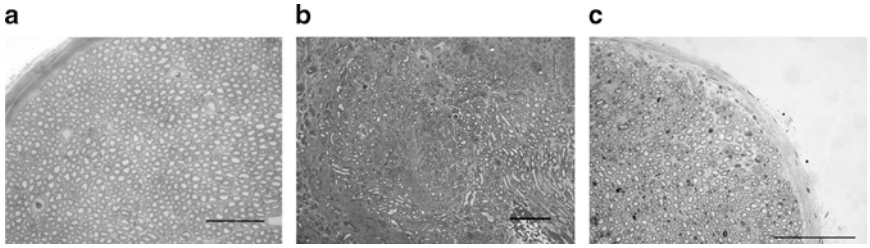

Fig. 5 Facial nerve transverse sections. (**a**) Normal Intact Group rat. (**b**) ESN Group rat. (**c**) EEN Group rat. Scale bar 50 μm. EEN Group rat shows a better axon regeneration picture than ESN Group rat nearer to that of a normal rat

1. Intact control Group rats: the intact facial nerve appeared normal as connective sheaths, axon contents and organization.
2. ESN Group rats: the facial nerve showed figures of degeneration and regenerating axons, most of them small and not myelinated.
3. EEN Group rats: the facial nerve showed better regenerated axons and a tidy organization.

Discussion

To repair an injured peripheral nerve is something more than reconstruct the nerve continuity. A clear example is given by the fair functional results that can be obtained even with an end-to-end tensionless neurorrhaphy, made even early after the lesion without any adjunctive graft. For instance, after an end-to-end facial–facial nerve repair, the normal myotopic organization of the subnuclei in the facial motor nucleus is greatly lost so impairing function [10]. Examining the experimental and clinical reports on the matter, it seems reasonable to conclude that what appears, theoretically, as the best procedure surgically cannot be equally good functionally. Among the aspects that contribute to an impaired full recovery, there are probably factors like the number of neurons giving regenerating axons, the misdirected reinnervation, the hyper- and poly-innervation phenomena [5, 10].

When the proximal stump of a transected nerve is not available, the crucial point is the necessity of a donor nerve. The ESN technique has been proposed for this eventuality with the double aim of obtaining recovery of the recipient nerve and preserving function of the donor nerve. Theoretically, as for any technique of neurotisation, to facilitate motor recovery should be used a donor nerve that is not antagonist of the recipient one.

Controversies

On the efficacy of ESN various controversies exist. The first one is related to the origin of regenerating axons into the recipient nerve. Experimental studies with axonal tracers demonstrated that such axons origin mainly, as expected, from the donor nerve but also, as not expected, from the proximal stump of the same injured recipient nerve. In fact, neurons were found retrogradely labelled in the motor nucleus and posterior dorsal root ganglion of the donor nerve [3] and, surprisingly, also in the motor nucleus of the same recipient nerve [1, 12]. However, most of the regenerating axons were sensitive which made them unable for motor recovery [14]. Such sensory regenerating axons could also origin from the epineurial nerva nervorum injured while making the epineurial window and the suture.

Supposed that the axons reinnervating the recipient nerve come from the donor nerve, the questions are why the axons of the donor nerve sprout and how they overcome a barrier represented by both the thick perineurium and the endoneurium. These are perhaps two of the most controversial points. Some investigators [11, 15, 17] exclude axonal injury in the donor nerve, even when to an epineurial window a perineurial one is added: according to this view, axonal sprouting should be induced by neurotrophic factors released from the recipient nerve. Conversely, other authors [3, 8] observed that some mild axonal injury in the donor nerve, without functional effects, always occurs especially when the perineurium is stripped away. They conclude that some degree of axonal injury in the donor nerve is necessary to obtain a working ESN. Therefore, these authors considered that ESN is always, at least, a partial EEN.

However, whatever the mechanism underlying reinnervation of the recipient nerve, all authors agree that after ESN the best functional recovery is 60–70% of that obtained with EEN.

Our Study

Most of the experimental studies on ESN have been performed on peripheral nerves of limbs. As cited above, the anatomical studies with axonal tracers showed more labelled neurons in the dorsal root ganglion than in the ventral horn. This observation supports the inadequacy of ESN in restoring a satisfying motor reinnervation especially in districts with complex and precise motility like that of the facial

muscles. In this district, however, there is the clinical demand to find a surgical procedure able to preserve as much as possible the function of the donor nerve in case of hypoglossal–facial anastomosis (HFA) for facial reanimation. In fact, there are several clinical reports about the use of a variety of ESN techniques in which the hypoglossal nerve reinnervates the facial nerve [4, 7, 13].

The aim of our work was to make a step back starting from the assumption that the number of motoneurons involved in axonal regeneration is a good tool to evaluate the goodness of facial reanimation. Then, we made a thorough experimental study on such anatomical feature after facial–hypoglossal ESN. In a previous experimental work [6] on HFA and hemi-hypoglossal–facial anastomosis (HHFA), in accordance with other authors [9], we stated that the number of motoneurons in the facial nucleus of normal intact animals is 10–35% higher than in the hypoglossal nucleus. This finding could have been sufficient to avoid any surgical procedure that further reduces the number of hypoglossal motoneurons available for reinnervation of the facial nerve.

Analyzing the present results after facial–hypoglossal ESN or EEN in rats, it is evident that the motor reinnervation of the facial nerve was provided by both, the hypoglossus and the facial motornucleus, the entity of contribution given by the facial nucleus being inversely proportional to that given by the hypoglossus nerve (Table 1). In the ESN Group rats, in comparison with the number of motoneurons found in the facial nucleus of normal control animals, the number of labelled motoneurons in the hypoglossus and facial nucleus was about ¼ and ½, respectively. Altogether, the number of motoneurons in both the hypoglossus and facial nucleus corresponded to about 80% of the number of motoneurons in the facial nucleus of intact rats. This fact explains the good functional recovery of the facial muscles obtained in the ESN Group rats. As reported by other authors [2], the contribution of motoneurons from the facial nucleus through the proximal stump of the facial nerve, cut at the stylomastoid foramen and left in situ, is a constant finding in rat experimental models of HFA and was also found in the present study in both experimental groups. Very interestingly, the contribution of the facial nucleus was almost 4 times more consistent in the ESN Group rats than in the EEN Group rats (Table 1, Figs. 2 and 4). In both experimental groups of rats, the proximal facial nerve stump remained with interrupted axons able to regenerate (a condition not corresponding to that found in clinical practice where, generally, the proximal facial nerve stump is degenerated) and the higher "contamination" with facial motoneurons in the ESN Group of rats could be due to the insufficient grade of reinnervation of the recipient nerve by the hypoglossal axons causing a stronger attraction of axons from the facial source.

The anatomical data of the present paper are coincident with the findings of Tarasidis et al. [14] published in 1998: in his experimental study on different varieties of neurorrhaphy between peroneal and posterior tibial nerves he concluded that, since only poor sensory regeneration is obtained, clinical applicability of ESN is unlikely. We add that the meagre number of motoneurons from the donor nerve involved in ESN, while it could be enough to guarantee simple movements of lower limbs, it seems however inadequate for the more complex motor activity of facial muscles.

Conclusions

The most relevant point of this study on facial–hypoglossal ESN is the significant lower number of motoneurons provided by the donor hypoglossus to reinnervate the recipient facial nerve. This poorness of reinnervating hypoglossus motoneurons could be due to (1) the persistence of the anatomical barriers, the endoneurium and the perineurium, in the donor hypoglossus obstacles the axonal sprouting; (2) the lack of the important stimulus to axonal sprouting that is represented by the axonal damage of the same donor hypoglossus nerve.

According to the evidence that ESN guarantees an almost full preservation of the donor hypoglossus nerve function and a poor reinnervation of the recipient facial nerve, we think that it is inadequate for facial reanimation. In our opinion, in fact, it is not worth to preserve an intact hypoglossal nerve despite a fair facial nerve function.

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Anatomic Study in Cadaver of the Motor Branch of the Musculocutaneous Nerve

Alberto Isla and Julio Pozuelos

Abstract This study of 80 cadavers demonstrates that the anatomic position of the motor branch of the musculocutaneous nerve with respect to that of the sensitive branch of the same nerve is lateral in more than 88% of cases in humans.

The distance from plexus to the separation into the motor and sensitive fascicles was 8–9 cm long.

Given the lateral position of the motor component of the musculocutaneous nerve, the nerves that are going to be used to neurotize this area can be directed so as to increase the efficacy of the results for the flexor function of the arm.

Introduction: Brachial plexus lesions produce great morbidity and are relatively frequent in young adults. Innervating the coracobrachial, biceps and anterior brachial muscles, the musculocutaneous nerve is one of the priorities for nerve neurotization when plexus root avulsion occurs because it is essential for arm flexion. This nerve has both a motor and sensitive component, and the anatomic positions of the two components have not been much studied. When performing a neurotization anastomosis to the musculocutaneous nerve, being able to identify the motor component of the graft and attach it to the motor component of the musculocutaneous nerve could avoid a loss of many motor axons which would otherwise occur if the graft were attached to the sensitive component.

Objective: The present paper is based on a topographic anatomic study to locate and obtain the objective positioning of the motor branch of the musculocutaneous nerve in humans, as well as measure its length from the origin in the brachial plexus to the separation of both fascicles into branches.

Material and Methods: The study was performed in 40 cadavers, dissecting the musculocutaneous nerve along its course and measuring the distance from its *emergence* from the plexus until the separation between its motor and sensitive branches in both arms so as to be able to determine the positioning of the motor fascicle with respect to the sensitive fascicle.

Results: The distance from plexus to the separation into the motor and sensitive fascicles was 8.8 cm on the left side and 8.95 cm on the right side. The position of the motor branch with respect to the sensitive branch was lateral in more than 85% of the studied nerves, all the way from its origin in the brachial plexus until the definitive separation between both branches, on both the right and the left sides.

Conclusion: If the nerves that are to be used for neurotization of the musculacutaneous nerve are directly taken to the lateral fascicle of that nerve, which is generally the motor component, the treatment should be effective and should avoid the loss of motor axons resulting from anastomosing to the sensitive fascicle.

Keywords Cadaver anatomy · Musculocutaneous nerve · Peripheral nerve cadaveric measurements

Introduction

In brachial plexus lesions, whether complete or high incomplete lesions of the plexus due to incomplete avulsion, it is necessary to perform a neurotization, that is, employ regional nerves to reinnervate the lesioned areas that have a prioritary function [1, 3–5]. The musculocutaneous, axillar and suprascapular nerves must be re-neurotized when the lesions occur proximal to the plexus [7–9, 13].

The musculocutaneous nerve, which emerges at the brachial plexus, is a necessary candidate for neurotization due to its flexor function for the arm. However, the anatomic position of the motor branch of the nerve with respect to its sensitive branch has not been well characterised anatomically. The objectives in this paper are first of all to establish the anatomic relation of the motor branch with respect to the

A. Isla (✉) and J. Pozuelos
Service of Neurosurgery, Hospital Universitario, La Paz Paseo de la, Castellana, 261 28046, Madrid, Spain
e-mail: esilapa@mixmail.com

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sensitive branch of the nerve from its individualization, in the nerve cords of the plexus. Secondly, we shall measure the length of the motor branch from its emergence from the brachial plexus until its separation from the sensitive branch of the nerve, and lastly provide anatomic references to enable reneurotization processes that could avoid the loss of motor axons attached to sensitive objectives. This paper is based on the study of 40 cadavers.

Material and Methods

Material

Anatomic dissection was practiced on 40 formaldehyde conserved cadavers; 16 male and 24 female, aged 42–94 years old at the time of death (mean age 80.6 years).

Dissection Technique

The arm was placed in abduction and external rotation. An incision beginning 7 cm above the clavicle running behind the posterior border of the sternocleidomastoid muscle was made crossing the clavicle and directed toward the deltopectoral triangle as far as the axilla. The platysma muscle was opened. The posterior face of the omohyoid muscle was identified and cut to improve visibility. Dissection continued until the fascia of the anterior scalen muscle was identified; at this point an incision was made to expose the brachial plexus. Next, an incision was made over the clavicle to expose the fascia and subclavian muscle. An osteotomy of the clavicle was performed to expose the infra clavicular plexus (Fig. 1).

The incision continued to the axilla, resecting the majoris pectoralis muscle from the plexus and then removing the minoris pectoralis muscle at 1 cm from the corachoid apophysis, so as to completely expose the brachial plexus itself (Fig. 2).

Once the brachial plexus was exposed, the incision was continued along the abducted arm, between the biceps and triceps muscles until a point 5 cm proximal to the medial epichondyle. The deep fascia of the arm were dissected and identified and the entire lengths of the coracobrachial and biceps muscles were dissected. Then the separation of the musculocutaneous from the median nerve in the brachial plexus was identified, the trajectory of the former was followed to the elbow, observing its passage through the coracobrachial muscle to the point at which the motor and sensitive branches separate. Once the entire extent of the

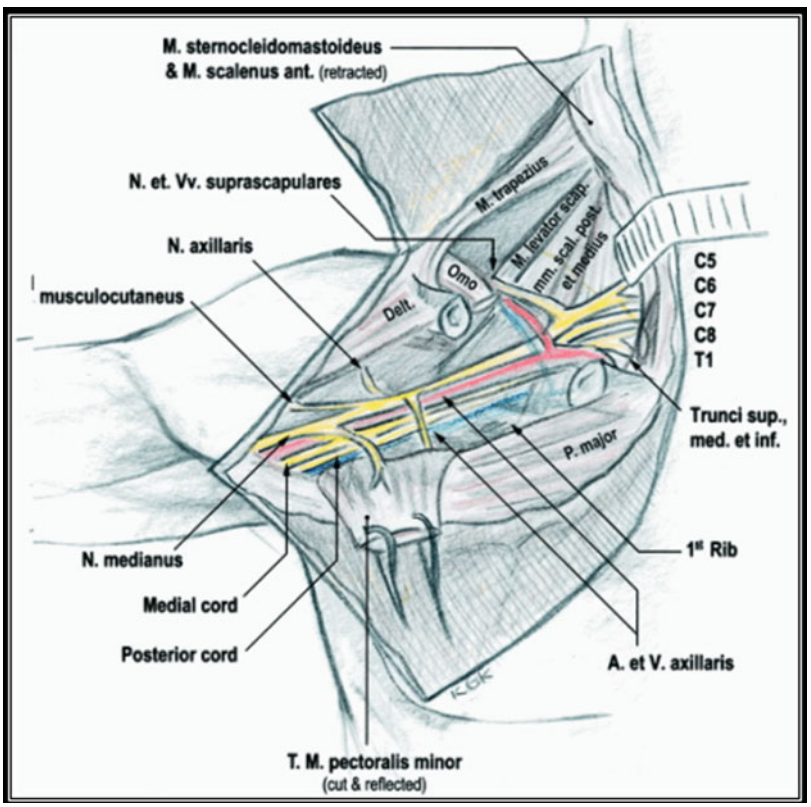

Fig. 1 Schematic drawing of the anatomy of the brachial plexus (from Neal et al. [9])

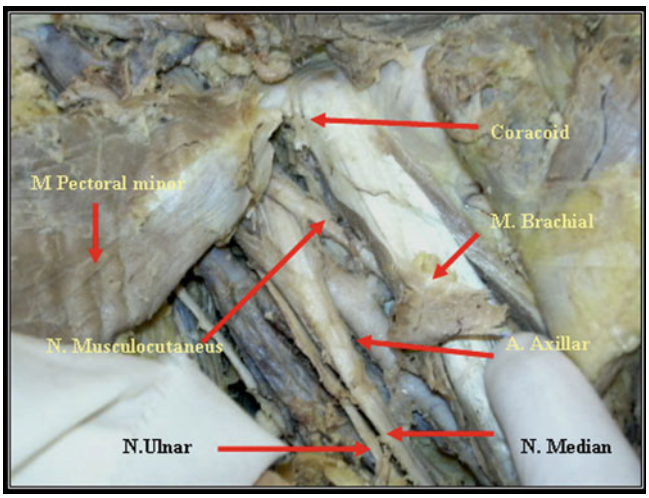

Fig. 2 Exposition of the inferior portion of the left brachial plexus identifying the separation of the musculocutaneous nerve from the median nerve

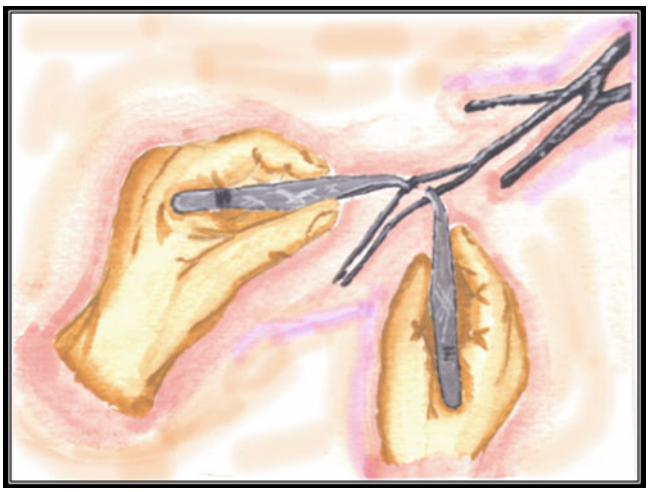

Fig. 4 Drawing representing the retrograde dissection employed to locate the anatomic position of the motor branch of the musculocutaneous nerve

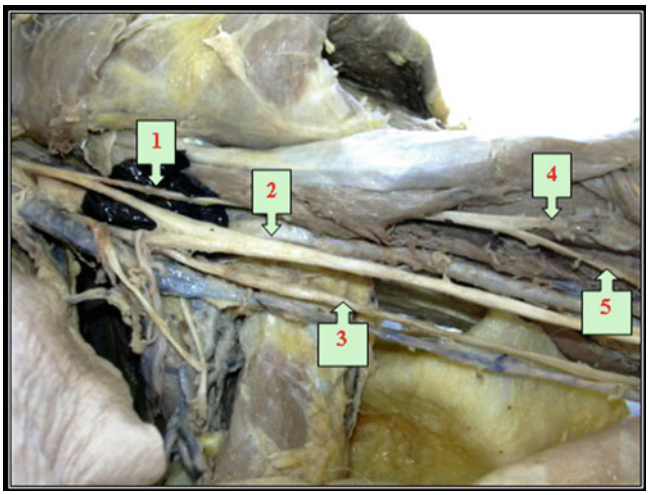

Fig. 3 Dissection of the terminal branches of the left brachial plexus in cadaver 1. (1) Musculocutaneous Nerve; (2) Median Nerve; (3) Cubital Nerve; (4) Motor Branch running to the biceps muscle; (5) Sensitive branch running to the forearm (lateral antebrachial cutaneous nerve)

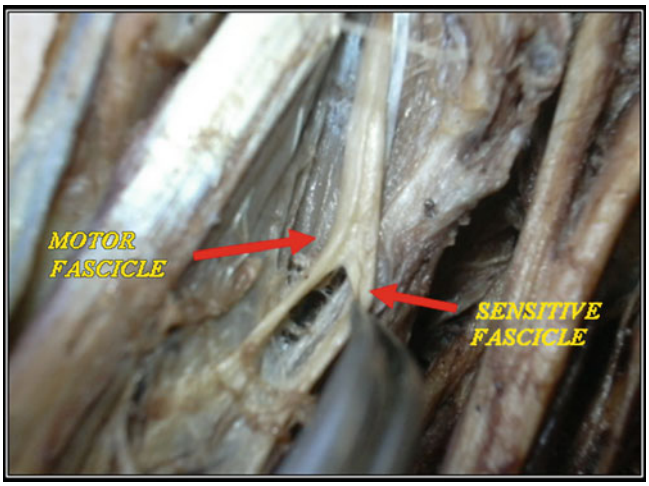

Fig. 5 Anatomic dissection showing the clear separation between both nerve fascicles once the epineural sheath is dissected

musculocutaneous nerve was identified (Fig. 3), the distance from the point of its separation from the brachial plexus to the point at which it separated into two branches was measured with a ruler.

Then, with the aid of a 5× Wentex lens and microsurgical instruments (Fig. 4), the nerve was dissected and the motor branch and sensitive fascicles were identified once the epineural sheath was dissected and separated from each other (Fig. 5), along the length of their course up to their emergence from the plexus, so as to establish the relative anatomic positions of the motor and sensitive fascicles along their joint trajectory.

Results

Forty cadavers were studied: 16 males and 24 females; mean age 80.6 years (range: 42–94 years). The brachial plexus was dissected and the musculocutaneous nerve located on both sides of all cadavers. The measurements are reported in Table 1.

Table 1 Measurement performed in both arms of 40 cadavers

Cadaver	Distance from brachial plexus to fascicle bifurcation		Fascicle location	
	Left	Right	Left	Right
1	3.5	2.5	Posterolat	Lateral
2	2.5	3.5	Posterior	Posterior
3	11	12	Lateral	Lateral
4	5	6	Lateral	Lateral
5	9	11.5	Lateral	Posterior
6	12	6	Lateral	Lateral
7	11	11.5	Lateral	Lateral
8	9	10	Lateral	Lateral
9	14	11.5	Lateral	Posterior
10	10	12	lateral	Anterolat
11	12	14	Lateral	Lateral
12	7	12.5	Lateral	Lateral
13	13	13	Lateral	Anterior
14	5	10	Lateral	Lateral
15	12	13	Lateral	Lateral
16	10	7	Lateral	Lateral
17	9	12	Lateral	Lateral
18	10.5	7	Lateral	Lateral
19	9	11	Lateral	Lateral
20	13	10	Lateral	Lateral
21	12	16	Lateral	Lateral
22	9	12	Lateral	Lateral
23	8	10	Lateral	Lateral
24	8	10	Lateral	Lateral
25	12	10	Lateral	Lateral
26	11	14	Posterolat.	Lateral
27	8	11	Lateral	Lateral
28	11	13	Posterior	Lateral
29	10	9	Lateral	Posterolat
30	11	12	Lateral	Lateral
31	8	10	Lateral	Latera
32	11	12	Lateral	Lateral
33	16	9	Lateral	Lateral
34	8	8	Anterior	Lateral
35	8	8	Lateral	Lateral
36	8	11	Lateral	Lateral
37	9	16	Lateral	Lateral
38	12	12	Lateral	Lateral
39	10	12	Lateral	Lateral
40	9	13	Lateral	Lateral

Musculocutaneous Nerve Motor Branch Anatomy in Cadavers

Results

Length

The mean distance from *emergence* from the brachial plexus until division into the two branches of the musculocutaneous nerve was:

Left side	8.8 cm
Right side	8.95 cm
Length of the left motor fascicle	8.8 cm
Length of the right motor fascicle	8.95 cm

Table 2 Musculocutaneous nerve motor fascicle position (80 nerves)

Position	Left	Right
Lateral	35	34
Posterior	2	3
Posterolateral	2	1
Anterior	1	1
Anterolateral	0	1

The results were analyzed with the SPSS version 11.0 Statistical analysis packet (*ELSEVIER*). Student's t-test was employed to analyze paired data and found no statistically significant differences in the lengths of the motor fascicles on the left and right sides (p=0.802).

Position

The results regarding position are shown in Table 2.

The position on the left side was lateral in 85.7% of the cadavers, and other in 14.3% of the cadavers. On the right side of the cadavers, the position was lateral in 88.2% of the cases and other in 11.8% of the cases. The McNemar test for paired data showed there was no significant right-left difference in the positioning of the motor fascicle (p=1.00).

Discussion

The musculocutaneous nerve is one of the terminal branches of the brachial plexus, providing the most important innervation for forearm flexing as well as sensitizing the lateral face of the forearm [6, 10–13].

Kawai [6] published a thorough study of brachial plexus anatomy particularly focused on describing the anatomy of the musculocutaneous nerve. He observed that the motor branch that connected to the biceps separated from musculocutaneous nerve at 7 cm from the coracoid apophysis; the length to the biceps short head was 11.7 cm and to long head was 13.7 cm.

Chirapattanakon and colleagues [2] employed the acromion as anatomic reference to locate the motor branch and reported it to be 13 cm from the acromion. In our own study, the reference point was the origin of the nerve in the brachial plexus, since we consider that point to be an

important surgical landmark to locate the origin of the motor nerve branch that innervates the biceps. Our measurements showed that the branch measured 8.8 cm on the left side and 8.945 cm on the right side (Fig. 6).

This datum is important because it can supply a known reference range for neurotization procedures that can be adapted to the surgical technique to be employed, particularly if sural nerve grafts are to be used in an anastomosis with the musculocutaneous nerve.

Modern microsurgical techniques employed in the neurotization process make a certain series of principles advisable. One is that of performing anastomosis as close as possible to the receptor muscle [8].

With regard to the position of the motor branch, Kawai [6] performed a topographic study that demonstrated that in 12 of 15 cases (80%), the fascicles for the brachial muscle and lateral cutaneous ante brachial fascicle are placed medially at 4.8 cm from the coracoid apophysis, while the fascicles for the biceps are lateral. Chiarapattanakon and colleagues [2] also studied the internal topography and demonstrated that the fascicles running to the biceps occupied a lateral position. In both cases, the methodology employed dissection followed by coronal sectioning of the nerve and staining. The results were examined in a microscope. Both papers describe a general lateral positioning of the motor branch of the musculocutaneous nerve; however, they do not report its position at the level of the separation of the nerve from the brachial plexus. In his paper, Kawai [6] reports that he was not able to topographically identify the musculocutaneous nerve at its point of origin. In our study, we demonstrated that in 70 of the 80 cases, the position of the motor branch was lateral even at the point at which the musculocutaneous nerve separates from the plexus, an important point when neurotization is being performed (Fig. 7).

Another interesting observation in two cadavers was the position of the lateral ante brachial cutaneous nerve after its separation from the motor branch. The sensitive branch, once it had separated from the motor branch that ran to the biceps, descended toward the forearm as an independent nerve. Immediately proximal to the elbow, the musculocutaneous nerve crosses the deep fascia and reaches the surface. At this point it is known as the lateral ante brachial cutaneous nerve and it innervates the lateral face of the forearm [11, 12]. In both cadavers, once separated from the motor branch, the sensitive branch was seen to turn back on itself so as to join the sheath that wrapped the median nerve and continue its downward course alongside the latter. This positioning was not observed in any other cadaver (Fig. 8).

None of the cadavers in our study lacked the musculocutaneous nerve, although this has been reported [14].

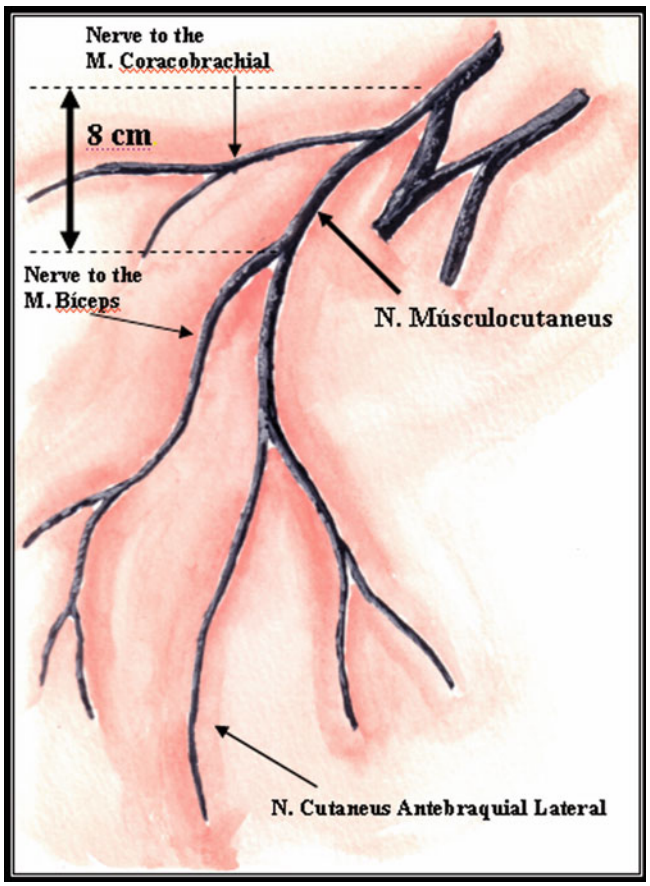

Fig. 6 Drawing of the length observed in the study with reference to the emergence of the musculocutaneous nerve from the plexus until its separation into the motor and sensitive branches

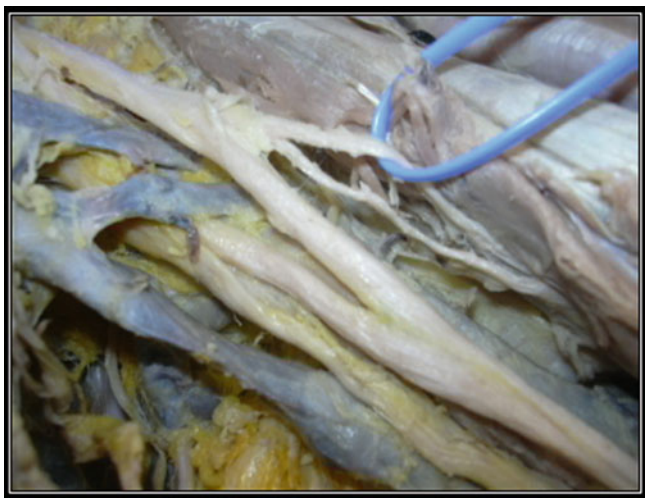

Fig. 7 Anatomic dissection demonstrating the anatomic position of motor branch of musculocutaneous nerve at the level of its emergence from the brachial plexus (*left arm*)

Fig. 8 Cadaver no 35, *left arm*. Observe the union between the sensitive branch of the musculocutaneous nerve to the sheath of the median nerve (*black arrow*)

Conclusions

The results of the measurements and observations in this study of 80 cadavers demonstrate that: The anatomic position of the motor branch of the musculocutaneous nerve with respect to that of the sensitive branch of the same nerve is lateral in more than 88% of cases in humans.

The distance from plexus to the separation into the motor and sensitive fascicles was 8–9 cm long.

Given the lateral position of the motor component of the musculocutaneous nerve, the nerves that are going to be used to neurotize this area can be directed so as to increase the efficacy of the results for the flexor function of the arm.

Conflict of interest statement We declare that we have no conflict of interest.

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Exposure of the Sciatic Nerve in the Gluteal Region Without Sectioning the Gluteus Maximus: An Anatomical and Microsurgical Study

Mariano Socolovsky, Lucas Garategui, Alvaro Campero, Horacio Conesa, and Armando Basso

Abstract *Background*: Complete sectioning of the gluteus maximus muscle is an extensive procedure when approaching the sciatic nerve in the buttock, resulting in significant morbidity and a prolonged postoperative recovery period. By contrast, dissecting through the muscle by splitting its fibers is faster, involves less damage to tissues and diminishes recovery time. The objective of the present work was to perform a cadaveric study to obtain measurements of the maximum, minimum and mean exposure that this minimally invasive approach can offer.

Methods: Both gluteal regions from each of ten fresh cadavers were dissected via a transgluteal approach, using a transverse curvilinear incision. After exposure of the sciatic nerve, the maximum length of exposed nerve was measured. As a final step, a 6 cm long sural graft reconstruction was performed, aided by a surgical microscope and microscopic techniques.

Findings: The mean sciatic nerve exposure obtained was 115.4 ± 17.9 mm, ranging from a maximum of 152 mm to a minimum of 90 mm. In all 20 cases, it was possible to perform microsurgical reconstruction under the microscope. We further illustrate these findings with three live patients in whom the transgluteal approach was employed to successfully expose and repair the sciatic nerve.

Conclusions: The transgluteal approach is useful in the operative repair of lesions of the proximal sciatic nerve. It is a less invasive technique than classical complete sectioning of the gluteus maximus muscle, and yields better aesthetic results and a faster return to normal daily activities. Complex lesions, like nerve trauma requiring grafts and nerve tumours, can be treated with minimal risk. Nevertheless, it is less comfortable for the surgeon, and the entire extent of the exposed nerve might not be visualized simultaneously during surgery.

Keywords Gluteal region · Nerve reconstruction · Peripheral nerve · Sciatic nerve · Sural grafts

Introduction

Over the past few decades, peripheral nerve surgery has witnessed numerous important developments, primarily due to the incorporation of several novel techniques for nerve transfer and suture to the surgical armamentarium [1–9]. Nevertheless, the approaches used to access the affected nerves have not undergone profound changes. In fact, most of the incisions used today were used in the 1920s [10–18] (Fig. 1).

Therefore, it is widely accepted that sectioning of the gluteus maximus muscle is necessary to achieve adequate access to the sciatic nerve at the buttock [11, 12, 15, 16, 19]. This classical approach involves an extended incision from the posterior inferior iliac spine to the midline in the posterior thigh, curving laterally at its mid-portion. Then, complete section of the gluteus maximus muscle at its insertion in the greater trochanter (leaving a cuff for reattachment at closure) and subsequent reflection of the muscle medially allows to a correct exposure of the entire sciatic nerve from the sciatic notch to the tight. Gluteal nerves and vessels are preserved. Unfortunately, sectioning the largest and strongest muscle in the human body – the gluteus maximus – usually is associated with a substantial fibrous reaction, severe pain, and prolonged post-operative recovery.

M. Socolovsky (✉) and A. Campero
Hospital de Clínicas, University of Buenos Aires School of Medicine, La Pampa 1175 Apt 5ºA, Buenos Aires, Argentina
Institute of Anatomy J. Naon, University of Buenos Aires School of Medicine, Buenos Aires, Argentina
e-mail: socolovsky@fibertel.com.ar

L. Garategui and H. Conesa
Institute of Anatomy J. Naon, University of Buenos Aires School of Medicine, Buenos Aires, Argentina

A. Basso
Hospital de Clínicas, University of Buenos Aires School of Medicine, La Pampa 1175 Apt 5ºA, Buenos Aires, Argentina

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Acta Neurochirurgica Supplementum 108, DOI 10.1007/978-3-211-99370-5_36,

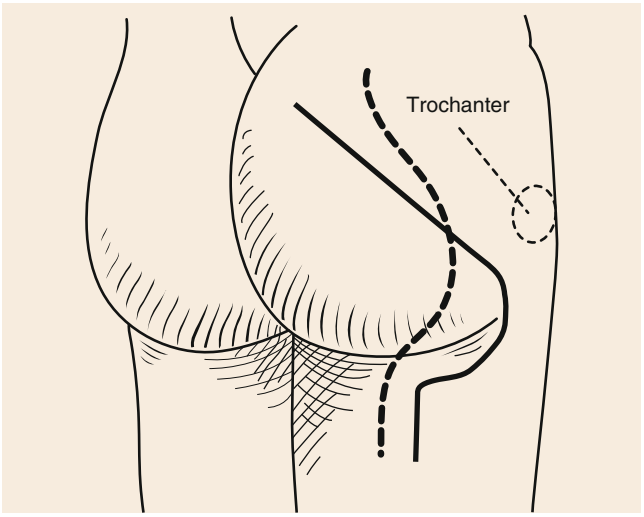

Fig. 1 Byron Stookey's incision for sciatic nerve approach with section of the gluteus maximus muscle (*full line*). The *dotted line* shows the skin incision described in modern textbooks [11, 12, 15, 16, 18, 19]. Both are very similar (modified from [17])

Recently, Patil and Friedman [20] sparked interest in the transgluteal approach as a means by which to widely expose the sciatic nerve in a manner that is less invasive, splitting the muscle fibers without sectioning the entire muscle. This associates with faster recovery than sectioning of the gluteus. Nevertheless, this technique is still rarely employed in complex reconstructions of the sciatic nerve, like autologous grafts that are common for nerve reconstruction after trauma.

The primary purposes of the current study were to assess the transgluteal approach on cadavers to determine (1) the maximum, minimum and average degree of sciatic nerve exposure provided by this approach; and (2) to determine the feasibility of using this approach when performing a 6 cm long reconstruction with grafts under a surgical microscope. In this manner, we sought to evaluate the potential usefulness of the transgluteal approach in sciatic nerve reconstructive surgery.

Methods and Materials

This work was done in the Anatomy Laboratory of the J. J. Naon Institute at the University of Buenos Aires School of Medicine. A total of ten fresh adult cadaver portions, sectioned at the level of the superior iliac crests superiorly and at the union of the medial and distal third of the thigh inferiorly, including both sides (20 gluteal regions) were dissected using the transgluteal approach, to achieve exposure and measurement of the sciatic nerve.

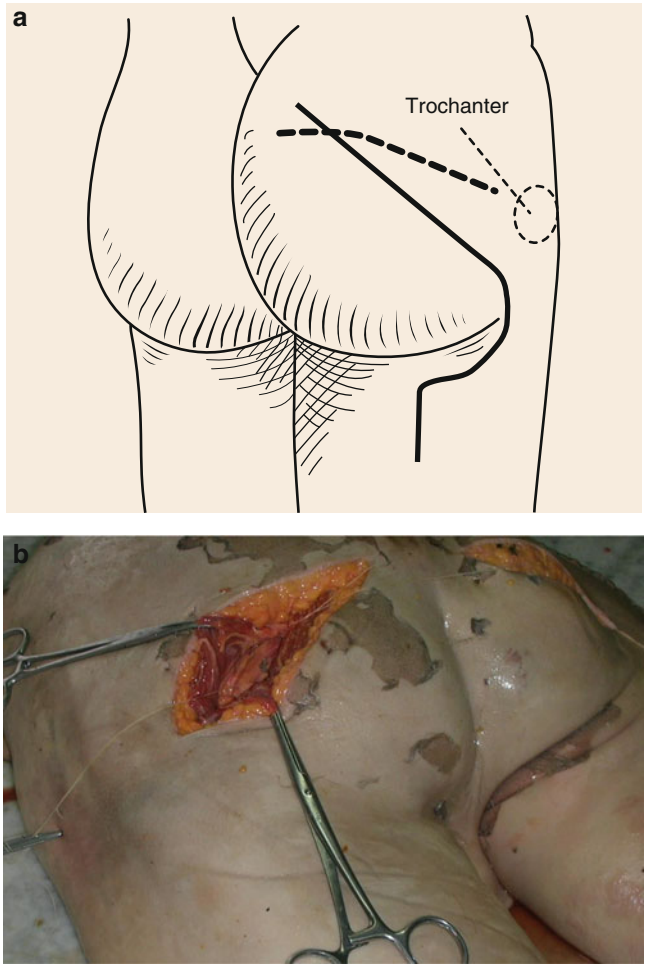

Fig. 2 (**a**) The *dotted line* depicts the skin incision performed in the present study for the transgluteal approach, not parallel to the sciatic nerve (modified from [17]). (**b**) Transverse skin incision to approach the sciatic nerve at the buttock, in a fresh cadaver, *left side*

The curvilinear incision started 4–5 cm lateral to the intergluteal line, at the midportion of the gluteal region, and was directed perpendicular to the main axis of the leg, in a curved fashion, its convexity pointing superiorly, ending in the direction of the trochanter at the lateral aspect of the gluteal region (Fig. 2). The skin, subcutaneous fat and gluteal fascia were divided, and wide exposure of the gluteus maximus muscle was achieved by subfascial dissection. Then, transverse dissection and splitting – but not sectioning – of the muscle fibers was performed. The sciatic nerve was observed easily, contained on the fat pad located immediately deep to the gluteus maximus muscle. Once the nerve had been located and repaired, the maximum length of nerve exposure was obtained by splitting gluteus fibers (Fig. 3). Proximally, the sciatic nerve could be exposed up to the piriformis muscle, which in any case was not sectioned to achieve greater exposure up to the sciatic notch. With a millimetre calliper, this measurement was obtained and

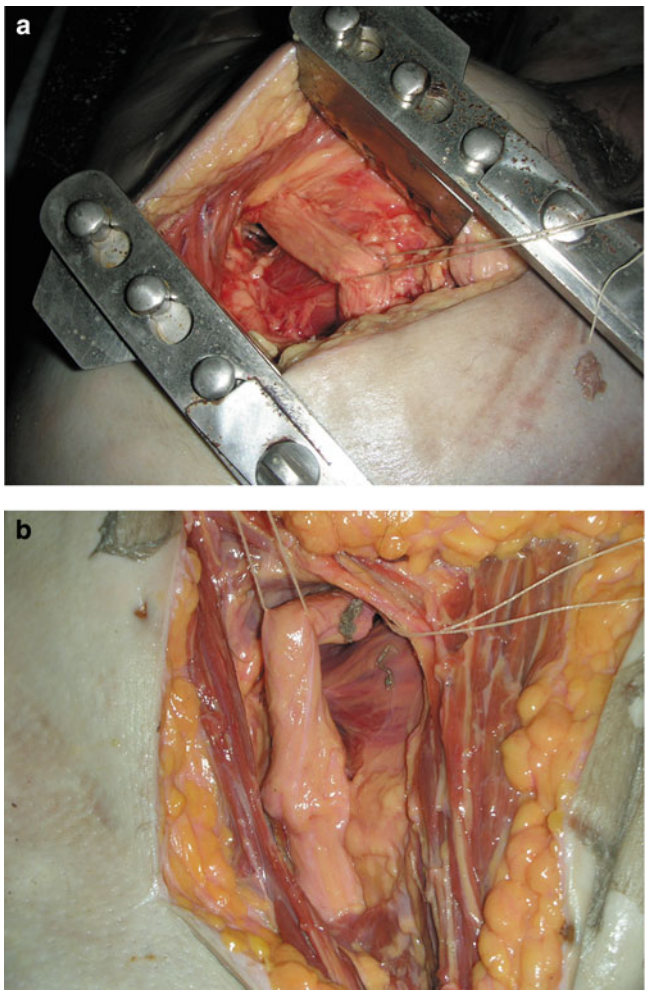

Fig. 3 (**a**) Exposure of the sciatic nerve in a fresh cadaver. *Left side*. (**b**) Maximum exposure was obtained by splitting gluteus maximus fibbers on a cadaveric dissection. With a millimetre calliper, the measure of the exposure was obtained

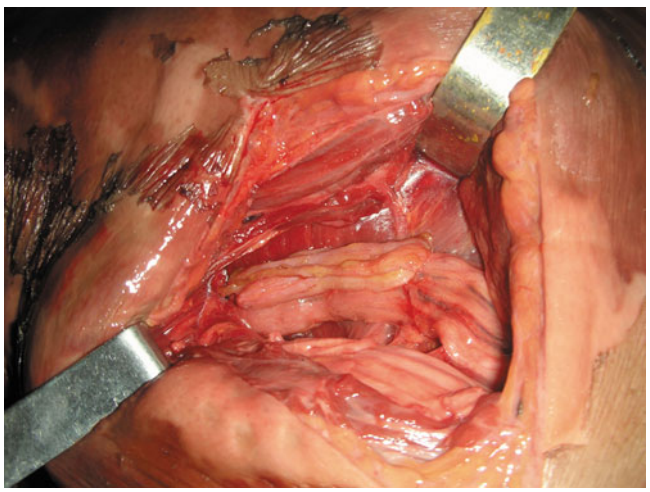

Fig. 4 A 6 cm nerve gap was reconstructed using nerve grafts 7 cm long, under microscope magnification

recorded. Then, a 6 cm portion of the sciatic nerve was resected; and, employing a surgical microscope and microsurgical techniques, this portion of the nerve was reconstructed in the classical manner [21, 22] with nerve grafts 7 cm long (Fig. 4). Statistical analysis included calculation of mean values and standard deviations.

Results

Anatomy of the Sciatic Nerve and Gluteus Maximus Muscle

Together, the nerve roots L4, L5, S1, S2 and S3 form the biggest nerve in the human body – the sciatic nerve – inside the pelvis. Its width is approximately the diameter of the fifth finger. It exits the pelvis through the greater sciatic foramen, and passes beneath the piriformis muscle, deep to the gluteus maximus and superficial to the external rotators of the hip (from superior to inferior: gemellus superior, obturator internus, gemellus inferior, obturator externus and quadratus femoris). The nerve has two main components, internal and external, which generally divide at the popliteal fossa, but can become separate as high as at the sciatic notch. The sciatic nerve transverses the space between the greater trochanter externally and the ischial tuberosity internally (these are important cutaneous landmarks in proximal sciatic surgery) to enter the posterior aspect of the thigh between the medial and lateral hamstring muscles.

The gluteus maximus muscle arises from the iliac crest and the sacrum, and inserts into the gluteal tuberosity of the femur. It is a powerful extensor of the thigh, and is essential for standing. It is innervated by the inferior gluteal nerve, a branch of the sacral plexus which enters the gluteus maximus muscle on its deep and medial surface, after passing below the piriformis muscle, 5 cm medial to the insertion of the muscle to the femur. The direction of the fibers is oblique, downward and lateral, in the direction of the greater trochanter [23–28, 35].

Numerical Data Obtained from Cadaveric Dissections

The data collected for each specimen are summarized in Table 1. The maximum length of exposure achieved was 152 mm and the minimum exposure 90 mm. The mean exposure of the sciatic nerve accessible with the transgluteal approach was 115.4 ± 17.9 mm. There was a slight difference in this mean value, when comparing right and left side, with

Table 1 Length of exposed nerve on both sides in ten fresh cadaveric dissections

Specimen #	1	2	3	4	5	6	7	8	9	10
Length of exposed nerve, right side (mm)	114	110	90	125	121	152	136	115	108	129
Length of exposed nerve, left side (mm)	90	103	92	105	125	114	152	121	99	131

the mean exposure length on the right side being 120.0 ± 16.9 mm, vs. 110.7 ± 18.4 mm on the left. With all ten specimens and on both sides, it was possible to reconstruct the 60 mm gap with a 70 mm graft under the microscope, employing 10.0 nylon sutures and microsurgical instruments.

Discussion

At present, literature describing surgical procedures for the management of proximal traumatic or tumoral lesions of the sciatic nerve in which sectioning of the gluteus maximus muscle is avoided, are scarce. This is not the case for compressive lesions (the so-called *piriformis syndrome* [29–32, 34]), wherein the nerve can be released via a small incision and splitting the muscle [20, 34]. It is a well known principle in peripheral nerve surgery that wide exposures assure a normal nerve both proximal and distal to the lesion, thereby allowing reconstruction. This may be the reason why complete sectioning of the gluteus muscle is so widely accepted.

Still, extensive sectioning of the gluteus is not inconsequential; and, even though the procedure generally causes no direct functional deficit, its morbidity is not deniable. The long incision, the extensive sectioning of fascia, and the muscle detachment from the femur make for prolonged postoperative rehabilitation. In addition, the risk of muscle suture rupture exists, potentially leading to the eventual need for further reparative surgery. Another non-minor morbidity of gluteus maximus sectioning is aesthetic: the scar formation is much thicker, deeper and more adherent to the skin and fat tissue. This is a well known fact among plastic surgeons, who avoid muscle division in gluteoplasty and many other procedures conducted in the gluteus region [33].

One possible criticism that could be made relating to the present study is that, even though measurement of nerve exposure was obtained, the acceptable degrees of exposure we observed should not be taken as definitive evidence that complex reconstruction can be done, because other elements should be taken into account, like the depth of the surgical field, interference of the split muscle fibers with microsurgical manoeuvres, the capacity for the surgeon to use a surgical microscope in the field, etc. This was the reason we decided to create a cadaver model and attempt reconstruction using a 6 cm nerve graft. In one of the biggest series of traumatic sciatic nerve lesions reconstructed with grafts, the reconstructions averaged 6–10 cm in length [12].

The employment of fresh cadavers also was an essential point of the present study. We chose to use fresh tissues because formalin-preserved tissues are much tougher, a fact that partially impedes retraction and elongation of muscle fibers and undoubtedly would alter results. With the transgluteal approach, retraction should be maximized to enhance exposure of the nerve.

The main finding of this study was that using a transgluteal approach, the accessed exposure of the sciatic nerve is at least 9 cm, can be as much as 15 cm, and averages just over 115 mm. These data are new in the literature and demonstrate that, when operating on a sciatic nerve lesion complete detachment of the gluteus maximus muscle may be preventable. It is a well known fact that a patient's return to normal daily activities occurs more quickly, that patients experience less postoperative pain, and that the rehabilitation period is abbreviated when a muscle is split, instead of sectioned, during surgery. The importance of this distinction is maximized when a decision is being made regarding the approach to use with a muscle that is as large and powerful as the gluteus maximus, which has enormous importance in most daily activities, because of its extreme contribution to stability and power during standing and walking.

Of course, in extensive lesions of the sciatic nerve, this approach can be insufficient and wider exposure may be needed. On the other hand, using modern imaging techniques, the precise location and extent of the lesion is known pre-operatively in the many traumatic and tumor-related sciatic nerve cases, so that surgeons can target their approach to optimize exposure even prior to stepping into the operating theatre.

In our anatomic dissections, it was clear that the more proximal portion of the sciatic nerve, as well as the piriformis muscle and the sciatic notch, virtually always is exposed with the transgluteal approach. Therefore, our approach's main limitation, relative to the classical procedure, relates to distal rather than proximal access. Nevertheless, if during a transgluteal procedure, the surgeon comes to recognize that the lesion is more extensive than what was anticipated initially, the skin incision can be continued distally towards the thigh, and complete detachment of the gluteus muscle easily performed, exposing more distal portions of the sciatic nerve (Fig. 5). As well, in contrast to what has been espoused in the work by Patil and Friedman [20], we prefer to make our skin incision transverse to the main axis of the body, not parallel to the nerve, for several reasons (1) the perpendicular incision yields a better aesthetic result, since

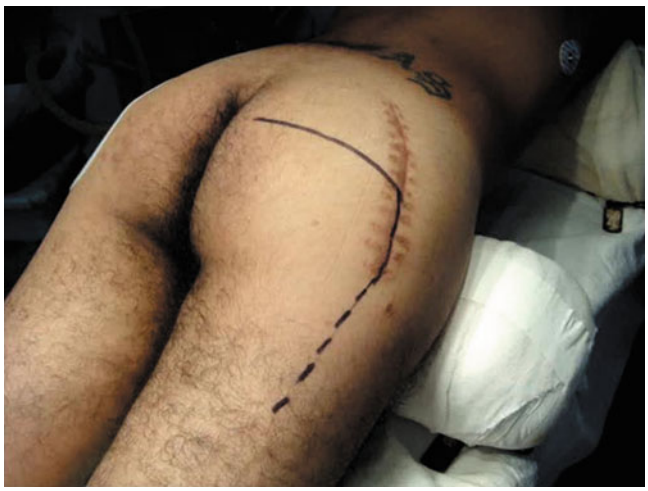

Fig. 5 Photograph taken from a real patient before surgery. Transgluteal approach to a iatrogenic sciatic nerve lesion. The transverse incision (*full line*) was originally planned, but if during surgery a longer injury is found, the transgluteal approach can be converted into a wider exposure by distal extension (*dotted line*). More distal sciatic nerve exposure is obtained by entire section of the gluteus maximus muscle near its insertion in the greater trochanter

the scar is easier to hide under clothes; (2) nerve exposure is not sacrificed; and (3) the incision can be extended distally to explore the sciatic nerve in the thigh, when needed. Utilizing an incision that is almost perpendicular to the gluteus maximus fibers does not interfere with exposure, because buttock tissues, in particular skin and fat, are soft and highly elastic.

One of the main limitations we have observed employing the transgluteal approach to repair the sciatic nerve is that the surgical field is somewhat deeper and narrower than when a complete section of the gluteus maximus muscle is performed. At the extremes of nerve exposure, some work is done near and partially under the gluteus maximus fibers. For this same reason, both exposed extremes of the nerve cannot be visualized simultaneously, and the assistant must move from one side to the other during the procedure. This obviously is less comfortable for the surgeon; but, as we have demonstrated, this fact does not interfere with graft reconstruction using microsurgical techniques. If such a complex surgery can be completed successfully via the transgluteal approach, procedures that are less technically demanding, like neurolysis, should be even easier. It also should be underlined that the present report merely describes an anatomical study performed in cadavers, so that specific surgical considerations are necessary when translating this procedure into use in live patients. For instance, special care should be taken to avoid damaging vessels that transverse the muscle, as they could retract into the pelvis and cause an intrapelvic haematoma [12, 16, 20].

Case Presentation

Over the period between June 2005 and June 2008, a total of 13 transgluteal procedures were performed in our department to expose proximal lesions of the sciatic nerve. Given the fact that this paper is an anatomic study, we will augment our discussion with a short presentation of three cases. In the future, the whole series will be presented as a separate article.

Case #1

A 5-year old boy received an intramuscular injection of penicillin in his right buttock, during which he suffered immediate, intense pain that radiated into his thigh and leg. Shortly thereafter, he developed mild paresis of the leg and foot, while his pain persisted. Six months after the episode, he was evaluated by a peripheral nerve surgeon (MS), who deemed that exploration of the nerve was indicated due to persistence of both motor and sensory signs. MRI studies were normal, so that a transgluteal procedure was employed. This approach provided exposure that was extensive enough to perform neurolysis under the microscope, as the nerve was found to be adherent to extensive fibrosis. After surgery, the boy's pain disappeared and his motor function gradually returned. One year after surgery, at final evaluation, the patient had no pain and his paresis had disappeared (Fig. 6).

Case #2

A 24-year old woman suffered a shotgun injury that traversed her pelvis from one side to the other and required an urgent laparotomy and bladder repair. Once recovered from that emergency, she started to complain of severe burning pain in her left leg and foot, and was noted to exhibit moderate paresis in the same distribution. Given the bullet trajectory and her symptoms, the left sciatic nerve was presumed to be directly affected. After failed conservative treatment, a decision for operative exploration was made. As in the previous case, a transgluteal approach allowed for wide exposure, and adherent scar tissue between the sciatic nerve and the traversed sciatic notch was relieved via neurolysis. The patient's postoperative course was uneventful and her pain resolved immediately. Motor weakness improved gradually, so that she was able to return to her previous occupation as a police agent 6 months postoperatively (Fig. 7).

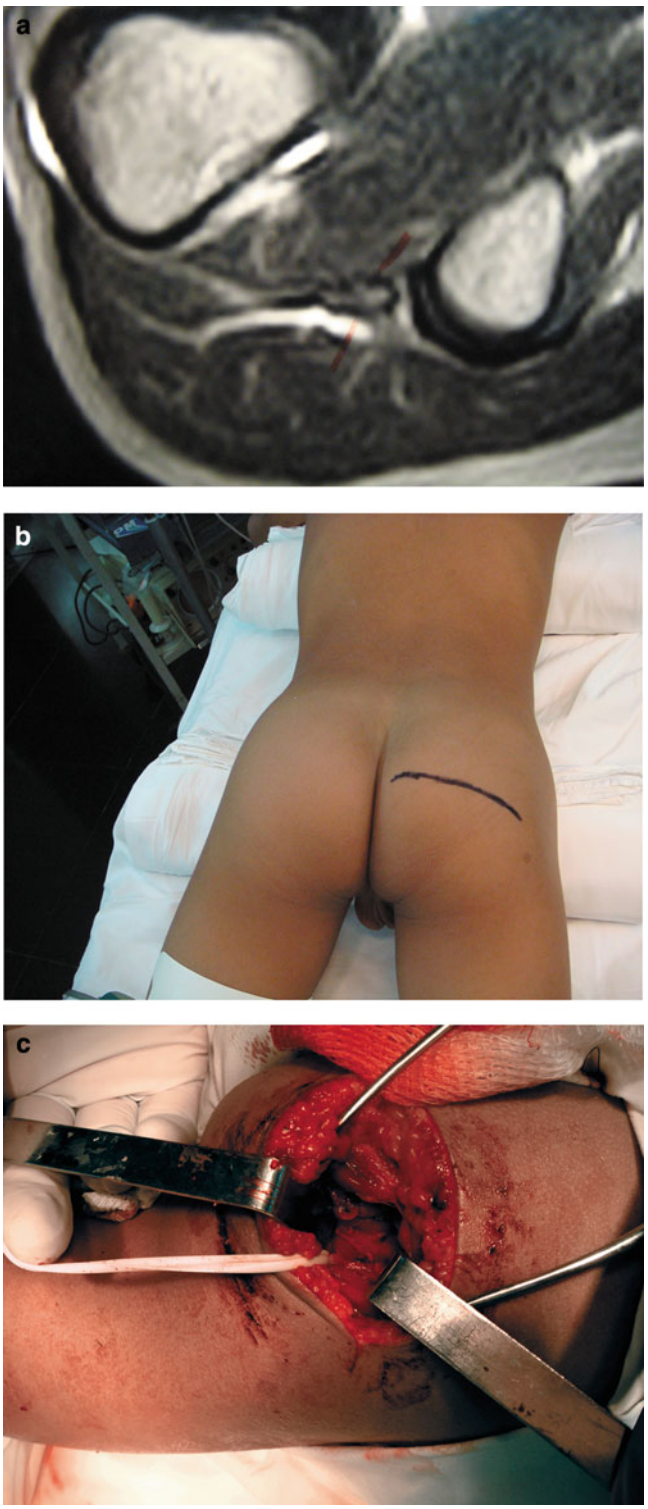

Fig. 6 (**a**) Skin incision for sciatic nerve exposure. (**b**) Contrast-enhanced MRI showed a fibrotic lesion surrounding the nerve (see *mark*). (**c**) Transgluteal approach successfully allowed to perform a neurolysis of the nerve under microscope

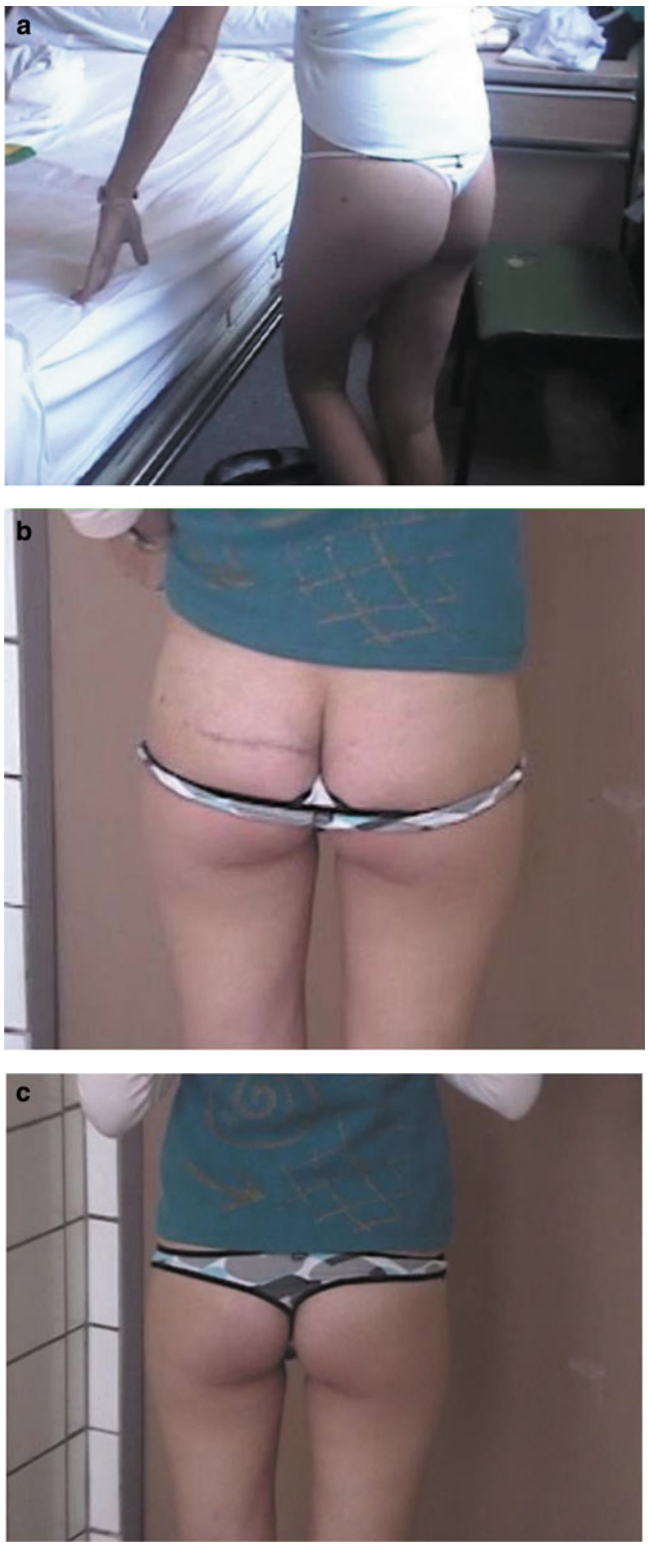

Fig. 7 (**a**) The skin mark in the left upper buttock is the entrance mark of the bullet. (**b**) The cosmetic result of the transgluteal approach is excellent in this young woman: no dense scar formation and no change in the gluteus region shape related to muscle section was observed. The transverse scar is easily hidden under the clothes

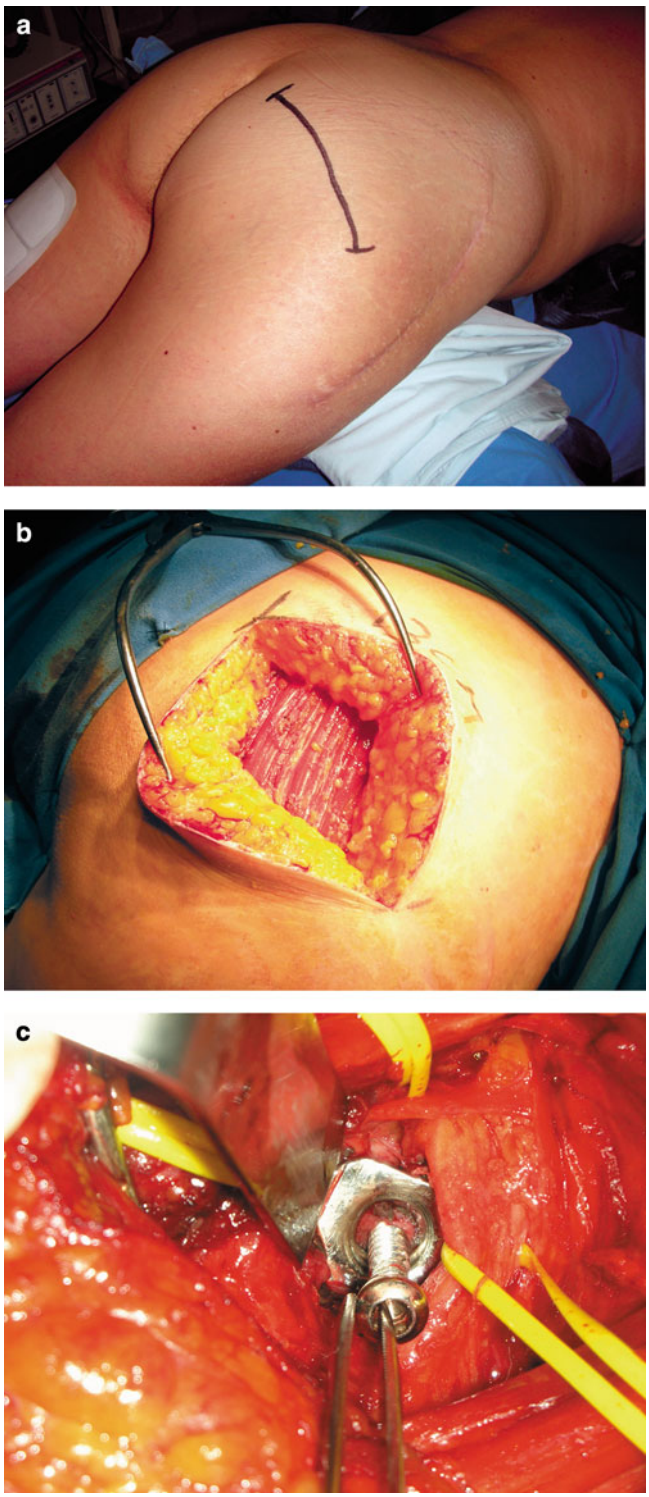

Fig. 8 (**a**) Skin incision for a transgluteal approach to explore a sciatic nerve injury after hip surgery. (**b**) The gluteus maximus fibbers before splitting. Extensive subcutaneous dissection allows to a better exposure of the nerve. (**c**) Metallic prosthetic material perforated the nerve, and was extracted before nerve reconstruction

Case #3

A 58-year old woman with congenital hip dysplasia underwent her third total hip replacement. Even though the surgeons failed to detect any unanticipated abnormalities or complications intra-operatively, except for extensive fibrosis secondary to the patient's previous procedures, she developed complete palsy and anaesthesia of the leg below the knee following surgery. Conservative treatment and subsequent electromyelograms revealed no improvement, so that a decision to explore the nerve was made 8 months after hip replacement. The transgluteal approach was used for exploration, during which part of a plate and two screws were found to be impinging upon the nerve. All external material was withdrawn. Unfortunately, the patient did not recover any motor function, but sensation on the sole of her foot reappeared approximately 18 months after surgery (Fig. 8).

Conclusion

The transgluteal approach is a useful means by which to operate upon lesions involving the proximal sciatic nerve. The technique is less invasive than classical complete sectioning of the gluteus maximus muscle, and yields better aesthetic results and a faster return to normal daily activities. Complex lesions, like those associated with nerve trauma requiring grafts and tumours, can be treated with less risk. If, after the transgluteal approach has been utilized, the lesion is found intraoperatively to be more extensive than what initially was anticipated, improved exposure can be obtained by extending the skin incision and sectioning the gluteus maximus muscle. On the other hand, the approach tends to be less comfortable for the surgeon, and the entire extent of the exposed nerve cannot be visualized simultaneously during surgery.

Conflict of interest statement We declare that we have no conflict of interest.

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Experimental and Clinical Employment of End-to-Side Coaptation: Our Experience

P. Tos, S. Geuna, I. Papalia, L.G. Conforti, S. Artiaco, and B. Battiston

Abstract The last 15 years have seen a growing interest regarding a technique for nerve repair named end-to-side coaptation. Since 2000, we have carried out experimental studies on end-to-side nerve repair as well as employed this technique to a series of selected clinical cases. Here we report on the results of this experience.

For experimental studies, we have used the model represented by median nerve repair by end-to-side coaptation either on the ulnar (agonistic) or the radial (antagonistic) nerve. For time course assessment of median nerve functional recovery we used the grasping test, a test which permits to assess voluntary control of muscle function. Repaired nerves were processed for resin embedding to allow nerve fibre stereology and electron microscopy. Results showed that, in either experimental group, end-to-side-repaired median nerves were repopulated by axons regenerating from ulnar and radial donor nerves, respectively. Moreover, contrary to previously published data, our results showed that voluntary motor control of the muscles innervated by the median nerve was progressively recovered also when the antagonistic radial nerve was the donor nerve.

As regards our clinical experience, results were not so positive. We have treated by end-to-side coaptation patients with both sensory ($n = 7$, collateral digital nerves) and mixed ($n = 8$, plexus level) nerve lesions. Results were good, as in other series, in sensory nerves whilst they were very difficult to investigate in mixed nerves at the plexus level.

Take together, these results suggest that clinical employment of end-to-side coaptation should still be considered at the moment as the *ultima ratio* in cases in which no other repair technique can be attempted. Yet, it is clear that more basic research is needed to explain the reasons for the different results between laboratory animal and humans and, especially, to find out how to ameliorate the outcome of end-to-side nerve repair by adequate treatment and rehabilitation.

Keywords Axon regeneration · Functional recovery · Peripheral nerve reconstruction · Termino-lateral suture

Introduction

Nerve repair by end-to-side coaptation has a long history and the first works referring to this technique were published in the second part of the nineteenth century [1, 2]. The basic concept of end-to-side nerve repair is simple: obtaining nerve fiber regeneration along the distal stump of a transected nerve by inducing collateral axonal sprouting from a neighbour healthy donor nerve.

A large body of literature has accumulated over the last 15 years showing that axon regeneration occurs after end-to-side repair and that regenerated nerve fibers are able to successfully innervate the denervated periphery and recover the lost function. Whereas most authors now accept that repopulation of the distal stump of a severely damaged nerve through end-to-side neurorrhaphy is possible, the question as to how axons can function when they are connected contemporarily to two different peripheries is still unanswered.

Empirical evidence has shown that the newly generated axons are able, after having reinnervated the periphery of the severed nerve, to lead to a variable degree of functional recovery [3–9]. However, clinical application of end-to-side coaptation have provided conflicting results so far [10–19]. In this review we will outline our experimental

P. Tos (✉), L.G. Conforti, S. Artiaco, and B. Battiston
Department of Reconstructive Microsurgery, Orthopaedic and Trauma Center – CTO, Via Zuretti 29, Torino, Italy
e-mail: pierluigi.tos@unito.it

S. Geuna
Dipartimento di Scienze Cliniche e Biologiche, Università di Torino, Torino, Italy

I. Papalia
Dipartimento delle Specialità Chirurgiche, Università di Messina, Messina, Italy

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and clinical results on the application of end-to-side nerve reconstruction.

Materials and Methods

Experimental

Our experimental studies were performed on Wistar adult female rats, employing the forelimb experimental model (median nerve) that has been proven to be superior to the hindlimb model for nerve repair studies [20–22]. Median nerve was used as receiving nerve in all experiments. The donor nerve was either the agonistic ulnar nerve or the antagonistic radial nerve. The median and ulnar nerves of the left upper limb were approached from the pectoral region. A 10-mm-long segment of the median nerve was dissected at a level corresponding to the mid of the humerus, and the proximal nerve stump was sutured to the pectoral muscle. A small window was then made on the epineurium of the ulnar nerve or radial nerve trying to avoid to damage the nerve fibers below. Finally the distal stump of the transected median nerve was approached to the epineurial window and then sutured to the ulnar or radial donor nerve.

Functional assessment of median nerve recovery was made by means of the grasping test modified by Papalia et al. [21]. This test allows obtaining an assessment of the flexion of the fingers by measuring the strength of the m. *flexor digitorum sublimis* and m. *flexor digitorum profundus* that produce this movement. Since these muscles are innervated by the median nerve, the grasping test can be considered as a tool for the assessment of the voluntary control of muscle function innervated from the median nerve.

From each animal, the nerve segment where the end-to-side coaptation was performed was withdrawn. The specimens were fixed in 2.5% glutaraldehyde, postfixed in 2% osmium tetroxide, dehydrated and embedded in resin for high resolution microscopic imaging and stereology. In each nerve, the morpho-quantitative assessment of myelinated nerve fibers was conducted using a DM4000B microscope equipped with a DFC320 digital camera and an IM50 image manager system (Leica Microsystems, Wetzlar, Germany). The 2D dissector stereological method was employed as described earlier [3]. Statistical analysis was performed using the one-way repeated measures analysis of variance (RM-ANOVA) test using the software "Statistica per discipline bio-mediche" (McGraw-Hill, Milano, Italia).

Clinical – Sensory Nerves

From 2002 and 2006, in the Department of Orthopaedics and Traumatology of the CTO-Maria Adelaide Hospital of Turin, we performed end-to-side nerve sutures for lesions of the digital collateral nerve in seven patients. The patient group (Table 1) included four men and three women, with a mean age of 42 (range 20–62). Two of the nerve lesions were localized in the digital collateral nerve of the thumb, and five of the digital collateral nerves were of the long fingers. The level of nerve lesion was in four cases the A1 pulley (1 thumb – 3 long fingers), in two cases the F2 of the long finger and in one case the IF thumb.

Four patients had come under our observation for treatment of iatrogenic nerve lesions occurring after flexor tenolysis for the trigger digit. In the other three cases, the nerve damage was caused by a more complex wound with substantial tissue loss. In the four patients with iatrogenic damage the operation was performed 2–10 months after nerve lesion. Two patients with traumatic lesions underwent an emergency intervention. In a third case, end-to-side neurorrhaphy was carried out at our Orthopaedic Center 6 months after the previously untreated nerve lesion.

The choice of primary reconstruction with end-to-side nerve suture was justified for three cases with traumatic lesion because of the loss of nerve substance, and in two cases of iatrogenic lesion after the failure of the tubulisation treatment. In the other two cases of iatrogenic lesion, the nerve reconstruction method was discussed with the patient and chosen as alternative to other available techniques (biological or synthetic tubulization, nerve autograft). From a technical point of view the method applied to repair

Table 1 Summary of clinical cases for collateral digital nerve by end-to-side coaptation

Patient	Age	Nerve lesion	Time to repair	Follow-up months	Previous surgery	2pd mm	Result
# 1	48	COLL THUMB	4	24	NEUROTUBE©	12	S3+
#2	28	COLL DIGIT IV	EMERG	16		15	S3+
#3	39	COLL DIGIT II	6	12		12	S3+
# 4	20	COLL DIGIT III	EMERG	24		14	S3+
# 5	49	COLL DIGIT III	10	8	NEUROLAC©	8	S3+
# 6	62	COLL DIGIT III	2	14		14	S3+
# 7	48	COLL THUMB	6	16		15	S3+

the nerve suture was the one described by Mennen [16]. After identification and preparation of the donor nerve and the distal branch of the injured nerve, an epineural window in the donor nerve was created before performing end-to-side suture with the help of magnifying instruments.

Recovery was assessed by two-point discrimination test and the sensitivity recovery test was based on the Highet British Medical Research Council scale, as modified by Mackinnon and Dellon [23].

Clinical – Brachial Plexus

Between 2001 and 2005 we have operated on 11 patients with end-to-side neurorraphy at the plexus level for traumatic lesions. Ten males and one female with a mean age of 30 years (range 16–55). End-to-side neurorrhaphy was performed as described by Mennen [16]. In every case, the choice to operate has always been the *ultima ratio*, when no other methods were possible. In every case, some neurotization procedures were associated thus making assessment of results difficult.

As donor nerve we employed: the phrenic nerve (8 cases, 4 of which with interpositional nerve graft), the hypoglossal nerve (1 case), the C5 nerve (1 case), and the C7 nerve (1 case). As recipient nerve we employed: the sovrascapular nerve (3 cases), the axillary nerve (2 cases), the primary middle trunk (1 case), the primary superior trunk (1 case), the secondary lateral trunk (1 case), the secondary posterior trunk (1 case), the secondary posterior trunk and secondary medial trunk (1 case), the C6 nerve (1 case).

Recovery was assessed by means of the British Medical Research Council scale at the shoulder and elbow level.

Results

Experimental

Histological analysis of repaired median nerves showed that nerve fibre regeneration along the repaired median nerve occurred in all operated animals irrespective of the donor nerve used. Stereological assessment showed that in both experimental groups, regenerated nerves had significantly ($p<0.05$) higher mean density and total number of myelinated axons as well as significantly ($p<0.05$) lower mean fiber and axon diameter and myelin thickness. Functional assessment of nerve recovery by means of the grasping test showed that voluntary motor control of the *flexor digitorum* muscles innervated by the median nerve recovered in all operated animals. The occurrence of partial recovery, also when an antagonistic nerve was used as the donor nerve, is in disagreement with the results obtained by Lutz et al. [15] although it should be noted that when the median nerve was repaired on the antagonistic radial nerve, functional recovery was delayed in comparison to reconstruction on the agonistic ulnar nerve.

Clinical – Sensory Nerves

The average follow-up period was 14 months (range 6–24 months). The results were considered stable 2 years after the intervention. An S3+ sensitive recovery was observed in all our patients (Table 1). The average distance of the two-point discrimination test, 2pd, was 12.5 mm (range 8–15 mm). No functional deficits of the donor nerve were found in any patient. One of our patients underwent a second treatment 14 months after the first reconstructive operation in order to treat a chronic neuroma of the proximal stump of the collateral injured nerve. In this case, after removal of the neuroma, we re-examined the end-to-side nerve suture which showed normal morphology of nerve branches at the neurorrhaphy level.

Clinical – Brachial Plexus

We managed to carry out a follow-up of minimum 2 years in eight patients. Motor function for the shoulder was M4 in 2 cases, M3 in 4 cases, M2 in 1 case and M1 in 1 case. For the elbow M4 in 2 cases, M3 in 1 case, M1 in 1 case and M0 in 4 cases. However, it should be pointed out that in seven out of these eight patients, clinical outcome was not attributable to end-to-side coaptation only; other neurotisations were concomitantly carried out. In the only patient who received end-to-side coaptation of suprascapular nerve on the hypoglossal nerve without any additional neurotisation, satisfactory recovery (M3) of active abduction of the shoulder was observed.

Conclusion

Experimental investigation of end-to-side coaptation showed that, in the rat, transected median nerve can be repaired using both the agonistic ulnar nerve and the antagonistic radial nerve. In all cases, end-to-side neurorrhaphy not only leads to axonal regeneration but also permits the partial restoration of voluntary control of the motor function lost after nerve

damage [9, 24]. Unfortunately, reports on the clinical application of end-to-side coaptation published so far did not show the same positive results observed in laboratory animals [10–19]. Yet, the number of patients treated is still limited making it difficult to draw conclusions about the clinical efficacy of this technique. Regarding digital nerves, although Mennen [16] reported that results of end-to-side nerve sutures are unpredictable, results of our clinical experience and analysis of the literature support the view that this technique is efficient for distal sensory re-innervation. For the repair of digital sensory nerve defects superior to 3–4 cm, the end-to-side suture technique may avoid the donor site morbidity required for autograft repair. In addition, end-to-side nerve suture may be considered a good therapeutic option in the case of a failed previous repair by means of another method.

Regarding brachial plexus, the case series reported in the literature showed favourable results in most patients reported by Mennen (62%) [16] and Haninec et al. (64%) [13] while negative results were reported by Pienaar et al. [25]. In our case series, clinical results were favourable especially in case of functional recovery of shoulder abduction.

While our case series is homogeneous regarding donor nerve selection (the phrenic nerve in 8 cases out of 11), the use of associated neurotization procedures using the spinal accessory nerve, the concomitant employment of end-to-side coaptation and neurotization may discriminate the real effectiveness of end-to-side neurorrhaphy and make function recovery very difficult. However, in at least one patient end-to-side coaptation of suprascapular nerve on the hypoglossal nerve without additional neurotisation led to satisfactory recovery of active abduction of the shoulder.

In conclusion, our experimental results suggest that end-to-side coaptation is successful in repairing transected peripheral nerves and that, contrary to what has widely been believed until now, recovery of voluntary motor function in the rat can also be expected when an antagonistic nerve is used as the donor nerve. While these results open promising perspectives for the employment of end-to-side nerve repair in human patients, the clinical results obtained so far support the view that end-to-side coaptation should still be limited at the moment, as the *ultima ratio*, to selected situations in which routine surgical nerve reconstruction techniques do not offer another solution; it will give an amount of "extra sprouting" without detectable loss of function. Yet, it is clear that more basic research is needed to explain the reasons for the different results between laboratory animal and humans and, especially, to find out how to ameliorate the outcome of end-to-side nerve repair by adequate treatment and rehabilitation.

Conflict of interest statement We declare that we have no conflict of interest.

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Considerations on the Treatment of Anterior Interosseous Nerve Syndrome

A. Alexandre, A.M. Alexandre, and A. Zalaffi

Summary Anterior interosseous syndrome (Kiloh–Nevin syndrome) refers to that constellation of signs and symptoms referable to weakness of the pronator quadratus, the flexor pollicis longus, and the flexor digitorum profundus to the index finger.

We present our series of 9 patients, affected by AIN Syndrome, and a group of 4 patients affected by pseudo–AIN neuropathies.

In the literature there is considerable controversy concerning the treatment, but we agree that understanding of anatomical variants of innervation combined with a thorough physical examination can provide important clues as to where pathology resides. Proper treatment needs a precise and accurate diagnosis; in fact medical treatment which we present is effective for nerve dysfunction and may avoid surgery, but surgical exploration is mandatory when EMG is suggestive of a severe lesion, and localizes the specific site on anterior interosseous nerve entrapment.

Keywords Anterior interosseous nerve entrapment · Anterior interosseous neuropathy · Anterior interosseous syndrome · Kiloh–Nevin syndrome · Median nerve

Introduction

Anterior interosseous syndrome refers to that constellation of signs and symptoms referable to weakness of the pronator quadratus, the flexor pollicis longus, and the flexor digitorum profundus to the index finger. Although the anterior interosseous nerve (AIN) supplies sensory fibers to the radiocarpal, midcarpal, and carpometacarpal joints, AIN syndrome by definition refers to a purely motor constellation of symptoms which compone the peculiar triad of findings of the Kiloh–Nevin [1] syndrome. These authors clearly described the anatomic explanation for the triad, and identified an isolated neuritis of the anterior interosseous nerve (AIN) as one potential cause. For this clinical situation Tinel [2] had offered the original description as a characteristic pattern of weakness of median innervated muscles, referring to it as a "dissociated paralysis of the median nerve."

The classic description of an acute brachial neuritis by Parsonage and Turner [3] in 1948 included weakness of the shoulder girdle. It is thereby impossible for this to have represented a neuropathy of the AIN.

In several other reports this constellation of findings mixes with weakness of muscles of the shoulder girdle, in association with supracondylar humeral fractures [4, 5], forearm fractures [6–8], an anomalous median artery [9], thrombophlebitis [10] and antecubital vein catheterization or phlebotomy [11] the use of a lateral epicondylitis forearm band [12].

We can thereby argue, as pointed out by Chin and Meals [13] that AIN syndrome refers not to a single pathologic entity, but to a common clinical manifestation of several different pathologies, which may or may not affect the AIN itself.

Although the syndrome is strictly motor, it may be associated with additional extrasyndromic signs which may suggest either that the underlying pathology resides outside of the AIN itself (median nerve or brachial plexus) or that aberrant anatomic features exist distal to the pathologic lesion in the AIN.

The causes of AIN syndrome are divided into two categories: compression neuropathies, neuritides, congenital anomalies, and anatomic lesions and discontinuities of the AIN itself, on one side, and pathologies affecting more proximal anatomic sites, but involving nerve fascicles destinated to the anterior interosseous nerve more distally

A. Alexandre (✉)
European Neurosurgical Institute (EU.N.I.), Via Ghirada 2, 31100, Treviso, Italy
e-mail: alexandre@eunionline.com

A.M. Alexandre
Department of Bioimaging and Radiological Sciences, Catholic University of Sacred Heart. Policlinico "A.Gemelli", Rome, Italy

A. Zalaffi
Neurosurgical Department, University of Siena, Siena, Italy

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(Pseudo–anterior interosseous neuropathies) [14] on the other side. A classic example of the pseudo–anterior interosseous neuropathies [3] is Parsonage–Turner syndrome, in which AIN syndrome is associated with weakness of the parascapular muscles.

Anatomy

Emerging from the two heads of the pronator teres muscle, the median nerve gives rise to the AIN from its radial aspect. The origin of AIN from the median nerve occurs 5–8 cm distal to the lateral epicondyle [15] and 22.4–23.4 cm proximal to the radial styloid [16, 17]. Coursing beneath the fibrous arch of the flexor digitorum superficialis muscle, the AIN enters the flexor digitorum profundis muscle belly an average of 1/3 the forearm length distal to the medial epicondyle [18]. The nerve then courses distally on the volar surface of the interosseous membrane.

Approximately 4 cm distal from its origin, the AIN gives rise to motor branches to the flexor pollicis longus, the flexor digitorum profundus to the index finger, and, variably, the flexor digitorum profundus to the middle finger [15]. It then supplies a motor branch to the pronator quadratus and terminates in sensory branches to the radiocarpal, midcarpal, and carpometacarpal joints.

Within the median nerve, at the level of the elbow, the motor fibers which will constitute the AIN lie posteriorly [19]. Sunderland described that fibers ultimately becoming the AIN form a distinct bundle within the median nerve 2.5 cm proximal to its macroscopic origin [20]. Spinner [21] has shown that this anatomic feature makes it possible for this fascicular component of the median nerve to sustain an isolated injury, giving rise to a clinical pattern mimicking an anterior interosseous neuropathy.

This is confirmed by the observations of Wertsch et al. [14], reporting median nerve compression at the antecubital fossa in cases of AIN syndrome associated with sensibility deficits, and by those of Hill et al. [22] reporting fibrous bands spanning from the deep head of the pronator teres to the brachialis fascia, as source of anatomic compression.

Spinner and Schrieber [5, 21] have identified at least eight anatomic features that seem to predispose an individual toward an anterior interosseous palsy.

Patients

The General Clinical presentation

Chin and Meals gave a clear and exhaustive description of the findings in true AIN syndrome [13], which by definition are paresis or paralysis of the pronator quadratus, the flexor pollicis longus, and the flexor digitorum of the index finger. Deterioration of handwriting has been described as a classic presentation in a series of patients with AIN syndrome [23].

Although there is no consistent history of onset of neuropathy, there are several different patterns of onset that provide important clues for determining etiology.

A history of trauma will obviously suggest either mechanical damage of the nerve, injury to the nerve, or compression neuropathy. The association between fractures of the supracondylar humerus [4, 5] and proximal forearm [6–8] have classic associations with anterior interosseous syndrome.

With anterior interosseous or pseudo–anterior interosseous neuritides, onset of neurologic symptoms is typically sudden and rapidly progressive. Patients often relate an antecedent prodrome of proximal volar forearm or shoulder pain, and these patients are generally suspected of exhibiting an inflammatory neuropathy.

AIN syndrome is suggested by the resting repose of the hand, which will exhibit an unnatural extension of the distal interphalangeal (DIP) joint of the index finger and interphalangeal (IP) joint of the thumb, compared with the gentle flexion arcade of the remaining fingers. The metacarpophalangeal joint of the thumb may compensate by assuming hyperflexion.

Weakness of the flexor pollicis longus and flexor digitorum profundus to the index finger is indicated by an inability to make the "OK" sign. Rather, the DIP joint of the index finger and the IP joint of the thumb are hyperextended during attempted tip-to-tip pinch.

The area of contact between the thumb and index finger is a flatter, broader area found more proximally. Attempting the "OK" sign, the affected hand will give the appearance of a *Playboy* bunny. The Spinner's sign [24] is that upon making a fist, the tips of the index finger and thumb remain conspicuously excluded.

Theoretically, contributions to resisted forearm pronation from the pronator quadratus and from the pronator teres are distinguishable. With the elbow bent at 90°, the patient is asked to forcibly pronate the forearm, against the resistance of the examiner. Flexion of the elbow at 90° delivers the pronator teres, which originates from the medial humerus, out of its optimal sarcomere length on the Starling length: tension curve, thus isolating contributions from the pronator quadratus distally. However, Stewart [25] finds this maneuver to be unreliable since weakness of pronation is due, to pronator teres involvement, indicative for "a lesion of the main trunk of the median nerve or an anatomic anomaly with the pronator teres being innervated by the AIN."

Abnormal sensibility in the median distribution in the presence of an anterior interosseous syndrome strongly suggests a proximal median compression neuropathy involving fascicles of the AIN.

Careful objective testing of the parascapular muscles can reveal subtle weakness of the shoulder girdle. Additional

testing to exclude Parsonage–Turner syndrome, acute brachial neuritides, or other proximal pseudo–anterior interosseous neuropathies is clinically prudent in any patient with anterior interosseous syndrome. Parsonage and Turner [3] were the first to describe anterior interosseous syndrome arising from a diffuse neuritis, presumably of anterior horn cells. In such cases, weakness of the deep flexors to the thumb and index finger is associated with varying degrees of weakness of the scapular muscles and usually is preceded or accompanied by pain [26].

On evaluating these patients one must keep in mind Martin–Gruber communications between the ulnar and median nerves in the proximal forearm, since they are present in approximately 15% of upper limbs [27]. Motor fibers targeted for typically ulnar-innervated muscles of the hand (most notably the adductor pollicis, abductor digiti quinti, and first dorsal interosseous [28], and the second and third dorsal interosseous muscles [24] may be carried temporarily in the median nerve. Therefore, when afflicted with either neuritis or compression neuropathy of the AIN, patients with a Martin–Gruber communicating branch may exhibit weakness or paralysis of these intrinsic muscles in addition to signature weakness of the flexor pollicis longus, pronator quadratus, and flexor digitorum profundus of the index finger. Sunderland observed that conversely, in the rare patient with ulnar innervation of the flexor digitorum profundus of the index finger, an anterior interosseous neuropathy may manifest as isolated weakness of thumb IP flexion and forearm pronation [20].

Specific Clinical Data of the Series

The series which is herein presented is made up of 9 patients, affected by AIN Syndrome, and a group of 4 patients affected by pseudo–AIN neuropathies.

All patients, studied and treated between 1998 and 2006, underwent EMG and CT/MRI investigation of the cervical spine.

AIN Syndrome

None of these cases came from acute open injury. Eight cases were classified as entrapment neuropathies Only the remaining patient had a history of possible blunt trauma, which was not anyway the precise and clear starting point of the dysfunction.

Presenting signs: all the 9 patients showed proximal volar forearm pain, and the Playboy Bunnie sign, while deterioration of handwriting was observed in 3 patients. Weakness or paralysis of typically ulnar-innervated muscles was present in the 2 patients bearing Martin–Gruber Communication.

Pseudo–AIN Neuropathies

Two out of these patients had a history of blunt trauma, one in a road accident, and the other on work accident.

Presenting signs: weakness of the scapular muscles, together with proximal volar forearm and shoulder pain was observed in all the 4 cases. Deterioration of handwriting was present in 1 patient, and Playboy Bunnie sign in three.

Electrodiagnostic Studies

Since the pronator teres is typically innervated by the median nerve, electromyographic testing of the pronator teres should logically distinguish anterior interosseous neuropathy from proximal compression of the median nerve affecting fascicles of the AIN.

Electromyographic studies may be quite helpful after a trauma, especially in case of blunt injuries.

Complete lesions are probably most amenable to immediate exploration, whereas surgical exploration of closed lesions may be deferred for some months.

The presence of positive sharp waves or fibrillation potentials indicate nerve degeneration and may provide an indication for surgical exploration.

As suggested by North and Kaul [15] we agree that any patient suspected of having AIN syndrome should receive electromyographic studies of the shoulder girdle to rule out neuralgic amyotrophy. Among patients manifesting signs and symptoms suggestive of anterior interosseous–like neuropathy, Parsonage–Turner syndrome is found with relatively high frequency.

Treatment

Treatment depends on recognition of the anatomic, inflammatory, infectious, post-traumatic, or compressive cause, and on the definition of the precise site of the lesion [14, 19, 24, 25, 29].

The treatment in our series was conservative by principle in all cases.

This medical treatment was performed once a week, and consisted in local injection of a mixture of antioxidants (Vitamine C) neurotrophic (Vitamine B) and vasoactive drugs (Naftidrofurile), and parenteric administration of Lipoic Acid and Vitamine E. In 5 out of the 9 Kiloh–Nevin syndrome patients, we went to open surgery with decompression of fibrous bands spanning from the deep head of the pronator teres to the brachialis fascia, since EMG had clearly identified the site of compression, and 6 weeks of conservative treatment did not offer significant results.

Pseudo–AIN neuropathies had significant (2 cases) or sufficient (2 cases) improvement by medical therapy and did not need further treatment.

Conclusions

In the literature there is considerable controversy concerning the treatment. Sunderland reported completely successful surgical treatments when fibrous bands constricting the AIN were found at operation. The resection of these bands, accompanied by anterior interosseous neurolysis resulted in motor recovery in every case [20].

Miller-Breslow et al. [30] reported nonoperative management in 10 patients with spontaneous AIN paralysis, with 80% success in 1 year. Spinner [24] treats spontaneous paralysis of the AIN nonsurgically initially but recommends surgical exploration within 12 weeks if no clinical or EMG improvement is evident. However, spontaneous recovery after 12 months is well-documented [30, 31] and some have considered waiting at least this long for spontaneous recovery before proceeding with surgical exploration.

This variety of observations and opinions may in large part be due to the broad range of pathologies resulting in a common triad of findings.

Understanding of anatomical variants of innervation combined with a thorough physical examination can provide important clues as to where pathology resides. Proper treatment is predicated on a precise and accurate diagnosis.

The medical treatment which we present is effective for nerve dysfunction and may avoid surgery, but surgical exploration is mandatory when EMG is suggestive of a severe lesion, and localizes the specific site on anterior interosseous nerve entrapment.

Disclosure of competing interest: no competing interests.

Conflict of interest statement We declare that we have no conflict of interest.

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Percutaneous Balloon Compression of the Gasserian Ganglion for the Treatment of Trigeminal Neuralgia: Personal Experience of 206 Patients

Marcos G. Baabor and Leonel Perez-Limonte

Abstract In a retrospective study of 206 patients diagnosed with trigeminal neuralgia (TN), we examined the results of percutaneous balloon compression (PBC) of the Gasserian ganglion performed by the same surgeon from September 1991 to November 2005. In these patients, 230 procedures were done. All patients had clinical follow-up for a minimum of 3 years while being evaluated for any recurrence of the symptoms. Initial pain relief was complete in 214 operated patients (93%) while in 16 operated patients (7%) it was not. From those, nine patients had another PBC performed immediately with eight of them becoming pain free while the remaining seven patients opted for medical treatment. From that last group, we found that six patients ended up experiencing resolution of their symptoms. In total, only 2 patients (1%) from the original 206 did not improve initially, while 99% had an excellent response. After a 3-year follow-up, only 35 patients (15%) had developed recurrent symptoms. In the majority of cases, the recurrence occurred between 2 and 3 year intervals (16 patients). There was no mortality. The low cost, low morbidity, low recurrence rate and high positive results make this procedure a valid option in the treatment of trigeminal neuralgia refractory to medical treatment.

Keywords Long-term follow-up · Percutaneous balloon compression · Trigeminal neuralgia

M.G. Baabor (✉)
Hospital Clinico Universidad de Chile, 11 de septiembre 1363, of 1502 Providencia, Santiago de Chile, Chile
e-mail: marcosbaabor@yahoo.com

L. Perez-Limonte
Department of Neurology, The Bonati Institute, 7315 Hudson Avenue, Hudson, FL 34667, USA
e-mail: llimonte@earthlink.net

Introduction

Trigeminal neuralgia (TN) is a painful, debilitating condition and the most common of facial neuralgias [1]. The International Association for the Study of Pain defines TN as sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve [2, 3]. The annual incidence of TN is 4–5 in 100,000 [4]. For the most part, medical treatment remains the mainstay in TN. A review of the literature identified 15 randomized controlled trials studying different medications [5]. From all of them, Carbamazepine (CBZ) [6–9] appeared to be the most effective with a 58–100% positive response rate. Other medications including oxacarbazepine [10], pimozide [11], gabapentin [12], baclofen, lamotrigine [13] and tizanidine [14] are felt to be somewhat effective as well. However, there is a group of patients whose symptoms are refractory to medical treatment and surgery remains the only viable alternative for treatment [15]. The following experience reflects our efforts trying to find the most minimally invasive, cost effective and safest technique while maintaining a high yield of positive results and low long-term recurrence. The technique becomes even more attractive because of the possibility of being performed in poor countries, in small rural hospitals and in ambulatory centers.

Materials and Methods

We performed a retrospective study of 206 patients from 1991 to 2005 that were suffering from TN refractory to medical treatment and/or who had failed prior to surgical intervention. All patients had undergone PBC of the gasserian ganglion by the same surgeon and had a minimum clinical follow-up of 3 years. Patients were only included in the study if they fulfilled the following criteria (1) A diagnosis of TN affecting any branch of the trigeminal

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Table 1 Premorbid conditions

Intolerance to Carbamazepine	70
Intolerance to Gabapentine	5
Hypertension	39
Diabetes mellitus	19
TMJ	9
CPA tumor	5
Multiple sclerosis	2
SUNCT	1
Prior surgery or other procedures	66

nerve which was refractory to medical treatment. (2) Recurrent TN after previous surgical intervention. (3) Patients with Classic TN although some cases of Secondary TN were selectively included (Table 1). Patients were excluded from the study if (1) They presented with severe sensory deficits along the trigeminal nerve distribution. (2) Had medical contraindications for general anesthesia. (3) Were pregnant. (4) Had any evidence of infection. The surgical technique performed was originally described by Mullan [16]. The procedure was performed under general anesthesia with intratracheal intubation. The air space of a No. 4 Fogarty catheter was filled with radiographic contrast to check the patency of the balloon. The catheter was inserted into the needle to a point marked on the shaft, indicating that the tip of the needle had been reached. Lateral views of the skull were obtained with a portable fluoroscopy unit. The entry point on the cheek was 2.5 cm lateral to the corner of the mouth and 0.5 cm upwards. A 14-gauge canula was used to enter the foramen ovale; there was no penetration of the intracranial space beyond the foramen ovale. A Kitchner wire was introduced to open the dura. Then, a No. 4 Fogarty balloon catheter was inserted through the canula until 17 mm of the catheter rested beyond the needle tip. The balloon catheter was inflated by slowly injecting 0.5–1.0 ml of contrast using a 1 ml syringe. The placement of the balloon was checked and immediately corrected if necessary. The duration of compression was between 1.3 and 3 min depending on the shape and volume of the inflated balloon with the surgeon attempting to obtain a pear shaped appearance of the balloon with 0.60 cc [17, 18] (Fig. 1).The catheter and canula were removed and the cheek was compressed for a few minutes. The patients were usually discharged after 24 h.

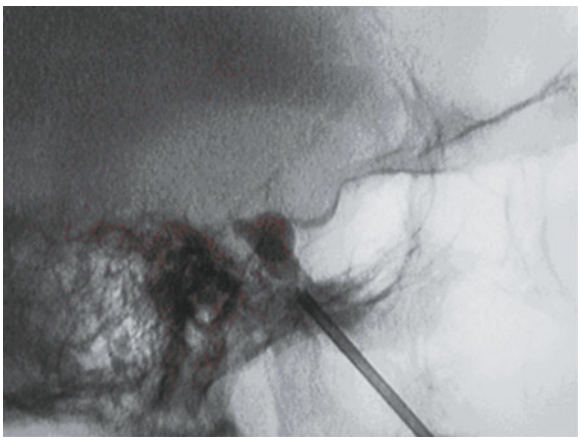

Fig. 1 Pear-shaped balloon in situ

Table 2 Distribution by age and sex

Age group	Women	Men	Total
0–19	0	0	0
20–29	0	1	1
30–39	5	2	7
40–49	19	14	33
50–59	32	18	50
60–69	44	21	67
70–79	28	18	46
80+	2	0	2
Total	*132*	*74*	*206*

Table 3 Distribution by branch and side

Branch	Right	Left	Total
I	4	1	5
II	15	10	25
III	17	8	25
I, II	21	10	31
II, III	53	24	77
I, II	0	0	0
I, II, III	28	15	43
Total	*138 (67%)*	*68 (33%)*	*206*

Table 4 Previous failed procedures

Microvascular decompression	22
Radiofrequency-thermorhizotomy	9
Percutaneous balloon compression	21
Glycerol gangliolysis	14
Total	*66*

Results

The group of 206 patients included 132 women and 74 men. The distribution by sex and age and by trigeminal branch and side is described in Tables 2 and 3 respectively. A total of 70 patients had demonstrated intolerance or a poor response to CBZ while 66 patients had previously failed different types of surgical intervention, including microvascular decompression (MVD), radiofrequency-thermorhizotomy (RF-TR) and percutaneous balloon compression (PGG) (Table 4). Symptoms were present in the majority of patients from 12 to 36 months prior to balloon compression. Surgical indications for the procedure are also described by group in

Table 5 Surgical indications

No response to medical treatment	89
Intolerance to medical treatment	75
Failed previous surgical intervention	66
Total number of procedures	*230*

Table 6 Morbidity: symptoms present at more than 2 months post operative

Persistent paresthesias	102 (44%)
Diminished corneal reflex	4 (1.7%)
Ophthalmoplegia	1 (0.5%)

Table 7 Time when recurrence occurred

12 months	5
12–23 months	9
24–35 months	16
36–47 months	3
More than 48 months	2
Total	*35*

Table 5. Intraoperative complications were easily managed during surgery. Persistent postoperative deficits were considered to be any postoperative symptoms that remained present for more than 2 months (Table 6). Other complications reported elsewhere in the literature, like infections, chemical meningitis, subarachnoid hemorrhage, extreme bradycardia or cardiac arrest were not seen. There was no mortality. From the 206 patients, in which 230 procedures where done, due to 3 bilateral cases and 21 reinterventions. 214 (93%) had an immediate positive response to the procedure while from the remaining 16 patients (7%), 9 underwent immediately another percutaneous balloon compression with 8 of them reaching a positive outcome after reintervention. From the seven patients that decided against another surgical intervention, six of them were able to achieve full symptom relief with medical treatment at that time. In total, complete symptom relief was obtained in 204 of the 206 initial patients for a 99% response rate. Post operative clinical follow-up was set up at a specialty neurosurgical clinic at 1 week, 1 month, 2 months, 6 months and once a year. It should be noted that in all cases there was a postoperative evaluation at least at 3 years from intervention. During the visits patients were evaluated for the presence of pain, paresthesias and any other neurological defect. We considered as recurrent symptoms any recurrence of pain regardless of severity, which may have occurred after the patient was pain free. From the initial 206 patients, a total of 35 patients (15%) eventually developed recurrent symptoms that were identified as per the above described criteria. Table 7 details the interval period in which the recurrences occurred. From this group, 21 patients underwent PBC again with complete pain relief while 14 patients received a new trial of medical treatment to which they were then responsive.

Discussion

In the last few years we have seen a tremendous effort from part of the medical community in trying to improve and develop surgical techniques which are minimally invasive with the important goals of reducing morbidity, improving post operative recovery rate and decreasing costs while continuing to maximize positive results and long term outcomes [19]. The treatment of TN refractory to medical treatment has traditionally included several methods like microvascular decompression (MVD), radiofrequency thermorhizotomy (RT-TR), stereotactic radiosurgery (SRS) and glycerol rhizotomy (GR) among others [20]. An exhaustive comparison between the different techniques is beyond the scope of this article, however, our personal experience suggests that PBD is effective, has a very low intraoperative morbidity and produces very satisfactory long-term results (currently at 3 years in our series). Recently published studies appear to support the fact that PBC and MVD have similar efficacy and superior effects to those of other modalities [15]. In addition, if one takes into consideration the risks associated with an open craniotomy and the need of a very experienced team to perform such a procedure, a minimally invasive technique like PBC becomes more relevant and feasible. Even though MVD appears to have the lowest recurrence rate (7–9%) from all surgical techniques, PBC still provides the second lowest acceptable recurrence rate (19.6%) [15]. Furthermore, the procedure can be repeated more than once [21] without significantly increasing the risks (unlike with MVD). The risks like anesthesia dolorosa and corneal hypesthesia and keratitis seen after RF-TR and the unacceptable high recurrence rates after SRS (60–70%) and GR (60%) make those surgical modalities less attractive in the surgical treatment of TN.

Conclusion

We conclude that at least in our experience, PBC is an excellent choice in the treatment of TN refractory to medical treatment, especially when considering older patients which present a higher surgical risk for MVD. We found that favorable results could be achieved with an average compression of 1.3 min, no less; however this is closely related to obtaining a pear-shaped balloon. Because this technique is also minimally invasive and has a lower cost, its availability and utilization in poor countries and in small rural clinics becomes of greater significance and importance.

Conflict of Interest Statement We declare that we have no conflict of interest.

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Erratum to:

Six Level Cervico-Thoracic Circumferential Reconstruction: Report of the Second Case of the Literature

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We regret that an error has occurred on page 187.
The correct author names should read as follows:

Massimiliano Visocchi and Giulio Maira

M. Visocchi (✉) and G. Maira
Institute of Neurosurgery, Catholic University – Medical School,
Rome, Policlinico Gemelli Largo Gemelli, 8 – 00168 Rome, Italy
e-mail: mvisocchi@hotmail.com

The online version of the original chapter can be found at DOI: 10.1007/978-3-211-99370-5_28

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