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Foreword

Since its inspired beginnings in 1993, the Annual Congress of the European Federation of National Associations of Orthopaedics has grown to become one of the most significant events in European orthopaedics. The annual congress in 2014 takes places in London at the EXCEL Centre and is unique in that it combines the Educational Programme of the British Orthopaedic Association as an integral part of the Congress available to all registrants.

The Congress is structured with varied educational approaches which include interactive expert sessions, evidence based medicine sessions, symposium both organised by clinicians and by Industry as well as the usual large number of free papers. This Congress is exceptional in having over four and a half thousand free papers submitted for consideration. Despite all this educational material, there is no doubt that the highlight of the congress remains the Instructional Lectures. Instructional Lectures are given by recognised experts across Europe in many varied aspects of orthopaedics involving all areas of the body and including basic science and tribology. The size of the congress makes it extremely difficult for a single clinician to listen to every Instructional Lecture. Therefore this book representing the fourteenth volume produced by EFORT represents a real gem in terms of educational material. It allows the reader to be acquainted with the current depth of knowledge in various areas of orthopaedic and traumatology practice and will continue to act as a very useful reference once the Congress is over. I count myself extremely fortunate in that I have every volume of the Instructional series (apart from one) which form a useful adjunct to my own personal library.

Once again this remarkable volume has been edited by George Bentley and produced in a wonderful format by Springer, and as the Chairman of the local organising committee in London, I would thank not only Professor George Bentley and his team for his superb editorial work, but also on behalf of EFORT I would like to thank the Instructional lecturers who not only have committed themselves to deliver remarkable lectures, but have taken on the added burden of producing a written format which allows publication.

I hope you enjoy the book and find it of great value.

London, UK

Steve Cannon
Chairman LOC, London

Preface

This 14th volume of the EFORT *European Instructional Lectures* is a collection of all the Instructional Lectures to be presented at the 15th Congress in London from June 4–6, 2013.

As previously, the topics were selected to reflect important aspects of current Orthopaedic and Traumatology thinking and practice by a group of specialists who also represent a range of expertise which is predominantly European.

Particular thanks go to the authors, not only for preparing and presenting their lectures but also for other activities such as paper reviewing and chairing of Symposia and Specialist sessions, participating in courses and demonstrations etc., which are vital for the rich totality of the Congress programme.

EFORT is constantly looking for new topics and authors and if you know of suitable lecturers and authors, please contact the chairman of the Scientific or Publications Committees via the Central Office.

Preparation of this print volume has been by Gabriele Schroeder and her colleagues in the Internationally-recognised Springer Company to whom we are very grateful.

My personal thanks go to, particularly, Susan Davenport and the EFORT Central office staff for their expert and unfailing support, as always.

This volume is dedicated to all those who have contributed, as lecturers, presenters, chairmen and exhibitors, to the ever-expanding Educational and Scientific development of EFORT, resulting in the greatest Orthopaedic and Traumatology fellowship in Europe.

The London Congress will be an unforgettable experience.

Stanmore, UK

George Bentley
Editor-in-Chief

Contents

Part I

General Orthopaedics

Bone Healing: The Diamond Concept

Peter V. Giannoudis, Michalis Panteli, and Giorgio Maria Calori

Abstract

The incidence of fracture non-union has been estimated to be as high as 10 %. The treatment of fracture non-union remains challenging even for the most experienced surgeons. The presence of a poor soft tissue envelope, deformity, avascular bone edges, reduced bone stock, low-grade infection and patient related co-morbidities are some of the important contributing factors that need to be addressed. Evaluation of the complexity of the non-union and formulating the appropriate pre-operative plan and treatment modality requires good understanding of the pathogenicity of this condition and having extensive surgical experience.

The state of both the mechanical and biological environment, is thought to play a crucial role in the decision making process regarding revision surgery. Application of the so-called 'diamond concept' provides the optimum mechano-biological conditions for bone repair and should be considered in cases where difficulties to achieve union are anticipated.

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Introduction

Fracture healing and bone regeneration represent a complex and well-orchestrated physiological process that involves timed cellular recruitment, gene expression and secretion of multiple signalling molecules [1]. In response to injury and fracture, bone has a unique intrinsic capacity for repair and regeneration [2, 3]. In contrast to the majority of tissues in the human body that heal by the formation of a scar of inferior quality, bone generated by the process of fracture healing encompasses its former biochemical and biomechanical properties [4]. This phenomenon can be described as a regenerative process that recapitulates aspects of embryonic skeletal development,

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combined with normal responses to acute tissue injury [1, 5].

Types of Bone Healing

With regards to the histology of bone healing two basic types have been described, depending on the stability of fixation of the fracture's bone fragments [2, 3, 6].

1. The primary (direct) healing pattern occurs when there is absolute contact of the bone fragments (anatomical reduction) along with almost complete stability (commonly obtained with open reduction and internal fixation) and therefore minimisation of the inter-fragmentary strains [7, 8]. In this type of healing that rarely happens in nature, the disrupted continuity of the bone is re-established with regeneration of lamellar bone and the Harvesian system, and has no need of any remodelling [8, 9].
2. The secondary (indirect) healing pattern occurs in the vast majority of clinical cases and depends on the formation of fibrocartilaginous callus that matures to mineralised cartilage and finally bone [2, 7]. Callus is formed as a physiological reaction to the inter-fragmentary movement and involves both intramembranous and endochondral ossification [2, 7–9]. It originates from committed osteoprogenitor cells of the periosteum and undifferentiated multipotent mesenchymal stem cells (MSCs) [7].

Fracture Healing and Bone Repair

Several types of tissues are involved in the process of fracture healing including cortical bone, periosteum, undifferentiated fascial tissue that surrounds the fracture, and bone marrow [9, 10]. Bone repair follows a well defined chain of events starting with haematoma formation, followed by inflammation, angiogenesis and granulation tissue formation, fibrous tissue formation, fibrocartilage, hyaline cartilage (soft callus), cartilage mineralisation, woven bone (hard callus), and finally remodelling [2, 6, 11]. The process of remodelling can last for several months.

In more detail, following an injury the bone architecture and the surrounding soft tissue continuity are both disrupted. The concomitant tearing of the blood vessels at the site of injury leads to bleeding, activation of the coagulation cascade and therefore the formation of a haematoma that encloses the fracture area [12]. The haematoma contains cells that originate from the peripheral and intramedullary blood, as well as bone marrow cells [8]. Different cellular populations have been described including inflammatory immune cells, neutrophils, monocytes and macrophages (activated by the coagulation process), fibroblasts and MSC's [2, 12]. Through the different type of mediators secreted, the formed haematoma exhibits a complex micro-environment that can exert different effects on diverse cell populations [2].

All stages of fracture healing are well coordinated but any insufficiency to one or more of these pathways can alter the physiological sequence of fracture healing. This interruption can lead to complications such as an impaired fracture healing response expressed as delayed union or non-union. In order to reverse any deficiency to one or more of these pathways, planned targeted interventions should be well-timed and well-aimed [7].

Biological Pre-requisites for Successful Union

Certain biological pre-requisites have been identified during the complex process of fracture healing. Different types of cells are recognised to interact with local and systemic regulatory molecules, cytokines, hormones and extracellular osteoconductive matrix [7, 11].

Osteogenic Cells

The first element for an unimpeded fracture repair is a vibrant cell population [7]. These cells include specific mesenchymal stem cells (MSC's) that under the appropriate molecular signalling are recruited, proliferate and differentiate to

osteogenic cells [8]. These MSC's originate from the surrounding soft tissues, cortex, periosteum, bone marrow and systemic circulation (mobilised from remote haemopoietic sites) [8], with their transformation to cells with an osteoblastic phenotype occurring in areas of high cellular density [13, 14].

Since the identification and quantification of the role of MSC's in osteogenesis, several in vitro and in vivo studies concentrated on the use of genetically engineered MSCs [15–19] and differentiated osteoblasts to enhance fracture healing [20, 21].

Growth Factors

Several signalling molecules exerting a direct influence on the faith of MSC's have been isolated within the fracture haematoma. These are categorised into three groups: the pro-inflammatory cytokines; the transforming growth factor-beta (TGF-β) superfamily and other growth factors; and the angiogenic factors [3].

The major signalling molecules include: transforming growth factor-β (TGF-β) that upregulates the undifferentiated MSC's [10, 12]; bone morphogenic proteins (BMP's) that promote the differentiation of MSC's into chondrocytes and osteoblasts, and osteoprogenitor cells into osteoblasts [9, 10, 12]; fibroblast growth factor (FGF) that enhances mitogenesis of MSCs [10, 12]; insulin-like growth factor (IGF) that promotes proliferation and differentiation of osteoprogenitor cells [10, 12]; platelet-derived growth factor (PDGF) that facilitates mitogenesis of MSCs and is responsible for macrophage chemotaxis [10, 12]. Vascular endothelial growth factor (VEGF) is responsible for the blood vessel invasion of hyaline cartilage, growth-plate morphogenesis, and cartilage remodelling, by regulating recruitment, survival and activity of endothelial cells, osteoblasts and osteoclasts [12]. An increased secretion of factors promoting the recruitment of inflammation cells and angiogenesis is also evident (tumour necrosis factor-α (TNF-α), interleukin-1 (IL-1), IL-6, IL-11 and IL-18) [8, 10].

Many of these molecules have been extensively studied to evaluate their clinical effectiveness in enhancing fracture healing. BMP's represent the sole clinically approved agents for applications related to fracture repair [1]. BMP-7 is FDA(Federal Drug Administration) approved for treatment of long bone non-unions, whereas BMP-2 has recently gained FDA approval for the treatment of open tibial fractures and spinal fusion surgery [1]. The clinical data on their safety and efficacy appears to be positive [22–25], whereas their application for off-label indications is also promising [22–31].

PDGF has also demonstrated promising results in the enhancement of fracture healing when used in animal studies [32, 33]. Other growth factors that are currently under investigation include growth and differentiation factor-5 (GDF-5) [34], insulin-like growth factor-1 (IGF-1) [35, 36], growth hormone (GH) [37] and platelet-rich plasma (PRP) [38–40].

Osteoconductive Scaffolds

During the natural process of indirect fracture healing, a fibrin-rich granulation tissue derives from the fracture haematoma [8]. This extracellular matrix provides a natural scaffold (osteoconductive properties) where all the cellular events and interactions take place, including cell adhesion, migration, proliferation and differentiation [1, 7, 41].

In the clinical setting, the ideal material to be used should mimic the native characteristics of the tissue, provide a source of cells capable of promoting proliferation and differentiation, as well as acting as a scaffold for angiogenesis, cell migration and attachment [13].

Various materials simulating some of the properties of this extra-cellular matrix have been clinically used. Autologous bone graft harvested from the iliac crest remains the "gold standard" for bone augmentation in non-unions [6, 42]. The Reamer-Irrigator-Aspirator (RIA) technique has also been used for obtaining from long bones and particularly the intramedullary (IM) canal of the femur autologous bone graft avoiding some of

the complications related to the iliac crest harvesting [43]. Other porous biomaterials used as bone void fillers include allograft or xenograft trabecular bone, demineralised bone matrix (DBM), collagen, hydroxyapatite, polylactic or polyglycolic acid, bio-active glasses and calcium-based ceramics [7, 44]. Modern scaffolds recently introduced involve osteoconductive synthetic metallic materials (Porous Tantalum, Trabecular Titanium etc.), offering a three-dimensional reticular frame where osteoblasts and osteoclasts proliferate producing bone [44–46].

Mechanical Environment

The process of inflammation and angiogenesis depend largely upon the mechanical conditions [2] and should therefore be taken under consideration in optimising fracture healing. Mechanical stability is essential for the formation of callus and its progressive maturation from woven to lamellar bone [7], whereas in case of rigid fixation no callus is evident (primary bone healing).

Mechanical stability at the fracture site is relevant to the selected type of fixation and can be achieved using ORIF (open reduction internal fixation), locking plating systems, intramedullary nailing and external fixation systems [41]. Plaster-of-Paris also represents a form of stabilisation using non-invasive external immobilisation support. In general terms it can be said that any surgical intervention (external or internal fixation systems) that improves fracture stability enhances the physiological process of bone repair.

Vascularity

Blood supply and revascularisation are essential for a successful fracture healing, including the final stage of remodelling [8]. The process of revascularisation involves not only neo-angiogenesis, but also the apoptosis of chondrocyte cells, the cartilaginous degradation and the removal of cells and extracellular matrices for blood vessel in-growth [8]. During uncomplicated bone repair, the medullary, periosteal and osseous blood supply can be enhanced according to the physiological needs [12].

Two molecular pathways mainly regulate the vascularisation process: the angiopoietin-dependent pathway and the vascular endothelial growth factor (VEGF)-dependent pathway, with the second being considered as the key regulator of vascular regeneration [8, 47]. VEGF is an osteogenic, pro-resorptive, oxygen-sensitive, signalling molecule that can regulate the function of osteoblasts, osteoclasts and osteocytes [48]. Evidence of the importance of this molecule has been reported with the inhibition of VEGF activity, by neutralizing VEGF receptor [49]. On the contrary, exogenous administration of VEGF enhanced blood vessel formation, ossification, and new bone (callus) maturation [49]. Evidence is now emerging that VEGF can be used to promote angiogenesis and osteogenesis, therefore improving bone repair [50–52].

Host

The optimal treatment of these challenging clinical problems should be tailored and individualised to the mechanical and molecular biology of the host. Identified risk factors for impaired bone healing amongst others include: poor blood supply, poor apposition of fractured bone ends, interposition of soft tissues or necrotic bone between bone fragments, inadequate immobilisation, infection, drug use (e.g. corticosteroid therapy or nicotine), advanced age, and systemic disorders such as diabetes or poor nutrition [12].

Apart from the previously described biological variation of the host, genetic predisposition is believed to be yet another important element of fracture healing [53–55]. Gene therapy is an emerging but rapidly developing approach to the treatment of non-unions, with encouraging results [56, 57].

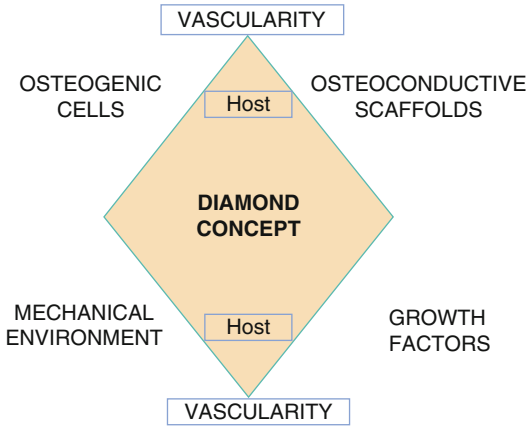


Fig. 1 Schematic representation of the diamond concept conceptual framework to promote bone regeneration

"Diamond Concept"

The so-called "Diamond Concept" has been proposed for the successful regeneration of bone and the treatment of fracture non-unions and bone defects [6, 7, 58, 59]. It represents a conceptual framework, which takes into consideration all the essential biological pre-requisites for a successful fracture healing response. It supports the implantation of MSCs, an osteoconductive scaffold and application of a growth factor to reconstitute the molecular milieu known to be necessary for the initiation and successful completion of bone repair. However, prior to any intervention and implantation of any or all of these constituents, the non-union bed of the host should be optimised, in terms of vascularity, containment and possessing adequate mechanical support where molecular and physiological processes will evolve promoting an early and successful osteogenesis [59] (Fig. 1).

Following a successful implementation of the "Diamond Concept", the non-union bed should have been transformed to a 'biological chamber', the so called 'local bioreactor', capable of supporting efficiently all the vital interactions between cells, growth factors and the underlying osteoconductive matrix facilitating a successful outcome [59]. In a sense the 'biological chamber' constitutes the centre of the highest biological activity, where all the cascade of events of bone repair and regeneration progress in a time-dependent fashion so that bone continuity can be restored [59]. The induced membrane formed following the application of the 'Masquelet technique' appears to be the ideal material to surround this 'biological chamber', as it can be produced naturally and possesses unique osteogenic promoting properties [60, 61].

"Diamond Concept" in the Clinical Setting

The "Diamond Concept" has been applied in the clinical setting in recalcitrant non-unions with multiple failed previous interventions, and the results obtained are very promising [6, 29–31]. However, one may argue whether it is always necessary to apply the conceptual framework of the diamond configuration (signals, cells, scaffold and/or revision of the fixation) for a successful outcome. The issue of whether there is still adequate mechanical stability present, and as such there is no need for revision of the fixation, can be addressed by careful evaluation of the radiographic findings of the affected extremity. Is there evidence of loosening or osteolysis of the interface between the bone and the existing implant? Is there failure of the metalwork? Does the patient report the presence of substantial painful stimuli whilst mobilising? How long the implant has been in situ prior to our planned intervention? Will the existing implant following our intervention continue to provide adequate mechanical support for the subsequent 6–9 months or else until the anticipated amount of time for union to occur has been reached? These are some of the important parameters that need to be answered in order to decide whether revision of the fixation is mandatory. The decision whether to apply only one of the biological constituents (monotherapy) of the 'diamond

concept' or all of them simultaneously ((cells, signals and a scaffold) – (polytherapy)) remains more challenging. Will it be sufficient to implant only osteoprogenitor cells? Only a growth factor or perhaps only a scaffold? How can I reach a sensible decision to ensure that my biological based therapy would be enough to promote successfully bone regeneration? Obviously the natural history of the non-union or else the bone defect area is crucial to be accurately documented. How many previous interventions have taken place without success? Are we dealing with a recalcitrant non-union? What is the state of the surrounding soft tissue envelope? Is there muscle wasting, local atrophy? Does the colour of the extremity/skin look compromised? Is there a history of underlying host pathology (i.e. diabetes, peripheral vascular disease)? Is the patient a smoker? These are some of the important factors to be evaluated to allow us to take the right decision.

Table 1 Non-union scoring system

		Score[a]	Max.	score
The bone				
Quality of the bone	Good	0		
	Moderate (e.g. mildly osteoporotic)	1		
	Poor (e.g. severe porosis or bone loss)	2		
	Very poor (Necrotic, appears avascular or septic)	3	3	
Primary injury – open or closed fracture	Closed	0		
	Open 1° grade	1		
	Open 2–3° A grade	3		
	Open 3° B–C grade	5	5	
Number of previous interventions on this bone to procure healing	None	1		
	<2	2		
	<4	3		
	>4	4	4	
Invasiveness of previous interventions	Minimally-invasive: Closed surgery (screws, k wires, …)	0		
	Internal intra-medullary (nailing)	1		
	Internal extra-medullary	2		
	Any osteosynthesis which includes bone grafting	3	3	
Adequacy of primary surgery	Inadequate stability	0		
	Adequate stability	1	1	
Weber & Cech group	Hypertrophic	1		
	Oligotrophic	3		
	Atrophic	5	5	
Bone alignment	Non-anatomic alignment	0		
	Anatomic alignment	1	1	
Bone defect – Gap	0.5–1 cm	2		
	1–3 cm	3		
	>3 cm	5	5	

Table 1 (continued)

Soft tissues				
Status	Intact	0		
	Previous uneventful surgery, minor scarring	2		
	Previous treatment of soft tissue defect (e.g. skin loss, local flap cover, multiple Incisions, compartment syndrome, old sinuses)	3		
	Previous complex treatment of soft tissue defect (e.g. free flap)	4		
	Poor vascularity: absence of distal pulses, poor capillary refill, venous insufficiency	5		
	Presence of actual skin lesion/defect (e.g. ulcer, sinus, exposed bone or plate)	6	6	
The patient				
ASA Grade	1 or 2	0		
	3 or 4	1	1	
Diabetes	No	0		
	Yes – well controlled (HbAlc < 10)	1		
	Yes – poorly controlled (HbA1c > 10)	2	2	
Blood tests: FBC, ESR, CRP	FBC: WCC >12	1		
	ESR > 20	1		
	CRP >20	1	3	
Clinical infection status	Clean	0		
	Previously infected or suspicion of infection	1		
	Septic	4	4	
Drugs				
Steroids		1		
NSAIDs		1	2	
Smoking status	No	0		
	Yes	5	5	

[a]Higher score implies more difficult to procure union

In order to address the above issues a non-union scoring system was developed so that the clinician can be assisted to reach the right decision [62]. It takes into account the bone/anatomical criteria and soft tissues condition, as well as the patient's characteristics, co-morbidities and drug use (Table 1), [62]. According to this non-union scoring system, scores from 0 to 25 would be considered straightforward non-unions and should respond well to standard treatments. Scores from 26 to 50 would require more specialised care. For patients with scores from 51 to 75, specialised care and specialised treatments should be sought. Finally, patients with scores above 75 may be candidates for consideration for primary amputation [62]. Application of a biologically- based therapy should be considered in patients with a score of more than 26 points and when the score is above 51 points the diamond concept must be applied (Fig. 2).

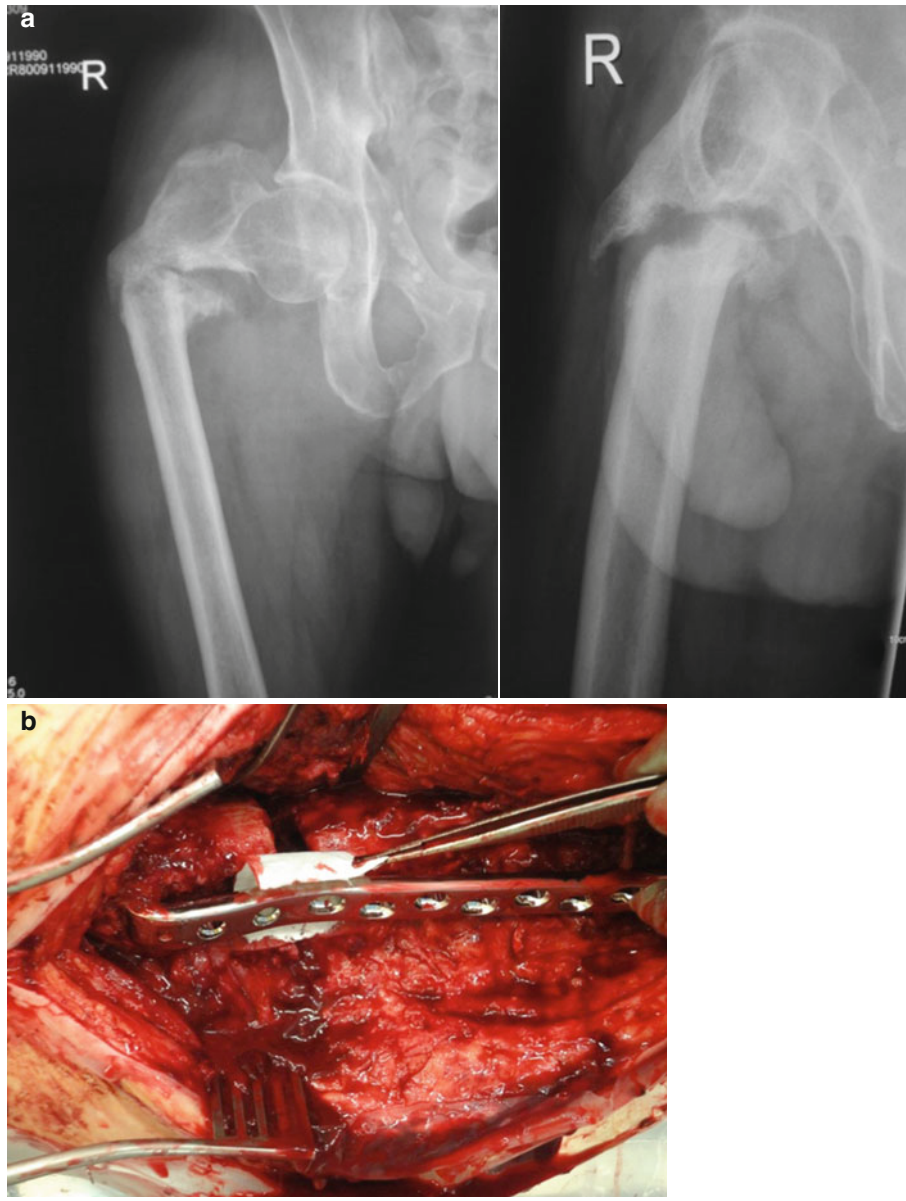
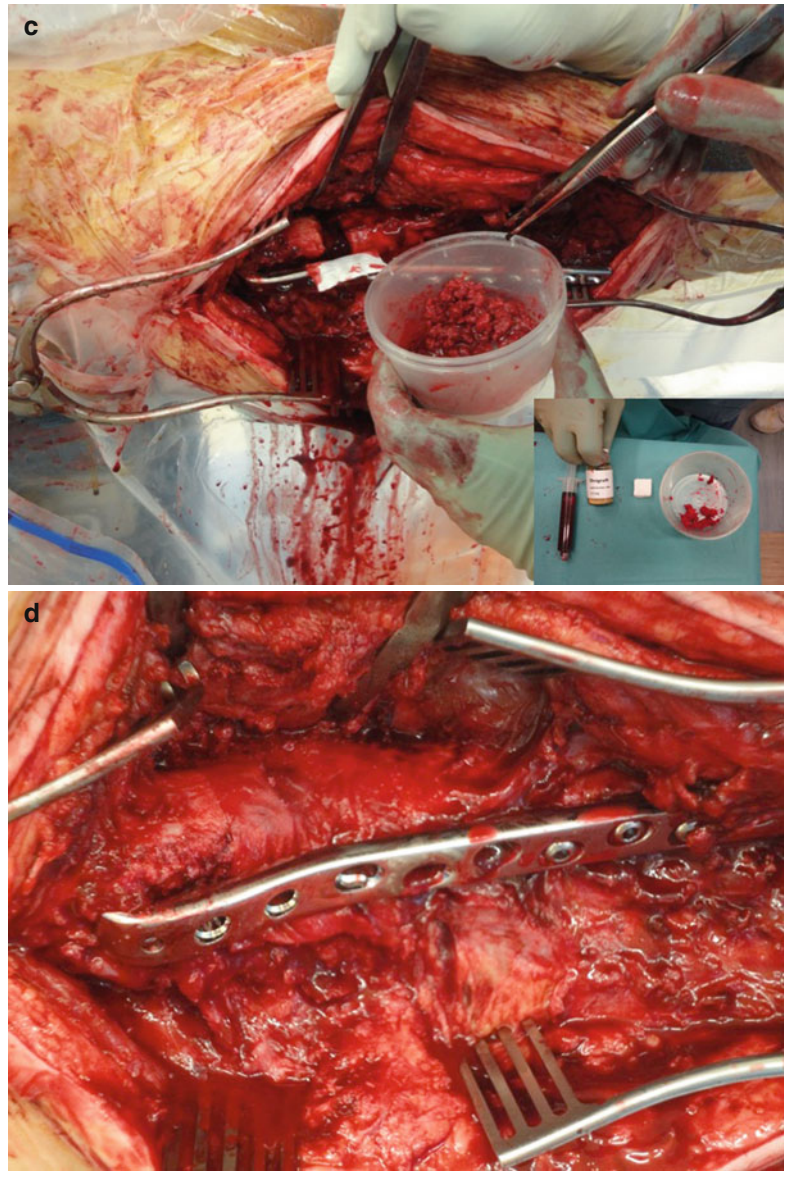
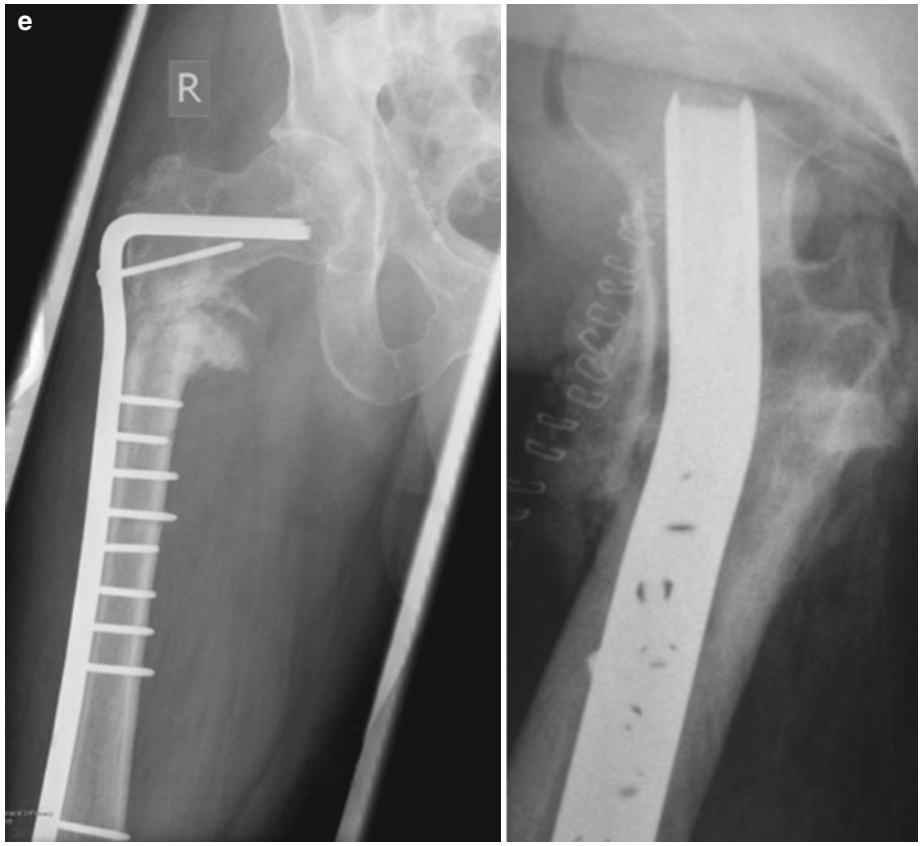


Fig. 2 (**a**) Radiographs AP, Lateral of a subtrochanteric non-union of a male patient 40 years of age. The patient had sustained a previous fracture that was stabilised with a cephalomedullary nail which was associated with implant failure and infection. The radiographs seen are 12 months after the removal of the failed implant. The initial non-union had been managed with temporarily stabilisation with an external fixator and several operative procedures for the control and eradication of the infection. In total the patient had undergone five previous procedures. He was a smoker. There was muscular wasting in the right lower extremity and a leg length discrepancy of 3 cm. Radiographs revealed signs of bone disuse and porosis. He was on a long-term prescription of non-steroidal anti-inflammatory medication. His non-union score was (bone component = 16, soft tissue component = 2, patient component = 8). Total points 26 × 2 = 52. (**b**) Intra-operative photograph illustrating that the right femoral non-union has been stabilised with a blade-plate following debridement of the non-union site. A collagen membrane (white material shown between the plate and the bone was inserted for the containment of the graft material. (**c**) Introperative photograph illustrating the diamond concept application: implantation of a growth factor (BMP-7), concentrated bone marrow aspirate (osteoprogenitor cells) and bone graft (scaffold). (**d**) Containment of the implanted graft using the collagen membrane. (**e**) Post-operative AP and Lateral radiographs. (**f**) Four months follow-up radiographs revealing osseous union of the previous right femoral subtrochanteric non-union

Fig. 2 (continued)





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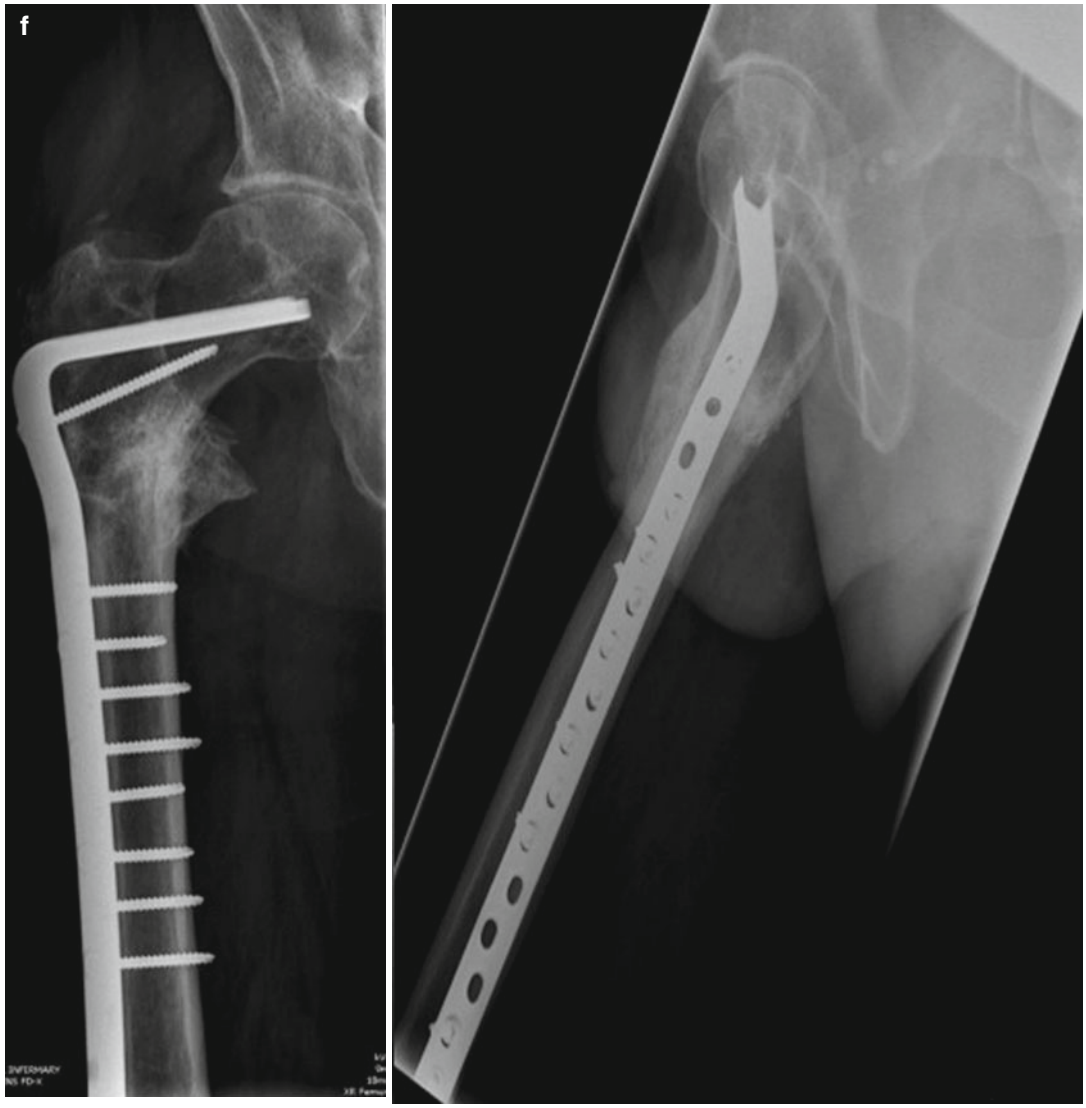

Fig. 2 (continued)

Conclusion

Several cells and molecules are actively involved in fracture healing, each having a distinct temporal expression pattern and role. A better understanding and deeper knowledge of the pathways involved would give us the opportunity to target each of these cascades independently. "Tissue engineering" is expected to revolutionise the treatment of patients with impaired bone healing, providing novel treatment strategies in the years to come [41]. However, there are several challenging technical issues that still need to be overcome. The "diamond concept" attributes equal importance to both the biological and mechanical environment and provides the clinician with a stepwise approach in dealing complex clinical cases of non-unions [41]. Moreover, the concept of the 'biological chamber' sitting at the heart of the diamond concept allows the clinician to consider in a more structured way the underlying molecular environment. With combination of therapies, the results of these difficult clinical conditions may be optimised providing a better, cost-effective treatment modality.

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The Dangers of Peri-operative Smoking in Orthopaedic Surgery

Alain C. Masquelet

Abstract

Tobacco smoking is a major worldwide hazard. It has been proved that its detrimental effects are due to nicotine and carbon monoxide, which impair the microcirculation and tissue oxygenation. Smoking adversely affects bone mineral density, increases the incidence of hip fractures and alters bone and wound healing processes. Tobacco has been proved to be a factor in causation of post-operative complications, cardiopulmonary failure, soft tissue and bone infection and delayed union or non-union. A systematic smoking-cessation programme should be observed from at least 6 weeks prior to surgery by all involved professions.

Introduction

People have become aware of the various harmful effects of smoking since a definitive association was established in the 1960s between tobacco smoking and lung cancer. Physiological effects of nicotine and other products found in cigarette smoke are more and more well known by scientists and information has been publicly propagated widely. Moreover the alarming reference work of Robert Proctor [50] has revealed how cigarettes came to be the most widely used drug source on the planet thanks to more than a century of manipulation by the tobacco industry. Also, big tobacco manufacturers continue to deny the negative effects of smoking by intensive publicity and collusion with some scientific and political agencies. Nonetheless, the detrimental effects of cigarette smoking on post-operative outcomes are yet underestimated by surgeons and patients although a considerable literature and consistent studies have been published since 2000. All surgical specialities are concerned but this paper aims to inform more specifically Orthopaedic surgeons by reporting the general physiological effects of cigarette smoke, the musculo-skeletal effects of cigarette smoking, the existence of peri-operative complications directly resulting from cigarette smoking, the effects of cigarette smoking cessation and how to help smokers to quit around the time of surgery.

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Physiological Effects of Cigarette Smoking

Cigarette smoke consists of two phases:

- A volatile phase which contains nearly 500 gases (e.g. carbon monoxide, benzene.)
- and a particulate phase of approximately 3,500 chemical products which contains nicotine and carcinogenic substances.

Nicotine is now considered as the principal addictive component of cigarette smoke. It has a half life of 3 h and is metabolized by the liver, giving the nicotine which can be used to evaluate recent cigarette smoking by detecting it in a smoker's urine. Nicotine is responsible for vascular disturbances by stimulating the sympathic nervous system.

Carbon monoxide reduces the amount of oxyhaemoglobin by taking the place of O_2. Combined action of nicotine and carbon monoxide decreases tissue perfusion and oxygenation, increases platelet aggregation and blood viscosity resulting in microclotting [5].

The immune system is impaired by cigarette smoking: white blood cell functions and antibody responses are decreased and the T-lymphoblasts are inhibited in the cell cycle. Paradoxically the level of auto-antibodies tends to be increased in smokers, notably antinuclear rheumatoid factors which are involved in rheumatoid polyarthritis [41, 61].

General Musculo-Skeletal Effects of Cigarette Smoking

Bone metabolic activity is reduced in smokers by the combined action of reduced blood supply, tissue hypoxia and effects on arteriolar endothelial receptors. The role of smoking has been incriminated in the development of osteonecrosis of the femoral head in adults and Legg-Calvé-Perthes' disease in children [6, 19, 22].

The effect of nicotine on osteogenesis and osteoblast formation appears paradoxical and to be dose-dependent. Osteoblast formation and function are inhibited at high levels of circulatory nicotine, whereas they are stimulated at low levels [3, 14, 23, 52]. In a study on rats, nicotine alone did not affect mechanical properties of healing femoral fractures, whereas tobacco extract not containing nicotine significantly reduced it [58]. Different studies suggest that nicotine replacement is safe with regard to bone healing and may even accelerate fracture healing with a dose-dependent effect [36].

On the other hand collagen synthesis is impaired by exposure of osteoblast-like cells to high concentration of both nicotine and cigarette smoke [17, 26]. Carcinogens in cigarette smoke inhibit osteoblast formation and differentiation. Another negative effect of smoking on bone may be the depletion of bone marrow by T3 lymphocytes inducing decreased calcium absorption in smokers which may also be a factor of decreasing bone formation and increasing resorption [18, 32]. Smoking has also been involved in disturbances of sex hormones; female smokers tend to enter the menopause 2 years earlier than non-smokers [40, 43]. The level of osteocalcin which is secreted solely by osteoblasts and used as a marker of bone formation is decreased in recently menopausal female smokers [24]. Increased resorption and decreased formation result in significant deleterious effects on BMD even in young people [39]. All these harmful biological effects increase the risk of fractures amongst smokers. Meta-analysis of prospective studies demonstrated an independent association between smoking and hip fracture risk both in men and women (RR = 1.85) [28, 33].

Peri-operative Complications in Orthopaedic Surgery

One should differentiate general complication and local complications at the surgical site. The most common complications associated with smoking are wound healing, infection, delay in bone healing and cardio pulmonary complications.

General Complications

Tobacco smoking is one of the most important risks of cardiac and pulmonary diseases. Smokers who undergo a general anaesthetic have an increased

risk of complications which is associated with pulmonary and cardiac diseases and not directly linked with tobacco smoking [15, 46]. Nonetheless differences between past and current smokers have been found, which indicate a statistically significant decrease in pulmonary complications for the former [55]. No difference between past and current smokers has been found on mortality.

The average length of stay was reported to be increased in current smokers. The duration of hospital stay was linked both to general complication and local complications [55].

Local Complications

Soft Tissue Healing and Wound Infection

Smokers are known to be at increased risk for wound and soft tissue complications as compared with non smokers [47]. Cigarette smoke induces an alteration of the normal process of healing by disturbing the function and the migration of fibroblasts, mesenchymal stem cells, acute-phase proteins and growth factors [63]. Moreover smoke creates free radicals which cause direct cellular damage [51]. Increased risk to free and local flaps and digit replantation failures among smokers has been observed [5, 11, 53] but surprisingly, the rate of micro-vascular anastomosis failure was not found significantly increased by smoking [34]. Tendon healing and ligament healing appear to be affected by cigarette smoking in experimental studies involving rats or mice [20]. Degenerative tears of the rotator cuff were found to be more prevalent and longer-lasting in smokers with a dose and time-dependent relationship [7, 27]. In one series smokers also had a 7.5 times higher risk of distal biceps tendon rupture [56]. According to several studies smoking altered significantly the long term outcome in primary anterior cruciate ligament reconstruction [29, 31, 60]. A randomised study performed on healthy voluntary adults, who had experimental an incision just lateral to the sacrum, showed a higher rate of infection in smokers whereas 4 weeks of abstinence reduced wound infection to the level of a non-smoker [59].

Delayed Bone Union or Non-union

Association between smoking and spinal fusion non-union has been well described by Brown et al. [8] who found the rate of non-union to be five times higher in smokers. This conclusion was confirmed by other studies [4, 21]. Osteotomies and joint fusion have been found to be associated with an increased risk for delayed union or non-union in smokers compared with non-smokers. This concerns particularly healing of ulna shortening osteotomy for carpal impaction (7.1 months in smokers vs. 4.1 months in non-smokers) [12], ankle joint fusion with a risk of non-union in smokers 3.75 times that of non-smokers [13], hind foot fusion with a risk of non-union in smokers to be 2.7 times state of non-smokers [25]. In patients who underwent an osteotomy for knee deformity, time of healing was longer in smokers than in non-smokers [62]. Risk of scaphoid non-union after surgical treatment in smokers was 3.7 times that of non-smokers [37].

Although the detrimental effect of smoking on fracture healing may not be due to nicotine, several retrospective studies have found that fractures are more prone to worse outcomes in smokers [1, 2, 13, 45, 57]. Operative management of Ankle fractures is associated with a six times greater risk of delayed or non-union in smokers than in non-smokers [48]. Finally, smokers are 3.7 times more likely to develop a bone infection [9] and 3.8 times more likely to develop a non-union [10, 16].

Smoking Cessation Reduces Peri-operative Complications

The effects of smoking may at least be partially reversible. Immune functions appear to recover after 6 weeks of abstinence, wound healing after 3–4 weeks, pulmonary function after 6–8 weeks [55]. A recent review of six randomized trials on the effect of cessation showed a relative risk reduction of 41 % for post-operative complications with each week of cessation prior to surgery increasing the magnitude of effect by 19 % [44].

Trials of at least 4 weeks smoking cessation had a significantly larger treatment effect than shorter trials [49]. Observational studies demonstrated relative risk reduction of 0.76 on total complications with a longer period (more than 4 weeks) cessation, producing an average 20 % larger reduction in complications than shorter periods. Two randomized smoking cessation studies involved Orthopaedic patients.

In the first one the group of patients who undertook 6–8 weeks of smoking cessation prior to their operation had significantly fewer complications requiring treatment as compared with a control group of smokers particularly with regard to wound complications [46]. In another study of randomized patients undergoing hip or knee replacement and other operations (hernia repair, laparoscopic cholecystectomy) post-operative complications where reduced from 42 % in the control group (smokers) to 21 % in the intervention groups (6 weeks smoking cessation programmme). Abstainers had fewer complications than those who only reduced smoking or those who continued to smoke [38].

Encouraging Patients to Stop Smoking Pre-operatively

From a general point of view, the attitude of physicians has increasingly changed over the last 10 years. Before 2000, retrospective studies had shown a correlation between negative effects and surgical outcomes, but level of proof was weak and a true uncertainty remained. A precautionary approach was generally taken and consisted of simply advising candidates for surgery to quit or to reduce smoking. Since 2000, prospective and randomized studies have resulted in the same conclusion with a high level of proof: tobacco smoking in the peri-operative period increases the risk of general and local complications. Uncertainty has been removed and the precautionary approach which is indicated in uncertain situations has become obsolete. Medical Doctors involved in peri-operative management have now, not only to inform the patient but also, and chiefly, to propose and undertake preventive actions. This means helping the patient to stop smoking in order to decrease the risk of adverse outcomes.

Elective surgery offers a great opportunity for physicians to help smokers stop, as peri operative smoking is linked to surgical complications including wound infections, cardiac and pulmonary functions, prolonged hospital stay, general infections and vascular or intestinal anastomotic leaks. Recent study [42] undertaken by the French Society of Orthopaedic and Traumatology (SOFCOT) confirmed that most of surgeons do not seize this opportunity [54]. One important reason may be the lack of awareness since surgeons and patients are often not fully informed of the detrimental effects of smoking on surgical outcomes. Other reasons include time constraints, lack of expertise in cessation counselling and sometimes a perceived lack of effective smoking cessation interventions. Although many interventions are available (nicotine replacement, behavioural feed-back,) convincing a smoker to quit in the time before surgery is challenging. The announcement of surgery may increase the desire to smoke in anxious patients. Other obstacles can arise since surgeons may find cancelling an elective operation both frustrating and costly. On the other hand, a patient who is refused an operation by surgeon can find a different surgeon willing to perform the procedure. Refusing to operate on a smoker may appear as a possible discrimination. But one should remind all patients that operating on active smokers results in higher health care costs and higher risks of surgical complications.

In fact, arranging appropriate smoking cessation services need not be complicated or time intensive [35]. Surgeons should use the Ask-Advise-Refer strategy, in identifying surgical candidates as smokers and refer them to other trained professionals such as the patient's primary care physician, respiratory therapists, toll-free telephone quit lines or web programmes. The dilemma of a National health service is between an authoritative demand for smokers to quit and the option to provide incentive-based cessation programmes for patients to quit smoking [30].

Informations and assistance to quit smoking is relatively easy to manage in elective surgery. When the surgeon meets a patient for a consultation for the first time, the "four rules" recommendations can easily be applied:

- Is the patient smoking?
- If yes, the addictive dependency must be assessed by the shortened Fagerström test which comprises the quantity of cigarettes per day and the delay between waking and the first cigarette. A delay of less than half an hour suggests a strong addictive dependency to nicotine.
- To explain to the patient the increased relative risk of wound necrosis, superficial and deep infections and delay in bone union; which is multiplied by 3, compared with non-smokers.
- To propose gently a programme of smoking cessation 6 weeks before surgery, based on nicotine patches. Controversies have arisen about the role of e-cigarettes and their efficacy in smoking cessation and in harm reduction. Their long term safety is also discussed. Nonetheless, in the context of minimal support, e-cigarettes are at least as effective as nicotine patches and are a cheaper alternative.

The most difficult situation is probably the management of a smoker in an emergency just after trauma. Physiological and psychological consequences of the trauma, anxiety resulting from the announcement of imperative surgical treatment, obligation to remain on an empty stomach, and withdrawal symptoms, often result in aggressive behaviour which increases the risk of complications. The solution is to undertake emergency replacement nicotine therapy, before surgery.

Surgeons must be aware that surgery is a powerful opportunity to help patients quit smoking. Patients and physician should be convinced by the evidence that pre-operative smoking cessation is safe and significantly reduces complications and length of hospital stay. National surgical professional societies should promote greater use of the AAR strategy. Collaborations with primary care physicians, anaesthesiologists, and other involved professions can facilitate smoking cessation.

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Sarcopenia and Osteoporosis: What Orthopaedic Surgeons Should Know

Cornel C. Sieber

Abstract

Sarcopenia, the age-associated loss of skeletal muscle and function, is an integral part of the physical component of the "frailty syndrome". There is evidence that sarcopenia can reach levels where mobility, balance and functionality overall are hampered. So, the diagnosis of sarcopenia should be part of the standard diagnostic and therapeutic repertoire of Geriatric Medicine and Orthogeriatrics. From a pathophysiological point of view, both sarcopenia and frailty share many components, very importantly the one of a low-inflammatory state. The propensity to lack adequate responses to internal and external stresses in frailty, highlights that other domains are involved in this multidimensional syndrome.

As with muscle mass, bone mass is declining irrespective of gender or life-span. Both Geriatric Medicine and Orthogeriatrics in addition very often deal with patients suffering from fragility fractures due to osteoporosis. In essence, sarcopenia as well as osteoporosis often develop in parallel and the Orthopaedic surgeon seeing elderly persons with fragility fractures is also confronted with sarcopenia and the clinical signs of frailty. In this mainly multi-morbid population, a close interplay between the Orthopaedic surgeons and Geriatricians therefore helps in the management of this fast-increasing population.

Sarcopenia

Since the term sarcopenia was described in the late 80s and early 90s [1, 2], there has been a continuous research interest in the age-associated decrease of muscle mass and muscle strength. Nevertheless, studies elucidating the clinical aspects of sarcopenia – including the overlap with the frailty syndrome – have been performed with a relevant time-lag [3–6].

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Although popular among geriatricians and even non-professionals for decades, the term "frailty" has been attributed to the concept of a geriatric syndrome much later [3]. Since then, it has attracted a wide-spread scientific interest among researchers and clinicians. How can these two entities then be interrelated and which conclusions should be drawn? This is delineated in this chapter.

Definition of Sarcopenia

Sarcopenia has emerged as a core concept to understanding function and by that, independence, in older age. As muscle mass counts for about 40 % of body mass, its decline with age is not just a part of senescence [5, 6]. After the age of 50 years, about 1–2 % of muscle mass is lost per year [9]. In addition, muscle strength is lost even faster with age [10], pointing in the fact that the loss of muscle mass is only partially responsible for strength and functionality in old age.

This loss of muscle mass is more pronounced in men than in women, the former showing a higher absolute muscle mass in earlier years, but a steeper decline in later adulthood and old age. Sarcopenia is present when there is a less-than-expected muscle mass in an individual of a specified age, gender and race. Using the definition of Janssen [7], the prevalence for class II sarcopenia – two standard deviations below that of young adults – above age 80 was calculated at 7 % for men and at 11 % for women in the United States.

Besides muscle mass itself, strength should be a component of the definition of sarcopenia. The relevance of strength and functionality for an elderly person's capability to cope with the demands of daily life is obvious.

Sarcopenia Beyond Muscle Mass Loss and Locomotion

Even though the focus of sarcopenia research has mainly been concentrated on locomotion (e.g. gait speed, falls), muscle tissue is abundant and important in other body tissues. Loss of muscle mass in these organs also hampers functionality in affected persons. As muscle mass loss is a general phenomenon of aging, its loss beyond a certain threshold renders a person more vulnerable to different health outcomes (see below for "frailty"). Cardiac output, respiratory capacity, glucose homeostasis and insulin sensitivity, amino-acid supply, as well drug bio-availability and tolerance (due to changes in body composition) are such factors. Sarcopenia may aggravate other diseases as well as their prognosis by negatively influencing their progress. Such diseases include congestive heart failure, chronic obstructive lung disease, diabetes mellitus, chronic kidney disease, and even stroke and dementia.

Diagnosing Sarcopenia

There have been several consensus conferences how to diagnose sarcopenia in recent years. What is common in all of them is – different to osteoporosis – that the diagnosis of "just" a reduced muscle mass is not enough to make the diagnosis. Indeed, besides a reduced muscle mass – preferentially measured by bio-impedance analysis (BIA) – there must also be signs of a loss of strength and/or function. The first one is mainly measured by handgrip strength, whereas the latter is measured by gait speed. Relevant cut-off points for handgrip strength in relation and gender as well as for gait speed (<1.0 m/s) are published [3].

Inasmuch such cut-off points are also reliable for persons with obesity and sarcopenia (so-called "sarcopenic obesity") has still to be explored [13]. This is an important research channel, as we soon will see an important elderly population suffering from obesity and sarcopenia in parallel, hampering their functional status and therefore their independence.

Definition of "Frailty"

The Frailty Concept

Frailty may be regarded as a geriatric syndrome of decreased reserve and resistance to stresses,

Table 1 Criteria for the phenotypic definition of "frailty" developed by Fried et al.

Weight loss	>5 kg/a
Exhaustion	Depression scale CES-D (2 points)
Weakness	Grip strength (lowest 20 %)
Gait speed	5 m (slowest 20 %)
Low physical activity	kcal/week (lowest 20 %)
Diagnosis of pre-frailty	1 or 2 criteria met
Diagnosis of frailty	3 or more criteria met

resulting from cumulative declines across multiple physiological systems, causing vulnerability to adverse health outcomes including falls, hospitalisation, institutionalisation and mortality [14]. This could imply that a common underlying biological process is responsible for its development. Concepts focussing on inflammatory processes, hormonal changes and body composition follow this hypothesis (Table 1).

Frailty is a multi-dimensional entity comprising physical, psychological and sociological components. Up to now, most research has clearly been performed on the physical and disease-related aspects of frailty, while the other two areas are still predominantly unexplored. Frailty may be seen as a continuum stretching from early stages that cannot be identified clinically under the circumstances of everyday life and which only will be obvious when the individual faces external stresses, to late stages with full-blown frailty that is easily recognized because it interferes with daily routine activities and comes close to a state of disability [15].

Pathophysiology of Frailty

Several pathophysiological processes are related to the development of frailty [16]. A predominant role has been attributed to inflammatory mechanisms. Increased CRP-values and pro-inflammatory cytokines were associated with the presence of frailty [17–19]. Especially increased IL-6-levels have repeatedly been observed with a close association of an increased risk for being frail.

A series of studies concentrated on the relationship between nutrition and frailty. It was shown that frailty is significantly associated with a daily energy intake below 21 kcal/kg bodyweight as well as a low protein intake [20]. From the Women's Health and Aging Studies, we know that pre-frail and frail individuals had a higher prevalence of being deficient for vitamin B12, vitamin D and alpha-tocopherol than non-frail individuals [21]. The simultaneous prevalence of more than one vitamin deficiency was also significantly higher for the pre-frail and frail individuals.

The current understanding of the involvement of the above mentioned multiple factors in the pathogenesis of frailty is summarized in Fig. 1. It also shows that sarcopenia plays a central role in this concept.

Diagnosing Frailty

The two most widely utilized approaches are the phenotypical definition of frailty developed by Fried and co-workers based on data from the Cardiovascular Health Survey and the Frailty Index developed by Rockwood and co-workers [22, 23].

The Fried definition proposes five items: weight loss, exhaustion, weakness, slow walking speed, and low levels of physical activity. Frailty is diagnosed when at least three criteria are met. An individual is said to be pre-frail when one or two of these criteria are present.

Based on the results of several recent studies, the criterion weight loss may be regarded as one-dimensional as higher BMI-values above BMI 30 kg/m^2 are also associated with a loss of functionality which may be an expression of being frail. Furthermore, the weight loss thresholds given in the Fried criteria may be too high for a European population, as shown in a study in community-dwelling older persons [24]. In this study, a good applicability of the Frailty assessment by the Fried criteria can be demonstrated in a general practitioner setting. So, due to a reasonable time to perform the test, the Fried criteria could also be used on Ortho-geriatric wards.

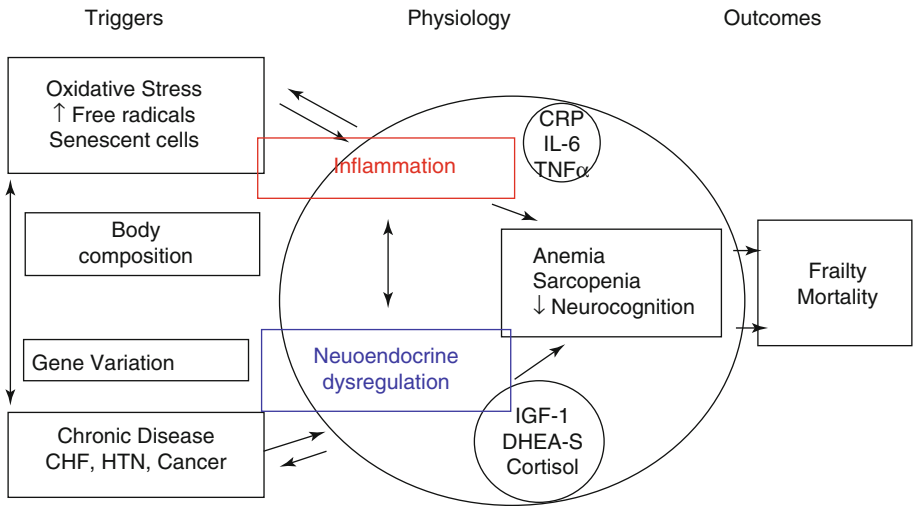

Fig. 1 Modal pathway to adverse outcomes in the elderly (Adapted after Walston J, 2007, personal communication)

The relationship between frailty and a wide spectrum of clinical diseases like coronary heart disease [25], Parkinson's disease [26], stroke [27], Alzheimer's disease [28] and venous thromboembolism [29] and has been explored by different research groups. This underlines the growing interest of clinical researchers in this geriatric syndrome.

Pathophysiological Overlaps Between Sarcopenia and Frailty

Pathophysiological overlaps between sarcopenia and frailty are important. When taking the factors contributing to sarcopenia as detailed in two recent articles [5, 30]. They include in particular the following components:

Different hormonal axes show significant changes during aging. Growth hormone, insulin like growth factor-1 (IGF-1), but also sex hormones including testosterone, oestrogens and the pro-hormone dehydroepiandrosterone sulphate decrease with age. Some of them have been used in an attempt to counteract the sarcopenia process. Nevertheless, studies using one single hormonal replacement have been disappointing. Present concepts favour a multiple hormonal dysregulation leading to frailty [31]. So, the absolute burden of several anabolic hormonal deficiencies partly predict frailty, suggesting a generalized endocrine deficiency in frail elder persons [32].

Besides different endocrine axes, growth hormone has received a special attention as being a strong anabolic hormone, its plasma levels decreasing in the normal aging process as does the muscle mass. A correlation with growth hormone and the IGF-1 axis in relation to skeletal muscle aging is aging has indeed been described [33]. The substitution of low growth hormone levels to counteract the sarcopenic process and frailty has been to date disappointing, but its use is still debated, especially as part of a more orchestrated intervention including several anabolic substances [34].

Anorexia is frequent in older persons, especially in those showing signs of frailty. A correlation between anorexia, subsequent weight loss and sarcopenia and the frailty syndrome has therefore been put forward [35]. As anorexia often leads to protein-energy malnutrition – being a major cause for sarcopenia – a further interlink between sarcopenia and frailty can be found.

Inflammatory signals as part of the "inflamm-aging" concept [36, 37] – also related to nutrition – are associated with muscle wasting (sarcopenia, cachexia), which then may lead to frailty and functional decline. Most studies have focused on interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF-alpha). Studies have demonstrated

an independent association of pro-inflammatory cytokines such as tumour necrosis factor alpha and interleukin 1 and 6 with lower muscle strength, lower physical performance and a higher risk of disability in sarcopenic persons [38].

Insulin resistance predicts not just frailty, but diabetes mellitus also accelerates muscle strength loss [39]. This is corroborated by findings, that insulin resistance is not only correlated to frailty, but also to gait speed, pointing out a link to sarcopenia and frailty [40]. Inasmuch frailty is associated with insulin resistance and glucose metabolism in relation to changes in body composition still needs confirmation. More specifically, this correlation may also depend on increased abdominal fat linking frailty to sarcopenic obesity [41].

Low vitamin D levels are clearly related to functional muscle strength loss and falls as an indirect sign of sarcopenia [42–44]. The correlation of a low vitamin D status as a single parameter for frailty risk is also described. Nevertheless, even though lower vitamin D levels in community-dwelling older men are independently correlated with frailty, it does not predict a further progression in the following years [45]. Similar findings are described for women, where low vitamin D levels in addition are associated with an increased risk of incident frailty or death during follow-up [46], findings challenged by others, where such a correlation could only be found in men [47]. In summary, low vitamin D levels as a single biomarker only modestly predict progression of frailty, but vitamin D deficiency at a serum concentration <15 ng mL as a punctual measurement is paralleled by an around fourfold increase in the odds of frailty [48].

Finally, with regard to functionality, a further link between vitamin D status, inflammatory load and the 6-min walk has been described in frail elder persons with heart failure [49, 50].

Grip strength – strongly correlated with sarcopenia – is also a predictor of falls, physical disability and the frailty syndrome [51].

The strong correlation of gait speed as a functional parameter in the lower extremities with functionality per se and even mortality has therefore also found its way in the description of frailty [52, 53].

Osteoporosis

As for sarcopenia, the prevalence of osteoporosis rises with advancing age as is not at all just confined to women (postmenopausal osteoporosis). Indeed, the demographic shift is accompanied with many elderly men also reaching a life-expectancy well above 80 years, an age where many of them suffer from osteoporosis.

There is clear correlation between sarcopenia – and osteoporosis and the risk of falls with consecutive fragility fractures. Besides the important role of vitamin D for both muscle and bone (see above), the therapeutic approaches have to separate drugs with an osteoclastic effect and those with a dual effect, meaning an additional osteoblastic effect. For the latter, parathyroid hormone and strontium ranelate have been proven to have positive effects. The role of bisphosphonate have lost some importance due to the question of the adverse side-effects when given in the long-term (>5 years). When dealing with elderly persons with a reduced kidney function, denosumab seems to be a good alternative.

In essence, there exist a broad palette of drugs to treat osteoporosis, a fact which is not mirrored in the treatment of sarcopenia at the present stage.

Future Challenges

Sarcopenic Obesity

Changes in body composition, especially a relative and absolute increase in fat mass, may be seen as another important aspect in the pathogenesis of frailty. In this context, it has recently been shown by data from the Cardiovascular Health Study, that frail individuals are characterized by higher weight, more central obesity, higher insulin resistance and a higher probability for the metabolic syndrome [54].

Obesity is been defined as an increased body mass index (BMI). Despite this, BMI does not say anything about body composition. An increased reduced balance [55]. When screening for nutritional status, the BMI can be replaced by

the calf-circumference [56], indirectly correlating body weight with body composition.

This means that obesity can very well be related to sarcopenia, functional decline and the frailty syndrome. This interrelationship is well described both for research and treatment strategies in an aging and more and more obese society [57].

Neuronal Alterations

The interplay between muscular innervation and muscle structure and function has not attracted much attention until recently. It is well established that the number of motorneurons is declining with age. We therefore search for a subgroup of patients with sarcopenia suffering from neuronal changes leading to a subgroup of sarcopenia. Drey et al. could show that indeed motorneurons may be reduced in patients with sarcopenia, and that in parallel the motorneuron units innervate more muscle fibres [58]. In addition, we investigated inasmuch the 22kk-peptide agrin could serve as a biomarker of sarcopenia [59]. These data are still preliminary but point in the direction that there can exist different forms of sarcopenia, which most probably in the future will help to introduce specific therapies for subgroups for the clinically so-important syndrome of sarcopenia [60].

Cachexia and Sarcopenia

In the consensus paper of Evans and colleagues [61], they use for the diagnosis of Frailty three out of five of the classification items out of the Fried frailty criteria. The question now arises if sarcopenia, frailty and even cachexia share common pathways and clinical presentation. As sarcopenia is always part of cachexia but not vice versa, one can differently argue about the interplay of these three clinical entities:

- Frailty is an umbrella syndrome, under which both sarcopenia and cachexia can be covered
- sarcopenia and frailty are brothers and sisters, and cachexia is a combination of the two in states of high inflammatory states
- sarcopenia is one of the phenotypes of frailty, cachexia is another one, and even quite different ones such as psychological and social failure to cope with internal and external stressors.

If the last feature may fit best, this has implications for diagnosis and especially treatment of frailty. It will need to tackle the specificity of different pathophysiological origins of frailty separately. It then also means that research and drug/treatment developments for frailty have to concentrate on the specific predominant backgrounds. Sarcopenia may well need different therapeutic approaches as does cachexia. This is substantiated by the fact that nutritional interventions are successful for sarcopenia and frailty, but much less for cachexia. Such a concept can also help to critically analyze present therapeutic strategies involving nutritional interventions and physical activity programs, which well may differ in their goals and success.

With regard to cancer cachexia, an interesting cross-link to both frailty and sarcopenia has recently been published [62]. The diagnostic criterion of cachexia was weight loss adding to individuals who already show signs of a diminished BMI (<20 kg/m^2) or reduced skeletal muscle mass (sarcopenia). Assessments for a clinical classification and management should include the following domains: anorexia or reduced food intake, catabolic drive, muscle mass and strength, functional and psychological impairment. The items muscle mass, muscle strength and functional impairment depict the overlap to sarcopenia, as these parameters are an integral part of the sarcopenia definition.

Strictly speaking, one can summarize that the definition of cachexia by Evans and colleagues uses different items of the frailty definition whereas the one of Fearon and collaborators for cancer cachexia takes the sarcopenia definition, in addition demanding weight loss or a BMI <20 kg/m^2. The latter two items are not part of the sarcopenia definition and therefore point in the direction that weight loss or a low BMI adds up to sarcopenia to a state of cancer cachexia. The reasons for this weight loss may indeed be quite diverse, one of them being the inflammatory

load. It is to be hoped that biomarkers of inflammation are better defined and thresholds found, as this may influence therapeutic strategies.

Therapeutic Interventions

The "magic" prevention and treatment strategy for sarcopenia and indirectly also for osteoporosis is a protein-rich diet, especially when combined with regular physical activity. For both treatment avenues exist well-delineated meta-analyses and treatment guidelines [63–65].

Especially with regard to an adequate protein intake, a recent international consensus has been developed counselling for a daily protein intake of 1.0–1.2 g protein per kilogram body weight [66]. As this is often not easy to reach for elderly persons in a normal diet, the use of oral protein-rich supplements is worth considering in many elderly persons after fragility fractures [67, 68].

When considering that a diet rich in anti-oxidant can counteract oxidative stress – both from internal and external sources – and by that inflammatory processes such as sarcopenia and frailty, it may well be that such processes do not just reduce the risk of becoming sarcopenic and frail as part of functional decline, but also the risk for other components of the frailty syndrome [69, 70].

Conclusions

Sarcopenia as many other geriatric phenomena, involves a number of underlying causes and mechanisms. Factors involved are not just intrinsic changes within the muscle tissue itself, but also neuronal, humoral, and lifestyle factors. Inadequate protein intake and physical inactivity may accelerate sarcopenia.

Sarcopenia – as the frailty syndrome – may be regarded as a non-specific clinical sign that can be an age-associated phenomenon, but that may also be caused by a multitude of clinical conditions that are independent of the aging process. Sarcopenia is a fundamental component of frailty but it may be seen as too one-dimensional while the general condition of the elderly individual is determined by a complex interplay of multiple factors that will, in several instances, be missed by the diagnosis of sarcopenia alone.

Osteoporosis in the (oldest) old – if not due to specific problems such as long-term corticosteroid therapy – is nearly always accompanied by sarcopenia. Therefore, the Orthopaedic surgeon dealing with elderly persons with fragility fractures should always look for accompanying sarcopenia and if present, treat this "Duo" together.

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Management of Infected Total Joint Arthroplasty

Burak Beksaç

Abstract

Periprosthetic joint infection is one of the most challenging complications of total joint replacement surgery. Until very recently, the infection diagnosis was not clearly defined in the orthopaedic literature. This review outlines the new definition of periprosthetic joint infection, the utility of various clinical, serological and radiological tests in the prevention and diagnosis of infection. Treatment strategies and principles are also reviewed in the light of the current literature.

Introduction

Periprosthetic joint infection (PJI) is one the most common serious complications of total joint arthroplasty (TJA) surgery and a reason for re-operation [1]. PJI is as much devastating to the patient as challenging for the surgeon to treat, often necessitating long treatment time, multiple surgeries with high costs and may result in patient disability, lower functional status, and rarely, limb loss or mortality.

The incidence of PJI is 1–7 % in primary TJA and much higher following revision.

Many authors have classified PJI, but the usefulness of these classifications as a guide to treatment is limited. PJI is considered as acute post-operative in the first month following the initial surgery. Acute hematogenous (infection) may present at any time following TJA, and is seeded to the implant from a distant haematogenous source with symptoms in less than 4 weeks from surgery. Infection is chronic (late) if the duration of the symptoms is more than 4 weeks. Although this classification provides a chronological pathogenetic description for PJI, its usefulness to guide treatment is limited as some recent studies showed that factors such as the host type, the virulence of the infecting organism, status of the soft tissues and bacterial biofilm are important factors and should be assessed to successfully treat PJI.

Diagnosis

The diagnosis of PJI is not a straightforward one, as different clinical and laboratory parameters are used to define the infected joint. Different authors [2–6] published different sets of signs, symptoms and tests to define PJI, which have contradictory points, and contradictory

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Table 1 The Musculoskeletal Infection Society's new definition parameters for diagnosis of peri-prosthetic joint infection (PJI) [8]

Definition of periprosthetic joint infection
Based on the proposed criteria, a definite PJI exists when:
1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from two or more separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. When four of the following six criteria exist:
(a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,
(b) Elevated synovial white blood cell (WBC) count,
(c) Elevated synovial polymorphonuclear percentage (PMN%),
(d) Presence of purulence in the affected joint,
(e) Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
(f) Greater than five neutrophils per high power field in 5 high power fields observed from histological analysis of periprosthetic tissue at 400 times magnification.
Please note that a PJI may be present if less than 4 of these criteria are met.
The panel also acknowledged that in certain low-grade infections (e.g., *P. acnes*), several of these criteria may not be routinely met despite the presence of PJI.

P. acnes Propionibacterium acnes

(infected vs. non infected) results [7]. Recently, in a combined effort to improve the scientific uniformity and accuracy of the definition of PJI, the Musculoskeletal Infection Society released a new definition of peri-prosthetic joint infection [8], to be accepted as the gold standard and provide uniformity in this field (Table 1).

The most commonly identified aetiological organisms are *Staphylococcus aureus* and *Staphylococcus epidermidis. S. aureus* typically produces early infection whereas *S. epidermidis* and other epidermal flora result in delayed acute haematogenous infection. *S. aureus*, *S. epidermidis*, β-hemolytic Streptococcus and gram-negative species are highly virulent and difficult to eradicate because they produce a biofilm glycocalyx.

Preventative Measures

Peri-operative parenteral antibiotics use is proven to decrease PJI. The ideal timing of administration should be between 30 and 60 min before skin incision to reach peak bone concentrations. The most recommended agents are the first and second generation cephalosporins, cefazolin and cefuroxime. If the patient is allergic to penicillin or there is a reason that the routine prophylactic agents cannot be used, teicoplanin and vancomycin are reasonable alternatives. The duration of prophylaxis should be 24 h, as longer periods do not lower the incidence of PJI and help the evolution of antibiotic-resistant organisms. A preoperative single dose of cefazolin was as effective as three doses of cefuroxime in a retrospective review of 1,367 total hip arthroplasties [9].

The use of antibiotic cement is not routine in primary arthroplasty surgery, but recommended in revision total joint arthroplasties [10, 11]. A recent prospective study [12] of 31,086 THAs reported that the revision rate due to PJI was 0.8 % and influenced by the type of fixation (cemented, uncemented, or hybrid). Compared to cemented hips, uncemented hips had a higher adjusted risk of revision due to infection (RR: 1.5, CI: 1.0–2.2, p = 0.03). The rate of revision due to infection presented by hybrid fixation was not different to cemented fixation (RR: 1.1, CI: 1.6 0.7, p = 0.7). In a study demonstrating the increasing risk of PJI conducted by the Nordic Arthroplasty Register Association (NARA), the use of cement without antibiotics and hybrid configurations were found to be risk factors for infection [13]. Nonetheless there are concerns that are related to the routine use of antibiotic cement during primary arthroplasty such as the type and dose of antibiotic; cost; emergence of resistant organisms; weakening of the mechanical properties of the cement

and possible failure of the fixation. The recommendations of International Consensus Meeting [14] (ICM) for these issues are as follows:

There is no clear data on which antibiotic and what dose should be added to cement and there is a difference between various cement formulations with regard to their ability to prevent infection. Some cement formulations have been shown to have better antibiotic elution profiles than other formulations [15–20]. Due to the cost [21], ICM recommended that the routine use of antibiotic cement during elective primary arthroplasty should be limited to patients at high risk of PJI, such as those with diabetes or immunosuppressive conditions.

The concern that remains is whether hand-mixing of antibiotic with cement can lead to a significant reduction in the mechanical properties of cement and subsequent failure of the prostheses [22, 23]. Because of the latter issue, ICM recommended that either pre-mixed antibiotic cement should be used or if hand-mixing of cement is being considered, the dose of antibiotic added to cement should remain around 1–1.5 g per 40 g pack of cement.

Current Recommendations of Diagnostic Tests for PJI

The surgeon should always carry a high index of suspicion for PJI, to make a timely diagnosis, allowing for the best opportunity to eradicate infection. The diagnosis of PJI is a combination of clinical judgment, serological tests, joint aspiration and analysis, and intra-operative microbiological and histopathological examination of joint fluid and tissue samples.

The clinical suspicion should be based on clinical signs and symptoms: Fevers persisting beyond postoperative day 5, extended drainage from the wound, wound erythema, and rest pain in the setting of an otherwise well-looking arthroplasty should raise suspicion of infection and initiation of a serological sepsis work-up.

Radiographic studies such as X-rays, computed tomography and magnetic resonance imaging have limited usefulness in the diagnosis of infection. Radiographs may show bone defects and periostitis in chronic infections, where the utility of CT and MRI scans is limited by the artifacts, which are created by the implants. The routine use of these advanced imaging modalities is not recommended for PJI diagnosis.

The clinical use of radionuclide scanning modalities such as 99Tc, Indium-111 labelled leucocytes scans is valuable. Monoclonal antibody fragment (Fab) scintigraphies have also been investigated and were recommended in the American Academy of Orthopaedic Surgeons (AAOS) guidelines but only when suspicion of PJI remains but is not confirmed by the results of joint aspirations and if surgical intervention is not planned, but these recommendations are based on weak to moderate evidence [24]. Recently, positron emission tomography using fluorine-18-fluoro-2-deoxy-D-glucose (FDG-PET) revealed some promising results with high sensitivity and specificity level, in differentiating between aseptic and septic causes of pain in the hip following THA [25, 26]. But additional studies and more evidence are required to establish its role in the diagnostic workup of PJI.

Laboratory Evaluation

If there is a clinical suspicion of PJI, initial investigation consists of measurement of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell (WBC) count. Serum ESR and CRP are excellent screening tools and sensitive markers of PJI with relatively poor specificity and can be influenced by other infectious and non-infectious inflammatory diseases, including extra-articular infection [27–31]. The combination of an elevated ESR and CRP with traditional thresholds has been shown to be a more accurate predictor of PJI than isolated elevations of the ESR or CRP alone [6, 29, 30]. If both markers are negative the likelihood of infection is nil.

Joint aspiration is the next step if the serological markers are above normal limits. The hip should be aspirated under fluoroscopic guidance to improve accuracy (Fig. 1). The patient should be off antibiotics for preferably 3 weeks. The

aspirated synovial fluid should be sent for Gram stain, aerobic and anaerobic cultures, cell count and differential and leucocyte esterase strip test. Many studies [5, 32] suggest that a WBC count of >1,700 cells/μL or a polymorphonuclear neutrophil (PMN) percentage of >65 % after the acute post-operative period is predictive of an infected knee joint [32, 33]. Schinsky et al. performed an investigation involving these markers in hip joint aspirate and recommended threshold values of >4,200 cells/mL for the WBC count and >80 % for the PMN percentage [6]. Diagnosis of peri-prosthetic joint infection during the acute post-operative period is complicated by the natural increase in inflammatory markers during this time. The cut-off values of serum and synovial fluid markers values for acute and chronic infections were discussed in many studies and the International Consensus Meeting on PJI [14] values are shown in Table 2.

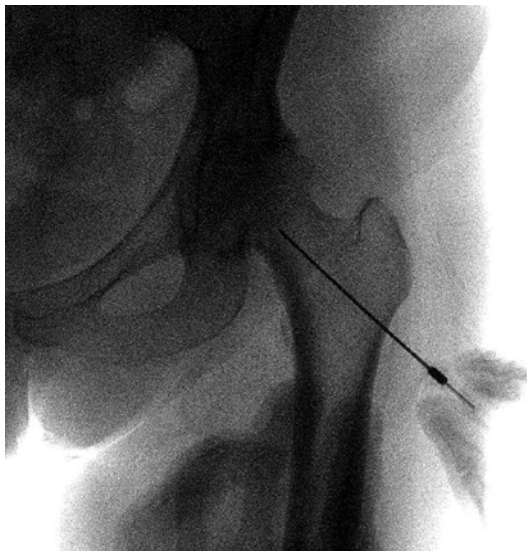

Fig. 1 Hip aspiration under fluoroscopic guidance

The usefulness of Gram stain of the joint aspirate in diagnosing PJI is limited as it has a high specificity but very poor sensitivity [34, 35]. The current recommendation is to avoid the routine use of this test to diagnose/refute infection [14].

Intra-operative frozen sections of intra-articular tissue samples are useful to diagnose PJI. Although this tool has been promoted by many clinicians [36, 37] and is supported by the AAOS guidelines [24], the accuracy is much influenced by the experience of the pathologist. A frozen section is considered positive if bacteria, and 5 or 10 PMN were identified per high power field. The difficulty of comparing the previous reports on frozen sections was that the authors used varying degrees of 'magnification' and varying definitions of 'PMN per high power field'. Currently the standard is that a frozen section is considered positive if there is more than 5 PMN in five or more high power fields, at (×400) magnification.

Leucocyte esterase strips are mainly used for urinary tract infection detection. Recently, reports were published to use this easy, inexpensive, quick test to diagnose PJI [38–40]. The results showed very high specificity and sensitivity of the strip test using synovial fluid. The leukocyte esterase concentration also showed a high correlation with the ESR, CRP, synovial WBC count, and synovial PMN percentage [39]. This simple test is considered very useful and accurate but one study [38] reported that the utility is limited by blood or debris in the synovial fluid rendering them unreadable in one-third of cases.

In a study [41] of confirmed infected arthroplasty patients, multiple synovial fluid inflammatory markers were studied with a proteomics protocol to determine the concentrations of the inflammatory proteins in each sample, and ROC curve analysis was used to establish the optimal

Table 2 The cut-off values of serum and synovial fluid markers values for acute and chronic infections agreed at the International Consensus Meeting on PJI [14]

	ESR	CRP (mg/L)	Synovial WBC	Synovial % PMN
Acute PJI (<6 weeks)	Not useful in acute PJI	>100	>10,000 WBC/mL	>90 %
Chronic PJI	>30 mm/h	>10	>3,000 WBC/per mL	>80 %

threshold of each potential marker for diagnosing peri-prosthetic joint infection. Using the optimal threshold of 4,270 pg/mL, IL-6 was the most accurate predictor of PJI, with a sensitivity of 87 % and a specificity of 100 % [41]. The high accuracy of IL-6 was also confirmed by another study [42].

Current Methods of Treatment

The treatment of a PJI is multi-factorial, including consideration of the duration of symptoms, patient immune status and co-morbidities, and the infecting organism(s). The options are antibiotic suppression without surgical intervention, debridement and component retention, one-stage exchange, two-stage exchange, resection arthroplasty and amputation.

Antibiotic suppression alone may be considered in the extremely frail patient who would not tolerate surgery and/or the infection is caused by a pathogen that is of low virulence and sensitive to antimicrobial agents [43]. Patients with multiple failed attempts to eradicate infection and who are not willing to undergo surgery are without options other than to try to control the infection with chronic antibiotic suppression [44]. In these cases, identifying the micro-organism before starting any antibiotic regimen is strongly recommended. Taking into account the low probability of infection eradication and limited clinical experience, the authors of ICM on PJI [14] recommended the following two phases of antibiotic treatment:

1. treatment to remission and
2. chronic suppression. The first phase of antibiotic treatment should be continued until clinical signs of infection disappear and systemic inflammatory parameters (ESR, CRP) improve for at least 3 months. After this period, chronic oral antibiotic suppression should be initiated using monotherapy of antibiotics with a good safety profile and high oral bio-availability [14].

Debridement and component retention are often used in patients with acute post-operative or acute hematogenous infections, within 2 weeks of the start of symptoms, in presence of a well-fixed and aligned implant, an antibiotic-susceptible organism, and sufficient soft-tissue coverage (Fig. 2) [45]. Recent studies [46, 47] suggested that MRSA had very low (16–37 %) eradication rates and streptococcal infections that were believed to be well treated with irrigation and debridement with implant retention had a low (65 %) eradication rate [48]. With inconsistent rates of infection eradication [48] and in the light of recent evidence, it is suggested that there is a decreased utility for surgical intervention with prosthesis retention [48].

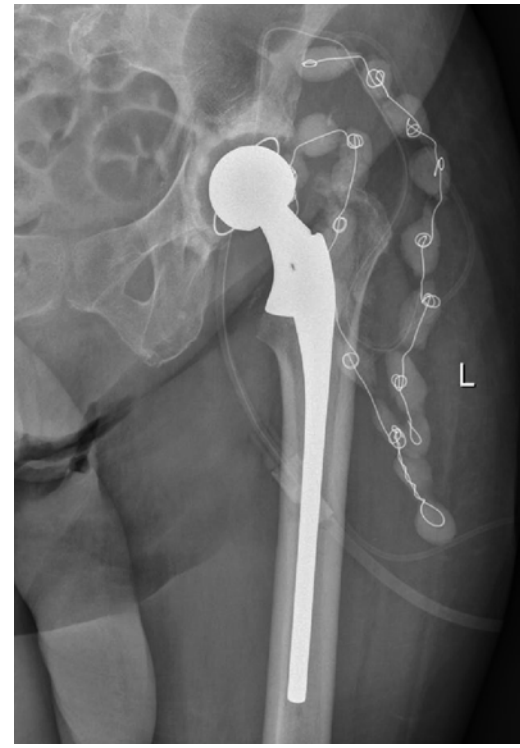

Fig. 2 AP radiograph of an acutely infected cemented hip arthroplasty, treated with debridement and component retention and hand-made antibiotic cement beads

One-stage exchange for PJI is a popular and successful treatment option, mainly in Europe [49–56]. The principles of one-stage exchange are as follows:

Pre-operative determination of the infecting organism(s) and respective antibiogram sensitivity are essential to specify the antibiotics to be loaded to the bone cement, which allows a

high local antibiotic elution directly at the surgical side. A specific antibiotic treatment should be planned by an infectious disease specialist. Systemic sepsis and the need for soft tissue reconstruction (flap) are contra-indications for one-stage exchange. The surgical success relies on the complete removal of all pre-existing hardware, including cement and restrictors and an aggressive and complete debridement of any infected soft tissues and bone material. Post-operative systemic antibiotic administration is usually completed after only 10–14 days [49]. The indication for one stage exchange is decreased when the infection is polymicrobial, the organism is gram-negative, especially Pseudomonas, and in MRSA and group D Streptococcus infections. Cementless revision in one stage exchange is not favoured, as the antibiotic addition to the cement is one of the key factors to provide very high doses of local antibiotic concentration. The success rates of eradication of infection were reported to be 83–93 % [49–51, 57].

Two-stage exchange is the gold standard of PJI treatment in North America [58]. In the first stage, aggressive debridement and removal of the all infected material and tissues are performed. In the case of the hip, an extended trochanteric osteotomy may be performed as this has been shown [59, 60] to heal and unite well, and not increasing the risk of recurrence of infection or osteomyelitis. After the removal of implants, either an articulating or static antibiotic spacer is placed [61, 62]. The advantages of an articulating spacer are that it preserves bone stock, restores proper limb length, prevents soft tissue contractures, and facilitates re-implantation [63, 64]. The alternatives for articulating spacers for septic hip and knee revisions include pre-manufactured spacers, intra-operative self- (hand) made spacers and spacers made using a mould (Fig. 3) [61]. There are no differences in the rate of infection control between manufactured spacers and surgeon-made articulating spacers used in the hip and knee. However, issues of cost, ease of use, and antibiotic delivery should be considered [14]. Intra-operatively prepared spacers have the advantage of being able to adjust the type and amount of antibiotics specific to the infecting organism. The antibiotics to be added to cement should be specific to the infecting organism, heat resistant, as it may become inactive during cement polymerization, water soluble to be released from the spacer and not allergic to the patient. The surface area of the spacer and the type of the cement, with high-viscosity cements containing methacrylate – methyl methacrylate (MA-MMA) co-polymers having better antibiotic elution profiles than other acrylic bone cement formulations with only MMA, are the main parameters for the amount of antibiotic released. For the same reason, hand mixing in a bowl without vacuum is recommended as bubbles facilitate elution of the antibiotics. The surgeon should be aware of potential systemic toxicity of the high dosage of antibiotics and assess the patient`s hepatic/renal functions pre-operatively and follow it post-operatively, as there are toxicity reports in the literature [65, 66]. A complete list of antibiotic type and amount that can be added to bone cement may be found in the Proceedings of ICM for PJI [14]. In patients with extensive bone loss, lack of soft tissue or ligamentous integrity and if there are concerns about further compromise of host bone with further ambulation, the surgeon may choose to use a static spacer.

There is no consensus among clinicians about what is the optimum time between the two stages of infected joint replacement, as reported times varies from 6 weeks to 1 year. The ideal duration of antibiotic therapy (IV alone or combined IV and oral) is not known. Decreasing the interim period of antibiotic treatment reduces cost and risk of bacterial resistance and complications of the therapy. There has been a recent trend for earlier second stage implantation but most of the literature recommends antibiotic therapy with duration between 6 and 12 weeks. There is some evidence suggesting that time intervals greater than 6 months result in sub-optimal results in restoring patient function and eradicating infection [67]. Improvement in the clinical signs of infection along with progressive sequential decreases in the values of ESR and CRP have been used to determine the ideal time for re-implantation [4, 6, 68–71]. In addition, no ideal cut-off value has been determined for these inflammatory markers, as several studies have

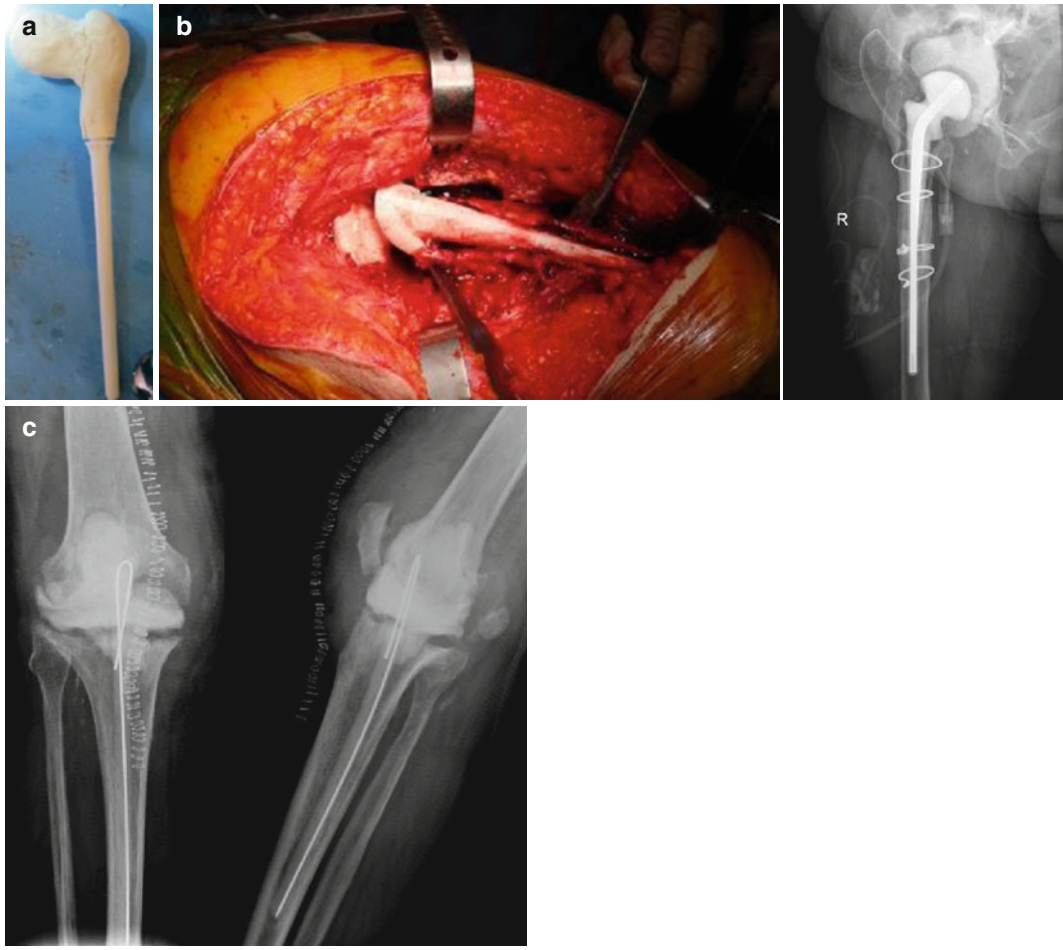

Fig. 3 Examples of spacers. (**a**) Hand-made hip spacer; (**b**) Pre-manufactured hip spacer- intra-operative photograph and post-operative X-ray view; (**c**) Static knee spacer with intramedullary antibiotic rod extension

shown that although these parameters were not normalized, the joints were sterile during the second stage surgeries [29, 69]. New inflammatory markers such as pro-calcitonin [72], leukocyte esterase [39, 41, 73], IL-6, and others [42] are being investigated and hopefully decisive and accurate cut off levels for re-implantation may be determined in the near future. An antibiotic "holiday period" at the end of the treatment period is desirable to identify persistence of infection before re-implantation. Two weeks period is considered adequate for control of clinical and serological parameters, but there is also no agreement on the duration of this time.

The clinical success of two-stage exchange has been reported to be between 85 and 95 % [64, 74–77]. In their recent systematic reviews, Romano et al. demonstrated that a two-stage exchange provides, a better outcome with respect to the eradication of infection in the knee [78] and similar results for the hip, although the difference in infection control was less successful [79]. Cemented reconstruction has the advantages of being more versatile, allowing the surgeon to add antibiotics to the cement, with the requisite adequate bone stock and meticulous cement technique. Uncemented reconstruction was thought to have higher recurrence rates, which was proved not to be the case in recent studies [80, 81].

In spite the advances made in the field of PJI, there is a considerable group of patient that

presents with persistent or recurrent infection following two-stage exchange [75, 82, 83]. The predictors of recurrent or persistent infection after two-stage knee exchange has been investigated and culture-negative peri-prosthetic joint infection, a methicillin-resistant pathogen, and increased operative time during re-implantation have been found to be independent predictors of recurrence of the infection [84]. Another study [85] comparing the success rates of infection eradication with regard to type of pathogens showed that gram-negative pathogens had as low a success rate (52 %) as two-stage treatment of an infection caused by MRSA (51 %), whereas the success rate for treatment of methicillin-sensitive gram-positive organisms (69 %) was considerably better [85]. Another study [86] investigated the rates of recurrence and de novo infection rates following failed two-stage exchange. In this group of patients there was an infection recurrence rate of 31.5 % and in the rest of the group at least one new pathogen was isolated. The authors stressed the minimization and optimization of co-morbid risk factors in the patients that may contribute to the low success rate of PJI treatment and recurrence of infection [86].

Resection arthroplasty remains an option when multiple two-stage procedures fail to eradicate infection, in patients with limited ambulatory capacity or severe medical co-morbidities. Patients with resistant organisms including MRSA and Enterococcus PJI experienced higher rates of salvage surgery (definitive resection, fusion, or amputation) and should be informed regarding possible outcomes [87–89]. A Girdlestone procedure is reported to successfully eradicate infection and eliminate pain, although all patients need ambulatory aids to mobilize and have up to 10 cm. of shortening of the involved extremity [90].

In patients with very limited chances of obtaining a functional, painless joint, unlikely to be reconstructed because of bone and extensor mechanism defects, in patients with extremely high medical risks and general status, and with polymicrobial infections or those due to highly resistant organisms for which there is no effective antimicrobial therapy, arthrodesis of the knee should be contemplated [45, 47, 69, 75, 89, 91–96]. The arthrodesis may be performed in one or two stages considering host factors, quality of debridement of infected tissues, bone loss. External fixation is favoured over internal fixation devices such as intramedullary rods and plates in a one-stage arthrodesis.

Amputation for treatment of PJI affecting the knee or the hip may be appropriate in a non-ambulatory patient, in necrotizing fasciitis resistant to aggressive debridement, severe bone loss that precludes arthrodesis (knee), inadequate soft tissue coverage, and multiple failed attempts at staged exchange and resection arthroplasty, or peripheral vascular disease and neurovascular injury [7, 45, 47, 75, 89, 94, 97–99].

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Indications for Vacuum-Assisted Wound Closure: When, Where and Why?

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Abstract

Vacuum-assisted wound closure relies on the application of negative pressure through an occlusive dressing. It acts by drawing the wound edges together, removing wound exudate and decreasing oedema, as well as by stimulating cell proliferation and differentiation, thus improving angiogenesis and promoting formation of granulation tissue. As this technique has become more popular over recent years, it is being applied for more and more indications. In orthopaedic surgery, it is used especially in wounds with a soft tissue defect, including exposed hardware; open fractures, especially of the lower extremities; for the fixation of skin grafts and flaps. The aim is to prevent breakdown or infection of high-risk surgical incisions; to accelerate closure of fasciotomies, and to improve the management of infected wounds. High-level evidence regarding the effectiveness of this technique and its superiority to other methods is scarce, and more studies are needed to clearly define the situations in which negative pressure wound therapy may be most useful.

Introduction

Drainage of wounds following surgery in order to avoid dead spaces and accumulation of excess fluid has been a long established technique for over 50 years [60], since the introduction of suction drainage and "later on" the Redon bottle in the 1950s. Several articles on negative pressure wound therapy were published in the Russian literature in the 1980s, and Chariker reported treatment of enterocutaneous fistulae using a wall-mounted suction device with a gauze interface. In the 1990s, two groups separately established

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treatment protocols for negative pressure wound therapy: in Germany, Fleishmann's group developed a technique using a polyvinyl alcohol foam, occlusive dressing and Redon drainage bottles for the treatment of open fractures [18], fasciotomy wounds [19], and wound infections [20, 21]. Meanwhile, Argenta and Morykwas [1, 55] published reports on a commercially available system (Vacuum Assisted Closure or VAC®, Kinetics Concepts Inc [KCI], San Antonio, TX) using polyurethane foam and a portable, adjustable vacuum pump. Several other commercial negative pressure systems have become available. As the technology became more popular, indications for its use have increased. In spite of its widespread use, only a few high-level studies exist regarding application of vacuum-assisted wound closure. The aim of this review is to summarize the evidence regarding the mechanism of action and indications for vacuum-assisted wound closure in the trauma setting.

Mechanism of Action

Vacuum-assisted wound closure is thought to act primarily by (1) contraction of the wound edges; (2) decrease of wound oedema and removal of wound exudate; and (3) stimulation of cells surrounding the wound surface. Secondarily, it is also believed to improve angiogenesis, promote formation of granulation tissue and decrease the bacterial bio-burden [47, 57, 62, 78]. However, several aspects of these hypothetical mechanisms are currently under debate [6, 27, 60].

Contraction of Wound Edges

Following traumatic or surgical skin disruption, the tensile forces of the surrounding tissues are interrupted, leading to wound gaping and soft tissue retraction and fibrosis. Vacuum-assisted wound closure exerts a contracting effect, drawing the wound edges together [60, 62] and avoiding the formation of a dead space [42].

Decrease of Wound Oedema and Removal of Wound Exudate

Negative pressure wound therapy facilitates removal of excess interstitial fluid, along with soluble proteins and electrolytes, thereby maintaining osmotic and oncotic gradients between the wound bed and the surrounding soft tissues. Wound exudate may contain an excess of matrix metalloproteases (MMP) and other factors, and has been associated with poor wound healing. Studies have suggested that modulation of MMP may be a mechanism of action of vacuum wound therapy [59]. Furthermore, the occlusive dressing prevents wound desiccation, avoiding scab formation and necrosis, and stabilizing the wound environment.

Constant evacuation of excess fluid reduces interstitial pressure, allowing capillaries collapsed by local oedema to re-open. Treatment with negative pressure has been shown to reduce the circumference of the affected extremity and reduce the surface area of the wound, and could be useful for resolving muscular oedema following a compartment syndrome [16, 19].

Stimulation of Cells Around the Wound Surface

Local negative pressure and flow of interstitial fluid creates shear and strain forces around the cells, leading to cellular micro-deformation. Additionally, as ions dissolved in the interstitial fluid flow past opposing charged glycoproteins, electric fields are created that in turn stimulate production of growth factors and other cellular responses [68]. It is well known that these forces can lead to an increase in cellular mitosis rates and tissue growth, as this principle is widely applied in distraction osteogenesis and expansion of dermal tissue [48]. In animal models, negative pressure therapy has shown to enhance production of growth factors such as vascular endothelial growth factor (VEGF) and fibroblast growth factor-2 [35]. Expression of Ki-67, correlated with cell proliferation, was significantly increased in another model using diabetic mice [69]. Significantly

higher levels of interleukin-8 (IL-8) and VEGF were detected in wound fluids of patients with traumatic wounds treated with negative pressure. Histological examination revealed increased expression of CD31 and von Willebrand factor, markers of increased neovascularisation [43]. All together, these factors would promote angiogenesis and formation of granulation tissue, as has been observed in clinical and animal studies. Morykwas et al. [55, 56] showed a significant increase in formation of granulation tissue following application of negative pressure to porcine skin wounds. Other studies have shown quicker wound closure in patients treated with negative pressure for chronic wounds such a diabetic foot wounds and in vascular ulcerations [78, 79].

Increase in Local Blood Flow

Due to one or more of the aforementioned factors, an increase in local blood flow to the wound may seem reasonable. Using a Doppler laser probe in a porcine model, Morykwas et al. [55] demonstrated a fourfold increase in local blood flow after applying −125 mmHg of negative pressure, but a decrease of blood flow with higher levels of vacuum. He also observed that the local tissue perfusion associated with continuous negative pressure began to decline after 5–7 min, but that this decrease was offset by intermittent negative pressure with maximum effect using a 5 min "on"/2 min "off" cycle. Timmers et al. [80] showed increased Doppler readings when a VAC device was applied on intact human skin, with increasing perfusion up to −500 mmHg using the VAC pump with a polyurethane foam. However, Wackenfors et al. [87] observed an area of hypoperfusion surrounding the wound edge treated with vacuum closure in a porcine groin wound model, and speculated that cycling the negative pressure could rescue the area of hypoperfusion by resultant hyperaemia in the "off" phase. Kairinos et al. [36] used a radiotracer technique to study tissue perfusion in healthy human subjects and found a decrease in perfusion that correlated with increased levels of suction. Further studies are necessary to elucidate the precise effect of negative pressure treatment on wound perfusion and the appropriate type of negative pressure most suited for each wound type.

Decrease in Bacterial Burden

In their original study on pigs, Morykwas et al. [55] described a decrease in bacterial load by the fifth day of treatment with vacuum-assisted closure. On the other hand, Mouës et al. [58] randomized 54 patients with acute and chronic wounds to receive either VAC treatment or moist dressings. No significant difference was observed in quantitative bacterial load between groups. However, qualitative analysis of the bacteria cultured showed a decrease of gram-negative bacilli such as *Pseudomonas aeruginosa*, and an increase of *Staphylococcus aureus* strains. Lalliss et al. [44] later confirmed these observations in a study on goats. In a retrospective chart review, Weed et al. [90] observed that the bacterial bioburden increased while negative pressure wound therapy was applied. In a randomized study of vacuum-assisted wound closure versus conventional treatment for acute and chronic wounds, Braakenburg et al. [9] was unable to detect a difference in bacterial load.

In conclusion, according to current evidence, the role of negative pressure wound closure as an independent factor in reducing bacterial burden is unclear.

Applications in Orthopaedic Surgery

As the technique became more widespread over the last 15 years, the possible applications of vacuum-assisted wound closure have become more varied [2, 78, 88]. Negative pressure wound treatment is now widely used in many settings; however, the relative paucity of published high-quality evidence regarding this modality of treatment is surprising. Several systematic reviews have not provided clear evidence on the superiority of this technique over conventional wound therapy [29, 31, 34, 82]. Furthermore, conclusions on efficacy and safety based solely on

published reports may no longer hold true after taking into account unpublished data. Manufacturers finance a large number of the studies on vacuum-assisted closure.

Industry-sponsored trials are more likely to report favourable outcomes [61], potentially leading to a publication bias [66]. These issues have recently cast some doubts regarding its superiority compared to conventional treatment [29, 31, 34, 65, 82].

Common indications in Orthopaedic surgery include (1) wounds with a soft tissue defect, including exposed hardware, and open fractures, especially of the lower extremities; (2) fixation of skin grafts and flaps; (3) surgical incisions at risk of breakdown or infection; (4) fasciotomies, and (5) infected wounds.

Wounds with Soft Tissue Defects

Soft tissue coverage is an important element regarding management of Orthopaedic injuries. In the context of high-energy trauma or repeat surgeries such as in revision arthroplasties, the soft tissue envelope is often severely damaged (Fig. 1);

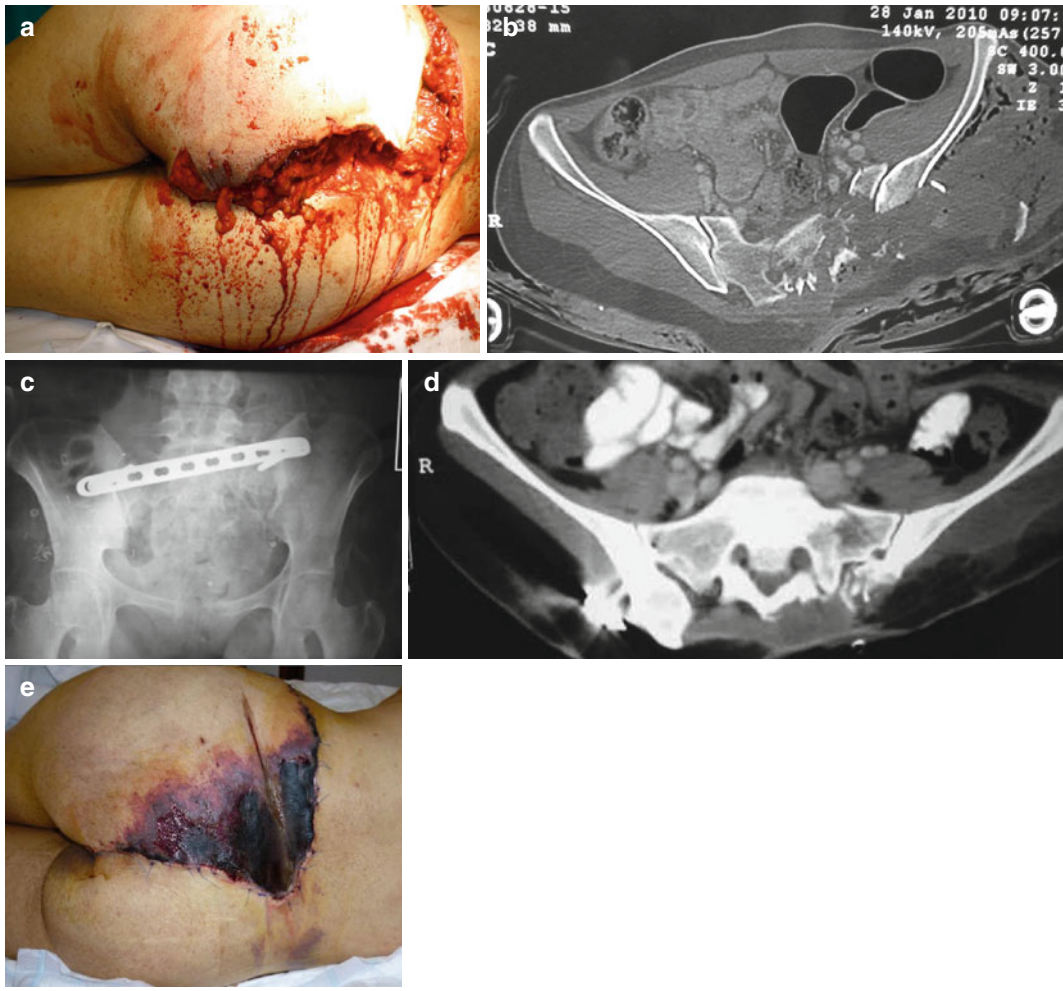

Fig. 1 A 31 year old woman hit by a train. Open pelvic fractura with extensive soft tissue injury (**a**, **b**). After initial treatment (direct ligation of the superior gluteal artery, internal fixation with a 4, 5mm plate, angiography, and colostomy) (**c**, **d**), the patient developed soft-tissue necrosis (**e**). Wound after debridement (**f**), and after six weeks with using negative pressure therapy (**g**, **h**), rotational flap (**i**). Final result at 2 years, following plate removal

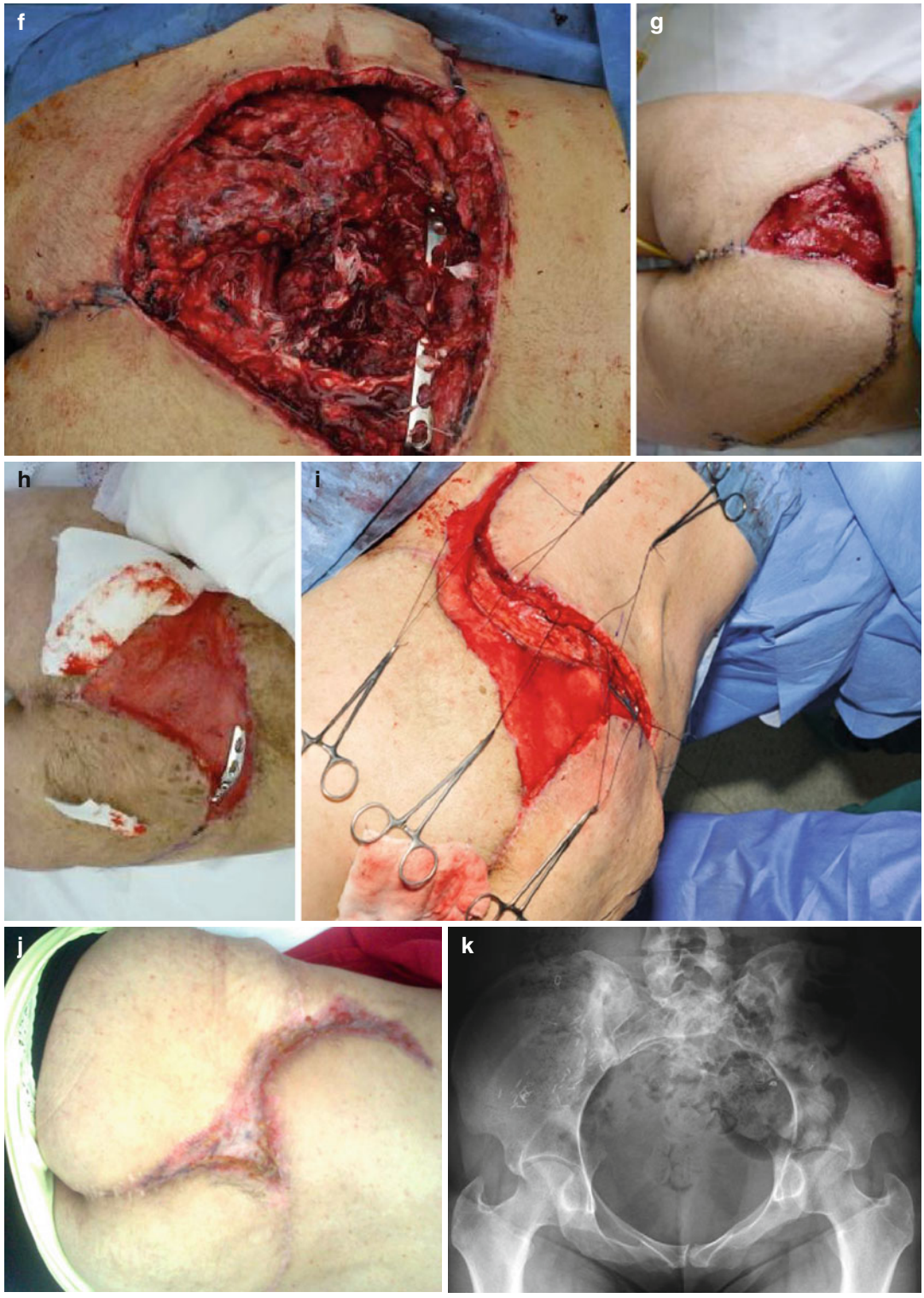

Fig. 1 (continued)

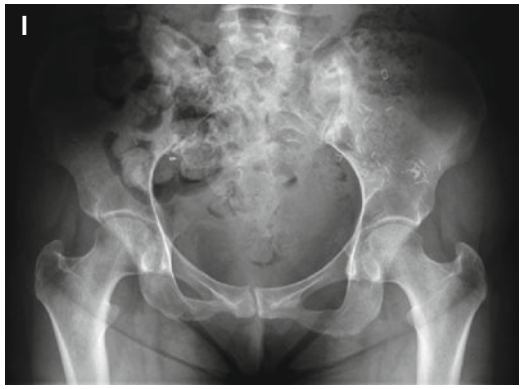

Fig. 1 (continued)

this is associated with compromised viability and bacterial contamination. Adequate surgical debridement and irrigation are key factors in order to reduce bacterial load and remove devitalized tissue prone to infection.

Conventional moist dressings require frequent changes, which lead to patient discomfort, increased workload, and repeat exposure to possible nosocomial contamination [9]. In 1986, Godina [28] reported a significantly lower infection rate in patients in whom flap coverage had been performed in less than 72 h following injury. The "fix and flap" approach, based on the results of this and other studies, comprises aggressive debridement and prompt fracture fixation and soft tissue coverage. In many cases, concomitant life-threatening injuries in the multiply-injured patient or technical issues such as surgeon or operating theatre availability make the "fix and flap" approach unfeasible. In these situations, negative pressure wound therapy could serve as a temporary treatment until definite wound coverage is possible [10, 42].

Several authors have observed that vacuum therapy may reduce the need for major soft tissue reconstructive procedures [15, 32, 33, 64, 73]. DeFranzo et al. [16] observed that when used on wounds with exposed bone and tendon, in several cases enough granulation tissue was formed over exposed tissue to obviate the need for a soft tissue transfer. Dedmond et al. [14] observed a 50 % decrease in the need for free tissue transfers or muscle flaps in a retrospective case series of paediatric open tibial shaft fractures. Other authors have also published favourable results in paediatric patients following lawnmower [70] and other injuries [26, 54]. A recent quantitative meta-analysis [79] of negative pressure therapy versus standard wound care in chronic wounds found that the size of the wound was significantly smaller and time to healing was significantly shorter in the vacuum therapy group. On the other hand, Mouës et al. [58] found no significant difference in terms of time to "ready for surgical therapy" status in their randomized study of acute and chronic full thickness skin defects.

To date, we have found only one randomised controlled study [72] evaluating the impact of vacuum therapy on severely contaminated open fractures. Patients treated with negative pressure wound therapy were only one fifth as likely to develop an infection; however, they found neither a significant difference in the number of debridement procedures or time to definite closure, nor a reduction in the need of flap coverage.

In a retrospective study comparing vacuum-assisted closure versus treatment with Epigard® in patients with open fractures, Labler et al. [40] observed a trend toward less infections using negative pressure therapy, in spite of more serious fractures and an injury severity score that precluded early coverage. Blum et al. [7] observed a decreased rate of deep infections in patients treated with negative pressure versus conventional dressings in his retrospective review of 229 open tibial fractures. However, a longer time to wound closure and a higher proportion of free flaps was also observed in the vacuum treatment group, although this may be due to a higher proportion of grade IIIB fractures in this group. Rinker et al. [67] found a lower rate of infectious and flap-related complications after wound coverage following vacuum treatment for 1–6 weeks for open tibial fractures. A retrospective review of open extremity fractures treated in Hannover, Germany, showed no increase in skeletal or soft tissue complications in spite of a mean time to definitive wound closure of 4 weeks [75]. However, several retrospective case-control studies have shown that delayed coverage by using negative pressure therapy for more than 7 days in

Gustilo IIIB/IIIC open tibial fractures significantly increased the risk of infectious complications [5, 11, 33, 49].

Based on these conflicting results, flap coverage should be performed as early as possible [73] in a physiologically stable patient; if surgical delay is required, negative pressure therapy is a valid option as a bridging treatment until coverage is feasible. It is accepted the effectiveness of vacuum-assisted wound therapy is comparable to standard wound dressing, at least in the initial post-traumatic period [38].

DeFranzo et al. [16] stated that coverage was possible even when exposed hardware was present; ideally, vacuum therapy should be applied within 72 h of hardware exposure. Vacuum therapy has also proven to be an effective adjunct for closing complex deep spinal wounds with exposed instrumentation in instrumented spine fusions complicated by surgical wound infection [52]. Several other studies [41, 63, 85, 86] have also shown promising results with vacuum-assisted closure following complications of spinal surgery, but more high-level studies are needed.

Vacuum-assisted closure is especially appealing in the setting of combat-related wounds, which have a high risk of infection due to cavitation with necrosis and contamination. The safety of vacuum therapy during aeromedical evacuation has been evaluated in several studies [17, 78], and vacuum-assisted wound treatment was seen to be a valid option for definite treatment of high-energy soft tissue wounds in a deployed wartime environment [23, 47].

Most of the authors reiterated that vacuum-assisted therapy was not a substitute for thorough debridement of all non-viable bone and soft tissue. Furthermore, adequately vascularised soft tissue must be available in order for vacuum therapy to work.

Fixation Rate of Skin Grafts and Flaps

The current evidence base is strongest for use of vacuum therapy on skin grafts [3, 89]. In a recent consensus document [39], this application was awarded a grade A or B recommendation depending on the clinical situation ("Negative pressure wound therapy must/should be considered"). In a randomized controlled trial evaluating split thickness skin grafts on burn patients, vacuum therapy was associated with a decreased loss of skin graft and a reduced hospital stay [50]. Negative pressure therapy was also found to improve the graft take rate and reduce the time to complete healing of free composite tissue grafts [39, 73].

Surgical Incisions at Risk of Breakdown or Infection

The bolstering effect characteristic of vacuum therapy, which facilitates graft incorporation, seems promising in treating surgical incisions at risk for wound breakdown, as well as de-gloving injuries and draining haematomas. In this setting, Labler described using negative pressure therapy for severe pelvic injuries with Morel-Lavallé lesions [42]. Stannard et al. [71] randomized patients with post-traumatic haematomas with persistent drainage to receive treatment with vacuum-assisted closure versus a standard pressure dressing, and found decreased drainage and fewer infections in the group treated with negative pressure. In the same study, he found similar results in patients randomized for vacuum therapy over surgical incisions for stabilization of tibial plateau, pilon or calcaneal fractures. Negative pressure therapy was also shown to be useful for prevention of wound breakdown following elective foot and ankle procedures such as total ankle replacement [13].

A prospective multicentre randomized clinical trial also led by Stannard et al. [74] compared the incidence of wound dehiscence and infections of surgical incisions after high risk fractures (tibial plateau, pilon, calcaneum) when using vacuum therapy versus standard care, and found an almost twofold higher risk of infection in patients treated with standard dressings. In addition, wound dehiscence was significantly less likely in patients treated with vacuum-assisted closure. However, a similar randomized trial by another group [51] was unable to detect differences in wound dehiscence or infection rates, so further

study is warranted before widespread adoption of this technique for high-risk wounds.

Closure of Fasciotomy Wounds

Vacuum therapy is thought to decrease oedema, accelerate formation of granulation tissue and apply uniform tension over the entire wound bed. Thus, it may be an interesting adjunct in the management of fasciotomy wounds, and early studies by Fleischmann et al. [19] showed promising results. A retrospective chart review [92] by the group in the USA that has licensed the most commonly used commercially available system also showed that vacuum treatment after fasciotomy for compartment syndrome allowed for a significantly higher rate of primary closure and a shorter time to healing among patients treated with the VAC® device compared with wet-to-dry saline gauzes.

However, other recent studies have shown opposite results. A retrospective chart review [22] performed by another group observed a nearly sixfold higher chance of needing a skin graft when being treated with negative pressure wound care following a fasciotomy. A recent randomized trial [37] observed a significantly longer time to definite wound closure and higher costs when treating fasciotomies with negative pressure.

In summary, it is unclear whether negative pressure wound therapy has beneficial effects in the treatment of fasciotomies following compartment syndrome.

Infection

The efficacy of antibiotic pouches for the management of traumatic wounds makes the idea of applying vacuum therapy in combination with antibiotic or antiseptic infusion onto the wound bed, or together with antibiotic-laden cement, seem appealing. Another future direction is the use of foam dressings impregnated with silver [24, 25, 76], which may help reduce bacterial rebound.

Fleischmann et al. [20] published a paper in 1997 describing vacuum therapy for the treatment of acute and chronic infections in 313 patients, with a 3.9 % recurrence rate of infections. The following year, they published a modification of their technique in which bacitracin or polyhexanide was intermittently instilled into the sealed area [21]. Several commercially available vacuum pumps later incorporated modifications that would allow for instillation of antiseptic fluids or antibiotics into the wound bed. A historical case control study [81] compared vacuum therapy combined with instillation of polyhexanide antiseptic solution to conventional treatment with polymethylmethacrylate (PMMA) beads and intravenous antibiotics for the treatment of osteomyelitis. The patients treated with VAC® and instillation had a 10 % recurrence rate, compared to 58.5 % recurrences for the historical controls. In addition, the length of hospital stay was shorter and the number of surgical procedures lower. Lehner et al. [46] reported that more than 80 % were able to retain their implant after using instillation negative pressure wound therapy to treat patients with infected orthopaedic implants.

However, some authors have observed that vacuum therapy may reduce the effectiveness of antibiotic-laden cement beads. In an animal model using goats [77] high levels of antibiotics were found in the effluent samples recovered from the pump's canister, and bacterial count was higher in wounds treated with a combination of negative pressure and antibiotic-loaded PMMA beads. Another study found local antibiotic concentrations were not affected, provided the fascia covering the cement was closed [45].

The use of negative pressure wound therapy as a co-adjuvant in the treatment of local infections seems promising, but formal recommendation cannot be made until well-designed studies in humans are available. It is important to note that vacuum therapy cannot substitute adequate surgical debridement.

Precautions and Contra-indications

Failure to maintain an adequate vacuum seal and then applying negative pressure wound therapy is the most common problem. Loss of vacuum may lead to desiccation of the wound bed, eschar

formation, and wound infection [12]. The potential causes of loss of suction are a puncture of the occlusive dressing, power loss of the motorized suction pump, clogging of the drainage system, or excessive fluid build-up underneath the occlusive dressing. While negative pressure systems using wall-mounted suction or drainage bottles have shown favourable results as well as the commercially available electrical pumps, the electrical pumps have the advantage of alarm systems alerting to these incidents (loss of power, loss of vacuum seal, or excess of fluid in the canister), as well as allowing for intermittent vacuum cycles and precise adjustment of the level of suction.

In 2009, the US Food and Drug Administration issued a warning [53, 83] alerting the existence of serious complications, including death. To date [84], they have reported on 12 deaths associated with vacuum therapy systems, mainly due to extensive bleeding. Extensive bleeding occurred in patients with vascular grafts (such as femoral and femoral-popliteal grafts), in sternal and groin wounds, in patients receiving anti-coagulant therapy, and during removal of dressings that adhered to or were embedded in the tissues. A case of life-threatening bleeding due to erosion of an anterior tibial artery in the vicinity of a grade IIIB open fracture of the fibula has been described [91]. Retention of foam dressing pieces and foam adhering to tissues or embedded in the wound was noted in several injury reports, requiring surgical procedures for removal of the retained pieces. Other complications described are worsening infection from original open infected wounds, fluid depletion due to aspiration of interstitial fluid [4] and toxic syndrome [30]. Circumferential application of negative pressure wound dressings should be avoided. Table 1 lists some of the contra-indications and precautions regarding vacuum-assisted therapy.

Table 1 Contra-indications and precautions with negative pressure wound therapy [8]

Contraindications	Precautions
Exposed vital organs	Active bleeding or a risk of bleeding (e.g., difficultly achieving wound haemostasis, use of anticoagulants)
Inadequate debridement of the wound	Exposed blood vessels close to the wound
Untreated osteomyelitis or sepsis within the vicinity of the wound	Difficulty maintaining a seal
Untreated coagulopathy	Uncontrolled pain
Necrotic tissue with eschar	Patient non-compliance with or intolerance to the procedure
Malignancy in the wound	
Allergy to any component required for the procedure	

Discussion

Vacuum-assisted wound therapy has been shown to be a safe technique if simple precautions are followed, with clinical results at least similar to conventional wound treatment. Clinical and basic research has proven it relies on sound physiological principles such as elimination of excess fluid, stimulation of growth through mechanical deformation and stabilization of the wound environment. Although this treatment modality is more expensive than traditional methods, the cost is offset by an increase in patient comfort, a reduced workload for healthcare personnel, and possibly a lower length of stay. It is possible to apply negative pressure therapy with commercially available portable pumps, as well as with homemade systems; though they are more expensive, commercial devices present a series of safety precautions unavailable with homemade systems.

Vacuum therapy does not serve as a substitute for adequate surgical debridement and control of infections. In Orthopaedic surgery, it has proven to be of greatest use as a bridging therapy until definite soft tissue coverage is possible in the multiply-injured patient in whom damage-control orthopaedics precludes early “fix and flap” treatment. Many other possible indications exist in acute traumatic as well as in elective orthopaedic settings (Table 2). One of the most promising future developments could be the use of vacuum therapy in combination with local antibiotic or antiseptic treatment in order to treat orthopaedic infections.

Table 2 Evidence-based recommendations for negative pressure wound therapy (NPWT) in orthopaedic trauma

Use of NPWT for soft-tissue coverage in open fracture wounds
NPWT **should** be considered when primary closure is not possible after or in between debridements as a bridge to definitive closure (Grade B)
NWPT **should** be stopped when delayed surgical closure is possible (Grade B)
NPWT **may** be used to downscale the complexity of closure procedures (Grade B)
Use of NPWT in skin grafts and flap procedures
NPWT **must** be considered to improve the rate of graft success (Grade A)
NPWT **should** be considered in wounds/patients with high risk of graft loss (Grade B)
It is **possible** to use NPWT as a treatment for flaps which have suffered partial necrosis after debridement of necrotic tissue to manage secondary defects (donor sites) which cannot be closed primarily (Grade D)
Use of NPWT for the prevention of wound dehiscence in high-risk surgical incisions of the lower extremities
NPWT **may** be used to prevent wound dehiscence and shorten wound drainage in high-risk surgical incisions (Grade C)
Use of NPWT for management of fasciotomies following compartment syndrome
NPWT **may** be used to improve the healing of fasciotomy incisions (Grade C)
Use of NPWT as co-adjuvant therapy for infections
It is **possible** that NPWT in combination with local antibiotic or antiseptic therapy could serve as an adjunct to treatment of musculoskeletal infections (Grade D)

Modified from Krug et al. [39]

The paucity of high-level evidence evaluating the efficacy of negative pressure wound therapy is surprising given its widespread use and numerous possible indications. Methodological issues in several of the few randomized studies performed, industrial sponsorship of a great number of studies and the existence of a possible publication bias raise flags of concern. As a consequence, several systematic reviews and clinical audits have placed the superiority of this treatment modality in doubt.

Further well-designed clinical studies are needed to ascertain the precise situations in which vacuum-assisted wound therapy may prove to be superior. Meanwhile, provided it is used with the necessary precautions, it remains a valid treatment alternative, especially for unstable patients, with soft tissue defects following trauma, to bolster skin grafts or de-gloving injuries, or for the treatment of other labour-intensive or high-risk wounds.

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Part II

Trauma

Early Total Care vs. Damage-Control Orthopedic Surgery: Evidence Based?

Christian Kleber and Norbert P. Haas

Abstract

The management of musculoskeletal injuries in multiple-trauma has changed tremendously over the last decades. From the initial concept "patients are too ill to operate" to early total care (ETC) to damage-control Orthopedic surgery (DCO) and now individual concepts based on anatomical and physiological injury severity. Despite the undisputable benefit and decrease of mortality of these concepts in multiple-trauma management, fundamental evidence and large prospective randomized multicentre trials are still missing.

In this article we present the advantages and disadvantages of ETC and DCO. The crucial step for successful management of multiple-trauma is the allocation of the right surgical principle (ETC/DCO) to the right patient. This most important task is presented and discussed in a separate chapter.

Introduction

Trauma is still the leading cause of death among people <44 years of age. Due to improvement of critical care medicine, the mortality rate has significantly decreased in the last decades [1]. New insights in the pathophysiology of multiple-trauma revealed a change in surgical management strategies with a shift from the classical tri-modal to a new bi-modal distribution of traumatic death [1]. In 1980 Harlan Stone first described a surgical technique of abdominal packing in coagulopathic bleeding [2]. The term "damage control surgery (DCS)" was described for the first time in 1993 by Rotondo and Schwab et al., showing a landslide reduction of mortality from 77 to 11 % in patients with combined visceral and major vascular abdominal injury [3]. The new surgical concept for emergency operations with primary bleeding control fluid, resuscitation, stabilization of haemodynamics and scheduled definitive procedure was born. Further investigations revealed the lethal triad with metabolic acidosis, impaired coagulation, haemodynamic instability, infection and pulmonary complications contributing to morbidity and mortality [4]. Based on the second-hit theory

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trauma surgeons realized that surgical procedures are also iatrogenic injuries to the immune system and organ function of severe multiple-trauma patients [5]. A review article in 2011 analyzed 26 studies (16 retrospective, 10 prospective) and confirmed the post-operative second-hit in multiple-trauma related to pulmonary dysfunction, coagulopathy, pulmonary embolism and inflammatory response [6].

Damage Control Surgery

In the beginning of DCS the primary focus was visceral surgery [7, 8]. Damage control laparotomy is an abbreviated laparotomy with the goal to obtain surgical bleeding control and prevent contamination from whole visceral organs followed by temporary abdominal closure, in order to prevent abdominal compartment syndrome [9]. Techniques for bleeding control are ligation, direct suturing, temporal shunting of vascular injuries, packing and splenectomy in the presence of splenic injury (AAST Grade 4–5 Moore). Furthermore, several techniques for temporary abdominal closure were developed (towel clip closure, temporary silos, vacuum-assisted closure, open packing, absorbable or permanent meshes) [10, 11]. Second-look operations for depacking or definitive surgery are planned within 24–36 h [12]. But until now no clear evidence for DCS is available. A Cochrane analysis from 2010 and 2013 revealed no randomized control trial for DCS [7, 8].

Damage Control Resuscitation (DCR)

According to the changes of surgical management of multiple-trauma and the new pathophysiological understanding of traumatic coagulopathy, fluid resuscitation and mass transfusion protocols have also tremendously improved in the last decades [13]. Today damage control surgery and resuscitation are the two cornerstones of successful multiple-trauma management. Techniques for DCR are aggressive re-warming, early blood product supply to reverse coagulopathy, recovery of normal physiology, enhancement of microcirculatory oxygen supply and the principle of permissive hypotension [13]. The principle of permissive hypotension can reduce mortality by restricted fluid resuscitation until surgical or interventional bleeding control [13]. The use of catecholamine should be avoided unless non-responsiveness to fluid resuscitation and attendant sTBI (severe Traumatic Brain Injury) or spinal cord injury. Mass transfusion protocols and lactate or base-deficit-guided fluid administration protocols go hand-in-hand with damage control surgery and both significantly contribute to the increased survival in multiple-trauma patients.

Damage Control Orthopedic Surgery (DCO)

The History of DCO

Trauma surgeons worldwide learned from the experience of DCS and developed simultaneously orthopedic management strategies for multiple-trauma. Analogous to visceral surgery a paradigm change occurred and changed osteosynthesis of musculoskeletal injuries in multiple-trauma over the past 50 years. In the 1960s most femur fractures were treated conservatively with traction or cast because patients were considered to be "too sick to operate" [14]. In 1970–1980s studies revealed the reduction of mortality due to early fracture stabilization [15]. The new philosophy of early total care (ETC) was born [14]. From this time-point trauma surgeons improved osteosynthesis techniques (minimally- invasive, angle-stable implants) but strove for as fast as possible primary definitive osteosynthesis neglecting the side-effects of extensive surgery. In the 1990s evidence evolved that primary osteosynthesis in multiple-trauma can have negative effects and may pre-dispose for adverse outcomes. After the first report of adverse events in severe traumatic brain injury (sTBI) while femoral nailing a paradigm shift occurred [16]. Scalea et al. introduced the name "damage control orthopedic surgery

(DCO)" in 2000 using external fixator in femoral fractures for multiple-trauma [17]. The name DCO is a homage to naval principles, preventing warships from sinking after torpedo attacks. Simultaneously in Germany Tscherne et al., at the Department of Orthopedic and Trauma Surgery in Hanover were using a staged protocol for multiple-trauma patients with femoral fractures and external fixators since the 1980s [18]. From that time point several studies showed decreased incidence of multiple organ failure (MOF), adult respiratory distress syndrome (ARDS) and mortality, but most of the studies addressed only femoral fractures. For other common injuries of e.g. tibia and humerus no studies referring to DCO exist. At the beginning of the twentieth century negative aspects of DCO evolved leading to the recent controversy of ETC vs. DCO in multiple-trauma.

For both, ETC and DCO, definitive evidence is still missing. An initiative of the German Trauma Society with a multi-center randomized control trial in 2010 failed due to insufficient data acquisition [19]. A systemic review of Nahm et al. in 2012 revealed the data heterogeneity of ETC/DCO in multiple-trauma [20]. A major problem is that no uniform, worldwide classification of multiple-trauma exists. Heterogeneous combinations of injuries with completely different pathophysiological mechanisms are compared at different end-points mostly using the incidence of MOF (multiple organ failure), ARDS (adult respiratory distress syndrome) or outcome. One exemplary prospective randomized trial and 16 retrospective trials investigated the incidence of MOF and ARDS in ETC/DCO [20]. Two prospective randomized and six retrospective studies compared ETC and DCO in multiple trauma [20]. Thirteen retrospective studies investigated sTBI and seven retrospective studied chest injury and the method of fracture stabilization [20]. This demonstrates the clear need for a uniform classification of multiple-trauma and large multi-center prospective randomized trials to prove the positive impact of ETC and DCO in the right patients.

Knowing that both concepts have beneficial effects, the present understanding of ETC or DCO in multiple-trauma management is, that the allocation of the right patient to the right therapy is crucial. In the following chapter we describe the advantages and disadvantages with recent evidence for the different aspects of ETC or DCO and give a clinical guideline whether ETC or DCO should be used.

Early Total Care (ETC) in Musculoskeletal Trauma

Early total care in multiple-trauma means appropriate definitive osteosynthesis as soon as possible. Early fracture stabilization within 24–48 h after trauma can decreases mortality, the incidence of pneumonia, ARDS, ventilation time, thrombosis, enhance pulmonary function, decrease narcotic requirements, improve pain control and decrease pulmonary embolism via early mobilization [21]. Additionally, patients have shorter hospitalization periods and invoke lower total costs [22]. Disadvantages of ETC are the potential high blood loss compared to DCO, extensive soft tissue injury with inflammatory boost, increased risk of pulmonary embolism and adult respiratory distress syndrome (ARDS) [15, 23]. But the incidence of pin track infections, secondary infections (femur <3 %, tibia <9 %) and need for additional surgery is significantly lower in ETC compared to DCO [24]. These results indicate the disadvantages of invasive DCO (e.g. external fixator) but also non-invasive DCO techniques like skin traction have negative effects. A prospective single centre study comparing ETC of femoral fractures to skin traction concluded that ETC is beneficial due to higher incidence of MOF in the skin traction group and increased total costs [21]. In general, the crucial factor is not the type of DCO compared to ETC. So what indicates the method we should choose? Patients with a moderate injury severity score (ISS), less than 18, and delayed fracture stabilization showed a trend to increased pulmonary complications, indicating that patients with moderate injury severity benefit from ETC [25]. But also patients with high ISS >17 and femur fracture were also successfully treated by nailing after aggressive fluid resuscitation prior to surgery [26]. These

two studies underscore that it is not only the anatomical injury severity but the responsiveness to fluid resuscitation and physiological condition prior to surgery. ISS is not reflecting the physiological injury severity. Also specific injuries and osteosynthesis techniques (nailing, plating, minimally-invasive) are not indicative. Nailing of femoral fractures in thoracic trauma for example does not generally worsen outcome but is associated in some patients with higher incidence of ARDS [14, 27]. The main factors for ARDS are mass transfusion, thoracic trauma and femoral reaming [15, 23]. Taking the longer operation time of ETC compared to DCO into account, patients with femoral fracture and reamed nailing are at higher risk of ARDS. Early stabilization of femur fractures with sTBI does not worsening the outcome [14].

The type of nailing in femoral fractures was investigated in two prospective randomized trials and showed a higher incidence of pulmonary complications in reamed femoral nailing compared to undreamed but failed to prove statistical significance [28, 29]. In the only study dealing with pelvic injuries in a small cohort of 15 multiple-trauma patients early internal fixation within 72 h gave no increase of MOF or ARDS compared to delayed fixation [30]. A retrospective trial on costs in femoral fractures with ETC and DCO showed significantly higher total costs in DCO concluding that from the economic point of view, ETC is less deficient compared to DCO [22].

Summarizing, ETC is beneficial in moderate injury severity or responsiveness to fluid resuscitation. The ISS or an isolated injury (sTBI, thoracic trauma) without physiological parameters (lactate, base deficit) is inadequate to safely allocate ETC or DCO in multiple-trauma. Furthermore, nailing in thoracic trauma is not generally contra-indicated and undreamed nails might be beneficial. ETC in moderate injury severity is economical compared to DCO.

Damage-Control Orthopedic Surgery (DCO)

The damage-control orthopedic surgery principle avoids long operation periods, extensive surgical approaches, uses quick and safe surgical procedures to restore mechanical stability and prevents bleeding and further contamination. Techniques of DCO are temporary conservative intervals via casts (e.g. upper extremity), extension or skin traction (femur, acetabulum, tibia) and external fixator [31]. Concomitant vascular extremity injuries are treated with direct hemorrhage control, ligation, suture, anastomosis or temporary shunting to preserve the injured extremity [32]. A prospective trial showed shorter operation times and lower blood loss in DCO compared with ETC [33]. Therefore, external fixation for example is a far quicker (22–35 min) procedure compared with nailing (125–136 min) in femoral fracture [17, 34]. The blood loss and post-operative systemic inflammation (thromboxane B2 compared to un-/reamed nailing; neutrophil elastase) was lower in the external fixation group compared to nailing group [35, 36]. The post-operative inflammation in primary nailing compared to a staged algorithm is significantly higher [27, 37]. These facts indicate the benefit for multiple-trauma patients of preventing second-hit because post-operative inflammation can induce endothelial dysfunction with organ- or multiple-organ failure. DCO is recommended in high injury severity, severe thoracic, pelvic and sTBI. A retrospective study showed a reduction of predicted (TRISS) compared to the observed mortality in femoral fractures with DCO [15]. Beside external fixation, skin traction is another possible option for DCO. In a retrospective study of femoral fractures, skin traction showed a lower sepsis rate and shorter length of hospitalization compared to external fixation [38]. Independent from the type of DCO, in abdominal trauma delayed internal fixation of musculoskeletal injuries is associated with a better outcome [39]. If successful resuscitation is not achievable, ETC of femoral shaft fractures increases the mortality in patients with severe abdominal trauma [39]. Negative effects on sTBI due to hypoxia, hypotension (eightfold higher) and increased fluid requirement while nailing of femoral fractures, but equally long-term neurological outcomes are also reported [16, 40]. Pelvic injuries in haemodynamically-unstable or in extremis patients should be mechanically stabilized and

rapid bleeding control via packing or embolization achieved. External fixation and non-invasive external pelvic stabilization are feasible methods for damage control [41]. Beside the emergency interventions the optimal timing of conversion from DCO to secondary definitive osteosynthesis is important. Secondary osteosynthesis between day 2 and 4 after trauma compared to 5–8 days after trauma revealed a significantly higher incidence of MOF in the early group with IL-6 levels >500 pg/dL ($r = 0.96$, $p < 0.001$) [42].

Summarizing, DCO is a quick procedure for bleeding control and mechanical stability in severe multiple-trauma and is beneficial regarding blood loss, operation time, post-operative inflammation and outcome. Especially patients with sTBI and abdominal injuries benefit from DCO. The post-traumatic inflammatory response is significantly lower in DCO compared with ETC. Considering the advantages of ETC the question arises: What patient needs ETC/DCO?

Spine Damage Control (SDC)

Analogous to femoral fracture and pelvic injury the optimal time point of reduction and stabilization of unstable thoracic and lumbar spine injuries in multiple-trauma is a controversy. ETC in spine injuries means operation within 24 h compared to delayed definitive stabilization. A review of Dimar et al. including 11 articles showed shorter hospitalization periods, ICU stays, ventilation days and lower pulmonary complications in patients treated with early decompression and stabilization of their thoracolumbar fractures (24–72 h after trauma) [43]. SDC is defined as a staged procedure of immediate posterior fracture reduction and instrumentation within 24 h (day-1 surgery). After stabilization and restored physiology a scheduled 360° spinal fusion based on biomechanical aspects (thoracotomy, thoracoscopy, lumbotomy, vertebral corporectomy, decompression, anterior fusion) if necessary is performed. More than 2/3 of these patients needed exclusively posterior stabilization. A prospective cohort study revealed that SDC is a safe and efficient treatment strategy in multiple-trauma [44]. A retrospective trial for unstable thoracic spine injuries compared early stabilization (<3 days) with late fixation (>3 days). The authors present significant lower pneumonia rates, less ventilation days, shorter ICU stay and lower total costs in the early stabilization group [45]. A review of thoracolumbar spine fractures confirmed these results [46]. No differences regarding spinal cord injury and the time-point of decompression and stabilization have been found in a national trauma databank study [45, 47–49].

Decision-Making and Guidelines

The issue of correct and optimal treatment of musculoskeletal injuries in multiple-trauma has been a controversy for 30 years. Patients benefit from early fracture stabilization but the optimal time-point and method are still a controversy [15]. No uniform algorithm on how to treat extremity fractures in multiple-trauma exists [50]. Rixen et al. performed a literature study from 1951 to 2002 and, due to insufficient evidence, could make no recommendation for ETC or DTC [50]. We know from the ETC concept and a randomized prospective multicentre trial that haemodynamically-stable multiple-trauma patients benefit from early fracture stabilization [51]. On the other hand femoral fracture is a predictor for ARDS and statistically predictive for mortality (OR 1.606, CI 95 %) and pulmonary complications (OR 1.659; CI 95 %) [15, 23]. Bilateral femoral fracture is associated with increased risk of systemic complications [15, 23].

But what is a stable or unstable patient [51]. Pape et al. revealed in a prospective multicentre randomized clinical trial three different patient types [51]. Stable patients with ETC (<24 h after trauma) present shorter ventilation time compared to DCO, but borderline patients had a higher incidence of ARDS in ETC group compared to DCO [51]. Borderline patients were defined as [52]:

- Blood pressure 80–100 mmHg
- Received 2–8 blood units within 2 h
- Lactate 2.5 mmol/dL
- Platelets 90–110,000/ml
- Fibrinogen 1 g/dl
- Body temperature 33–35 °C
- Thoracic trauma AIS >2
- Horovitz index 300

- Abdominal trauma Moore < III
- Pelvic type B/C injury (AO classification)
- Extremity trauma AIS 2–3

The pre-operative condition of the patient is imperative for the decision-making for the type of initial stabilization (ETC or DCO) in multiple-trauma [51]. It is not the concept that every patient with musculoskeletal trauma receives primary definitive osteosynthesis or all patients receive external fixation and secondary definitive osteosynthesis. ETC and DCO today go hand-in-hand. With regard to the advantages of ETC, and in respect of the pathophysiology of multiple-trauma, we understand ETC today as early appropriate care (EAC) [53]. DCO should not be abused in every patient. DCO is a powerful tool to successfully resuscitate haemodynamic unstable, in extremis and severe multiple-trauma patients. Before surgical decision-making the trauma surgeon has to estimate the total injury severity, know the patient's physiological status and anatomical injuries. Furthermore, multiple-trauma is a dynamic disease and demands repeated re-evaluation. Haemodynamically-stable patients receive ETC, unstable patients DCO. In borderline patients individual decision-making based on the dynamic of the physiological parameters and response to fluid resuscitation is made. Simultaneous operations in borderline patients can save operation time. Always choose the safest and less invasive surgical procedure that the patient endures. Stabilize the patient and restore physiology on ICU.

Management of multiple-trauma with musculoskeletal injury needs an individual concept for each patient. Therefore, consider damage control in the following patients [17, 19, 21, 24, 25, 42, 54–59]:

- Age >65 years
- Haemodynamics/circulation: Blood pressure, heart rate
- Metabolic criteria: acidosis pH < 7.2, lactate >2.5 mmol/L, base deficit >8
- Hypothermia <35 °C
- Mass transfusion requirement >10 packed red blood cells (pRBC)
- Coagulopathy: increased prothrombin (PT), partial thromboplastin time (PTT), thrombocytopenia, hypofebrinogenaemia
- Poor response to fluid resuscitation (<12 h after trauma; lactate/base deficit clearance)
- Injury Severity (ISS >25)
- sTBI (AIS >3)
- Multiple penetrating torso trauma
- Thoracic trauma (AIS >3)
- Poor oxygenation/ventilation (Horovitz index <200)
- Abdominal trauma (AIS >3; penetrating trauma combined with major vascular injury)
- Pelvic disruption
- Bilateral femur fracture
- Operation time >90 min
- Borderline patients

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Acute Management of Traumatic Bone Defects in the Lower Limb

T. Begue and J.C. Auregan

Abstract

In severe trauma of the lower limb, acute management needs to refer to Damage Control Orthopaedics (DCO). When additional bone, loss is encountered, surgeons face more challenging situations and decision about treatment of the bone loss is difficult. Critical size defects are those exceeding 5 cm and they cannot be treated by conventional bone grafting due to graft resorption and additional procedures needs for complete fusion.

The induced membrane technique, so-called Masquelet technique, is dedicated to treat very huge bone defects up to 25 cm, using a two-stage procedure with a cement spacer insertion for six to eight weeks then filling the chamber created around by autologous cancellous morcelized bone graft.

Ilizarov techniques can be used either by immediate shortening, acute shortening followed by compression-distraction techniques, or bone transport. Advantages and pitfalls include difficulty for shortening over 3 cm, length of external fixation with infection pin sites, docking site non-union, and extrusion of transferred bone due to retraction of soft tissue in the defect.

Free vascularized fibula transfer is the last option for acute reconstruction for traumatic bone loss in case of femoral bone loss with a double-barreled technique or tibial defect over 12 cm.

Tissue engineering will modify solutions by combining mesenchymal stem cells, specific scaffolds, and growth factors such as bone morphogenetic proteins (BMP).

Introduction

In severe trauma of the lower limb, the level of injury of the bone, the soft tissue environment, the presence of arterial damage and duration of ischaemia and nerve injury, in particular plantar nerve disruption, are all parts of the decision of

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whether or not to preserve the limb, Different scores have been chosen [1–3] to try to define which limbs must be reconstructed, and those which may need immediate amputation. None of them emphasises the importance of the amount of bone defect. In addition, as scores are difficult in determining what to do, recent authors [1, 4, 5] have emphasized preference for "damage control management" (DCO), not only in polytraumatized patients but, as an extension, in severe multi-tissue injuries of the limbs especially the lower limb. We have based our initial bone treatment management on this Damage Control Orthopaedics method of evaluation and proposals.

In DCO, severe trauma of the lower limb includes any type of fracture. Most often those fractures are open and the severity of the bone lesion is part of the whole injury. The soft tissue lesion is a second critical criterion for complete management of the fracture. In fact, in very severe lower limb injury there is a patchwork of bone lesion from simple fracture to comminuted ones with bone defect, surrounded by a massive destruction of the soft tissue where correct analysis of viable and unviable ones is very difficult to assess. All injuries make management of such trauma quite challenging, and may lead to amputation, non-union or malunion, infection, joint stiffness and poor function [3]. For Meinig [6], management of traumatic bone defect must be done in three consecutive phases which are phase I: initial patient management; phase II: interim management – skeletal fixation and definitive soft tissue coverage; phase III: final bone defect reconstitution. Time schedule of all those procedures are not well defined, and we think that they can be done in a shorter time. In our unit, management of this type of injury, even in a single lesion of the leg, is done using the DCO guidelines. Serial débridement of soft tissue within the first days after the injury is done, and temporary external fixation is the standard of care for the fracture. Such procedures help to remove compromised tissue and avoid any huge bacterial contamination. At the end of the first week after the injury, definitive treatment can be done, with removal of the ExFix, secondary and definitive internal fixation, and soft tissue coverage to resolve all defects.

In some cases, either due to the severity of the initial trauma, or due to secondary dead bone resection, a bone defect can be seen. The extent of the bone defect tends not to be a limiting factor for limb salvage in the lower limb, even if time for complete healing is quite high [6, 7]. Treatment of such bone defects may be difficult when its length is "critical", and different treatment protocols have been proposed such as conventional cancellous bone graft, open-air cancellous Papineau grafting [8], fibula transfer in a non-vascularized or vascularized manner, and bone transport [3, 9].

"Critical-Sized" Bone Defect in the Lower Limb

As critical-sized bone defect is mentioned, one can argue that the definition of such clinical situation is unclear. From animal models, researchers have defined a critical sized bone defect as "the smallest osseous defect in a particular bone and species of animal that will not heal spontaneously during the lifetime of the animal" [10]. From a clinical point of view, critical sized bone defects can be defined as segmental bone losses exceeding 2–2.5 times the diameter of the injured bone [10–12]. So the size is different in the lower limb in the femur and the tibia. We can assume that a segmental bone defect, which is a complete cylindrical defect with no contact between the proximal and the distal fragment can be considered as a critical sized bone defect if the length is of 7–8 cm in the femur, and 5–7 cm in the tibia [7].

As part of the DCO management, this defect must not be considered at the time of early care of the open fracture, but after the serial débridement and bone excision, as the defect may be more important at the end of the first stage after débridement of the fracture site. In our unit, we identify this critical sized defect at time of definitive total care, using clinical and radiological measurements.

All authors agree that critical sized defects in the lower limb will not heal without secondary intervention [13]. As the treatment scheduled may be different on the basis of the results of each

bone in the lower limb, the way to identify a critical sized defect is important. In the femur, numerical X-ray analysis is essential, as the diameter of the bone may be quite different between gender and ethnicity of the patients. Discussion with radiologists will help to evaluate correctly the real size of the defect. CT-scan may be used but is not mandatory, as precise evaluation is not really needed. For Dugan et al. [11], a critical sized defect in the femur can be considered as less as 2.2 cm of bone defect, but they have considered, in their study, only polytraumatized patients which may give more challenges for healing as others bone segments may be involved in the initial trauma. Tibial bone defects are easier to evaluate as the bone is close to the skin, and direct measurement can be done. For Calori et al. [9] a critical sized defect leads to non-union and this can be observed when the defect is over 3 cm whatever is the bone involved. Based on different literature considerations, we can assume that any defect which is over 3 cm must be carefully considered as close to a critical sized defect and a specific treatment protocol in emergency must be added to the fixation device used.

Localisation of the defect is another major point. Diaphyseal defects need, for a correct healing process, to obtain cortical bone at the end of the process. In most cases, both ends of the defect are of Haversian (cortical) bone type, where fusion is hard to obtain. Alternatively, cancellous bone from the metaphysis or the epiphysis is easier to reconstruct and to fuse. In the latter, the main problem is the adjacent joint function after healing has been achieved. Then, the ideal treatment must be able to reconstruct the missing bone while allowing immediate function of the muscles and joints located around the defect. In addition, such clinical situations are associated with soft tissue damage, and its treatment must be included in the operative protocol. As we know, early soft tissue reconstitution aids in the prevention of deep sepsis as well as preparing an environment advantageous for bone grafting [6, 13].

When dealing with critical-sized bone defects, surgeon must consider whether the defect is a cavitary one, where some contact between the fragments ends is still present, even if the surface of contact is very poor, or a segmental one, where a complete cylinder of bone is missing, with a tendency of the soft tissues to fill the defect if it is left without specific treatment.

Based on all the above conditions, the treatment protocol can be considered to have two possibilities:

1. in the acute phase, the surgeon decides to maintain the defect, either segmental or cavitary, and the difficulty is how to do it, and when to treat it? ;
2. in the acute phase, the surgeon decides to remove the defect using acute shortening techniques, and the difficulty is how and when to restore the normal length of the limb? The different options are discussed in the following chapter.

Conventional Cancellous Bone Graft for Treatment of Large Bone Defects

This type of graft is the first to be tried when the surgeon has decided to maintain the bone defect. Autologous bone grafting remains the gold standard in the reconstitution of such defects. Autograft is the only material that provides osteogenic cells (osteocytes, osteoblasts, marrow stem cells), osteoconductive matrix (inorganic mineral), and osteo-inductive molecules (BMP's, transforming growth factor-beta, vascular endothelial growth factor, and others) [6, 14]. All those criteria have made conventional cancellous bone grafting as the "gold standard" against which all others techniques must be shown to produce better results.

With defects of 2 cm or less, traditional anterior iliac crest bone graft is usually sufficient as 5–72 ml can be harvested. Larger defects can still be grafted with iliac crest by multiple harvest sites such as the contralateral site or use of the posterior iliac crests with amounts of 25–90 ml being obtained. In addition, the use of a small acetabular reamer may result in less donor site pain and larger volume of graft.

The most recent development in autologous harvest techniques is the intramedullary canal harvest. A recent review confirms that the use of

the Reamed Irrigator Aspirator [9]. In a single pass, reaming of the femur produces significant amounts of bone graft (25–90 ml) with low rates of complications and post-operative pain. While the rate of complication is lower than that described in conventional iliac crest harvest, iatrogenic femoral fracture has occurred. In addition, studies of RIA harvest material suggest that it is rich in growth factors, viable cells, and morcellized trabecular bone. The RIA harvest can thus be considered biologically equivalent to iliac graft. The bone marrow harvest, however, lacks any structural properties that can be achieved with tri-cortical iliac harvest [6].

There are very few publications about the treatment of critical sized defects by conventional bone graft, either solid or cancellous. In our practice, when this type of graft is used, we have observed a fusion at bone ends, but bone resorption at the most central part of the graft leading to non-union. Partial healing can be noted as the amount of bone defect has been treated, but with additional procedures needed to get complete fusion of the defect. Those results were also reported by Pelissier et al. [15], as this author had bone resorption in 5 of 14 cases (35.7 %), to be compared to a 8.33 % rate with other procedures available. In the same paper, the mean bone defect size was 4.37 cm in the conventional graft group versus 9.58 cm in the other procedure group. We can assume that conventional bone graft is not suitable for critical sized defects.

"Induced-Membrane" (Masquelet) Technique

Maintaining the volume of the defect without filling it as a primary treatment protocol leads to retraction of the soft tissues inside the defect, and the graft bed must be rebuilt at the time of the grafting itself [3]. In 2000 [16], we published an original technique where the defect is filled up, at the initial phase, by a cement spacer. Since then, the procedure is known as the Masquelet technique or the Induced Membrane technique. The initial fracture management is according to the Damage Control Orthopaedic concept [1], with limb alignment and external fixation. In the following days, additional débridements are done with resection of all dead or devitalized tissues, including bone fragments if needed. At the end of the first week, a comprehensive evaluation allows the replacement of the external fixation by an internal, either plate or nail, whist at the same time performing flap coverage of the skin defect if needed. Treatment of the bone defect can be done accordingly.

The induced membrane technique consists of a reconstruction of the segmental or cavitary defect with a cement spacer built with commercially available PMMA-antibiotic beads or surgeon-fabricated PMMA-antibiotic spacers [6]. The technique is easily performed. PMMA cement is prepared, and a tubular or appropriately shaped spacer is fabricated to span the defect and overlap the native bone ends [17]. Overlapping bone ends allow a continuous reconstruction with the non-injured periosteum, which will be of value for the second procedure. Antibiotic cement is utilized as an adjunct to around the bone defect to prevent deep sepsis. The cultivation of an "induced membrane" has clinical and basic science advantages for delaying definitive autologous bone transfer into segmental defects [17, 18]. The global concept is a two-stage procedure dedicated to wide diaphyseal bone defects with the use of a cement spacer placed within the osseous void, in the first phase. In contact with the PMMA cement spacer a pseudosynovial membrane forms. The cement spacer remains in place for 4–8 weeks to allow the membrane to fully develop biochemically and physically.

The second stage is carried out with removal of the spacer by breakage, maintaining the membrane intact, filling the defect by bone grafting within the induced biomembrane [19]. The intramedullary canals must be opened and freshened on either end of the defect, removing the membrane only at this level. This must be done also in cavitary defects to get a close contact between living bone and graft [7]. The pseudomembrane induced by the spacer prevents graft resorption and favours its vascularisation and corticalisation [10].

The role of the membrane in healing has been examined in animal models. Histological and immunochemical analysis has revealed that the membrane is made of a type I collagen-heavy matrix, and fibroblastic cells are the dominant cell type. The inner aspect of the membrane is

epithelial-like and composed of fibroblasts, myofibroblasts, and collagen bundles. This tissue is highly vascularized, and the PMMA spacer causes a mild foreign-body inflammatory response; giant cells and macrophages were discovered on histological evaluation [17, 18, 20]. The membrane contains a high concentration of vascular endothelial growth factor and an angiogenic factor that has been shown to increase the vascularity of the surrounding tissue [18, 20].

Soft-tissue repair, if needed, is performed with a muscle flap during the first stage (spacer insertion) operation. The first role of the spacer is mechanical, as it prevents fibrous tissue invasion of the recipient site. Moreover, since the spacer behaves as a foreign body, absence of infection after 2 months is an excellent indicator of favourable local conditions for bone grafting [10]. The definitive fixation implant should have sufficient mechanical properties to function during the duration of bone reconstitution. Stable fixation is mandatory as biological reconstruction using the induced membrane technique cannot be associated with dynamisation. With early restoration and maintenance of the limb in the anatomical position, patient comfort, rehabilitation, and function are greatly enhanced which is a distinct advantage over distraction osteogenesis [6]. In a recently published experience, 40 patients with an acute bone defect were treated with this technique [21]. Bone defect sizes were from 2 to 10 cm. All patients healed, with a final reconstruction close to a normal bone (Fig. 1). Donegan et al. [19] has used this strategy in five patients treated acutely, with bone union obtained in all cases. All defects were above the critical sized level, either in the femur or in the tibia. Different types of bone substitutes have been used in the Masquelet techniques, as well as bone morphogenetic proteins, demineralized bone matrix, or allograft [7, 10, 15, 19, 20]. All authors agree on the importance of elution of several growth factors, the prevention by the membrane of graft resorption and promotion of revascularization and consolidation of new bone. Excellent clinical results have been reported, with successful reconstruction of segmental bone defects >20 cm [20]. For Taylor et al. [20], if an IM nail is in place, nail removal or exchange is not recommended because of the potential for destabilization. Excellent results have been reported with maintenance of the original IM nail [22].

The main disadvantage of the induced membrane technique is that of a two-stage procedure. Some authors have proposed a similar technique in a one-stage manner using Cylindrical Titanium Mesh Cage (CTMC) and polylactide membranes technique [10]. It is a one-stage procedure that relies in the use of cylindrical hollow mesh implants, consisting of biodegradable polylactide membranes or titanium cages [12, 23]. The cylindrical implant surrounds the segmental defect and is packed with cancellous allograft. The bone cage interface is protected by means of internal or external fixation. Initially reports were of cases which included titanium mesh-allograft reconstructions of large tibial diaphyseal defects, which were protected by intramedullary nailing. Cylindrical polylactide mesh membranes and titanium cages demonstrate marked similarities in the treatment of segmental long-bone defects when applied in combination with bone graft [10]. Biocompatibility of the mesh material (lactide and/or titanium), fenestrated design and ability to enclose bone graft are some of advantageous biological properties of those devices. Moreover, a graft composite consisting of allograft chips mixed with demineralized bone matrix or rhBMP-2 has been successfully used [10].

Acute Shortening, Compression-Distraction and Bone Transport

As an alternative to staged care, fractures with bone loss may be effectively managed with bone transport techniques. Inspired by Ilizarov's philosophy, this can be accomplished by acute shortening of the fractured area and immediate or secondary lengthening of the bone. The advantage of this approach is its inherent simplicity. Nevertheless, different types of shortening have been described [24]. Isolated acute shortening and bone healing is the more simple technique [13]. The goal is to remove completely the defect, ending with both bone ends in contact waiting for fusion. If this is a suitable technique in the upper extremity, this type of management is more controversial in the lower extremity, as any final limb discrepancy will lead to gait disturbance. After bone union,

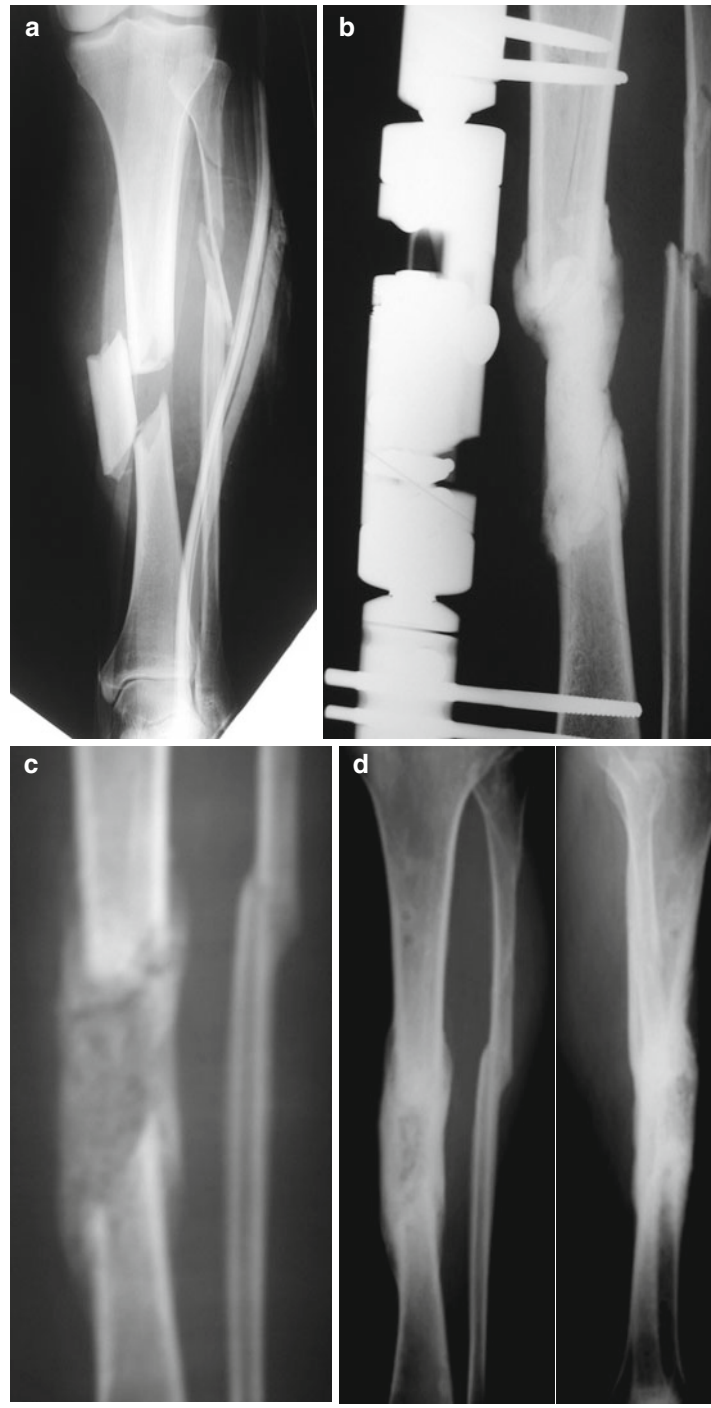

Fig. 1 (**a**) Emergency X-ray of a IIIA open fracture of the tibia. Segmental bone is devitalized outside the skin. (**b**) Segmental reconstruction with a cement spacer overlapping bone ends, and external fixation. (**c**) Autologous cancellous bone graft: appearance after 4 months. (**d**) Final appearance after 3 years

additional techniques will be required for lengthening. The concept of isolated shortening is to create an ideal biomechanical environment to promote union without any need for bone grafting as direct cortical contact encourages primary osseous union [13]. Other techniques include acute shortening with compression-distraction at the fracture site, or acute shortening and progressive lengthening after a corticotomy distant from the fracture and progressive bone transport [24, 25].

All techniques have their own advantages and pitfalls. The main advantage of acute shortening is to cure immediately the bone defect, as bone ends will come into contact. Doing this, in case of associated soft tissue defect, allows direct wsound closure to be done without any additional plastic surgery. This may help in circumstances where plastic surgeons or trained trauma surgeons in flap surgery are not available, i.e. in undeveloped countries, or with mass or war trauma. This technique needs external fixation either with a circular or a monolateral stable frame. Doing this, the duration of hospital stay can be lowered which is of value as it lowers costs and additional co-morbidities. Surgeons can expect fusion when apposition of bone ends is achieved and in a compressive situation. Nevertheless, the high level of "docking site" non-union is high [8, 24, 26, 27]. Pitfalls include a long time of external fixation with a high rate of pin site infections, skin scars, and non-union at the site of distraction. But the main pitfall concerns the amount of acute shortening that vessels, nerves and soft tissue of the lower limb can tolerate. All authors [24, 26] have fixed the maximum length of acute shortening to 3 cm, which is rather limited, and cannot be enough for large bone defects of critical size. For the later, Sen et al. [26] has proposed a gradual shortening at a rate of 2 mm/day with good final results. If acute shortening doesn't need additional surgery in the upper limb, this type of technique in the lower limb leads to a discrepancy needing to be compensated later [24]. Based on clinical results [24, 28], isolated acute shortening can be used in the tibia, but must be excluded in the femur. Immediate contact can be expected for defects lower than 3 cm, but are dependent on the vascularisation of the foot in larger defects. In all cases, partial resection of the fibula is needed, and late lengthening must be considered due to functional consequences.

After acute shortening, leg length discrepancy can be overcome by distraction lengthening at the fracture site at a rate of 1 mm/day after a latency period of 10 days [10, 24], or during the shortening phase through a corticotomy at a proximal or distal level depending on fracture localization, until there is equalization of leg-lengths [25, 26]. In the paper of Sen et al. [26], 24 patients were treated using the shortening-lengthening technique in an acute manner. There were 14 Type IIIA and 10 Type IIIB fractures according to Gustilo classification. The mean defect was of 5 cm (3–8.5).

The author prefers an alternative method to provide solid union. It is to compensate for bone loss by transporting healthy bone to the fracture site, hence bridging the bone defect [26]. This is done by simultaneous corticotomy and lengthening down to equal length. Mean healing time in this series was of 7.5 months [4–11]. Using the healing criteria of Paley and Maar [29], the Index of External fixation was of 1.4 month/cm. The author has reported the incidence of 52 complications which was 2.08 per patient. Different major complications were seen such as equinus deformity, hardware complications, too rapid fusion, limb leg discrepancy, adjacent joint stiffness, mal-union and osteitis.

For Sen et al. [26], these findings support the argument that, when compared with bone transport series and the length of time for external fixation, the treatment period was shortened and the rate of complications and secondary interventions were decreased in patients who underwent simultaneous acute shortening and lengthening. At the same time, according to the results, mal-alignment, such as angulation and translation, were not observed if the shortening-distraction technique was used in the acute post-traumatic period when the plasticity and mobility of the soft-tissue is still present. For Rigal et al. [24], stability of the construct is easier to obtain in a compression-distraction technique when compared to Bone transport. This may explain the lower risk of misalignment that can be observed during the progression of the bone fragment. Needs for additional bone grafting at the docking site are still controversial with this technique [24, 26]. All authors agree that initial debridement and resection of dead bone are mandatory to expect a fusion within segmental bone ends after compression with no complementary procedure.

El-Rosasy [25] experienced this technique in ten acute tibial fractures (seven IIIA and three IIIB Gustilo types), with bone loss ranging from 3.0 to 7.0 cm. The author outlined some technical details for good final results. The amount of bone resection required was decided intra-operatively, so that

the bone limits are apparently healthy bleeding bone ends. Bone ends must be in contact either by wedging one bone end into the other or by a square osteotomy of the bone ends in order to obtain the widest area of contact, and get a stable fracture site. In case of a progressive shortening, bone ends must be cut perpendicular to the anatomical axis. Fixation is done, in this paper [25], with an external fixator. A circular frame similar to the Ilizarov must be chosen when dealing with osteoporotic bone, and if limb lengthening is of more than 5 cm, fixation of the foot was necessary. A monolateral external fixator can be used with good bone quality and short limb lengthening (less than 5 cm). The use of a monolateral fixator simplifies the fixation and is tolerated better by the patients.

All authors emphasize that acute limb shortening with immediate re-lengthening by corticotomy at a healthy level eliminates the problems encountered with bone transport by converting a complicated limb reconstruction into a simpler one, that is a linear limb lengthening. Bi-focal compression-distraction osteogenesis is a safe, reliable, and largely successful method for the acute treatment of open tibial fractures with bone and soft-tissue loss. Further non-operative or operative treatment can correct most complications [26].

The initial use of Ilizarov techniques for treatment of acute bone defects was bone transport without shortening. In such conditions, the defect is maintained, as well as the soft tissue defect when present [30]. The global procedure is well known as distraction osteogenesis. The Ilizarov method is a very satisfactory method for the reconstruction of long-bone defects that are accompanied by soft-tissue deficiency. Nonetheless, surgical experience and patient collaboration are needed for a successful result [10]. As mentioned by El Alfy et al. [30], in such techniques the defect is not removed but maintained as it is after iterative debridement. Soft tissue injuries associated with the bone loss can make reconstruction very difficult and limit the functional outcome. For this author, during distraction osteogenesis, bone and soft tissues are lengthened, giving an opportunity for a spontaneous closure of the soft tissue defects without the need for additional plastic surgery. This is due to the fact that during the distraction, the bone ends carry simultaneously the surrounding soft tissues. This technique was the usual practice in the early 2000s. Paley and Marr [29] reported on 11 fresh fractures treated with distraction osteogenesis including 8 cases with additional soft tissue defects, all treated by soft tissue transport in concert with bone transport. In the paper from Paley and Maar [29], the mean bone loss was of 10.7 cm [2–20]. The Paley criteria were an Index of External Fixation of 2.1 month/cm. In the same paper, the author proposed to modify the Distraction osteogenesis technique in acute bone loss, by doing not only one corticotomy, two different on the same bone, at the proximal and distal metaphysis levels, carrying the bone transport on the two segments. By doing this, the duration of external fixation is lowered and the Index of External Fixation was of 1.2 month/cm. To get the best outcomes, the surgeons must use circular frames that allow correction of mal-alignment, linear transport, and lengthening of the soft tissues when the bone ends are buried under the soft tissue (Fig. 2) [30]. If the bone ends are not well covered, during the bone transport there will be a protrusion of the bone due mainly to the retraction of the soft tissues into the defect. This can be resolved by using cement spacer pieces of cylinder and flap surgery during the initial phase, removing the pieces during the distraction [24]. The problem of management of the soft tissues during the distraction osteogenesis phase is an additional challenge to be taken addressed in these very difficult cases. Even if the distraction osteogenesis technique is of great value, this still-controversial way of management has some limits in acute treatment of bone loss in the lower limb.

The Ilizarov method is a very satisfactory method for the reconstruction of long-bone defects that are accompanied by soft-tissue deficiency. Nonetheless, surgical experience and patient collaboration are needed for a successful result [10]. Although successful bone restoration can be achieved with this modality. Distraction osteogenesis can be protracted, painful, frequently complicated by pin site infections, fluctuates in quality and quantity of the new regenerate, and has healing problems at the docking site with bone transport [12].

Saleh and Rees [31] have compared eight patients managed by bone transport with eight cases of bi-focal compression-distraction osteogenesis in bone loss. The mean duration of treatment was 16

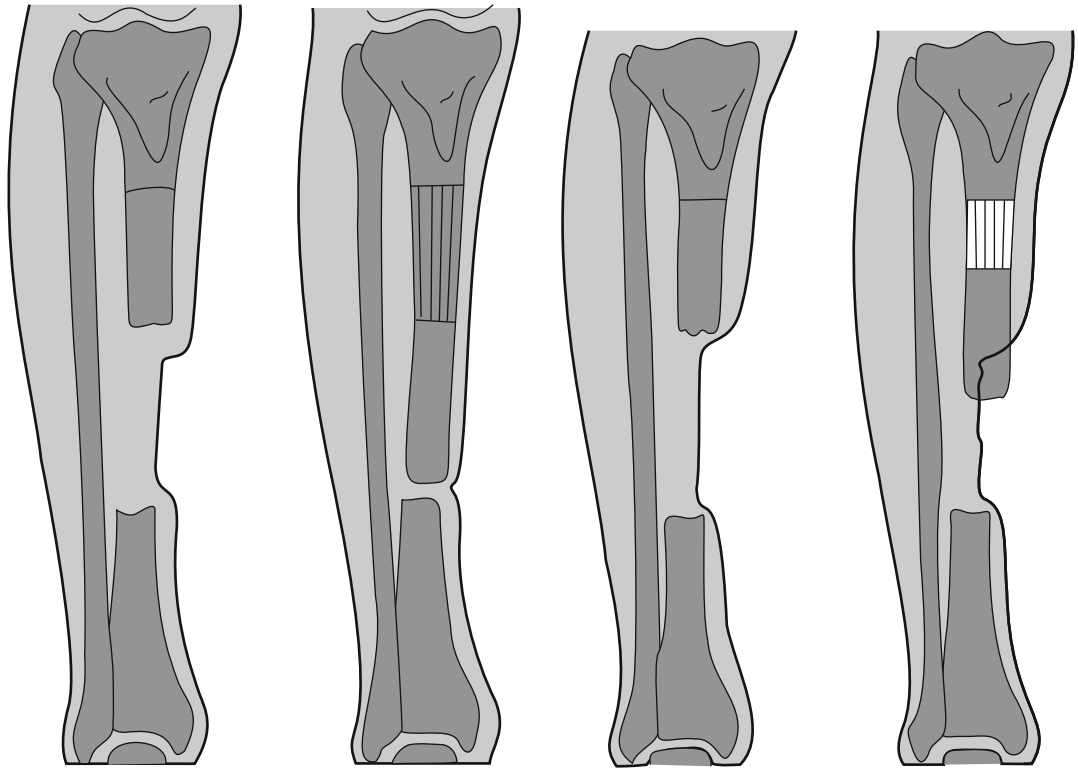

Fig. 2 Difficulty with retraction of soft tissues in the bone defect, and consequences during bone transport. *Left*: progression of soft tissue with the bone transferred with limited retraction of the skin. *Right*: extrusion of bone during bone transport with severe soft tissue retraction in the defect (From El-Alfy et al. [30], Springer Ed)

and 9.8 months, respectively [26]. Complication rates per patient were 1.0 in the compression-distraction group and 2.2 in the bone transport group.

In conclusion, the three approaches that are Acute Shortening, Compression-Distraction, and Distraction Osteogenesis alone, are not mutually exclusive but have their relative indications and difficulties. Distraction osteogenesis therapy is generally more protracted, technically very challenging, and accompanied by high complication rates. However, distraction osteogenesis can be spectacularly successful in the simultaneous management of soft tissue coverage, bone defect, and spatial deformity [6].

Free Vascularized Fibula Transfer

Different types of vascularized bone grafts have been proposed for treatment of bone losses. As accompanying skin paddle or muscle [32] may be harvested at the same time, the free fibula transfer is the most suitable vascularized bone graft for reconstruction of large bone losses in the lower limb. The amount of graft available goes up to 25 cm with a high-density, straight cortical bone with a good vascular pedicle and minimal donor-site morbidity [10]. Of particular interest with the fibula is the ability to fold the graft into two segments, getting a double-barrel graft that can treat large defects in the femur, mainly in the distal metaphyseo-epiphyseal area (Fig. 3). Although the free vascularized fibula has been well documented in the literature for reconstruction for post-tumoral resection in the lower limb, the correct positioning of this type of graft in a post-traumatic situation, especially in an acute management, is still discussed, with very few reports [32–35].

In the 14 cases reported by Pelissier et al. [32] only 2 were done for acute bone loss after trauma, each of them with a large bone defect of 15 cm. The authors have used a composite flap that

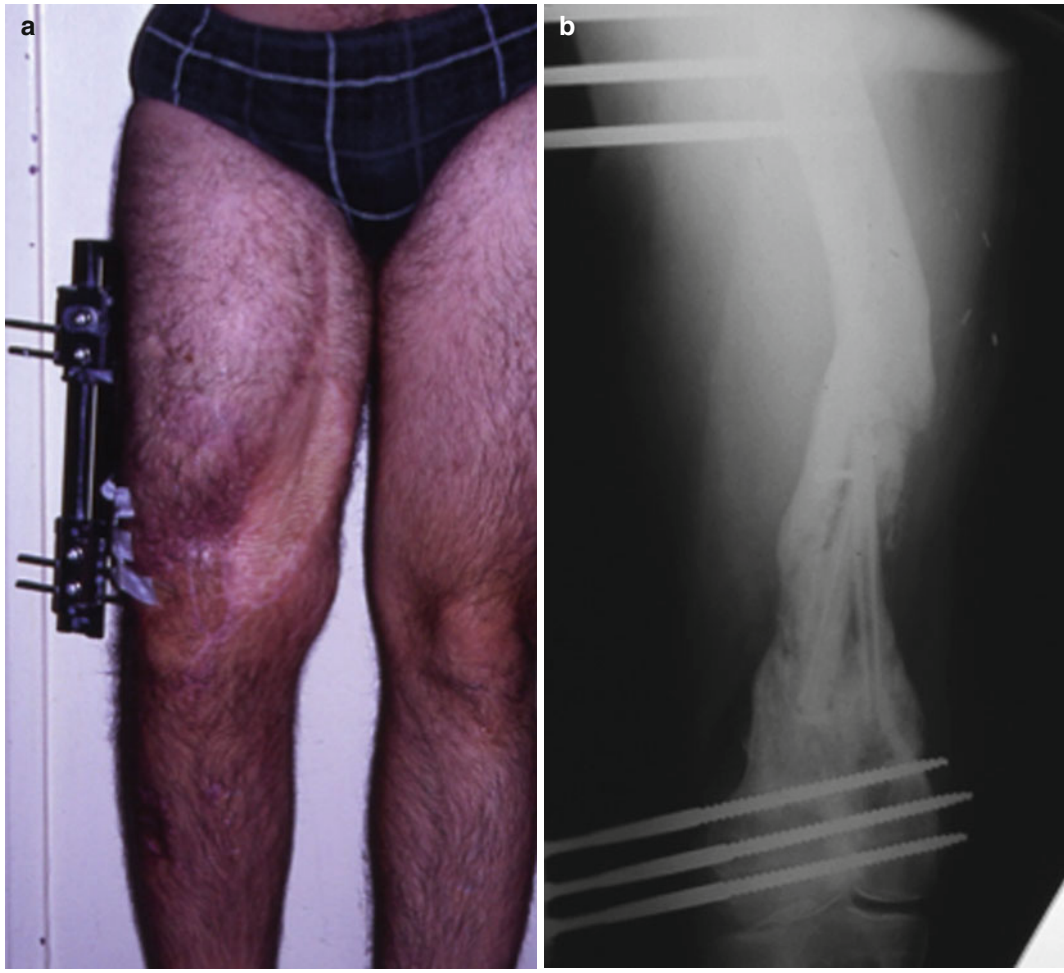

Fig. 3 (**a**) Clinical photograph of femoral defect treated by external fixation and free latissimus dorsi flap on the anterior thigh. (**b**) X-rays with a double-barrelled free fibular transfer for bone reconstruction

includes part of the soleus muscle to restore associated soft tissue defects. This composite flap is intended for extensive defects of the lower limbs involving bone and soft tissues. Bone healing was obtained in 11 months. Free weight-bearing was allowed 17 months after reconstruction [32].

According to Beris et al. [34], controversy regarding bone reconstruction using a free vascularized fibula graft in the acute phase may be linked to the risk of infection in a very technical demanding procedure. Large open fractures are contaminated with bacteria. Trying to get a non-infected bone graft site is the goal of early treatment of such challenging situations. Then, one option is to do the free vascularized fibula transfer within 6–8 weeks after trauma and soft tissue reconstruction. Beris has outlined that this is a difficult procedure due to increased scarring and limited recipient vessels in terms of their quality and location. Immediate one-stage procedure can be done, using composite transfers such as vascularized osteoseptocutaneous or osteomuscular fibula graft, immediately after radical debridement of the lesion site. The advantages of this procedure include simultaneous bone and soft-tissue reconstruction, early bone stability, stimulation of bone union and decreased time for bone healing, prevention of soft-tissue and vessel scarring, and increased rate of infection management [34]. In the author's experience, a one-stage procedure does not add risk of infection but on the contrary, increases the rate for resolving infection.

In a comparative study between free vascularized fibula transfer and bone transport, El Gammal et al. [33] was able to follow 13 free fibula vs 12 Ilizarov cases. Of particular interest are the inclusion criteria as bone defects were at least 6 cm long, none were cavitary defects, and none has involved the knee or ankle joint, so that these cases are exactly those discussed in this chapter. Operative time and blood loss were significantly higher in the free fibula group. External fixation time was longer in the Ilizarov group (10.58 months) vs 6.92 months for the free fibula group. Full weight-bearing time was similar in both groups, and above 9 months. Defect size was found to have the most significant effect on the results. The author recommends using free vascularized fibula for traumatic tibial defects of 12 cm or more, whenever experience is available [33].

A literature review of all cases of free vascularized fibula transfers published for management of acute lower limb trauma is still very unsatisfactory as only 20 papers encountered the previous-mentioned criteria. Among them, there are 11 case reports. This outlines the controversy of using such a demanding procedure in a very challenging situation where the infection rate seems the main drawback. The advantages of free vascularized fibula include maintained graft vascularity and so ability to hypertrophy in response to load [15, 33, 35], and resistance to infection [33, 34]. Its disadvantages are the need for microsurgical skills, possibility of total necrosis due to anastomotic complications, donor site morbidity, and occasional stress fracture [33].

The main drawback of the fibula transfer is the absence of soft-tissue coverage that is almost always needed in acute treatment of traumatic bone loss in the lower limb. The solution is additional plastic surgery such as local skin or myocutaneous flap, cross-leg, free skin myocutaneous flap, or composite flaps with the free fibula [32, 33, 35].

Protection of the vascularized fibula graft is needed during the first year and loading must be gradually increased for remodelling and hypertrophy. Stress fractures are common complications [10]. The type of fixation, associated with free vascularized fibula transfer, is still controversial. It seems that internal fixation raises the rate of stress fractures, so that external fixation with a monoplane frame [10] or circular one [35] must be preferred, as progressive loading and stress application can be achieved using this type of fixation. Large plates create unnecessary stress shielding and retard the hypertrophy of the fibula [35].

The double-barrelled fibula flap is indicated for femoral and proximal tibial reconstruction. For large defects over 12 cm, division of a single fibula will not provide adequate length [34]. The fibula presents the advantages of providing the greatest bony length and an excellent medullar and periosteal blood supply. In addition, its long cylindrical straight shape, mechanical strength, predictable vascular pedicle, and hypertrophy potential are criteria for some authors to use this demanding procedure in bone reconstruction of the lower limb [34].

Conclusions

Acute management of traumatic bone loss is still a very challenging situation even if there are different options available. Comprehensive literature review is rather difficult as all papers mix acute management and late bone reconstruction. The main criteria for decision-making are the bone defect size and the amount of surrounding soft tissue damage.

Small bone defects (less of 5 cm) can be managed using standard methods of fixation with autogenous bone grafting, and there is no evidence of a new or demanding procedure for a quicker or better outcome.

Management of large bone defects (over 5 cm) require specific techniques. Even if post-traumatic femoral defects of up to 15 cm have shown the potential for spontaneous healing after intramedullary nailing [10], large segmental bone defects, especially in the setting of an unfavourable wound environment, suboptimal surgical technique or biomechanical instability are usually characterized by low regeneration potential and will require more specialized surgical management.

The “induced membrane” technique seems to be a method of choice in all cases [7] as it maintains the limb length avoiding leg length discrepancy, allows acute flap surgery for soft tissue reconstruction in the post-traumatic period, gives some opportunity for diagnosis of infection in

those contaminated situations [21], and leads to a combined mechanical and biological favourable environment [19]. In the future, additional techniques of orthobiologics may help to limit the amount of bone graft needed [36, 37]. The main drawback of this technique is that of a two-stage technique needing additional anaesthesia. This situation may be improved by using new implant technologies with Cylindrical Titanium Mesh Cage (CTMC) and polylactide membranes technique [12], or custom-made products such as pre-determined bone segment with collagen-hydroxyapatite scaffold and autogenous platelet-rich plasma [38]. Part of the efficacy of the induced membrane technique is a non-infected and well-vascularized bone graft bed, so that all new techniques should be compared on this basis. In this technique, stability is mandatory, and future studies will help to determine which type of stable fixation is better [22].

Acute shortening, compression-distraction and Ilizarov bone transport must always be considered as they can correct associated deformity and shortening, address small areas of soft tissue defects, and allow immediate mobilization. Their disadvantages are long duration of treatment especially in long defects, pain accompanying the transport, frequency of pin tract infection, and occasional non-union at the docking site [33]. Based on previous published studies, in acute management of lower limb bone loss, it seems that compression-distraction techniques are the most suitable ones for reducing the number of complications. However, management of soft tissue involved in the trauma is still a significant problem with this type of procedure.

For long bone defects over 8–10 cm in length, the free vascularized fibula must be considered even if there is a high risk of septic complications and stress fractures. Exact positioning of this type of graft will be better defined in the future, as it is a very demanding procedure needing a high level of experience and must be limited to some surgical centres able to do it in a multidisciplinary surgical environment [15].

In conclusion, biological pseudomembrane seems to facilitate bone reconstruction. However clinical trials are needed in order for their effectiveness to be confirmed and their place in the armamentarium for the treatment of bone segmental defects to be clarified [10]. Addition of osteogenic proteins (BMP's), and their effect on bone healing and regeneration either in an induced membrane technique [18] or in an Ilizarov technique [39] must be studied more precisely. Such considerations will lead to the possibility of using tissue engineering for acute post-traumatic bone reconstruction, such as osteogenic cells, growth factors, and biomaterial scaffolds. The previously mentioned Masquelet and cylindrical mesh techniques may be the basis for tissue engineering procedures.

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Part III

Tumours

Diagnostic Strategy for Bone Tumours

Jacob Bickels

Abstract

Bone tumours are relatively rare and their diagnosis requires a staged multidisciplinary approach using clinical, radiographic, and histological analyses, when required. Patient's history and plain radiographs remain the key factors in establishing the correct diagnosis in the majority of these cases. Anatomical location of the lesion, pattern of bone destruction, and nature of the tumoural matrix can be assessed by plain radiographs and allow categorization of most lesions. Biopsy, when required, should be performed only at the conclusion of the clinical and radiological staging.

Identifying the histological type of a bone tumour is a critical step for its diagnosis and management. The differential diagnosis of a musculoskeletal neoplasm must be precise, and it is achieved by a staged multi-disciplinary approach using clinical, radiographic, and histological analyses, as appropriate. In a 1958 publication, Jaffe stated that a biopsy should be regarded as the final diagnostic procedure, not as a shortcut to diagnosis, and that biopsy must be preceded by careful clinical evaluation and analysis of the imaging studies [9]. The final diagnosis of a musculoskeletal lesion is based on those three parameters, and it must be questioned when all three do not match [1, 9]. Bone tumours are classified as either benign (latent, active, or aggressive – Table 1) or malignant (primary malignant tumours of bone or metastatic lesions).

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Biological Behaviour of Bone Tumours

Bone tumours are relatively rare and include a wide spectrum of histological types, ranging from lesions that usually heal spontaneously and convert to normal bone tissue (e.g., non-ossifying fibroma) to neoplasms that invade and destroy neighboring tissues and organs, metastasize early

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Table 1 Stages of benign musculoskeletal neoplasms

Latent	Remains static or heals spontaneously	Non-ossifying fibroma Enchondroma Osteochondroma
Active	Progressive growth but limited by natural barriers	Fibrous dysplasia Osteoid osteoma
Locally aggressive	Progressive growth, not limited by natural barriers	Giant cell tumor Aneurysmal bone cyst Osteoblastoma Chondroblastoma Chondromyxoid fibroma Eosinophilic granuloma

during the course of the disease and ultimately become life-threatening (e.g., Ewing's sarcoma). Tumours that arise from the mesenchymal elements of the musculoskeletal system exhibit certain characteristics that set them apart from other groups. Although each histological type has its own peculiar microscopic appearance, all histological types share some features in their biological behaviour, which reflect their common derivation.

Benign bone tumours grow in a centripetal fashion and spread as a ripple on a pond. The most immature tissue is found at the growing edge, i.e., at the periphery of the tumour. Lesions arising within bone are encapsulated by the fine connective tissue elements of the marrow, the endosteum, and periosteum. As the lesion extends along paths of least resistance between trabeculae and along haversian canals, the tumour remains separated from the bone by a thin, compressed layer of fibrous connective tissue. The presence of the tumour triggers a mesenchymal response at its periphery: the mesenchymal proliferation surrounding an intra-osseous lesion will mature unto reactive bone, whereas the mesenchymal response will be fibrous if the lesion penetrates into the soft tissues. This reactive tissue forms a pseudocapsule. Pseudocapsules associated with high-grade sarcomas may be invaded by nodules of neoplastic cells known as "satellites". High-grade sarcomata may also present with tumour nodules that grow outside the reactive rim but within the same anatomical compartment in which the lesion is located ("skip lesions") (Fig. 1) [7]. Unlike sarcomata, carcinomas usually infiltrate, rather than push, the surrounding tissues and ordinarily do not induce the

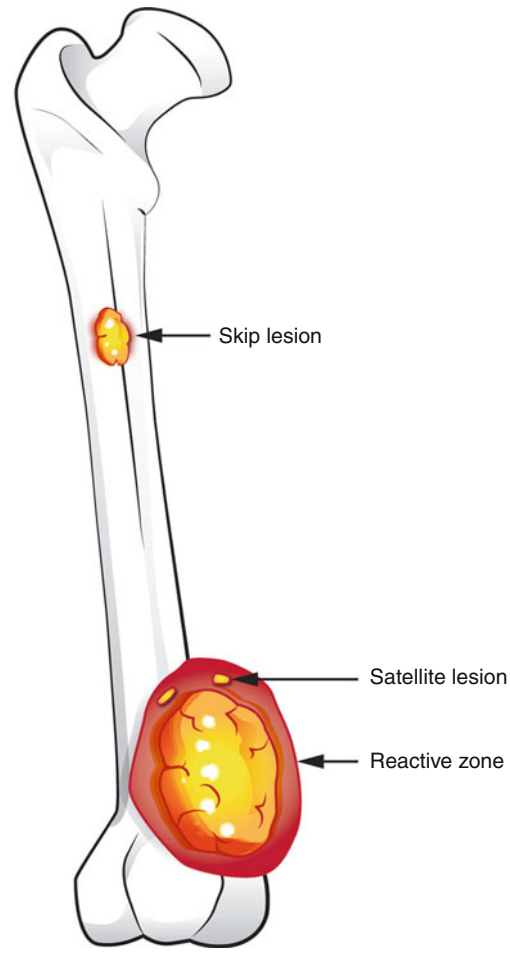

Fig. 1 Growth pattern of bone sarcomata. Sarcomata grow in a centripetal fashion, with the most immature part of the lesion at the growing edge. A reactive zone is formed between the tumour and the compressed surrounding normal tissues and may be invaded by tumour nodules that represent micro extensions of tumour (satellites) and not a metastatic phenomenon. High-grade sarcomas may present with tumour nodules that grow outside the reactive zone ("skip lesions") but within the same anatomical compartment in which the lesion is located

formation of a reactive zone and pseudocapsule. Metastatic disease from bone sarcomata is site-specific, first manifested by lung involvement in its early stage and by bone involvement later on.

Clinical and Radiological Evaluation

The age of the patient is associated with the nature of a given bone lesion. For example, primary sarcomata of bone are usually diagnosed in the second decades of life, while a destructive bone lesion in patients older than 50 years should be considered as being metastatic until proven otherwise. Latent bone lesions can be detected as incidental findings at any age: non-ossification of the distal femur may be detected on plain radiographs of the knee of a 9-year-old boy following a trauma to that site, while enchondroma at the same location may be detected on plain radiographs of a 60-year-old female.

Latent bone lesions are mostly asymptomatic and are usually detected incidentally on an imaging study done for another purpose. In contrast, benign-aggressive and malignant bone tumours are associated with pain that is distinctive by having an insidious onset that gradually becomes unremitting, progressive, and unresponsive to change in position or bed rest in most cases [2]. When these tumours are located in the pelvic girdle and lower extremities, the pain may be exacerbated upon weight-bearing and ambulation.

Despite advances in imaging techniques, a plain radiograph remains the key study in evaluating the nature of a given bone lesion. The cardinal principle in the diagnosis of solitary bone lesions is that the radiological appearance reflects the underlying pathology of the abnormal tumour tissue and its interplay with the host bone. All bone lesions can be described by the following parameters:

1. anatomical location,
2. interaction with the host bone, and
3. the characteristics of their matrix. Based on those features, it was claimed that the categorization of a lesion (latent, benign-aggressive, and malignant) and even its specific histological type can be made by a computer or telephonically without the diagnostician having to see the actual radiological image [12].

Anatomical Location

The anatomical location of the lesion within the host bone can be described as being confined to either the epiphysis, metaphysis, or diaphysis. Specific lesions have a typical anatomical location within the host bone: enchondroma is typically located within the diaphysis, osteochondroma and osteosarcoma in the metaphysis, giant cell tumour in the metaphyseal-epiphyseal region, and chondroblastoma in the epiphysis (Fig. 2).

Interaction with the Host Bone

A given bone lesion's interaction with its host bone is evaluated by two parameters: the pattern of bone destruction (e.g., geographic, permeative, or moth-eaten) and the nature of bone reaction at the host bone-lesion interface.

Pattern of Bone Destruction

In a *geographic* pattern of bone destruction, the tumour creates a large and well-circumscribed hole in the bone which is surrounded by normal spongy bone (Fig. 3). A *moth-eaten* pattern appears as multiple and confluent lytic areas (Fig. 4). In a *permeative* pattern, the spongy bone and adjacent cortices are invaded by numerous very small lytic lesions that do not modify their gross contours on imaging (Fig. 5). There generally is a correlation between the pattern of bone destruction and the rate of tumour growth, with the geographic pattern having been shown as being consistent with slow growth, the permeative pattern consistent with the most rapid rate, and the moth-eaten pattern consistent with an intermediate growth rate [12, 13].

Response of the Host Bone

The presence of a tumour within the host bone may induce a reparative process at its periphery. Reparative reactions are usually limited to cancellous bone, but they may also occur in the cortex

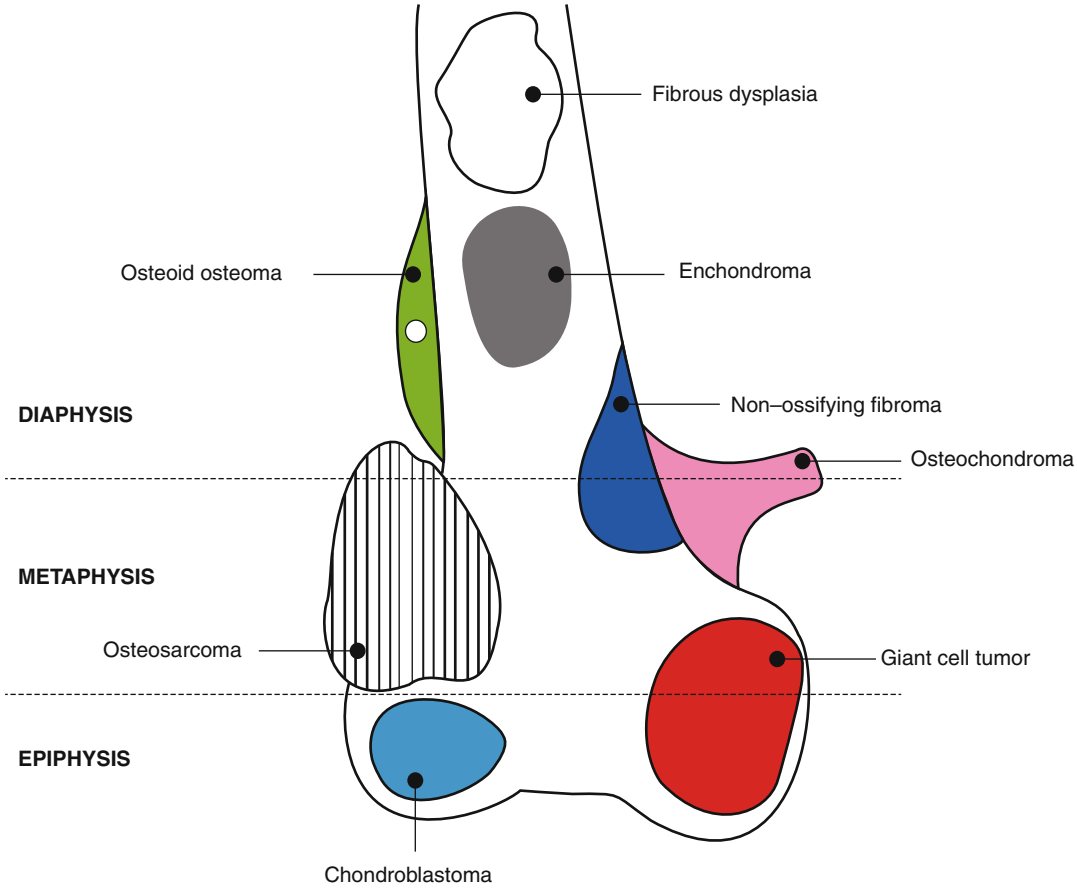

Fig. 2 The anatomical location of the lesion within the host bone can be a clue to its histological type

and in the overlying periosteum. As the tumour grows within the medullary cavity, the adjacent cancellous bone and inner surface of the cortex are resorbed by osteoclastic activity. The formation of new bone along the surface of the lesion is induced as the result of reciprocal and enhanced osteoblastic activity. In a latent or very slow-growing lesion, this osteoblastic activity results in the formation of a clear and thick sclerotic rim around the lesion (Fig. 6). Lesions that grow at a moderate pace allow a remodelling process that results in the expansion of the contour of the host bone, thus creating an expanded cortical shell (Fig. 7). Rapidly growing tumours erode the surrounding bone and do not provide the time required for new bone formation, resulting in the loss of the cortex and the characteristic patterns of a periosteal reaction, which is another form of host-bone response.

The periosteum is a labile structure that is capable of responding to pressure from an advancing tumour or from the presence of actual tumoral tissue by depositing new bone. The radiographic patterns of this osteoblastic response reflect the rate of aggressiveness of the process. Slow-growing tumours provoke the formation of a solid buttress of bone at their borders under the periosteum. More rapid growth of a tumour penetrating through an eroded cortex stimulates the formation of a lamellated periosteal new bone that may be either parallel to the cortical surface (“onion-skin”) or perpendicular to it (“spiculated” or “sun-ray”). The latter pattern usually indicates very aggressive tumour growth. In rapidly advancing neoplastic processes with cortical destruction and periosteal elevation of considerable degree, the separation of the periosteum

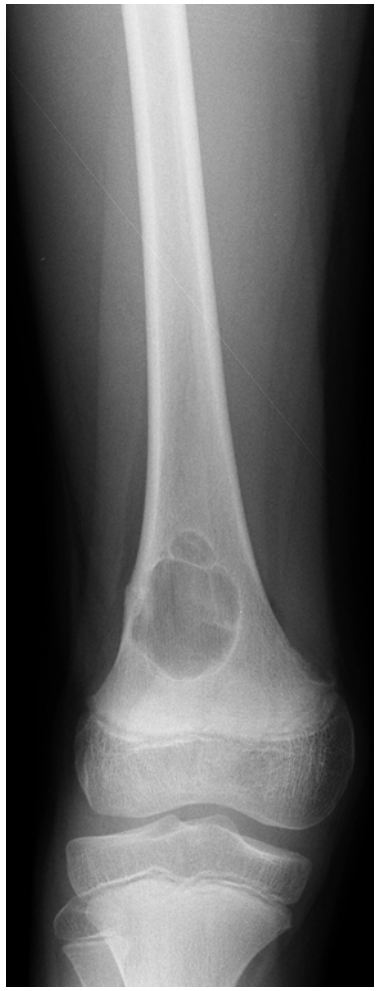

Fig. 3 Plain radiograph of the distal femur showing non-ossifying fibroma, causing a *geographic* pattern of bone destruction

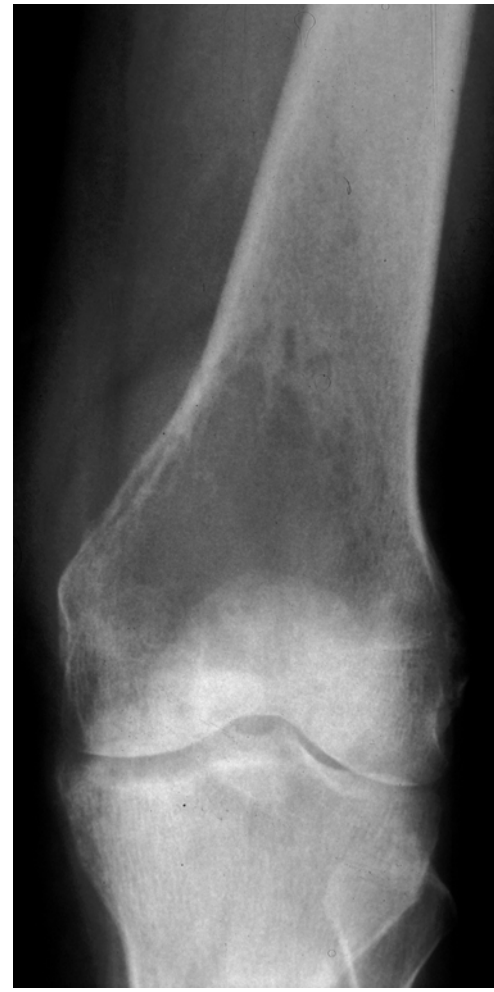

Fig. 4 Plain radiograph of the distal femur showing multiple myeloma, causing a *moth-eaten* pattern of bone destruction

from the still-intact cortex forms an acute angle with an open end towards the tumour's epicenter (Codman's triangle). This is most often present in malignant lesions and is an indicator for rapid cortical penetration with periosteal detachment (Fig. 8).

Tumour Matrix

The matrix of a mesenchymal tumour, which is its intercellular product, may assist in its correct identification. The matrix can accept mineral deposition in the form of calcification or ossification, thus allowing the distinction between bone- and cartilage-forming lesions. It is usually possible to differentiate between cartilage and bone matrix mineralization by the presence of stippled focal densities or as rings or arcs of peripheral calcifications in more lobulated cartilage areas. Osteoid mineralization can usually be recognized as amorphous densities when the bone is immature, or when it is trabecular in when ossification is more advanced. An extensively ossified matrix is referred to as a blastic lesion, and a lytic lesion is one in which the matrix has little or no ossification (Fig. 9). Fibrous dysplasia has a typical ground-glass matrix, which is the result of a mix-

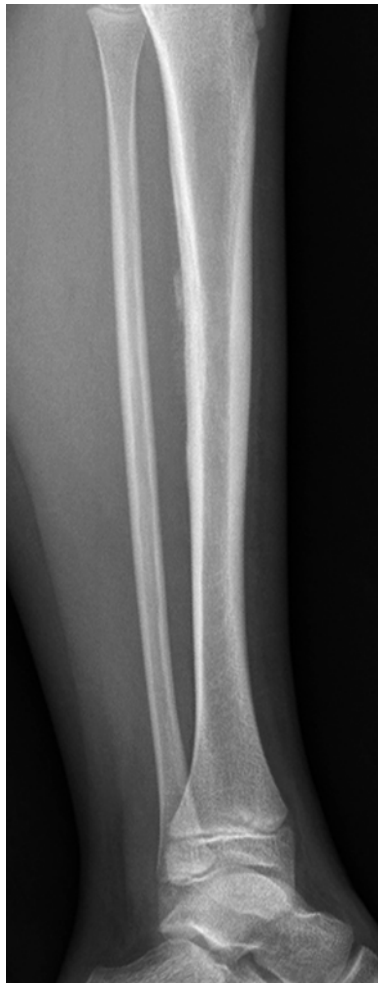

Fig. 5 Lateral plain radiograph of the leg showing Ewing's sarcoma of the mid-tibial diaphysis, causing a *permeative* pattern of bone destruction

ture of bone and fibrous elements (Fig. 10). Thus, the nature of a given bone lesion can be defined by the above-mentioned parameters of tumour-host bone interaction

Biopsy of Bone Tumours

Biopsy is the final and definitive step in the diagnosis of bone tumours. Anatomical alteration following a biopsy may interfere with a proper diagnosis and may even impair the possibility of performing a limb-sparing tumour resection. Biopsy of a musculoskeletal lesion should be performed only at the conclusion of staging accord-

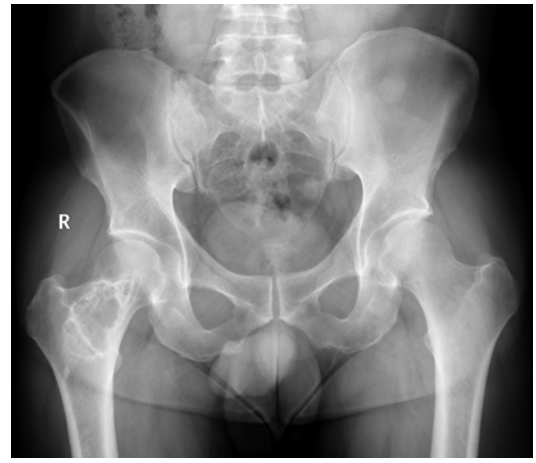

Fig. 6 Plain radiograph showing a latent cystic bone lesion of the right femoral neck surrounded by a thick sclerotic rim

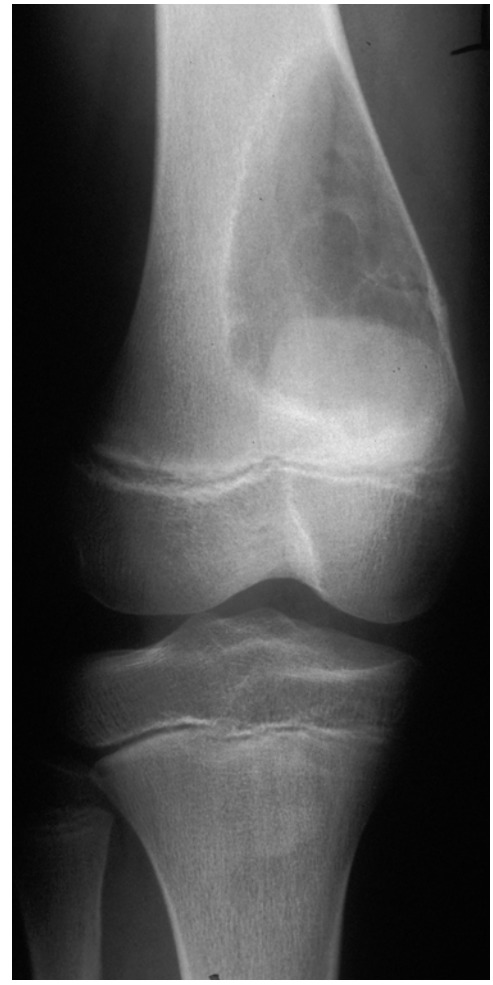

Fig. 7 Plain radiograph of the distal femur showing aneurysmal bone cyst, creating an expanded cortical shell

ing to the imaging studies that are essential for determining the characteristics and local extent of the tumour as well as the presence of metastatic disease. Staging helps determine the exact anatomical approach to the tumour, and delineates the region of the tumour that represents the underlying disease. A final and compelling reason for deferring biopsy until staging is complete is that biopsy superimposes both real and artificial radiological changes at the biopsy site and can thereby alter the interpretation of the imaging studies.

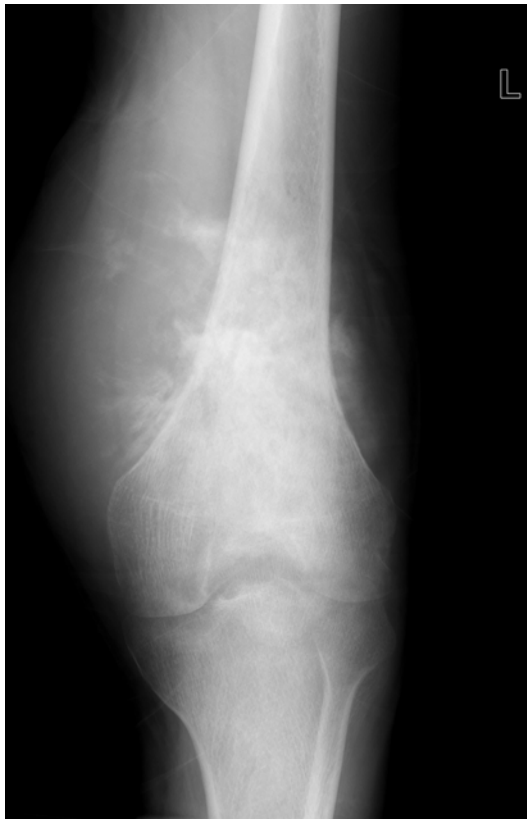

Fig. 8 Plain radiograph of the distal femur showing osteosarcoma, causing a spiculated periosteal elevation

Staging studies for a high-grade sarcoma of bone include computerized tomography (CT) and magnetic resonance imaging (MRI) scans of the affected bone in order to evaluate the local tumour extent, and chest CT and positron emission tomography (PET) scan to rule out the presence of metastatic disease. The CT scan provides anatomical data on the extent of bone involvement, and the MRI scan provides data on tumour extent within the medullary canal and in the surrounding soft tissues. As such, these two imaging studies provide complementary information and are both required to evaluate the full anatomical extent of a given bone tumour. A PET scan using fluorine-18-fluorodeoxyglucose (FDG) was shown to be as effective as the conventional imaging modalities in detecting the primary tumour, and superior to them in detecting bone manifestations and lymph node involvement of the disease [18]. However, PET-FDG was shown to be less accurate than CT in detecting lung metastases [18]. Complete staging is only required when the diagnosis of high-grade sarcoma of bone is in question. Benign-aggressive tumours do not require a metastatic work-up, and metastatic tumours are evaluated for the purpose of determining their specific histological type.

The presence of a bone lesion does not necessarily mandate a biopsy. The combination of medical history, thorough physical examination, laboratory data, and appropriate imaging studies allows accurate diagnosis of most bone tumours. Clinically and radiologically benign-appearing lesions do not require a biopsy. In contrast, a biopsy is indicated in benign-aggressive, malignant, and questionable lesions to confirm the clinical diagnosis and accurately classify the lesion before the initiation of definitive treatment (Fig. 11).

In 1982, Mankin et al. [14] evaluated 329 patients who underwent biopsy for bone or soft-tissue sarcomata. The rate of major errors in diagnosis was 18.2 %, and the rate of complications was 17.3 %. Unnecessary amputations were performed in 4.5 % of these patients [14]. These events occurred with far greater frequency when the biopsy was performed in a referring institution rather than in a specialized oncology centre. In addition to technical recommendations (discussed below), it was recommended that the patient should be referred to a specialized treating centre before the biopsy is done if a surgeon or an institution is not equipped to perform accurate diagnostic studies or definitive surgery and adjunctive treatment of musculoskeletal tumors [14]. In 1996, Mankin et al. reported a second study on 597 patients [15]. They documented

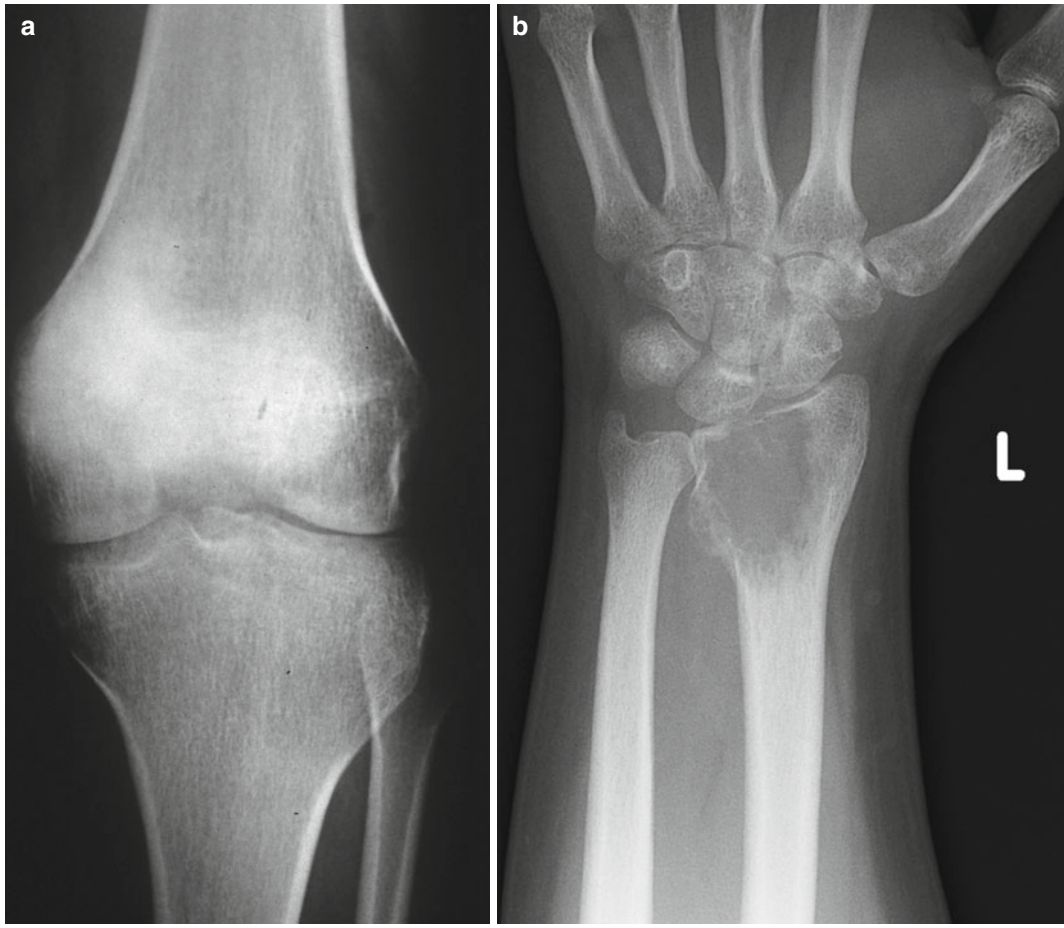

Fig. 9 Plain radiographs showing (**a**) osteosarcoma of the distal femur with a blastic matrix, (**b**) giant cell tumour of the distal radius with a lytic matrix

major errors in diagnosis in 13.5 % of the patients, a complication rate of 15.9 %, and unnecessary amputations in 3 %. The differences in outcome between referring and oncology centres were unchanged, and their recommendations were identical [15].

The site of biopsy within the lesion is of major significance because bone and soft tissue tumours may have regional morphological variations. As a result of that heterogeneity, multiple samples are required to establish a diagnosis. In contrast, carcinomas are commonly homogeneous, and a single tissue core or aspirate is sufficient for diagnosis. The term "sampling error" refers to an incorrect or inconclusive diagnosis, which occurs because the biopsy specimen was taken from a region that does not represent the underlying primary disease. Before performing a biopsy, the clinical findings and imaging studies must be evaluated by the surgeon and a radiologist who must be familiar with the biological and radiological findings of musculoskeletal tumours. The questions that must be answered before biopsy are the part of the lesion that needs to be biopsied, and the safest anatomical route to that site. Despite serious concerns regarding the potential of accelerated growth or metastatic dissemination of a malignant tumour after biopsy, there is no well-founded, objective evidence to show that biopsy promotes either adverse event. The real

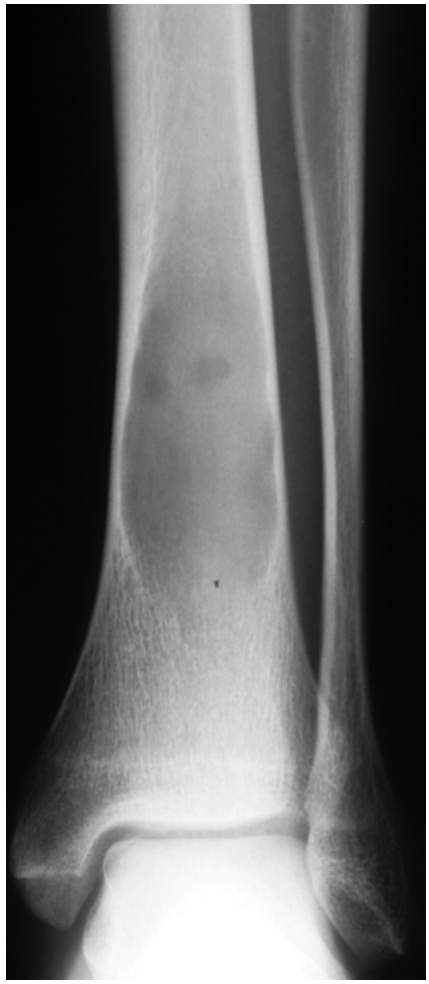

Fig. 10 Plain radiograph of the distal tibia showing fibrous dysplasia with its typical "ground-glass" matrix

risk of open and needle biopsies is that they may spread tumour cells locally and facilitate local tumour recurrence. The actual risk of local recurrence after biopsy is not well documented, but it is reasonable to assume that it is higher in open biopsy than in needle biopsy and that it is related to the width of the biopsy tract and adequacy of haemostasis.

A closed biopsy is relatively non-invasive, and the specimen is obtained after skin puncture by a needle or trephine. In contrast, an open biopsy is obviously an invasive procedure. It can be incisional, for which only a representative specimen is removed from the lesion, or excisional, for which the lesion is excised en bloc. Any surgical procedure, even the most minor one, is accompanied by a risk of complications, which may include iatrogenic injury to blood vessels or nerves, complicated wound healing, wound infection, and tumour cell contamination along the biopsy tract and subsequent local recurrence.

Open incisional biopsy is a reliable diagnostic method because it allows the pathologist to evaluate cellular morphological features and tissue architecture from different sites of the lesion. In addition, it provides material for performing ancillary studies, such as immunohistochemical analysis, cytogenetics, molecular genetics, and flow cytometric analysis. Needle biopsy of mesenchymal tumours had initially been criticized because the quantity of biopsy material was often considered to be insufficient for a routine histopathological evaluation and the ancillary studies that also require tissue. However, CT-guided core needle biopsies were shown to be safe and accurate in the diagnosis of bone tumours [16, 19]. Fine needle aspirations were also shown to have similar reliability in allowing accurate diagnosis in the majority of patients who have high-grade sarcomata [8]. Open biopsies may be unavoidable in cases when needle aspiration has not provided a clear diagnosis or in cases where the clinical-radiological diagnosis is inconsistent with a known histological entity.

In planning the definitive surgery, it was traditionally assumed that the biopsy tract is contaminated with tumour cells and that it should therefore be resected with the same safety margins as the primary tumour (i.e., wide margins). Binitie et al. reported 59 adult patients who had a deep and large soft-tissue sarcoma of the extremities and for which a core needle biopsy was done [3]. Definitive surgery in these patients did not include the biopsy tract and there was no increase in local tumour recurrence in those study patients compared with previously published data on local tumour recurrence when the biopsy tract was removed en bloc with the tumour [3]. Kaffenberger et al. reported similar observations among their 388 patients who underwent fine needle aspiration biopsy for high-grade sarcoma

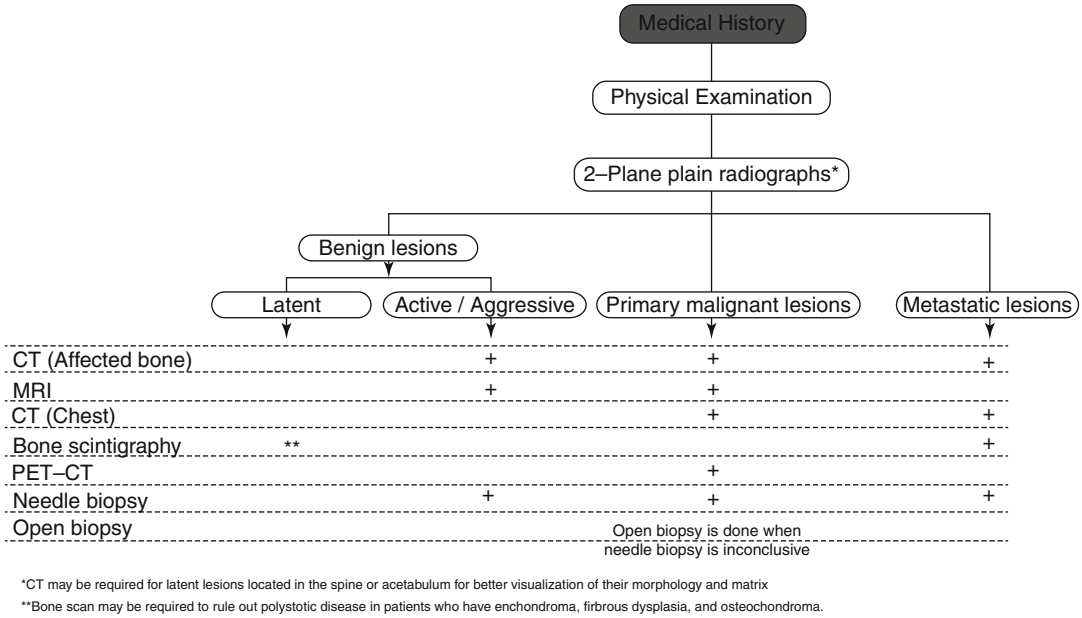

Fig. 11 Clinical and radiological processing algorithm of a bone lesion

[10]. A reasonable policy, therefore, would be to remove only the biopsy tracts that remain following an open biopsy (Fig. 12).

Important and meaningful advances have been made in mesenchymal tumour cytogenetics during the last two decades. Chromosomal translocation analysis has evolved from conventional chromosomal karyotyping and southern blot studies to more sophisticated molecular diagnostic techniques. Techniques such as reverse transcription-polymerase chain reaction and fluorescence in situ hybridization have become important tools for evaluating musculoskeletal neoplasms and for increasing the diagnostic accuracy of histopathological classification. Novel methodologies with diagnostic potential continue to emerge, such as cDNA micro-array and expression profiling [11]. A number of bone and soft tissue tumours have been shown to have recurrent and specific chromosomal changes, ranging from point mutations to chromosomal translocations. These changes not only serve as aids in the diagnosis and classification of bone and soft-tissue tumours – especially in the differential diagnosis of those of a confusing nature – but they have also guided molecular studies in establishing the underlying genes that are involved in tumour origin and progression. A number of tumour-specific gene fusions have been identified to date, and many have been shown to encode aberrant transcription factors [5, 11]. Knowledge obtained from these studies has translated into diagnostic, prognostic, and therapeutic applications for patient management [5, 11].

Conventional karyotyping depends on the availability of fresh, sterile tumour tissue, the success of tumour cell growth in culture, and the quality of metaphase cell preparations. It requires skilled personnel, which is mostly available in large centralized laboratories, and remains time-consuming, even with automated karyotyping systems. Although chromosomal abnormalities have been identified in a large variety of latent, benign, and malignant bone tumours, the vast majority is still accurately diagnosed on the basis of clinical, radiographic, and basic histopathological techniques [4, 6, 17]. The most common histological types in which chromosomal translocations are used for diagnosis include small blue round cell tumours, such as Ewing's sarcoma/primitive neuroectodermal tumour (PNET), poorly differentiated embryo-

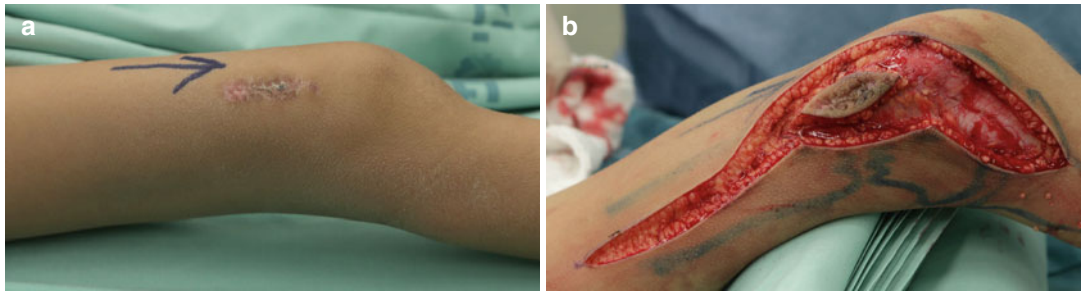

Fig. 12 Clinical photographs of a patient with osteosarcoma of the distal femur undergoing the definitive surgery of tumour resection showing (**a**) a biopsy incision along the medial aspect of the distal thigh, (**b**) biopsy scar, surrounding skin, and biopsy tract are kept adhered to the tumour and will be removed en bloc with it

nal rhabdomyosarcoma, and solid-alveolar rhabdomyosarcoma.

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Part IV

Paediatric Orthopaedics

New Trends in the Management of Osteo-articular Infections in Children

Manuel Cassiano Neves, Catarina Gouveia, Maria Joao Brito, Maria Favila Menezes, and Pedro Falcão

Abstract

Although many concepts regarding the aetiology, diagnosis and treatment of osteo-articular infection in children and adolescents have remained constant in the last three decades, recently we have seen some changes in the behaviour of the infectious agents, diagnostic tools and therapeutic attitudes that make it fundamental for the young surgeon to be familiar with these new concepts, as they can be used to guide evaluation and improve treatment.

Introduction

Although we have seen a decrease of incidence in the last three decades [16, 31] of osteo-articular infections (OAI), due to the improvements in the quality of life of the population, personal hygiene and general health, OAI in children still remains a challenge with significant morbidity worldwide. The bacterial behaviour has been changing over the years, creating new difficulties as to how to approach this problem [39]. In recent years we have seen new developments regarding the pathogenesis, diagnosis and treatment of paediatric OAI infections that increase the expectations of improving the diagnostic and the therapeutic approaches for this condition.

Osteo-articular infections in children and adolescents are rare. According to Gavilán et al. [30], the incidence of osteomyelitis in children is 0.2–1.6/1,000 per year with a wide variation all over the world. They are most common in childhood and have a small peak in the nenonatal period and at early school age [7, 55, 76]. The incidence of

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septic arthritis is between 5.5 and 12 cases per 100,000 children [27] or as low as 1/100,000 in the United States [28] with a peak incidence in the early years of the first decade. The incidence is higher in boys than girls (2.5:1) and the male-to-female sex ratio increases with age [27, 30, 76] with a seasonal variation peaking in late summer. In a combined group of osteo-articular infections in children the proportion of osteomyelitis to septic arthritis is 1.8:1 [28].

Changing Epidemiology

Staphylococcus aureus is still the most common bacteria causing septic arthritis (SA) in children [39, 53]. This predominance is even more obvious due to the near elimination of *Haemophilus influenzae* and reduction of *Streptococcus pneumonia* by widespread immunization [41]. Nevertheless, given the decrease in uptake of childhood immunization in Europe, these organisms should be regularly re-assessed.

Staphylococcus aureus has several virulence factors that explain its invasiveness [60]. In the last decades highly virulent strains of community-acquired-methicillin resistant *S. aureus* (CA-MRSA) have emerged [2]. There is, however, a wide geographical variation in CA-MRSA osteo-articular infections (OAI) prevalence, being 30–50 % in United States [2, 8], but less than 10 % in most European countries [38]. The molecular basis of this CA-MRSA virulence is still a matter of controversy [73]. The acquisition of Panton-Valentine leukocidin (PVL), more common in MRSA strains, has been associated with severe OAI in humans [11, 56]. Actually, the presence of a septic shock, plurifocal infections, necrotizing fasciitis or myositis, venous thrombosis or a concomitant pneumonia have been related with OAI caused by PVL-positive strains [8, 21].

Kingella kingae has been recognised as an important cause of OAI since the 1980s, probably due to improved molecular techniques [13, 100]. In several countries this organism is responsible for 43–82 % of OAI in children below 4 years [13, 22, 97, 100]. The clinical presentation is usually more insidious, with a less marked inflammatory response and a better prognosis than that of OAI caused by typical organisms [14]. However some authors don't describe these dissimilarities [4] and severe cases are now being reported [63].

Other less common agents remain stable. They include *Streptococcus pyogenes* and in neonates Group B streptococci (GBS) and Gram negative organisms [39]. In sexually active adolescents, *Neisseria gonorrhea* may be responsible for septic arthritis. In children with sickle-cell disease and *Salmonella* should be considered [5]. *Pseudomonas aeruginosa* has been traditionally associated with an infected puncture wound [39]. *Brucella Spp* and *Mycobacterium tuberculosis* may cause chronic mono-articular arthritis with a granulomatous reaction especially in endemic regions in southern Europe [20].

New Trends in the Diagnosis of Osteoarticular Infections

The initial diagnosis of OAI is based on the clinical history, laboratory investigations and imaging studies. Although it is fundamental to obtain a positive culture of the liquids aspirated from either the joint or the abscess we know that blood cultures and cultures from the aspirated joints are positive only in 30–50 % of the cases [62]. This means that in a large number of cases the treatment is only empirical and directed to a "suspected" agent. It is fundamental to improve the diagnostic tools in order to have a "directed/specific" treatment and recently we have seen some improvements in this field.

Laboratory Investigations

The identification of a pathogenic agent in OAI is a key point for successful treatment. In the presence of clinical signs of septic arthritis or osteomyelitis with an abscess formation, the cytological and cultural examination of the liquid aspirated, prior to the initiation of the antimicrobial treatment is mandatory.

The evaluation by laboratory markers should include:

- Complete blood count (haemogram)
- Erythrocyte Sedimentation Rate and C-reactive protein

- Blood cultures
- Gram staining, Acid-fast staining in the suspected diagnosis and Synovial fluid cultures
- Additional tests for specific micro-organisms (*N. gonorrhoeae*)

Haemogram

Classically an OAI will be associated with high peripheral white blood cell counts with a predominance of polymorphonuclear leukocytes [51, 62]. This is one of the four variables described by Kocher et al. [51] for predicting septic arthritis, together with history of fever, ESR >40 mm/h, non-weight bearing status WBC >12,000 cells/mm^3. But the classical picture is not always present. According to Khachatourians et al. [50] only 46 % of the cases with OAI presented at initial stage with an elevated peripheral white blood cells count.

Erythrocyte Sedimentation Rate and C-Reactive protein

These are two important markers are known as acute phase reactants. They are a group of proteins whose synthesis increases considerably in response to acute or chronic inflammation. ESR is elevated in 70–90 % of the OAI with a median value of 50–60 mm/h. CRP is another rapid indicator and levels are raised in almost all infections (levels greater than 20 mg/dl are considered elevated) [48, 75].

They have a better value as a negative predicting factor since negative values exclude a diagnosis of OAI. Decreasing of high values helps the monitoring of the therapeutic response and have a prognostic value (especially C-reactive protein) in the first days of treatment since if inflammation subsides, the CRP declines by 50 % a day [87].

Procalcitonin is an inflammatory marker that increases significantly as a response to a septic infection. In cases of a severe infection it can rise up to 100 ng/ml. High values of Procalcitonin are more related to Gram-negative and systemic infections. The projected specificity of procalcitonin in acute osteomyelitis (levels >0.5 ng/ml) in one study was 100 % with a sensitivity of 58.3 %. For septic arthritis the values were 100 and 27 % respectively. Thus, procalcitonin is a promising marker for predicting severe infection but its sensitivity for OAI seems to be low [9, 70].

Blood Cultures

Whenever there is a suspicion of OAI it is necessary to perform blood cultures. Blood should be obtained for aerobic and/or anaerobic cultures especially if systemic involvement is suspected and should be collected before starting antibiotic therapy. Blood cultures are positive in 40 % of the cases. This procedure enhances the possibility of identifying an agent, particularly in the presence of negative synovial cultures [31].

Synovial Fluid Cultures

It is indicated in the presence of fever and joint effusion. The fluid must be collected at an early stage and, if indicated, by ultrasound guidance (in particular in the hip joint). Needle aspiration should be performed with a heparinised syringe in order to avoid coagulation as a result of fibrinogenous increase. This will facilitate white blood cell count and the differential counting. Besides a macroscopic evaluation it should also include cytologic examination, microbiological examination for aerobic and anaerobic agents and a sensitivity test for antimicrobials. Additional examinations may be ordered in specific cases, as in the presence of less common agents (fungi or acid-alcohol resistant organisms).

A positive evaluation of the synovial fluid is specific for the diagnosis of septic arthritis. The white cell count, Gram staining and the cultural examinations are the most valuable to confirm OAI. White cell counts in the synovial fluid of more than 50,000 cells/ml with >90 % polymorphonuclears are very suggestive of a septic arthritis.

Only in 30–50 % of septic arthritis cases *Joint Fluid Gram staining* gives a positive result [44, 104]. The major advantage of a Gram staining is to offer immediate information about the type of bacterial infection (Gram-positive, Gram-negative, anaerobes) and to guide antibiotic prescription. We also need to bear in mind that micro-organisms seen on Gram staining may not grow in culture due to the bacteriocidal effect of the synovial fluid.

A *positive culture* is the key for establishing the diagnosis of OAI. The culture should be done for both aerobic and anaerobic agents. In children with ages between 6 and 48 months the synovial fluid should be inoculated in bottles for blood

culture in order to potentiate the possible identification of some agents like *Kingella kingae* [101].

Molecular Diagnosis

Osteo-articular infections in children can lead to devastating sequelae in adult life and only a correct diagnosis with a early detection of the infecting agent and premature direct antibiotherapy will help in preventing these complications.

The Polymerase Chain Reaction (PCR) in real time is a scientific technique in molecular analysis to amplify a specific region of a microbial DNA strand, the DNA target (or RNA) thereby aiding in the diagnosis. Although it is not a universal technique it can be performed even in the presence of small volumes of aspirates and as DNA does not disappear immediately after antimicrobial therapy, pathogens can be identified even after few days of therapy [61].

Yang et al. [104] described an adaptation of probe-based real-time PCR assay targeting *16SrRNA* gene for the diagnosis of *Staphylococcus aureus* in septic arthritis. The sensitivity and specificity of the probe based in real-time PCR assay in their series were 95 and 97 % respectively, versus synovial fluid culture. The total assay time from sample collection to result was 3 h which constitutes a major advantage when compared to 24–48 h needed for routine cultures [67, 103].

Another major advantage of this technique is the ability to identify micro-organisms with slow growth like *Mycobacterium tuberculosis* or bacteria that require specific conditions for culture such as *Kingella kingae.*

The limits for this methodology are still the elevated costs in some countries and the availability which makes it not a routine exam.

Imaging

Imaging is a very important tool in the exploration of a possible osteo-articular infection in children. It helps in localizing the infection and in differentiating between a septic arthritis and an osteomyelitis or in particular cases to identify both.

Plain Radiographs

In most of the infections plain radiographs maybe normal in the first days of the disease. In septic arthritis we may see an increase in the joint space and in later stages a dislocation (Fig. 1). In the presence of osteomyelitis radiographic signs will only appear between 7 and 21 days. Usually they consist of metaphyseal changes and periostitis which are both non-specific. In a study only in 20 % of the children presented abnormal radiographs at 10–14 days [6, 85].

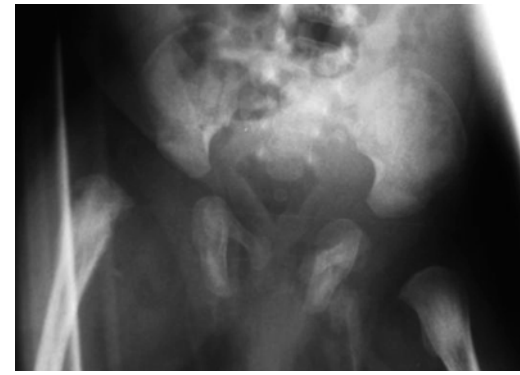


Fig. 1 Hip dislocation on the right side in a septic arthritis in a newborn

Ultrasound (US)

It is a safe, non-invasive, quick and effective way to investigate children with OAI and in particular for septic arthritis. It has become the investigation of choice especially in the assessment of deep joints like the hip and it allows detection of an effusion as small as 1–2 ml [35, 36]. A false negative rate of 5 % is observed and it has a 90 % sensitivity and a 45–100 % specificity. It helps the guiding of needle aspirations in particular in the deep joints [35]. However it cannot provide information that will allow the distinguishing of infective from non-infective effusions. In smaller joints like the sacro-iliac joint or the sterno-clavicular, the effusion cannot be perceptible and another imaging modality such as an MRI may be needed.

In the assessment of osteomyelitis, US shows at an initial stage subtle changes such as juxtacortical soft tissue swelling and periosteal thickening which is later followed by a sub-periosteal collection (Fig. 2).

Magnetic Resonance Imaging (MRI)

It is probably the most important imaging tool for the differential diagnosis of OAI. In children with septic arthritis that do not respond to appropriate

antibiotic therapy within 48 h, concomitant osteomyelitis should be suspected and MRI is indicated to make the differential diagnosis [52]. It helps also to differentiate septic arthritis from transient synovitis and is particular useful in the investigation of pyomyositis around the hip joint.

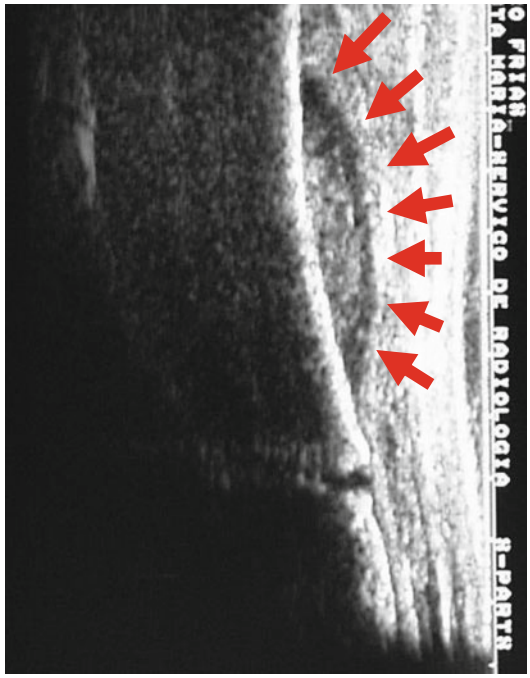


Fig. 2 Periosteal thickening followed by sub-periosteal collection seen in osteomyelitis. Ultrasound showing periosteum elevation with abscess (*red arrows*)

It has become the imaging modality of choice for the investigation of osteomyelitis in particular if the spine or the pelvis are involved (Fig. 3) [39]. Typical findings in the bone marrow include hypo-intensity on T1-weighted images, hyper-intensity on T2-weighted images and abnormal signal enhancement after gadolinium administration. In addition to defining the lesion area it also shows the degree of involvement of the adjacent soft-tissues and in particular intra-articular effusions. The drawbacks are the costs, availability and the need for sedation/general anaesthesia to perform the examination and this should be taken into consideration.

Computed Tomography (CT)

Due to the high dose of radiation CT should be used with caution in the evaluation process of OAI and should be used primarily in planning reconstruction of the sequelae of joint infections.

Bone Scanning

Bone scan with Technetium 99m was once a popular investigation to help identify the site/location of involvement and in particular in subtle cases with low clinical manifestations or in multi-focal infections [96]. Nowadays with the advent of MRI it is not so popular due to limitations on time, the high dose of radiation, availability and a low yield.

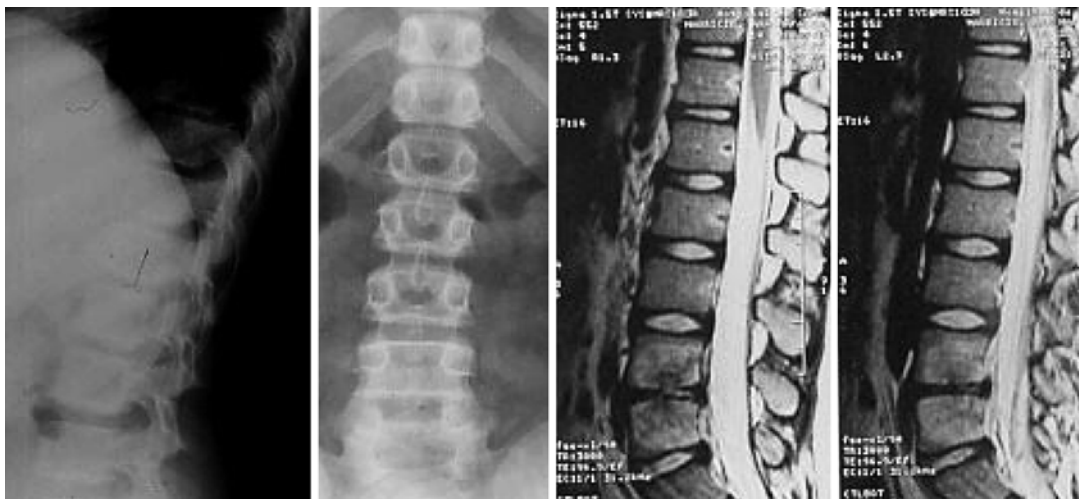


Fig. 3 Child with complaints of pain in the lumbar spine. Radiography not conclusive. MRI showing a L4L5 disc destruction compatible with spondylodiscitis

New Trends in the Treatment of Osteo-articular Infections

Moving Towards Shorter Courses and Oral Administration

The antibiotic regimen should be started immediately after aspiration of joint fluid. However, the antibiotic choice is still not established [20, 79]. It is guided by patient age, underlying predisposing conditions, synovial fluid penetration and mainly by local epidemiology of culture-positive infections [17]. There are several studies showing different antibiotic regimens effective in treatment of SA (Septic Arthritis) [17, 89]. Synovial penetration of most antibiotics is generally good but with slower and lower peaks when compared to serum concentrations [26, 54].

Since *S. aureus* is the most frequent cause of SA, the local pattern of *S. aureus* resistance dictates the antibiotic selection. In Europe, where CA-MRSA is yet less prevalent, a β-lactam antibiotics, such as oxacillin or high dose first or second-generation cephalosporin can be chosen, with adequate (although variable) bone penetration and good palatability [17, 38, 81]. Clindamycin is also a good option; besides covering CA-MRSA, it has an excellent bone and synovial fluid diffusion, a good bio-availability, although a worse palpability [58, 79, 83]. In regions were CA-MRSA is prevalent clindamycin or a combination of a β-lactam antibiotic and vancomycin has been recommended for empirical therapy [57, 79].

Kingella are sensitive to most penicillins and cephalosporins [99, 102]. Conversely, clindamycin and vancomycin do not provide adequate antimicrobial coverage against *K. kingae*, and should be used with caution for empirical treatment in children below 4 years in countries were *Kingella* predominates [102]. In these cases a first or second-generation cephalosporin would be preferable [58]. *Streptococcus pyogenes* remains unchangeably sensitive to penicillin and with the current breakpoint definition for pneumococcal full resistance to penicillin (MIC of 8ug/ml), high-dose penicillin also is appropriate as first line therapy for pneumococcal OAI [67].

The optimal length and route of treatment has been debated for decades [17, 82].

Although SA has traditionally been treated for 3–4 weeks, several reports currently suggest shorter courses of 2–4 weeks of sequential therapy, with 2–7 days of intravenous therapy [3, 43, 58, 81]. Jagodzinki established that 3 weeks of oral therapy was appropriate for patients who received 5 days or less intravenous treatment [45]. Peltola et al. treated patients with 2–4 days empirical intravenous therapy followed by oral therapy, with a mean total antibiotic of 10 versus 30 days [81]. No differences in outcome were identified between groups [81]. However, care must be taken, as this study was from a country with a low rate of resistant bacteria (89 % were MSSA and no MRSA was identified) and with a very short gap between symptoms and diagnosis.

In the United States, where CA-MRSA predominate, longer durations of 3–4 weeks have been recently proposed, probably related to the excessive frequency of complications [11, 57]. Certainly, if adjacent bone is affected, the gap between symptoms and diagnosis is higher than expected or if the micro-organism is atypical, treatment for more days is probably justified [20, 79]. In fact, there is no data on the length of treatment of newborns, immunocompromised patients or *Salmonella* arthritis. It is assumed that such cases require somewhat longer courses [20].

When choosing a shorter treatment course, clinical and laboratory monitoring become essential [79]. Sequential C-Reactive Protein (CRP) determinations provide an excellent method for monitoring SA [20, 77, 78]. If the patient is clinically recovering and CRP is declining, independent of the ESR, a change to oral antibiotic is probably safe, providing than high doses are used [78]. If no decrease in CRP values is observed or clinical improvement is compromised, further investigations should be carried out.

In conclusion, although there is no evidence to support treatment for months, with the intravenous phase lasting for weeks, the duration of

treatment is not agreed [71]. We recommend that a shorter sequential treatment can be applied for OAI in healthy children beyond the neonatal period, but must carefully monitored.

Surgical Approach

Septic Arthritis

Successful management of septic arthritis requires a correct diagnosis and treatment with antibiotics and joint drainage. It is accepted that delayed diagnosis and ineffective treatment are associated with several complications such as avascular necrosis (AVN), osteomyelitis, chondrolysis, systemic sepsis, leg-length discrepancy, and later osteoarthritis of the joint [12, 25, 92, 95].

Aspiration of the affected joint usually is performed for diagnostic (to confirm arthritis and identify the pathogen) and therapeutic purposes. It provides [12] sampling for laboratory diagnosis, decreases intra-articular/tissue pressure relieving pain, and promotes evacuation of purulent inflammatory material decreasing abscess formation and cartilage destruction.

Once the aspiration is done and we have a diagnosis of septic arthritis, antibiotics should be started and the joint promptly drained. Historically arthrotomy has been the method of choice for septic arthritis in particular of the major joints like hip, shoulder and knee. However in recent years there are several publications suggesting different approaches [12, 47, 65, 74].

There is no consensus regarding the choice of technique for surgical drainage [47, 65]. Classically, four types of drainage have been described [1]:

(a) Aspiration (single or repeated)
(b) Aspiration-lavage
(c) Arthroscopy
(d) Arthrotomy

Aspiration

Single aspiration is the method of choice for the diagnosis of a septic arthritis and at the same time functions as a treatment method. In the majority of cases one single aspiration can be sufficient to clear the joint. According to Pääkkönen, 73 % of the patients resolved with a single aspiration. In the same study 13 out 61 children (27 %) needed repeated aspirations. It is a less invasive procedure that decompressing the joint, improves blood flow and removes bacteria, toxins and proteases, but it can leave behind loculi of pus and necrotic synovium. Joint drainage should be repeated daily until effusions resolves [46]. It also helps in monitoring the effectiveness of antimicrobial treatment.

Although it was successful in 81 % of the cases in a minority (12 out of 62 children) it was necessary to convert to an arthrotomy.

Aspiration-Lavage

Aspiration and lavage with a saline solution it is considered also as a less invasive procedure, avoiding the risks of open surgery. In this particular case it is suggested to use a 14-gauge needle to allow an easy aspiration of the liquid and at the same time allowing for a good flow and pressure during the lavage. It removes more necrotic fragments than simple aspiration but it's not effective as arthroscopy or arthrotomy.

Arthroscopy

It is less invasive than arthrotomy, allows for quick recovery and return to activities [79]. Another advantage is the possibility of inspecting inaccessible areas of the joint filled with pus and breaking the pus loculations. It allows a safe synovectomy when indicated and gives the possibility of removal of any unstable cartilage.

Arthrotomy

This is a more invasive procedure but allows for nearly complete removal of all harmful substances, synovectomy and placement of irrigation-suctions systems if necessary. The main indications are [1]:

- Septic arthritis of hip, shoulder, sacro-iliac joint and sterno-clavicular joints
- Septic Arthritis not responding to multiple aspirations/antibiotics
- Thick pus
- Presence of negative prognostic factors (long time to the treatment, neonates, immunosuppression, vascular compromise, presence of pre-existing disease in the joint, concomitant osteomyelitis, infection by gram-negative bacteria)

No prospective randomized study has clearly shown that surgery (arthrotomy or arthroscopy) is superior to repeated aspiration or aspiration-lavage in the management of the infected joint. However several authors, including Goldstein et al. [34], postulated that factors responsible for cartilage degradation are better removed by an open procedure, being less harmful to the cartilage in a long-term.

Nord et al. [72] in an experimental study with goats found no difference between aspiration, arthroscopy and arthrotomy in damage to the articular cartilage.

The hip has been as been the most studied joint and most authors agree that in the septic hip, arthrotomy and washout are the best method of treatment [10, 25, 59, 68, 70].

However other studies showed no evidence for performing a routine arthrotomy. Goldenberg's study [33] supports repeated aspirations as definitive treatment, but he fails to define "total recovery" and no long-term follow-up is given in his study. Givon et al. [32] performed repeated aspirations of the hip joint with no complications seen and concluded that repeated aspiration is a safe and efficacious method of treatment septic hip arthritis.

Recently Pääkkönen et al. [74] published a study comparing treatment of septic hip with and without arthrotomy emphasising the fact that the majority of septic hips do not warrant surgical intervention beyond diagnostic joint aspiration.

As in the hip, authors are divided on the best way to drain the shoulder in children. Schmidt et al. [90] considered that septic arthritis of the shoulder in children should be treated by drainage of the bicipital recess and drilling of the metaphysis if concomitant osteomyelitis is present. Smith et al. [94] found no difference between aspiration, arthroscopy and arthrotomy.

Another controversy is arthroscopy versus arthrotomy. Since its advent, arthroscopy has gained popularity. Advantages over arthrotomy are the ability to inspect the joint, clear and remove all the pus, loculi and synovectomy, while being minimally-invasive allowing rapid recovery [29, 42, 91]. The knee is especially amenable to this form of treatment but it can be used in shoulder, ankle and hip as well. El-Sayed [24] compared arthrotomy and arthroscopy of infected hips and stated that arthroscopy proved to be an effective method of treating septic arthritis of hip and was associated with a shorter hospital stay, due to its minimally-invasive nature, while no statistically significance existed in the final clinical outcomes.

Randomized, prospective clinical trials comparing different techniques are needed.

Osteomyelitis

Recognizing osteomyelitis requires a high degree of suspicion. The diagnosis may be missed and it may lead to pus formation making a surgical intervention necessary. Conservative treatment with antibiotics only is useful just before the pus formation.

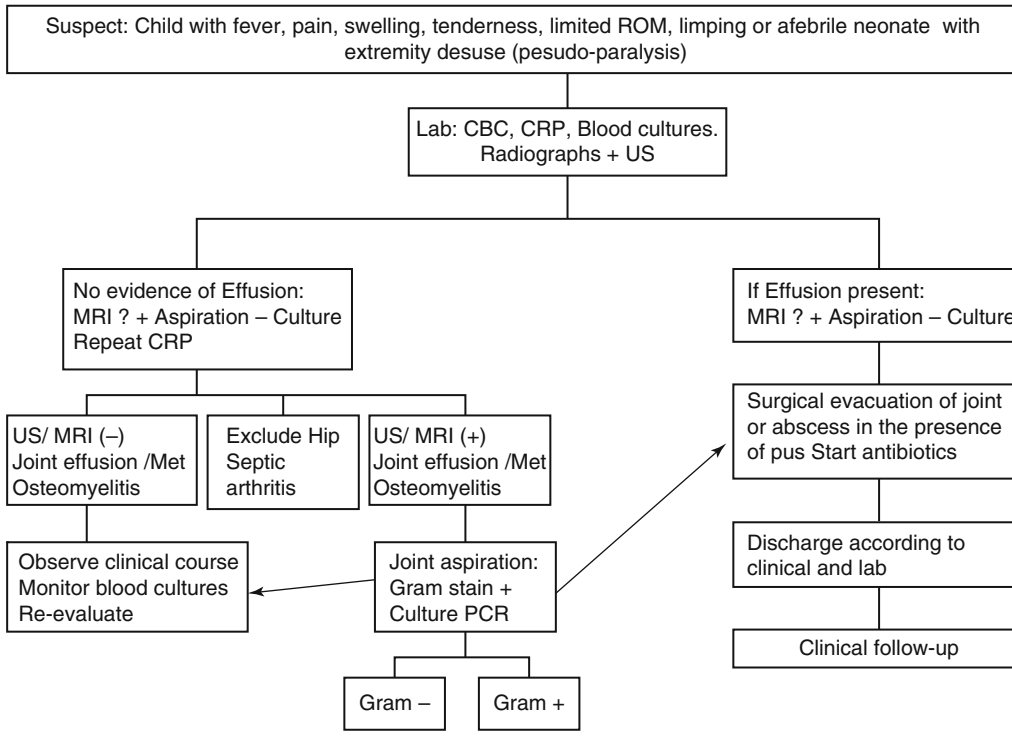
Nade [70] suggested five principles for the treatment of acute osteomyelitis:

- An appropriate antibiotic is effective before pus formation
- Antibiotics do not sterilize avascular tissues or abscesses, and such areas require surgical removal
- If such removal is effective, antibiotics should prevent their re-formation, and primary closure should be safe
- Surgery should not damage further already ischaemic bone and soft tissues
- Antibiotics should be continued after surgery

Surgical treatment is required if bone aspiration evacuates pus (from soft tissues, subperiosteal space or metaphysis), the child does not show signs of improvement despite treatment with antibiotics after 36 h, or plain radiographs show progressive bone involvement [1]. In concomitant septic arthritis and osteomyelitis, only arthrocentesis is indicated [1].

In a recent systematic review of the literature, Dartnell et al. [18] stated that surgery is

Table 1 Diagnosis and treatment of musculoskeletal infections



not routinely required and is reserved for concurrent septic arthritis, disseminated sepsis, failure to improve with antibiotics, or pelvic abscesses >2 cm.

A Diagnostic Protocol Approach-State of the Art in Diagnosis/ Treatment

In order to have a systemic approach to osteo-articular infections in children and adolescents we suggest the following:

For diagnosis and treatment (Table 1):

The diagnosis of an infection is based on the clinical examination and the identification of the infected agent, which makes the laboratory processing a key factor in the diagnosis. How to collect samples and process them is still a challenge due to the fact that sometimes the pus is scarce. In this situation it is necessary to prioritize the type of examinations available in order to improve the diagnosis. We propose the following methodology of pus processing (Table 2):

As stated before medical treatment is based on antibiotics. It is fundamental to have a systemized approach when choosing an antibiotic but the decision should be based on the knowledge of the country/regional incidence of the most prevalent bacteriological organisms. We know that although *Staphylococcus aureus* is still the most common agent prevalence may change from one region to another. This means that antibiotic protocols should be adjusted to the local needs. As a principle we suggest (Table 3):

Table 2 Pus processing

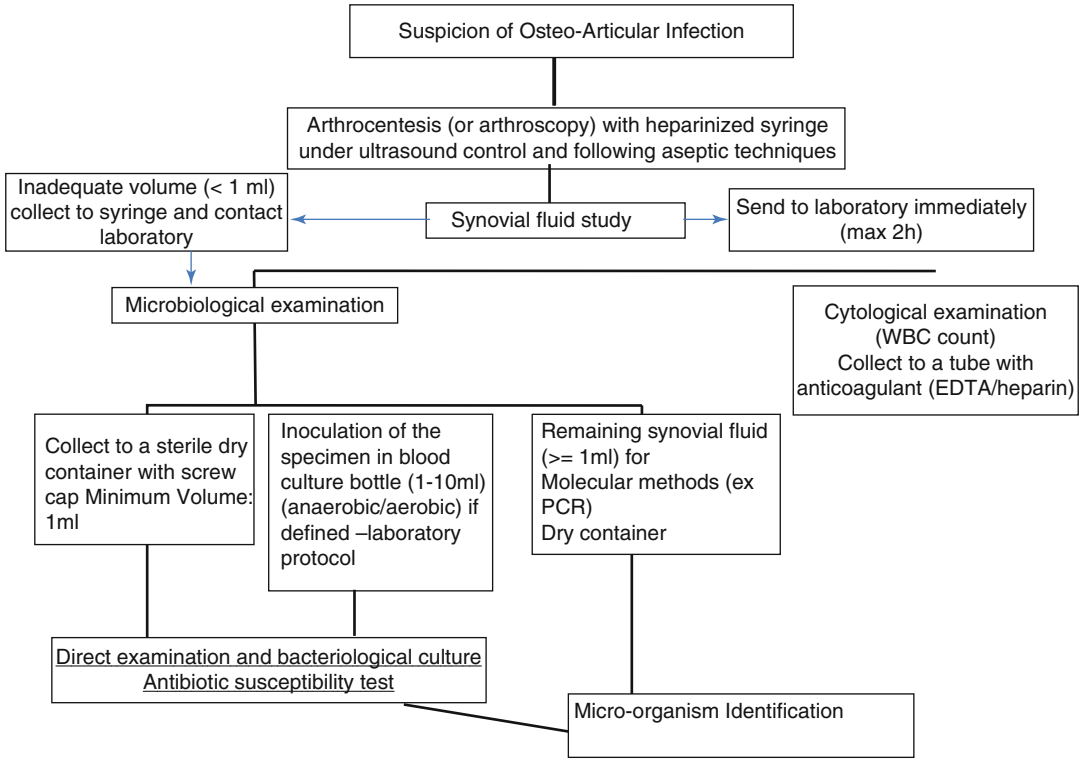
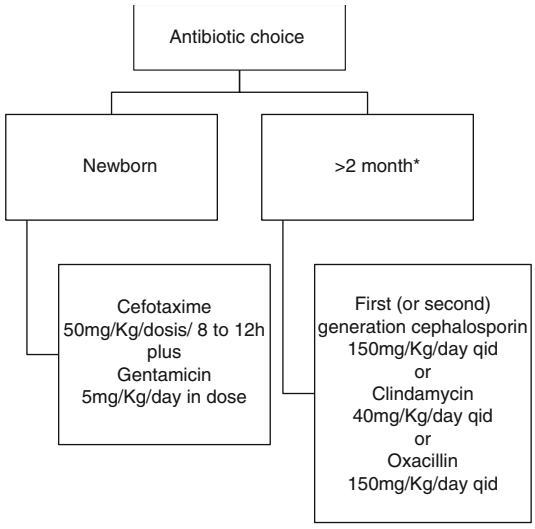


Table 3 Antibiotic protocol



Conclusions

Osteo-articular infections in children and adolescents are still a major challenge and a possible cause of disability in adult life if not properly diagnosed and rapidly treated. The aetiology can be diverse and the clinical presentations can change according to localisation, age and infecting agent which makes the diagnosis difficult. In order to have success and prevent major sequelae it is fundamental to establish a rapid diagnosis, identify promptly the infecting agent and start immediate medical treatment and appropriate surgery when necessary.

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Part V

Spine

Diagnosis and Treatment of Upper Cervical Spine Trauma in the Elderly

Christian Garreau de Loubresse

Abstract

Upper cervical spine trauma is frequent in elderly patients. The mechanism of injury is usually a low energy trauma, which explains the delay in diagnosis of this serious injury. There is no consensus on patient management. Both conservative and surgical management are associated with morbidity and mortality, although the risk factors have not been statistically confirmed by publications in the literature. Conservative treatment with a neck brace or a halo vest should be limited to stable fractures. Any instability should be treated with surgery. In these elderly patients surgery seems to result in a better rate of union, faster return to the same level of autonomy as before the injury, as well as in lower mortality than in non-surgical patients. Prospective descriptive studies are needed so that guidelines can be drafted for the management of this frequent, complex and sometimes life-threatening entity.

Introduction

As the life expectancy increases thanks to improved and increased access to healthcare, the elderly population is also increasing. In the European Union, epidemiological data show that one-fifth of the population will be over 65 in 2025, and one-third in 2060. The elderly subject has a particularly high risk of upper cervical spine trauma (UCS), with injuries that are completely different from those in young subjects. The association of stiffness due to diffuse secondary osteoarthritis and osteoporosis increases the risk of fractures from low energy traumas.

The cervical spine is divided into the upper cervical spine and the lower cervical spine by the C2-C3 disc. In most cases, trauma in elderly patients involves the upper cervical spine. Trauma in this complex region may cause life-threatening injuries and severe neurological or articular sequelae. The high rates of associated morbidity and mortality emphasize the importance of early diagnosis and appropriate management of these patients.

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Epidemiology of Cervical Spine Trauma in the Elderly

The frequency of cervical spine trauma is increasing in the elderly, while it is decreasing in younger patients [1–3]. Lomoschitz et al. [4] studied the epidemiology of cervical spine trauma in two sub-groups of elderly patients: patients over 65 and very elderly patients over 75. The older the patient, the greater the frequency of upper cervical spine injury. The location of the fracture was also influenced by the mechanism of trauma. Low energy traumas such as a fall from a standing or sitting position resulted in UCS involvement while the topographic distribution of high energy traumas was less specific. Naturally there is greater movement of the lower cervical spine, which explains why most of these injuries are found in younger patients. On the other hand, when stiffness develops in the posterior joints and the interspinous spaces between C3 and C7 due to degenerative bone disease, the risk of upper cervical spine trauma is increased. Fragile, osteoporotic bone is going to be injured by forced movements. The main fractures in the UCS involve the odontoid process, but also the atlas [5–7].

Classifications

C1 Fracture

The atlas is a ring of bone that surrounds the spinal cord and the odontoid process. The lateral masses joined by the anterior and posterior arches articulate with the occipital condyles by the superior facets and with C2 by the inferior facets. A complex system of ligaments provides stability. The transverse atlanto-axial ligament inserts into the anterior arch to ensure anteroposterior stability of the odontoid process. The apical and alar ligaments of the odontoid process limit rotation, flexion and inclination of the cranial-cervical junction. There are three types of C1 fractures:

Type I corresponds to fractures of either the anterior or posterior arches (Fig. 1).

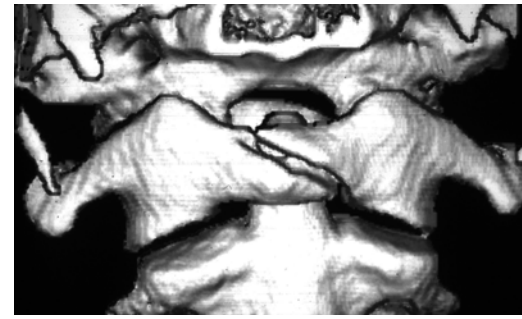

Fig. 1 Atlas fracture classification. Type 1

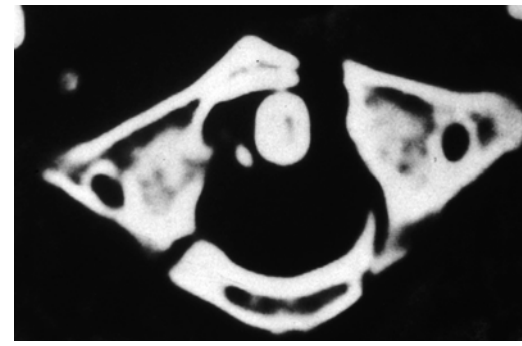

Fig. 2 Atlas fracture classification. Type 2, Jefferson fracture with anterior and posterior atlas arch fractures

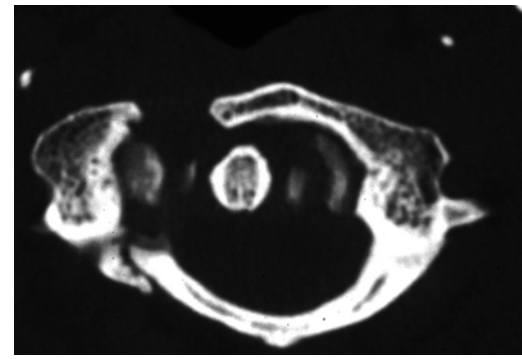

Fig. 3 Atlas fracture classification. Type 3: fracture of a lateral mass extended to an arch

Type 2 involves both arches or fractures with several fragments (Fig. 2). The Jefferson fracture is a four-fragment fracture.

A fracture of a lateral mass that extends to an arch is considered to be a type III fracture (Figs. 3 and 4) [8].

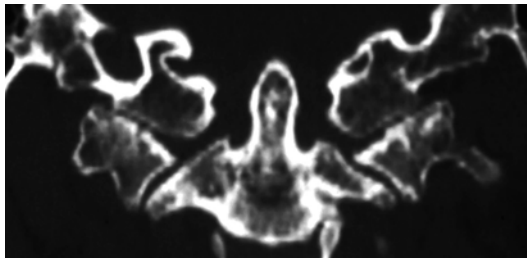

Fig. 4 Atlas fracture classification. Type 3: fracture of a lateral mass extended to an arch

C2 Fractures

C2 fractures mainly involve the odontoid process in elderly subjects. These fractures are usually classified by two systems. The Anderson and D'Alonzo classification (Fig. 5) [9] includes three types of fracture depending on the location of the fracture line:

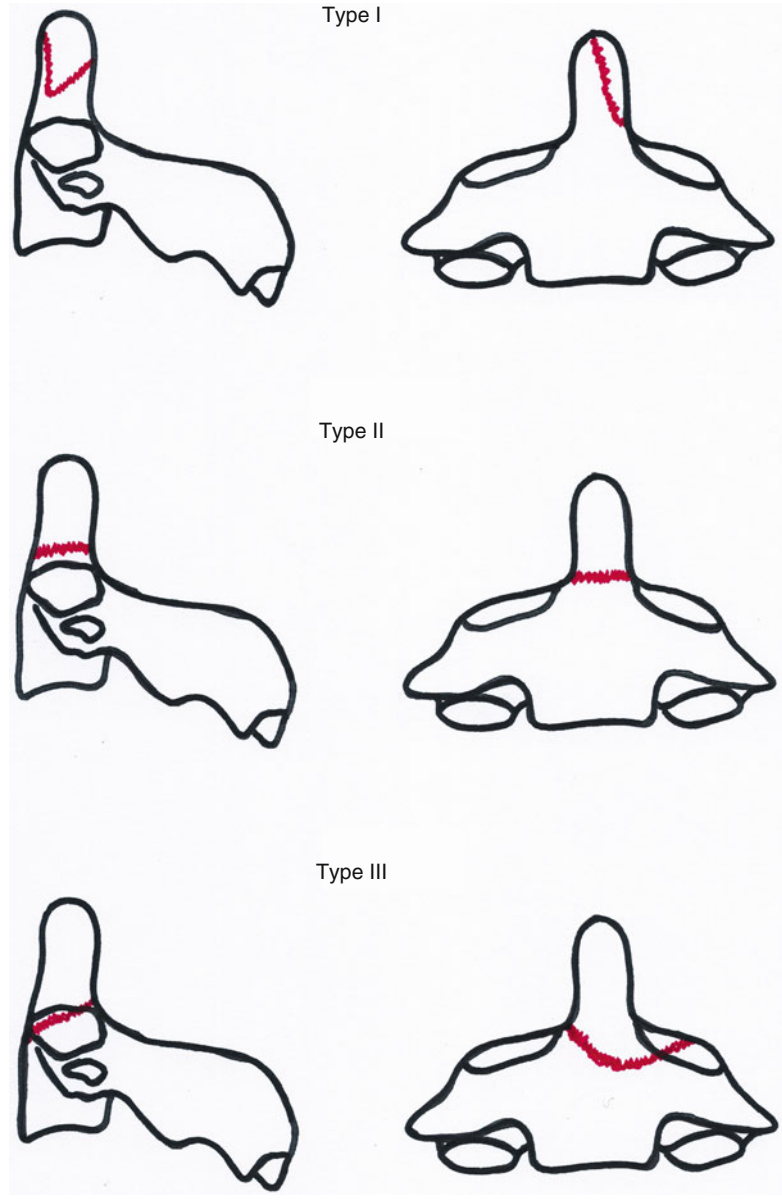

Fig. 5 Odontoid fractures. Anderson and d'Alonzo classification

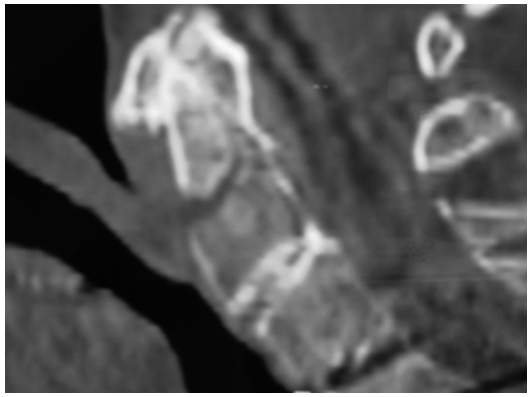

Fig. 6 Roy-Camille classification. Anterior oblique fracture line

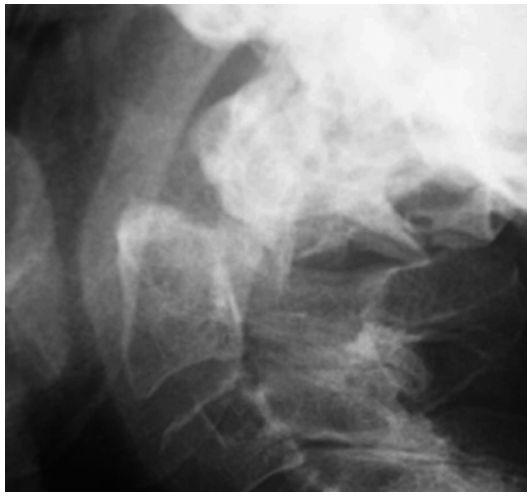

Fig. 7 Roy-Camille classification. Posterior oblique fracture line

Type I is an oblique avulsion fracture of the tip of the odontoid process.

Type II is a fracture at the junction of the dens and the body of C2.

Type III is a fracture of the vertebral body of the axis. The Roy-Camille et al. [10] classification is descriptive but includes the notion of stability for each type of fracture. There are three groups of fractures according to fracture line and direction. An anterior oblique odontoid fracture line (Fig. 6) is more stable than a posterior oblique fracture line (Fig. 7).

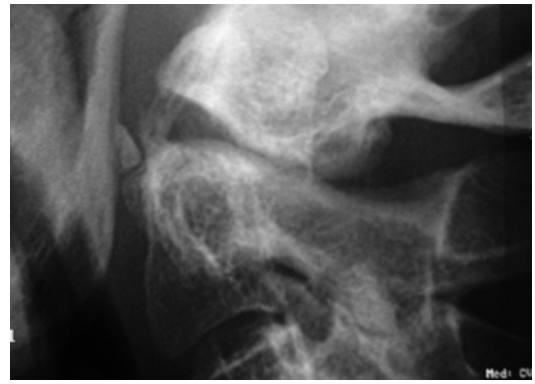

Fig. 8 Roy-Camille classification. Horizontal fracture line

Horizontal fracture lines are the most Unstable (Fig. 8).

Diagnosis

The diagnosis of UCS fractures in elderly subjects is sometimes difficult. The rule is to suspect a UCS fracture in the presence of even slight cervical pain after what might seem to have been very slight trauma, such as a fall from standing height. Neurological deficits are rare. In a systematic review of UCS trauma, only 6/692 patients had a neurological deficit [11]. Tetraplegia may be due to either medullary injury at the level of the UCS, or from decompensation of a pre-existing myelopathy of the inferior cervical spine [12, 13]. Clinical examination of the cervical spine may reveal reflex muscular tension, with sometimes very moderate pain, which explains the delay in diagnosis. Cervical stiffness can be another reason for consulting, and the patient should be questioned to identify any trauma, even benign.

X-rays of the cervical spine are essential and should include an AP open-mouth view. A haematoma behind the hypopharynx is seen as enlargement of the soft tissues across from the fracture site. The soft tissue should not extend more than 5 mm. beyond the anterior line of C2-C4 [14]. Bone structures are analyzed to make the diagnosis and classify the fracture. Isolated C1– C2 instability is rare in these cases.

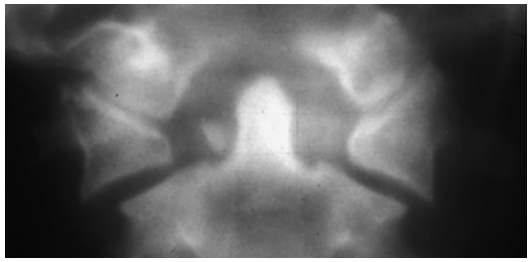

Fig. 9 Open mouth view and lateral overhang of lateral masses of the atlas

The diagnosis is based on AP X-rays showing an atlanto-odontoid interval of more than 3 mm. This anterior-posterior instability may be associated with a fracture of the lateral mass of the atlas, or a Jefferson fracture. A torn transverse atlantal ligament can be confirmed on an X-ray with the open-mouth view and lateral overhang of more than 6.9 mm of one lateral mass of the atlas (Fig. 9) [15]. These fractures of the odontoid process are dangerous for the spinal cord because of their displacement. Odontoid fracture angulation is measured by determining the angle between the posterior aspect of the C2 body and the tangent with the posterior aspect of the odontoid process. Fracture displacement is calculated by the distance between the tangents of the anterior aspect of the odontoid process, and the anterior aspect of the body of C2. A transverse line connects these two and the distance between them is sagittal fracture displacement [16]. If a fracture is found on X-ray, CT of the cervical spine can provide the location of the fracture, the direction of the fracture lines, displacement and confirm any instability [17, 18]. Whatever the type or severity of the trauma, a CT scan is indispensible in the presence of cervical pain or modified mobility that cannot by explained by simple X-ray. Anderson et d'Alonzo type II fractures were found in 95 % of the cases (803/846 reported cases of UCS fractures) in 23/24 studies evaluated in the systematic review by Jubert et al. [11]. Associated injuries were mainly atlas fractures. C1-C2 dislocation or fractures of the lateral mass of the axis were rare. Simultaneous fractures of the inferior cervical spine were very rare.

Treatment

Fracture union ensures stability of the spine and prevents neurological complications. Treatment of the elderly is difficult due to co-morbidities, the patient's general condition, the quality of bone and pre-existing spine deformities. There are numerous techniques ranging from conservative treatment with simple immobilization to reduction and the use of a halo vest or internal fixation.

Immobilization of the Upper Cervical Spine

Theoretically conservative treatment with immobilization should prevent rotation, extension-flexion and inclination of the cervical spine. This requires a rigid neck brace with chin, occipital and a forehead support. In practice this is poorly tolerated by elderly patients. There is a risk of pressure sores on the pressure points, in particular on the head and chin. This explains why less constraining immobilization is often used, with lighter, less rigid material that is less abrasive to the skin. The patient must remain in a brace for 3 months with X-ray follow up throughout treatment and until the end of immobilization.

Halo-vest

Halo vest placement is highly technical. After choosing the correct size, local anaesthesia is performed after applying a local antiseptic. The anterior pins are placed 1–2 cm above and lateral to 2/3 of the eyebrow. They are placed at 5 o'clock and 7 o'clock in the back of the head. Pins should avoid the frontal sinus, the supra-orbital nerve and the temporal artery and the mastoid. Halo ring placement follows a horizontal line that passes 1 cm above the pinna of the ear. Pin tension is 6–8 in./lb (0.7–0.9 Nm). They are screwed to the ring and blocked. The halo is attached laterally to the corset with rods. Reduction is controlled

by fluoroscopy. Specific instructions are given for pin care and for the skin under the corset. Pin tension should be checked again 24 h after the vest has been placed. AP open-mouth view X-rays are performed before the patient is released. Clinical and radiological follow-up is performed in a consultation at 15 days, then every month until union is obtained. After at least 3 months, if X-rays are good, the halo can be taken off the corset to perform dynamic lateral X-rays. When stability is confirmed, the halo vest is removed [19].

Interlaminar Posterior C1-C2 Arthrodesis

Stabilization of an odontoid process fracture is usually obtained indirectly by the interlaminar posterior arthrodesis described by Gallie [20]. The fracture is first reduced, then the posterior arches of C1-C2 are decorticated and an iliac autograft is performed and maintained by sublaminar wire fixation. Three months immobilization in a rigid occipital-cervical-thoracic brace is indispensible. The metal wires used initially are replaced by thin, braided sublaminar cables that are easier to use and less apt to break [21].

Posterior Internal Fixation

Trans-articular C2-C1 Screw Fixation

Described by Jeanneret and Magerl [22], this arthrodesis combines a graft between the posterior arches of C1 and C2 with ascending trans-articular screw fixation. The same authors especially recommend this procedure in elderly subjects with a contra-indication to anterior fixation due to, for example, thoracic kyphosis, limited cervical extension or degenerative lesions with a narrow cervical canal. Although biomechanical studies have shown that trans-articular fixation is more effective than sublaminar fixation, this technique is difficult to perform with a risk of vascular or neurological complications. Pre-operative CT should exclude the presence of any vascular anomalies or variants of the vertebral artery. Although erosion of the pedicle of the axis in contact with the artery was a source of risk in 18–23 % of cases, the estimated rate of injury to the artery was 2.2 % per screw [23]. In practice, the patient is placed in the prone position with a Mayfield head rest allowing fluoroscopically-controlled reduction. Long K-wires must be placed in the guide to direct oblique screw placement. After piercing the skin near C7, the entry point of the K-wire is located at the junction of the lamina and the articular mass and 2 mm above the C2-C3 joint space. A sagittal direction is taken at a 45° angle in relation to the horizontal line. The K-wire is advanced under fluoroscopic control through the C1-C2 joint space then into the mass of the atlas without fracturing the anterior cortex. Final screw fixation uses 3.5–4.5 mm diameter screws. The procedure is terminated by a graft and sublaminar C1-C2 fixation.

Screw-Rod Constructs

Stabilization of C1 and C2 can be obtained by a screw-rod construct with screw fixation of the lateral masses of the atlas and the pedicles of C2, which are joined by 2 rods. Technically, the posterior arches are exposed up to the C1-C2 lateral mass. The dorsal root ganglion of C2 is pushed downwards to expose the entry point of the C1 screw. The direction converges slightly with and is parallel to the atlas. The entry point for C2 screw fixation is in the cranial and medial quadrant of the isthmus surface of C2. All drilling is guided fluoroscopically. Screws that are 3.5 mm in diameter are used and joined with two rods. If necessary C1 can be reduced on C2 by manipulation of the implantation material. Arthrodesis is posterior and obtained by decortication of the posterior arches and the use of cancellous iliac grafts with no structural bone graft or wiring [24]. In a meta-analysis comparing trans-articular screw fixation (TAS) and the Screw-Rod Construct (SRC), there was no difference in the very low rates of mortality or iatrogenic neurological trauma between these two techniques. On the other hand a significant statistical difference was found with a higher incidence of injury to the vertebral artery, screw malposition and a lower rate of union with TAS [25].

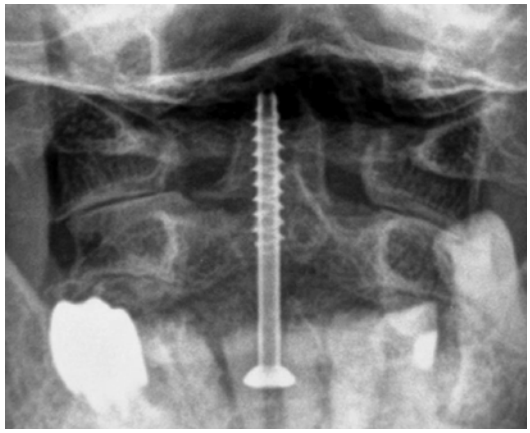

Fig. 10 Anterior screw fixation of an odontoid process fracture

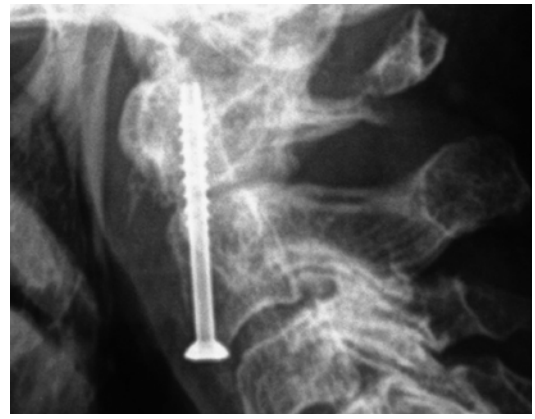

Fig. 11 Anterior screw fixation of an odontoid process fracture

Occipitocervical Fusion

This technique should only be used rarely in cases of complete loss of head movement in all planes. It is considered in the presence of unstable fractures at several levels and very rare occiput-C1 injury.

Anterior Screw Fixation of the Odontoid Process

Anterior screw fixation of the odontoid process is a difficult technique that should be performed only by an experienced surgeon. Installation of the patient is long but decisive for a successful procedure. The patient is placed in the dorsal decubitus position. The mouth is maintained open by a radiolucent retractor, or simple compresses. The head is stabilized in a headrest that allows imaging. Reduction is guided on the AP and lateral planes with two fluoroscopes. Before beginning surgery a wire is used to evaluate the necessary angle for odontoid screw fixation. In certain cases fixation may be disturbed by the volume of the thorax, a short neck or thoracic kyphosis. The surgical approach is by the lower cervical spine. Once the plane of the anterior vertebral ligament has been identified, dissection is continued to C2-C3. A guide-wire enters the posterior and anterior aspects of the body of C2. The direction and progression of the K-wire is fluoroscopically-controlled to the tip of the odontoid process. The length of the cannulated screw is chosen with distal threads to compress and stabilize the fracture. The indications for anterior screw fixation are type 2 fractures with a posterior oblique or horizontal fracture lines (Figs. 10 and 11). Contra-indications are fractures with anterior oblique fracture lines or with anterior comminution of the body of C2 [26].

Results and Outcomes

The results and outcomes of this type of management in elderly patients is based on a systematic review of the literature (Author's publication [11]) and several very recent publications [27–29].

Union

Rates of union were fairly similar and slightly better with surgery. Surgery with odontoid process screw fixation and posterior arthrodesis resulted in union in 76.9 and 86.6 % of cases, respectively. Treatment with a neck brace and halo-vest resulted in union in 79.4 %.

Morbidity and Mortality

The overall rate of short and intermediate term complications was 15.4 % (CI 95 %: 5.8–26.9).

Morbidity

The main complications with surgical treatment were dysphagia and respiratory difficulties. Conservative treatment was associated with local complications (migration or infections of the pins in the halo brace, skin abrasions) as well as respiratory decompensation. The main long-term complications were problems with union and non-union. The rate of non-union in the group with odontoid process fractures treated surgically (566 patients) was 10.2 %. The rate of non-union in patients treated conservatively (476 patients) was 12.2 %. Only four studies reported whether non-union required treatment or not [30–33]. Certain studies described a category of patients with stable non-union due to fibrosis of the fracture site. This rate of stable fibrosis in the surgery group was 9 and 8.4 % in the group that received conservative treatment. The stability of the fracture site provided by the fibrous callus prevented the development of neurological decompensation in these patients, and thus the need for revision surgery. The other factors for a poor prognosis that were most frequently mentioned in the elderly were very old age, co-morbidities and lesions associated with the initial trauma [34].

Mortality

A mean 18.7 % of patients died (210 deaths, all types of treatment included for 1,122 patients). One third of the deaths occurred in the surgical treatment group and the other two-thirds in the group treated with a neck brace or halo vest. However a direct comparison is impossible between these populations because there no statistical comparisons were performed. The main cause of death was cardiopulmonary-related, and patients died at least 3 months after the original trauma in 89.7 % of the cases. A secondary neurological deficit could also be considered a risk factor of death even if the association between the deficit and an UCS lesion is rare [1, 6, 35]. Decompensation of a cervical spondylotic myelopathy with a motor deficit following a low energy trauma increases the risk of mortality in elderly subjects [10, 36]. Moreover after a cervical spine fracture in elderly patients, the rate of death at 3 months is increased in those with a neurological deficit [35].

Influence of the Technique on Outcome

Management of these fractures is still a subject of debate [37]. For Smith et al. [38], the outcome is better following conservative treatment than surgical treatment. According to Andersson et al. [39], the rate of complications with anterior screw fixation is too high to be acceptable. On the other hand Omeis et al. [13] compared the different surgical techniques and did not find any significant difference in outcome or complications. Boakye et al. [40] reported that death is independent of the type of treatment and age is the main risk factor. For others [41], age, the presence of a neurological deficit, the number of co-morbidities and associated lesions could be risk factors for death and the type of treatment was not the only factor responsible for the patients' deaths. Finally in a prospective, multi-centre study, Vaccaro et al. [29] reported a significantly higher rate of mortality in the group without surgery than in those with surgery (annual rate of death of 26 and 14 % respectively). Selection criteria were not often clearly defined in the literature but were based on clinical practice, co-morbidities, the characteristics of the fracture as well as the surgeon's and patient's choices. Although odontoid process screw fixation is the most frequently performed surgical procedure, no studies have proven that it is more effective than other techniques. Most cases of conservative treatment use a rigid neck brace. Moreover, the mean duration of immobilization with a rigid neck brace or halo corset is often very long and can last 24 weeks [42–44]. This lengthy immobilization and its effect on the autonomy of these elderly patients may seem somewhat surprising.

Conclusion

Upper cervical spine trauma is frequent and should be suspected even after low energy trauma in elderly patients. Imaging and CT in particular can confirm the diagnosis and identify what may be multiple traumatic injuries. The choice of treatment must take into account the type of injury as well as the age

of the patient and especially co-morbidities. Mortality is nearly 20 % and requires close monitoring especially for cardiopulmonary decompensation.

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Part VI

Shoulder and Arm

Periprosthetic Fractures in the Upper Limb

Pierre Mansat

Abstract

Periprosthetic fractures around a shoulder or an elbow arthroplasty are not common, but remain a challenging complication. Osteopaenia, advanced age, female sex, and rheumatoid arthritis are medical co-morbid factors that may contribute to humeral or ulnar fractures and associated delayed healing and poorer function. Treatment strategy includes: identification of the cause of failure, exclusion the possibility of sepsis, evaluation of the local soft-tissue status, status of the prosthesis, selection of a prosthesis adapted to the revision procedure if needed and planning of the appropriate surgical technique. Classification must be used to determine the prognosis and treatment of these fractures: the location of the fracture in relation to the stem, the security of the fixation, and the quality of the bone. For fractures around an implant, if the fracture line overlaps most of the length of the prosthesis with a loose implant, revision with a long-stem implant should be considered. When the fracture overlaps the tip of the prosthesis and extends distally, open reduction and internal fixation is recommended. When the fracture is completely distal to the prosthesis and satisfactory alignment at the fracture site can be maintained with a fracture brace, then a trial of non-surgical treatment is recommended.

Peri-implant Fracture with Shoulder Arthroplasty

Incidence

Peri-prosthetic fracture during or following shoulder arthroplasty is not common with a frequency varying from 0.6 to 2.8 % [2, 5, 8, 15, 27, 29]. Reviewing 40 studies of humeral head replacement or total shoulder arthroplasty that included 3,584 patients, the rate of periprosthetic fracture was reported to be 1.2 % (range, 0–8 %) [28]. In studies of more

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than 2,500 primary total shoulder arthroplasties and 1,400 humeral head replacements performed over a 33-year period at the Mayo Clinic with a mean of 7 years of follow-up, the rate of intra-operative humeral fractures was 1.2 % (48 of 4,019) and the rate of post-operative humeral fractures was 0.9 % (36 of 4,019) [25]. Female sex and underlying diagnoses like rheumatoid arthritis and/or osteoporosis were significantly associated with a higher risk of intra-operative fractures, and co-morbidity was significantly associated with a higher risk of post-operative fractures [25, 26]. Campbell et al. [6] described osteopaenia of the humerus based on the ratio of the combined width of the mid-diaphyseal cortices to the diameter of the diaphysis at the same level. A ratio >50 % indicated normal bone, 25–50 % indicated mild osteopaenia, and <25 % indicated severe osteopaenia. Based on this definition, osteopaenia was a risk factor in 75 % of the periprosthetic humeral shaft fractures in their study.

Classification

Several classification systems exist for periprosthetic humerus fractures. The most accepted classification has been proposed by Wright and Cofield [30], which is based on the location of the fracture relative to the tip of the humeral prosthesis (Fig. 1).

- Type A fractures are centred near the tip of the stem and extend proximally;
- Type B fractures are centred at the tip of the stem but present with a variable amount of extension distally;
- Type C fractures are located distal to the tip of the stem.

Campbell et al. [6] proposed a classification system that included tuberosity and metaphyseal fractures and that may be more applicable for intra-operative fractures particularly those occurring with use of press-fit implants (Fig. 2).

- Region-1 fractures involve the greater and/or lesser tuberosities;
- Region-2 fractures involve the metaphysis of the proximal part of the humerus;
- Region-3 fractures involve the proximal part of the humeral shaft;
- Region-4 fractures involve the middle and distal parts of the humeral shaft.

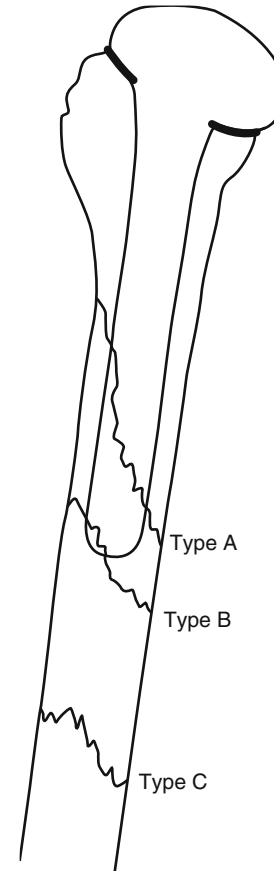

Fig. 1 Periprosthetic humeral fractures according to Wright and Cofield [30]

Treatment Strategy

The type of treatment is dictated by fracture location, displacement, and status of humeral component fixation.

Non-operative Treatment

A fracture with acceptable alignment occurring next to a well-fixed stem can be successfully managed non-operatively with functional bracing [6, 14]. Acceptable alignment can be defined as within 20° of flexion/extension, 20° of rotational and 30° of varus/valgus angulation [15]. Non-operative treatment can also be indicated when surgery is contra-indicated as with active infection and debilitating medical co-morbidities precluding the use of general anesthesia.

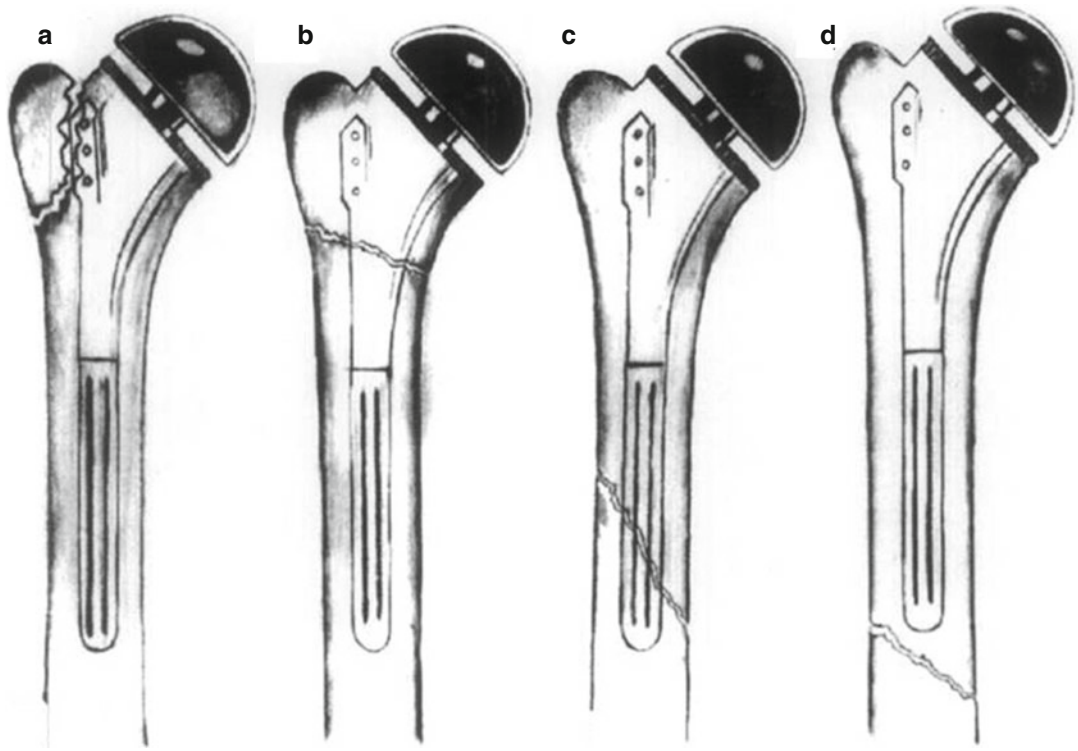

Fig. 2 Periprosthetic humeral fractures according to Campbell et al. [6] ((**a**) region 1; (**b**) region 2; (**c**) region 3; (**d**) region 4)

Surgical Treatment

Operative treatment may be indicated when there is prosthetic loosening, significant displacement, unacceptable angulation, or failure of a fracture to heal. Short oblique and transverse fractures as well as those distracted by the stem are more prone to delayed union and are more likely to require operative intervention. Surgery should be considered following failure to maintain fracture reduction. Pre-fracture loosening can be recognized by circumferential radiographic lucency or a shift in prosthesis position. When the prosthesis is loose the prosthesis should be revised with a long-stem humeral component. Revision stems may be cemented or, if there is adequate bone stock, may be cementless. The tip of the stem should extend two to three cortical diameters past the fracture site. Stable fixation at the fracture site can be augmented with allograft strut, cerclage wires, or plate-and-screw fixation. Autologous iliac crest or allograft bone graft can be used to supplement healing. Displaced fractures usually required operative intervention utilizing such implants as angular stable plates and cerclage as indicated. Humeral shaft fractures that are recognized intra-operatively should be managed with placement of a long-stem prosthesis and supplemental rigid fixation. Stable fixation allows for early range of motion (ROM) during rehabilitation as well as more satisfactory results from unrestricted shoulder and elbow movement. Union rates are better with this treatment than with non-surgical treatment of fractures located about the tip of the humeral prosthesis.

Surgical Technique – Indications

According to the Wright and Cofield classification [30], Steinmann and Cheung [26] have well described the surgical guidelines:

- Type A fracture: most type A fractures are minimally displaced and angulated due to the presence of the rigid intramedullary stem. Type A fractures may be comminuted or may be long and oblique, with substantial overlap

between the length of the fracture and the humeral stem. When there is substantial overlap between the length of the fracture and the humeral stem, as well as displacement >2 mm and angulation >20° in any plane, revision to a long-stem prosthesis is advised to by-pass the fracture by at least two cortical diameters (Fig. 3). Fixation should be supplemented distally with strut graft and cerclage wires. If necessary, plate and screws may be used instead of graft and wires to afford torsional rigidity.

- Type B fracture: for type B fractures with coexistent humeral stem loosening, revision to a long-stem prosthesis is recommended. In cases of severe osteopaenia, either a cortical strut graft with cerclage wires or plate fixation with cerclage wires is placed across the fracture site. Both cemented and cementless stems for periprosthetic humerus fractures have been used in small case series, with satisfactory union rates. A displaced or unstable type B fracture with a well-fixed humeral stem is managed with a hybrid plate. It is secured with cerclage wires or short locking screws proximally and screws distally, engaging eight cortices distally. Cortical onlay strut allografts act as biological plates, serving both a mechanical and a biological function, because allografts have the potential for remodelling and incorporation (Fig. 4).
- Type C fracture: ORIF of type C fractures is recommended after failed non-surgical treatment or failure to maintain reduction. This treatment is similar to that used for non-periprosthetic humeral shaft fracture. Plate-and-screw fixation is performed, with or without supplemental allograft struts. The length of the plate should be adequate to extend proximally. The plate should overlap the tip of the prosthesis by two cortical diameters to avoid the creation of the stress riser (Fig. 5).

Guidelines according to Campbell classification have also been proposed [6]:

- Region-1: these fractures are assessed for stability, and, if deemed stable, with the periosteum intact and without displacement, they may be treated with insertion of a standard implant without specific fixation. However, if any fracture motion exists or if there is any degree of displacement, suture fixation of the fractured tuberosity to the humeral implant and circumferentially around the proximal part of the humerus is recommended;
- Region-2: fractures are treated with a standard-length implant, cerclage fixation, and autologous bone-grafting.
- Region-3 and 4 fractures are best treated with longer stemmed implants with cerclage fixation and, in some cases, with supplementary allograft cortical struts.

Results

Relatively limited information has been published on the outcome of treatment of periprosthetic humerus fractures after shoulder arthroplasty. Results have been categorized in terms of fracture union, pain relief, and ROM (Table 1). Reported complication rates have been relatively high varying from 0 to 100 %. Complications included: hardware failure, delayed union, non-union. Other complications included neurapraxias (axillary nerve, radial nerve), frozen shoulder, and infection. Unsatisfactory results were primarily due to loss of motion.

Summary

The full spectrum of periprosthetic fractures around a shoulder arthroplasty has been classified. Implications of treatment and results naturally follow from the fracture type and the stem status.

Peri-implant Fracture with a Total Elbow Arthroplasty

Incidence

Periprosthetic fractures around a total elbow arthroplasty is not common but are being observed with increasing frequency and carry with them some very specific treatment considerations. Based on the Mayo Clinic experience with more than 1,000 linked Coonrad-Morrey implant

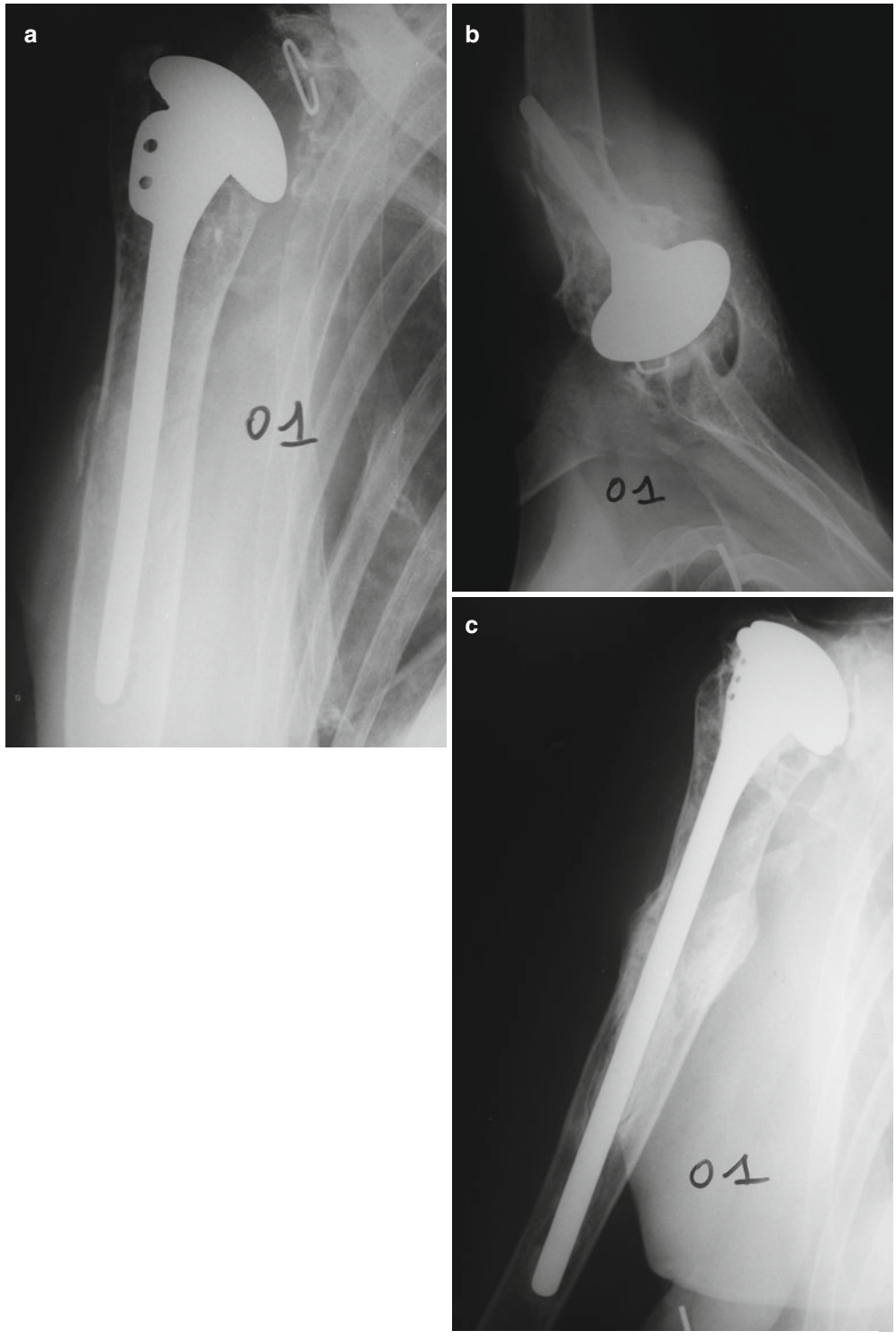

Fig. 3 Type A periprosthetic humeral fracture (**a**, **b**) treated by revision to a long-stem prosthesis (**c**)

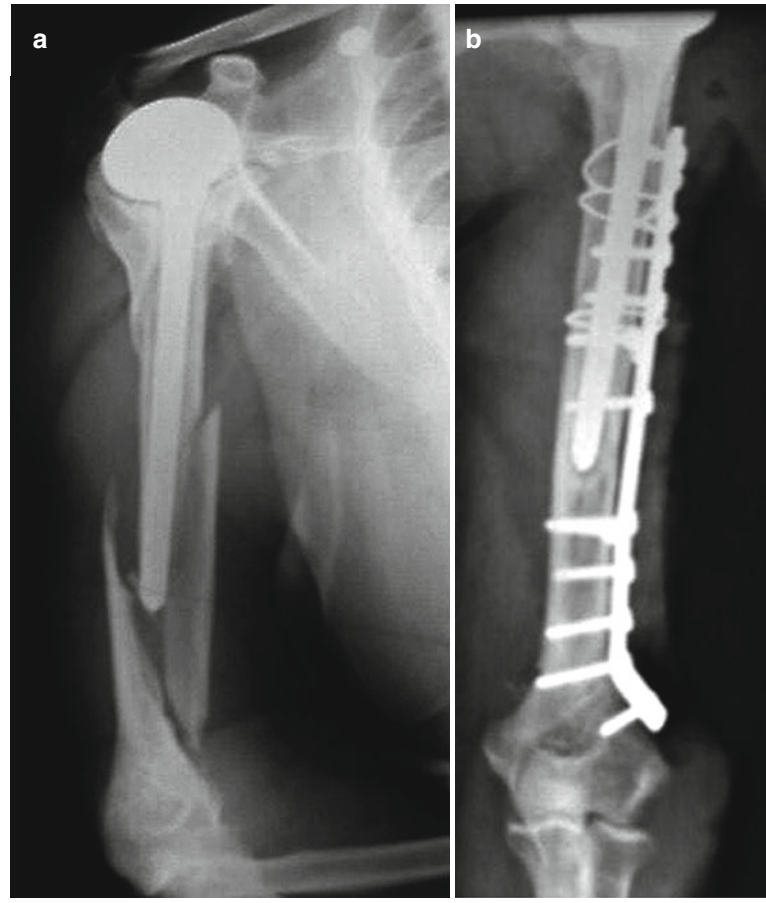

Fig. 4 Type B periprosthetic humeral fracture (**a**) treated with ORIF (**b**)

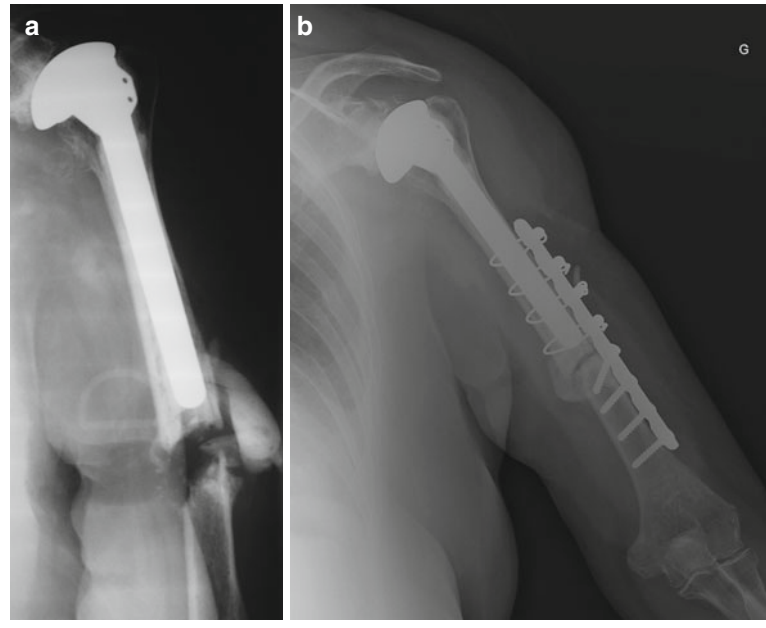

Fig. 5 Type C periprosthetic humeral fracture (**a**) treated with ORIF (**b**)

Table 1 Results of treatment of fracture around shoulder arthroplasties

Authors	N	Treatment	Age (year)	F/u (month)	Results
Boyd et al. [4]	7	–	–	–	All experienced complications 5 required surgery to achieve union 5 of 7 had reduced ROM
Wright and Cofield [30]	9	Nonsurgical (5) ORIF (2) Revision arthroplasty (2)	70 (45–85)	47 (4–196)	8 unions 3 satisf/6 unsatisf
Campbell et al. [6]		Nonsurgical (5) Standard arthroplasty (8) Long-stem arthroplasty (8)			
Worland et al. [29]	6	Nonsurgical (1) ORIF (1) Revision arthroplasty (4)	72 (67–94)	43 (13–85)	100 % union All satisfactory
Kumar et al. [15]	16	Nonsurgical (6) ORIF (10)	63 (37–76)	67 (4–191)	Union: 180 days nonsurgical to 278 days with ORIF 3 exc/4 satisf/9 unsatisf
Groh et al. [10]	15	Nonsurgical (5) ORIF + long-stem prosthesis (10)	58 (40–70)		100 % union rate (11 weeks)
Athwal et al. [2]	45	28 during primary TSA 3 during HHR 14 during revision arthroplasty			Complication rate: 36 %
Wutzler et al. [31]	6	ORIF (6)	75 (51–83)	15 (6–39)	100 % union rate
Singh et al. [25]	178	–	–	–	Female sex, underlying diagnosis risk factors of fracture
Sewell et al. [24]	22	Rev prosthesis (22)	75 (61–90)	42 (12–91)	12 very satisf/3 satisf/3 dissatisf
Andersen et al. [1]	36	ORIF (17) Revision arthroplasty (19)			Union rate: 97 % Complication rate: 39 %
Minéo et al. [20]	7	ORIF (7)	72 (68–75)		Union rate: 100 % Mean-time: 5 months

procedures a fracture was documented before, during, or subsequent to surgery in approximately 13 %. The complication was recorded in 9 % of primary surgery and in 23 % of revision procedures. The anatomical site of the lesion involves in an equivalent way the humerus and the ulna.

Treatment Strategy

Treatment strategy includes: identification of the cause of failure, exclusion the possibility of sepsis, evaluation of the local soft-tissue status, status of the prosthesis, selection of a prosthesis adapted to the revision procedure if needed and Planning of appropriate surgical technique.

Classification

Periprosthetic fractures in the elbow are classified according to the factors that determine their prognosis and treatment: the location of the fracture in relation to the stem, the security of the

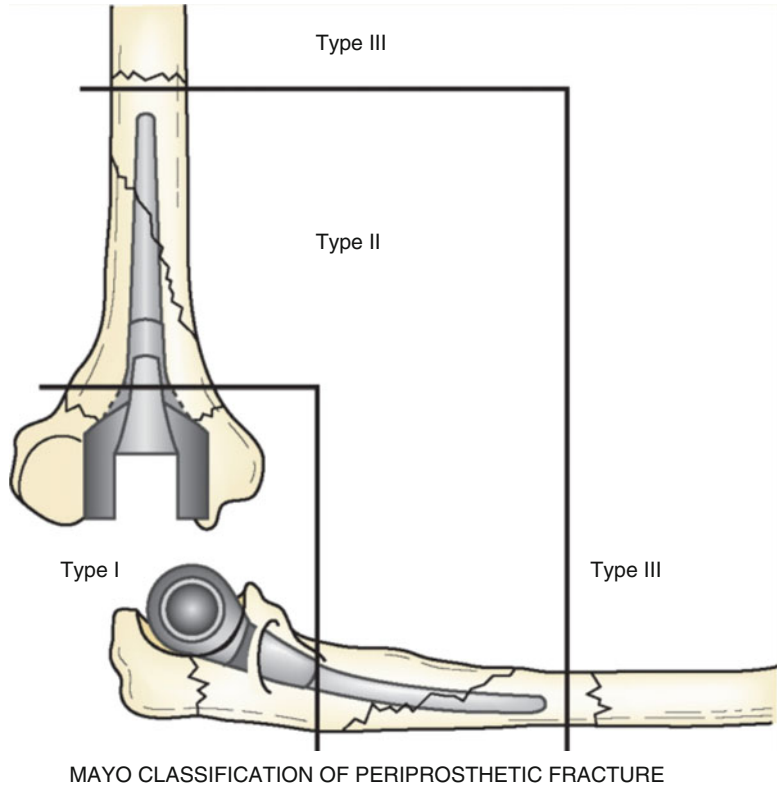

Fig. 6 Mayo classification of peri-prosthetic fractures around total elbow arthroplasties

fixation, and the quality of the bone. Dr Morrey has developed a classification system according to three anatomical locations of either the humerus or ulna [23]: metaphyseal (type I), stemmed shaft (type II) and beyond the stem (type III) (Fig. 6). The fracture is further characterized as associated with a well-fixed or a loose stem. Finally the bone stock is assessed as preserved or compromised.

Surgical Technique

The technical features of all revision options must address the management of the triceps, identity and protection of the nerves and protection of the osseous integrity. In all cases the ipsilateral iliac crest must be prepared. The previous posterior incision is used if possible. The ulnar nerve is always identified. The radial nerve is identified by palpation or isolated if an extensive approach of the humeral diaphysis is planned. The triceps is detached from the olecranon from medial to lateral but can be split. Per-operative specimens are always sent for cultures.

The fracture site is then identified. If the implant is well-fixed fixation of the fracture is performed. However, if the implant is loose it is removed and the medulla is cleaned of membranes, cement, and debris. The surgical reconstruction technique in each case is based on the severity of bone loss. Bone loss is considered to be moderate when techniques to augment the bone stock is not needed. Bone loss is considered to be severe when the cortical bone around the prosthetic stem is too thin, brittle, or even absent, such that bone stock augmentation by means of iliac bone graft, strut graft or an allograft-prosthetic composite is necessary.

Humeral Fracture

Type I – Humerus

Fractures of the condyles often occur intra-operatively but can also occur due to stress or fatigue failure post-operatively. There are minimal implications regarding treatment or prognosis with the linked Coonrad-Morrey device and nothing must be done. However, an intact condyle

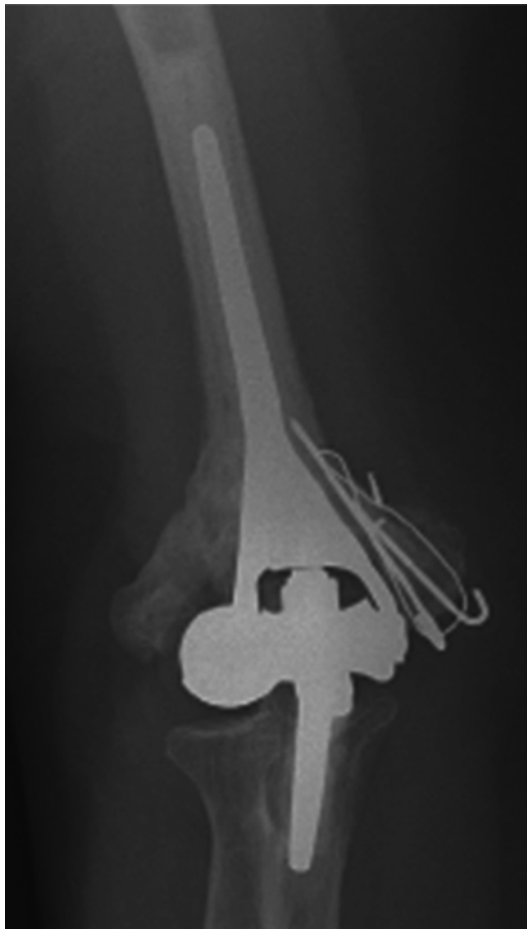

Fig. 7 Type I humerus fracture around a Latitude total elbow arthroplasty treated with ORIF

is essential for the stability of the linked GSBIII prosthesis or an unlinked arthroplasty. Hence, repair or reconstruction of the condyles is necessary (Fig. 7).

Type II – Humerus

Humeral shaft fractures around the stem or at its tip typically occur due to trauma or pathological fracture due to loosening or osteolysis around the component. Depending on the quality of the bone and the aetiology, the treatment varies but usually requires open reduction and internal fixation with cerclage wires, with or without additional onlay allograft struts or cerclage or plates [16, 23]. Fractures around a well-fixed stem are usually at the tip of the prosthesis. There are treated by open reduction and internal fixation. Fractures around a loose stem usually occur in the presence of osteolysis. Revision is almost always required with or without bone grafting depending of the remaining bone stock. If there is moderate bone loss around the humeral stem it is recommended to use strut graft to re-inforce the fixation [23]. Ideally the curvature of the strut is retained since this provides some angular stability to the construct when compressed with cerclage wires. The goal is to by-pass the fracture by a sufficient distance to provide stability. At least two circumferential wires are placed proximal and two distal to the fracture. If the stem is loose it has to be changed to a longer stem to by-pass the location of the fracture (Fig. 8). However, when the fracture is associated with a loose implant and severe bone loss, such that no cortical strut allograft augmentation could restore the diaphysis of the humerus and securely contain a new humeral component, massive allograft must be used [17]. The allograft is fashioned in such a way as to serve as a strut graft proximally at the humerus, while affording circumferential coverage of the implant at the articulation. Fixation is performed with cerclage wires (Fig. 9). Kawano and co-authors [13] have proposed an original method to treat this type of fracture using a locking nail threaded around the stem of the prosthesis.

Type III – Humerus

Fractures beyond the tip of the stem are treated as routine humeral shaft fractures with immobilization and functional bracing if non-displaced or with ORIF if displaced (Fig. 10). If the stem is not well fixed then the implant is revised. A longer-stemmed device is used as an intramedullary alignment and assists in the fixation. Struts can be employed to bridge the fracture. However with extensive osteolysis a massive allograft must be used [23]. However, when there is at the same time osteolysis in zone II and III, a massive allograft is preferred.

Ulnar Fracture

Type I – Ulnar

Peri-articular fractures of the ulna usually involve the olecranon because the coronoid is rarely fractured. The olecranon is particularly

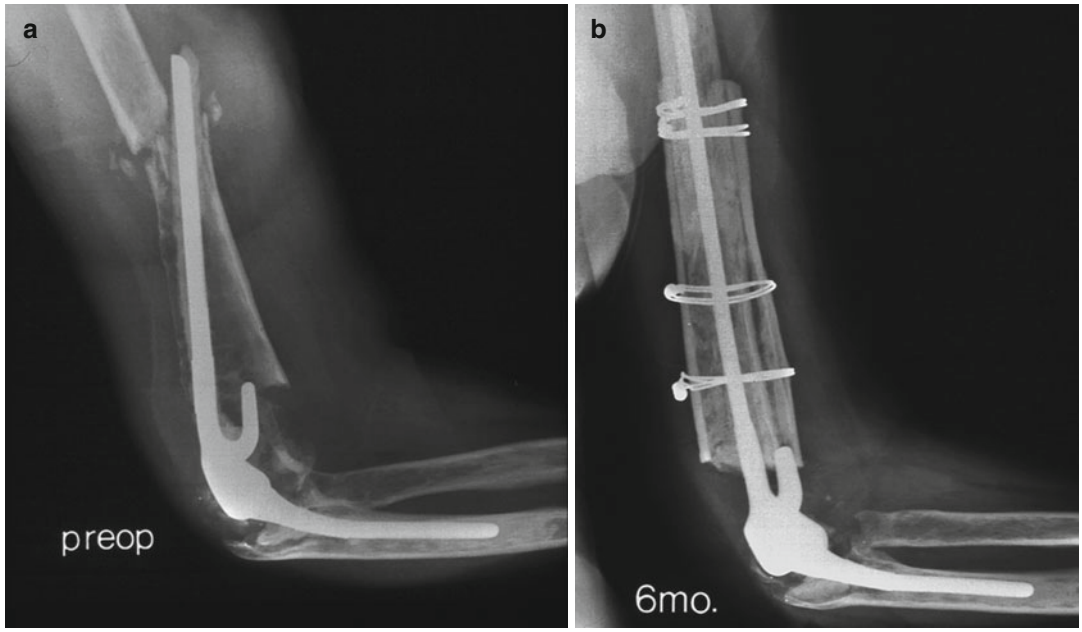

Fig. 8 Type II humerus fracture with preservation of bone stock (**a**) treated with revision to a long-stem implant and strut graft around the diaphysis (**b**)

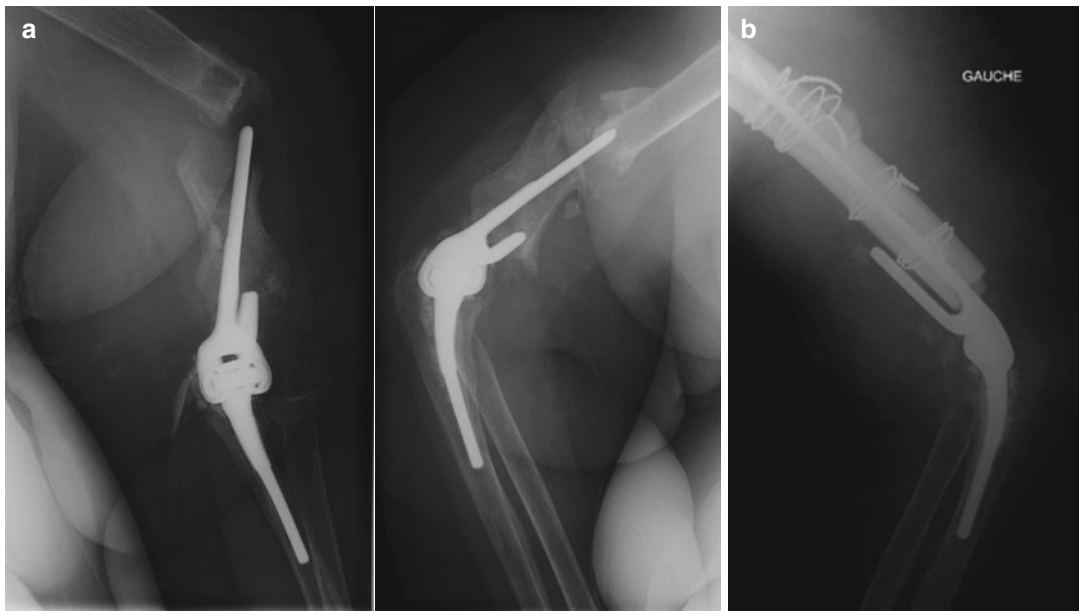

Fig. 9 Type II humerus with loss of bone stock (**a**) treated with an allogaft-prosthesis-composite (**b**)

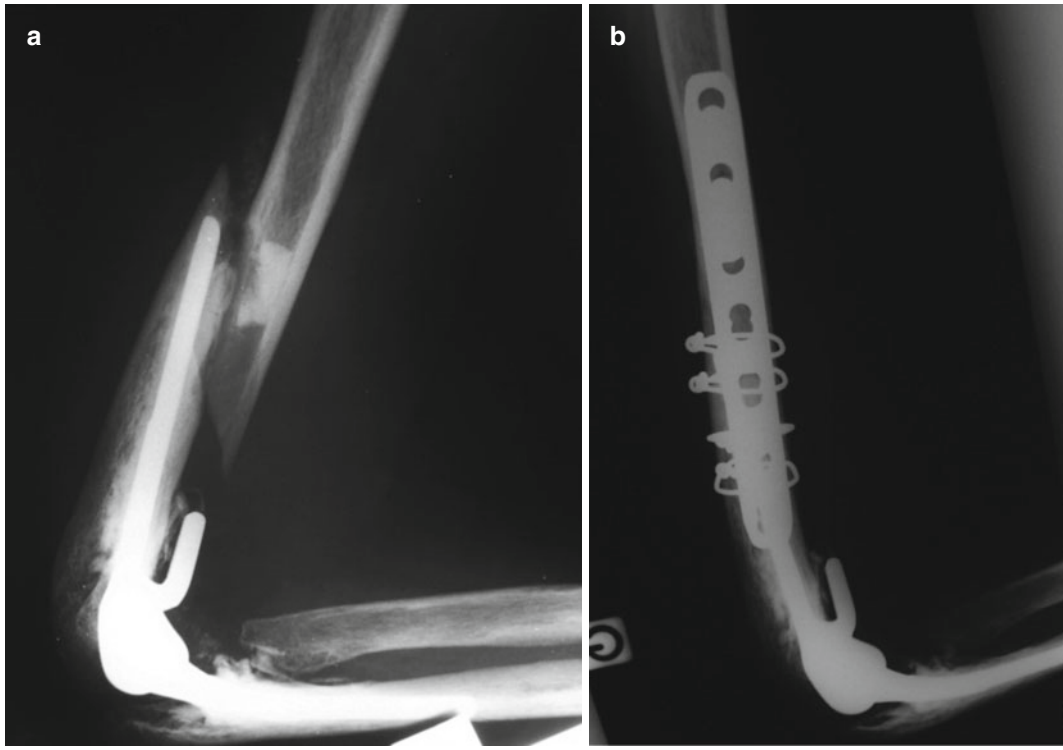

Fig. 10 Type III humerus fracture with a well-fixed implant (**a**) treated with ORIF (**b**)

prone to fracture in patients with rheumatoid arthritis, due to erosive thinning of the semilunar notch. Fracture can occur post-operatively due to forceful triceps contraction or as stress fracture. Treatment is usually determined according to whether or not the olecranon fragment is displaced. If not displaced, a period of immobilization is recommended. If there is significant displacement, the triceps will be weakened and open reduction is preferred. If the bone is thin, as is usually the case, it is simply reduced and held with heavy (N°. 5) non-absorbable suture through drill holes in the ulna. If the bone fragment is substantial, internal fixation is performed either with tension-band wiring or with a plate [18]. If the fracture displaces and involves the canal it can compromise ulnar stem fixation. Osteolysis may dictate reconstruction of the proximal ulna with an allograft ulna or fibular strut graft secured with circumferential wire.

Type II – Ulnar

Fractures around a well-fixed stem usually occur right at the tip of the stem. If there are displaced, they are treated by open reduction and internal fixation; if they are undisplaced, oblique and stable, they are managed by a period of immobilization. Transverse fractures tend not to heal. Fractures around a loose stem usually occur through a portion of the ulna that is weakened due to erosion from loosening or osteolysis. Some of these may present with minimally-displaced fractures, but revision is required for two reasons. First, the fracture is not likely to unite. Secondly, the loose stem will remain symptomatic and cause further endosteal erosion and the fracture is likely to displace. The primary objective is to by-pass the fracture with a longer stem and thereby stabilize it. Bicknell and co-authors [3] have proposed the use of iliac crest bone around the proximal ulnar component to replace a metaphyseal deficit (Fig. 11). Allograft strut reconstruction is used

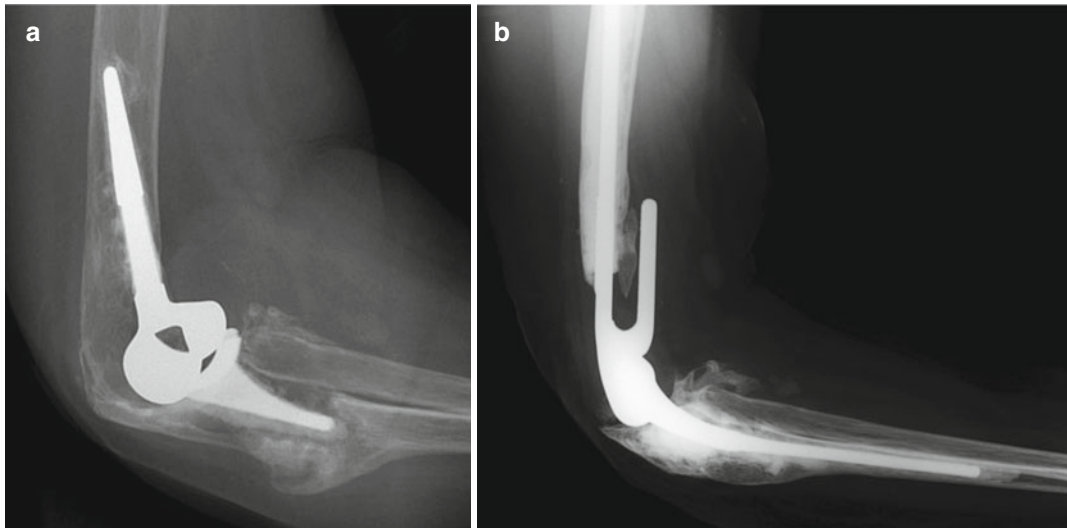

Fig. 11 Type II ulnar fracture (**a**) treated with revision to a long-stem implant with cortical bone graft from the iliac crest (**b**)

to re-inforce osseous deficiency with cortical defects around the prosthesis when it is not amenable to reconstruction with an iliac bone graft [12]. Cerclage wires are preferred to plate and screws to secure the graft around the prosthesis. Another method is the use of a fibular strut graft around the ulnar component. The goal is to bypass the fracture by a sufficient distance to provide stability. At least two circumferential wires are placed proximal and two distal to the fracture. One unique feature of ulna strut grafting is that the strut can be extended proximally to reconstruct an absent olecranon, thus providing a lever arm against which the triceps may function more effectively.

In massive, circumferential bone loss of the ulna, a massive allograft is needed. Morrey has described three type of allograft [21]. In Type I, the implant is inserted into a circumferential allograft, which is in turn inserted into an expanded lytic bone (Fig. 12). In Type II, the circumferential graft is modified to create a strut distally. The implant passes through the circumferential graft, which addresses the deficiency requirement for implant fixation. The strut part of the composite is fixed to the host bone by circumferential wire. In Type III, the implant is cemented in the proximal portion of an extended allograft. The allograft is secured "side by side" to the host bone with circumferential wire. A right fibula opposed to a left ulna works well as the flat side of the fibula opposes very well to the flat side of the ulna.

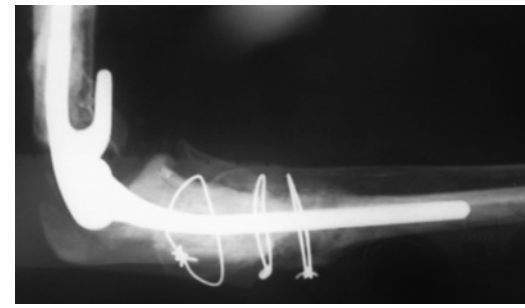

Fig. 12 Implant is inserted into a circumferential allograft, which is in turn inserted into an expanded lytic bone

Type III – Ulnar

Fractures distal to the ulnar stem are not common. They have been related to a specific trauma, or to a loose implant. The significance and management differs considerably depending upon whether or not the implant stem is stable or loose. If non-displaced it can be treated conservatively. If displaced with a well-fixed implant internal stabilization is needed usually with a

Table 2 Results of treatment of fracture around total elbow arthroplasty

Authors	N	Treatment	F/u	Results
Sanchez-Sotelo et al. [23]	11	Humeral fracture Strut graft	3 years	MEPS = 79 pts Union: 10/11 Compl: fracture (2), ulnar nerve (1), triceps (1), hum fract (1)
Mansat et al. [17]	13	Humeral and ulnar fracture Allograft-prosthesis-composite	42 months	MEPS = 67 pts Compl: infection (4), hum fract (1), allograft nonunion (1), ulnar nerve (2)
Kamineni and Morrey [12]	21	Ulna fracture Allograft bone strut	4 years	MEPS = 79 pts Compl: 4 soft tissues, 4 osseous
Loebenberg et al. [16]	12	Impaction grafting	2 years	MEPS = 83 pts Compl: loosening (2), fracture component (1), infection (1)
Marra et al. [18]	25	Ulna fracture Tension band (16) Excision (4) Suture (2)	66 months	MEPS = 86 pts 50 % bone union 45 % stable fibrous nonunion
Foruria et al. [9]	30	Ulna fracture Long-stem ulnar compoment + strut graft ± impaction graft ± allograft	5 years	MEPS = 82 pts Fracture healing = 100 % Compl: 4 infections, 1 loose component, 1 nerve dysfunction
Morrey et al. [21]	25	Humeral and ulnar fracture Allograft-prosthesis-composite		MEPS = 84 pts 92 % of allograft incorporated Compl: infection (3), fracture (3), nonunion (1), malunion (1), skin necrosis (1), triceps insufficiency (2), ulnar nerve (1)

plate. However, if it is associated with a loose implant, revision of the component is needed with often bone reconstruction [9].

Results

Treating peri-prosthetic fractures around a total elbow arthroplasty can be challenging. Experience with elbow surgery is needed for the appropriate therapeutic indication and adapted treatment. Usually good results can be expected with conservative treatment or ORIF of this fracture. Strut grafts give satisfying results varying from 70 to 90 % of the cases with an incorporation of the bone in more than 90 % of the cases [9, 12, 23]. However, with APC, results are less predictable [17]. However, Morrey and co-authors [23] have shown recently that better results are to be expected with larger graft-host contact areas in the three types of APC's with a 91 % rate of union. Complications are not uncommon and included infection, ulnar and radial nerve involvement, haematoma and wound problems, triceps insufficiency, and lack of incorporation of the graft in some cases (Table 2).

Summary

The full spectrum of periprosthetic fractures at the elbow is well defined by the proposed classification system. Implications of treatment and results naturally follow from the fracture type. For Type II and III fractures, principles of management are similar to those for periprosthetic fractures of the hip and long bones. If there is moderate or severe bone loss strut grafts are preferred to massive

allografts if possible. For Type I fractures the management is dependent on the implant type in the humerus, and a satisfactory outcome simply requires healing of the olecranon fragment in a minimally-displaced position.

Humeral Fracture Between Total Shoulder and Total Elbow Arthroplasties

Non-operative treatment with functional bracing can be proposed for periprosthetic humeral fractures occurring between ipsilateral shoulder and elbow arthroplasties. However, these fractures may not heal with non-operative treatment. Most often surgical intervention should be considered with osteosynthesis and autograft to maximize the healing potential. Strut allograft can also be used to improve fixation. Osteosynthesis can be performed with a locking plate, but dual plating constructs have been proposed to increase stability [7, 11, 19, 22].

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Part VII

Hip

Patient Safety in Fast-Track Total Hip and Knee Replacement

Henrik Kehlet and Christoffer Calov Jørgensen

Abstract

The multi-modal fast-track programmes have decreased hospital stay to 2–4 days after hip and knee replacement without increasing re-admissions. However, significant challenges exist to improve post-discharge safety regarding risk of general medical complications, cognitive dysfunction, rehabilitation, persistent pain, falls, dislocation, knee stiffness and infections. An increased understanding of the pathogenic mechanisms leading to individual post-discharge morbidities is required to improve outcomes.

Post-discharge Morbidity Challenges After Fast-Track Surgery in Total Hip and Knee Replacement

Fast-track surgery or enhanced post-operative recovery programmes are based upon a combination of single modality evidence-based revision of peri-operative care principles together with adjustment of logistical issues, in order to obtain early achievement of conventional discharge criteria and thereby reduce post-operative length of stay (LOS) [18, 31, 32]. The concept is now well-documented to reduce LOS to about 2–4 days with discharge to home after hip (THA) and knee (TKA) replacement and with reduced morbidity and no increase in re-admissions [15, 18, 28, 29, 45, 54, 56]. Although these results are positive compared to previous data, further optimisation of recovery may be achieved based on analyses of "Why in hospital" to delineate patient problems that may hinder early recovery [17]. However, despite that the principles of fast-track THA and TKA are well-established, several challenges remain to improve post-discharge patient problems of which not all are specifically related to the fast-track approach, but are common sequelae to these relatively major operations (Table 1). Since total joint arthroplasties are common operations, they facilitate high volume scientific studies and the outcome results may be of

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Table 1 Post-discharge safety issues after total hip and knee replacement

"Medical" morbidity	"Surgical" morbidity
Cardiopulmonary complications	Fractures
Thromboembolic complications	Dislocation
Cognitive dysfunction	Knee stiffness
Urinary complications	Infections
Rehabilitation/impaired muscle function	Bleeding
Falls	Re-admissions
Persistent pain	
Re-admissions	

general interest, as they are potentially transferable to other major surgical procedures with the same discharge problems.

This article will shortly summarise the post-discharge morbidity challenges after fast-track THA and TKA. The topic has been reviewed recently [18, 19, 28, 29] and mostly 2012 and 2013 studies are specifically referred to.

Peri-operative Pain

Modern peri-operative pain management is procedure-specific and aims at multimodal non-opioid analgesia where paracetamol and NSAID's/Cox2 inhibitors [13, 40] and high-volume local anaesthetic wound infiltration in TKA [8, 10, 30] are well-established. Additional use of gabapentinoids [59], ketamine [5] and a single pre-operative high-dose glucocorticoid [44] requires further dose-finding, efficacy and side-effect studies. The most important analgesic problem is focussed on the post-discharge phase, where very few descriptive or interventional studies have been published, especially regarding choice of combination of analgesics and duration. This is of major importance especially in TKA where a significant proportion of patients continue to have moderate to severe pain that may even persist in about 15–20 % of patients [38]. Finally, more efforts should be made pre-operatively to identify post-operative high-pain responders [43] to allow a differentiated analgesic approach and improvement of a multimodal pain programme [46].

Muscle Function and Rehabilitation

It is well-established that there is a pronounced loss of quadriceps muscle function and other lower extremity muscles amounting to about 70 % 2–3 days after TKA and about 30 % after THA. This may contribute to early general "weakness" potentially prolonging hospital stay [18], but may also increase the risk of post-discharge falls [24] and the need for rehabilitation [2]. Therefore, a major challenge for future studies is to define the mechanisms for the pronounced loss of lower extremity muscle function after THA and TKA [49]. Until these data are available and hopefully will reduce the need for rehabilitation efforts, future studies are required to define the exact time for initiation, duration and intensity of rehabilitation efforts, and detailed description of the rehabilitation techniques. Unfortunately, previous data from randomised trials do not allow firm conclusions on these issues [6, 11, 16, 47]. Since rehabilitation efforts after THA and TKA have major economic implications, there is an urgent need for scientific data to allow final conclusions.

Orthostatic Intolerance

It is well-established that orthostatic intolerance occurs after THA (and other major procedures) [4, 20], although there is no data from TKA. Previous studies have looked at early (24 h post-op) orthostatic intolerance, which is a maladaptive cardiovascular and autonomic nervous system response [4]. However, studies are required on the time course of post-operative orthostatic intolerance and especially whether this is important in the post-discharge period and may add to risk of falls, dislocation, etc.

Post-operative Delirium and Cognitive Dysfunction

It is well-established that THA and TKA in elderly patients increase the risk of post-operative delirium and longer lasting cognitive

dysfunction (POCD) [50]. The mechanisms may include pain, opioid use, sleep disturbances and the inflammatory response [37]. Preliminary data indicate that a multimodal opioid-sparing fast-track approach may reduce both delirium and POCD [36]. However, since especially late cognitive dysfunction has not been eliminated, further studies on identification of certain high-risk patients, post-operative sleep disturbances [34], better sleep drugs, reduction of post-discharge opioid use, and reduction of the inflammatory response should be performed. Recent improved monitoring techniques are available to assess post-discharge activity, sleep, cognition, pain etc. [35] calling for use in interventional studies.

Thrombo-embolic Prophylaxis

Current guidelines support the use of long-term thromboembolic prophylaxis after THA and TKA [27] although debatable in some countries [9, 42, 52, 57]. Since most data have come from studies with long LOS, it has been suggested that the fast-track approach with very early post-operative mobilisation may reduce thromboembolic complications and thereby the need for prophylaxis [33]. Preliminary data from several institutions, including a large prospective detailed cohort study [23], suggest that the usual recommendation for prolonged systemic prophylaxis with anticoagulants [7] may not be required.

Other Safety Issues

The concept of fast-track surgery was developed to provide the "pain- and risk-free" operation. In this context, early [45] and probably intermediate [51] mortality may be reduced after fast-track THA and TKA. However, several other safety issues need to be studied after an otherwise improved fast-track THA and TKA. Such factors include choice of anaesthesia where the previously documented use of regional anaesthesia may not be valid in fast-track THA and TKA [14, 39, 48]. Other factors include peri-operative blood management [12, 55] with a focus on treating pre-operative anaemia prior to surgery [21, 41], the choice of surgical approach and a detailed analysis of types of re-admissions between "medical" and "surgical" complications [26, 31]. Also, there is a need for future detailed studies on the specific role of conventional risk factors like old age and pre-operative pharmacological treatment of cardiopulmonary conditions [26], psychiatric diseases, diabetes, smoking and alcohol misuse [25], urinary and cerebral morbidity, and treatment regimens of post-operative urinary bladder dysfunction [3]. So far, studies from an optimised fast-track regime suggest that several of these conventional risk factors may not be as important as demonstrated from previous studies with "traditional" care, for instance age, pre-operative use of mobilisation aids, cardiopulmonary morbidity, smoking and alcohol misuse [25, 26]. Based on these and future studies, new peri-operative risk assessment scores in THA and TKA needs to be evaluated including the role of psychological factors such as pre-operative pain catastrophising and anxiety [43] and patient expectations [53] to allow a better understanding on post-discharge safety issues and patient-reported outcomes [22]. Finally, logistical issues such as the day of the week of surgery for a successful fast-track operation need to be considered [1, 18] as well as an integrated multidisciplinary approach to peri-operative care [18, 29, 58].

Conclusions

Fast-track THA and TKA has improved early and post-discharge morbidity regarding most post-operative organ dysfunctions. However, there is an urgent need for more detailed studies on the pathogenic mechanisms and interventions of early post-discharge morbidity problems in order to provide the "pain- and risk free" TKA and THA.

Conflict of Interest No conflict of interest.

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Part VIII

Knee

Knee Dislocation

Jacques Menetrey

Abstract

Knee dislocation is a devastating injury that necessitates a prompt diagnosis. Considering the final position of the tibia with respect to the femur, the dislocation can be classified as anterior, posterior, medial, lateral or rotatory. Reduction must be rapidly performed if necessary. Vascular and neurological status must also be repetitively evaluated. Emergency repair of any vascular injury has to be performed. In general, surgical repair of all ligamentous lesions is recommended in the "therapeutic window" between 10 and 20 days. Proper treatment leads to 80 % good to excellent results.

Introduction

Definition

Knee dislocation is uncommon and defined as the complete loss of contact between the articular surfaces of the tibia and the femur. In fact, knee dislocation is a misnomer, because a true dislocation is rarely encountered. Most of the time, the knee is reduced when the patient presents for medical care and the problem is a multiligament knee injury, defined most commonly as rupture of at least two to four major knee ligaments: anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), posterolateral corner (PLC), lateral collateral ligament (LCL), posteromedial corner (PMC), and medial collateral ligament (MCL). These lesions result in multi-directional knee laxities associated with vascular and neurological injury in about one fifth of cases.

Epidemiology

Traumatic knee dislocation is uncommon and represents less than 0.5 % of all joint dislocations [9, 39]. Schenk reported an incidence of 1.2 % in a series of general orthopaedic trauma [29], while others reported that knee dislocations account for 0.02–0.2 % of all orthopaedic injuries [8–10, 13, 26, 38]. Knee dislocation occurs in younger patients with a male-to-female ratio of 4:1 [9]. Half of them are secondary to motor vehicle

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accidents (high-velocity dislocation), approximately 30 % are sports injuries (low-velocity) and 10 % are from simple fall (ultra-low-velocity dislocations) [31]. Bilateral dislocations are rare and occur in 5 % of patients [9]. Several studies have reported ultra-low energy dislocations in morbid obese patients [24, 28, 30]. Five to seventeen percent of knee dislocations are open [12]. In 14–44 % of patients, knee dislocation is one component of multiple trauma [9].

Classifications

Considering the final position of the tibia with respect to the femur, the dislocation can be classified as anterior, posterior, medial, lateral or rotatory [9].

- Anterior knee dislocation accounts for 40 % of all dislocations, usually it occurs after a hyperextension of the knee in sports and in obese patients, and results in 39 % injury of the popliteal artery [5, 11].
- Posterior knee dislocation accounts for 33 % of all dislocations, is often caused by motor vehicle accident, and results in 44 % injury of the popliteal injury [5, 11].
- Medial knee dislocation accounts for 4 % of all dislocations, is caused by a forceful blow on the lateral side of the knee that leads to more ligamentous damage, and results in 25 % injury of the popliteal artery [5].
- Lateral knee dislocation accounts for 18 % of all dislocations, is caused by a forceful blow on the medial side of the knee, is sometimes irreducible by closed method, and results in 6 % injury of the popliteal artery and in neurologic injury [5].

Then, considering the anatomical injury pattern, as well as any associated neurovascular injury, Schenk has proposed the following classification system [29].

- KD1: intact PCL with variable injury to collateral ligaments;
- KD2: both cruciate ligaments disrupted with intact collateral ligaments (rare);
- KD3: both cruciate ligaments disrupted with medial or lateral ligament disrupted;
- KD4: both cruciate ligaments and both collateral ligaments disrupted;
- KD5: knee dislocation with peri-articular fracture.

This classification allows for establishing and organizing the clinical and surgical treatment of these injuries. Recently, another classification was described during the ESSKA's Symposium and redefined in the 10th Journées Lyonnaises de Chirurgie du Genou in Lyon to consider the pentads injuries in knee dislocation. In this system of classification, it is possible to identify the ligament injuries starting from the mechanism of injury and the relative positions of the tibia and femur [20, 21].

Finally, knee dislocation can be congenital, open or close, associated to fracture of the femur, the tibia, and/or the patella.

Clinical Evaluation

For acute knee dislocation, management and effective patient evaluation according to basic Advanced Trauma Life Support (ATLS) principles is the priority. Frequently, the knee is reduced on presentation and the diagnosis is often missed. According to the injury mechanism, one must have a high degree of suspicion about a knee dislocation, especially in the presence of an extensive swelling and bruising, and an uncontained haemarthrosis (Fig. 1). Neurovascular status has to be carefully and serially assessed. In case of a dislocated knee at presentation, close or, if necessary, open reduction must be performed under sedation as soon as possible. Then, a thorough clinical examination should be accomplished by an experienced surgeon. Indeed, ligament testing is difficult to perform in the acute phase due to pain, muscle spams and extreme laxity.

The incidence of associated vascular lesions in knee dislocation has been reported to be of 5–64 % [18, 19], but more recent studies have quoted a range of 7.5–14 % [1, 6, 10]. Pulses and sign of ischaemia must be carefully and repeatedly assessed (2–4 hourly over 24–48 h). In case of decreased pedal pulses, sign or symptoms of ischaemia, ankle-brachial blood pressure index

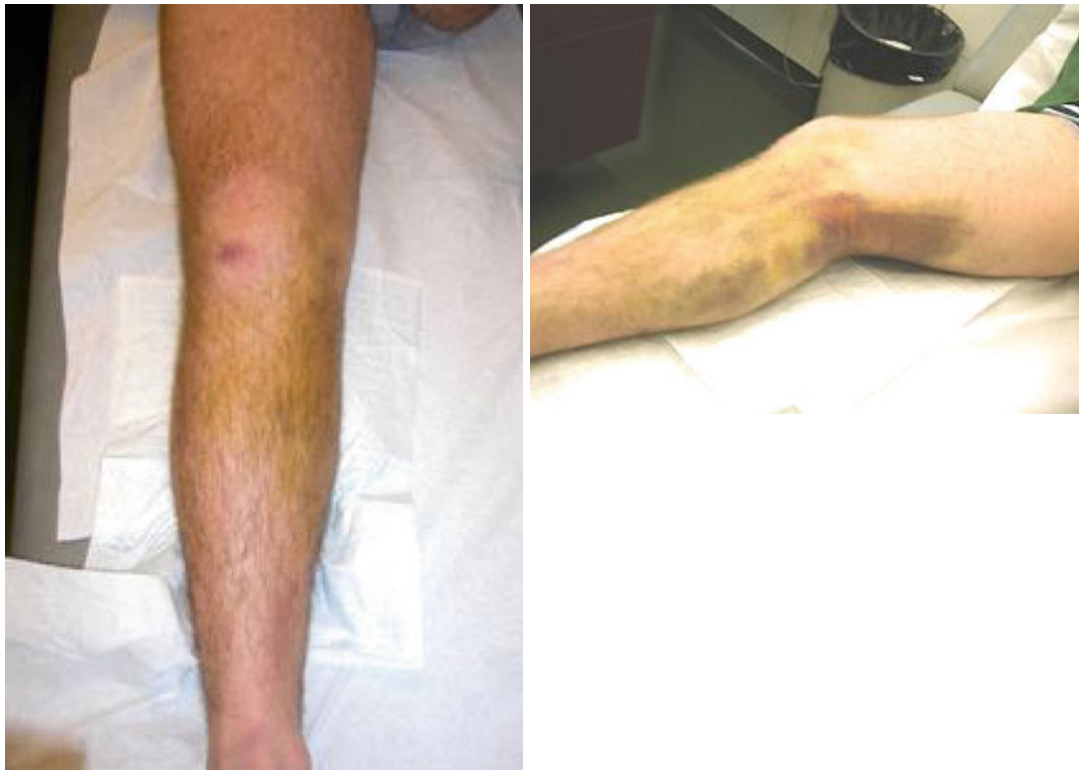


Fig. 1 Large swelling, bruising and uncontained haemarthrosis following a knee dislocation reduced at presentation

(ABI) <0.8, an immediate duplex ultrasound and/or an arteriography must be organized [36, 40]. Selective arteriography can be reserved if there is symmetric pedal pulses and no sign or symptoms of ischemia. However, careful assessment for signs of impaired circulation, asymmetrical or absent pulse should be performed regularly, repeatedly and documented. Indeed, distal pulse can be maintained for some time despite popliteal arterial injury by collateral circulation [23]. Intimal tear lesions are at least initially not flow limiting and are depicted by arteriography. In the past, this led to surgical exploration. However, recent studies have shown that the vast majority of intimal tears do not progress, and the current vascular surgical management with no flow limitation is simply a period of observation [34].

Peroneal nerve injury has been reported as having overall incidence between 14 and 45 % [6, 22, 27]. Nerve injuries are more frequently associated with posterior, postero-lateral, and medial dislocations. They are pathognomonic of severe lateral compartment injury and can go from neurapraxia to complete nerve disruption [7, 11, 32, 33]. From these neurological injuries, 30 % recover completely, 20 % lead to a residual deficit, and 50 % result in complete palsy and sensory deficit. Neurolysis or grafting have not been proven effective [11, 19, 33, 35].

Imaging

As all knee injuries, multi-ligament knee injuries should be investigated with the classical traumatic knee radiographs series including antero-posterior (AP), lateral and axial views. Radiographs allow for the verification of the congruency between femur and tibia as well the proper alignment of the patello-femoral joint (Fig. 2a and b). They also permit to demonstrate associated fractures or bony avulsions that will influence the strategy of treatment.

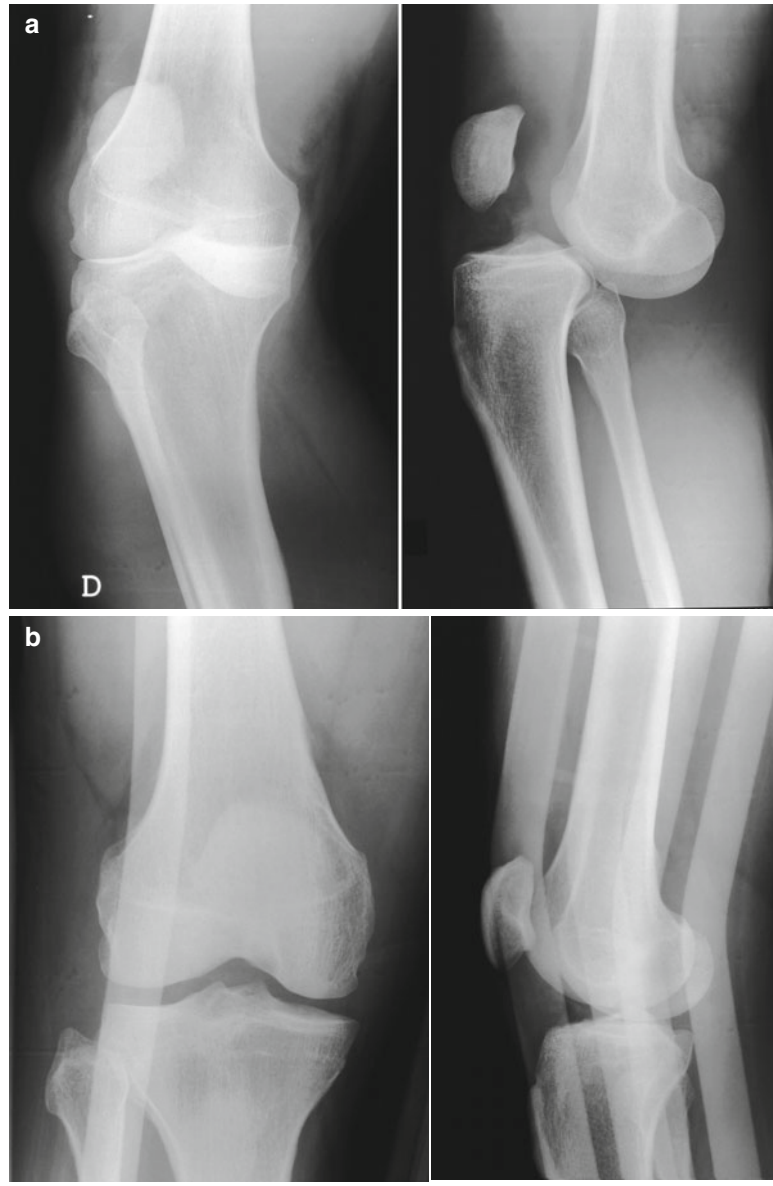


Fig. 2 (**a**, **b**) Antero-posterior and lateral radiographs allow for the verification of the congruency between femur and tibia

In the absence of vascular problems, MRI should be obtained in the first 3–5 days to assess extent of injury and allow for proper surgical planning. For example, if the PCL lesion appears to be a "peel off" lesion (proximal PCL disinsertion), a trans-osseous re-insertion can be performed and harvesting of a graft for the PCL is not required. MRI analysis should be performed methodically for injured structures: Anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), posteromedial corner (PMC), posterolateral corner (PLC), medial collateral ligament (MCL), lateral collateral ligament (LCL), medial meniscus (MM), lateral meniscus (LM), and associated cartilage lesions (Fig. 3a and b). Recently, Walker et al. have clearly stated that a close relationship between radiological findings and surgical considerations is crucial for optimizing the treatment of multi-ligament injury [39].

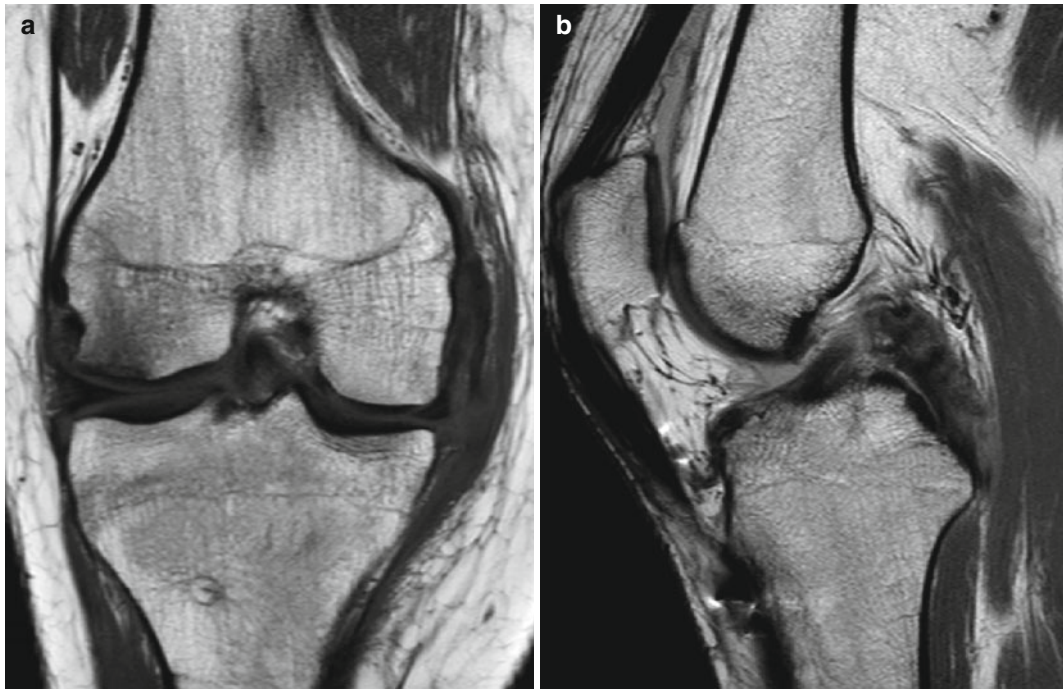


Fig. 3 MRI demonstrates the exact definition of the anatomical injury. (**a**) Mid-substance injury of the MCL with disinsertion of the medial meniscus. (**b**) Mid-substance injury of the PCL and ACL

Algorithm of Treatment

The algorithm we apply at the University Hospital of Geneva is as in Table 1. The only recent change is that we tend now to perform an immediate magnetic resonance (MR) angiography. In a small series of knee dislocations, findings were comparable to angiography [25]. This accelerates the diagnosis of asymptomatic vascular lesion.

Vascular injury must be depicted and treated within the first hours post-trauma (<6 h). If a knee dislocation should occur on a sports field, it is mandatory to rapidly transfer the injured athlete towards a medical institution, in which vascular imaging and surgery is available.

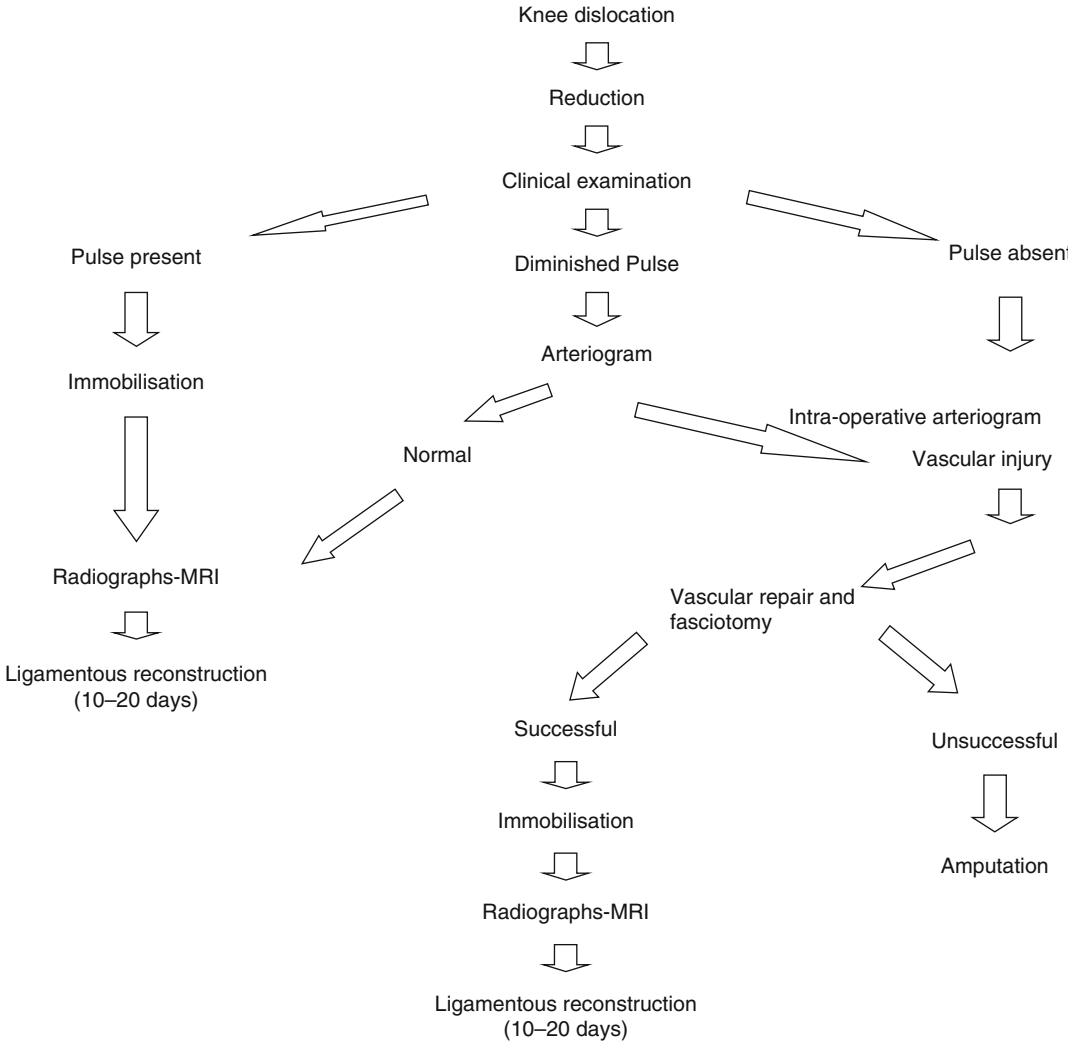
Following reduction and assessment of vascular status, early management consists of immobilization of the limb to provide analgesia, with stability and rest of the soft-tissue [9]. If the patients request vascular surgery, or in case of associated fracture and/or gross laxity, an external fixator can be applied concomitantly.

Treatment

Options of treatment are multiple and include cast immobilization, operative repair, early reconstruction of the PCL with late reconstruction of the ACL if needed, autograft versus allograft reconstruction of the ACL and PCL, and repair versus reconstruction of the LCL and PLC. There has been large debate regarding the most appropriate way to manage these difficult injuries and controversies exist [9, 14].

In young and active patients, the reconstruction of ACL and PCL, and repair/reconstruction of the PLC and/or PMC between 10 and 20 days post-trauma is recommended. In mid-age and low-demanding patients, the reconstruction of the PCL and repair/reconstruction of the PLC and/or PMC, with a delayed ACL reconstruction if needed, can be recommended. However, each case should obviously be discussed individually and a treatment "à la carte" proposed. In older patients with no demand and practicing no sport, the treatment may be conservative and functional.

Table 1 Algorithm of treatment applied at the University Hospital of Geneva



Open knee dislocations require an emergency reduction, a lavage-debridement, a "repair all that is possible" approach, and antibiotics. Secondarily, when soft-tissue lesions have healed, all clinically significant residual laxities can be corrected by ligamentous reconstructions.

In knee dislocation associated with fractures, we recommend first to restore the bone frame by fixing the fractures and to repair/reconstruct peripheral ligamentous injuries. The technique chosen for the fracture fixation should permit ligamentous reconstructions later. However, immediate mobilization should be possible in the post-operative period in order to prevent stiffness. Once the range of motion has been regained, and only in case of obvious residual laxity and instability, cruciates ligament reconstruction can be performed.

Conservative Treatment

In a selected category of patients, conservative and functional treatment has a place in the care of knee dislocation. Usually the treatment begins with immobilization in extension for 4–6 weeks. The treatment should be adapted to the injury pattern and be focussed on the PCL, posteromedial

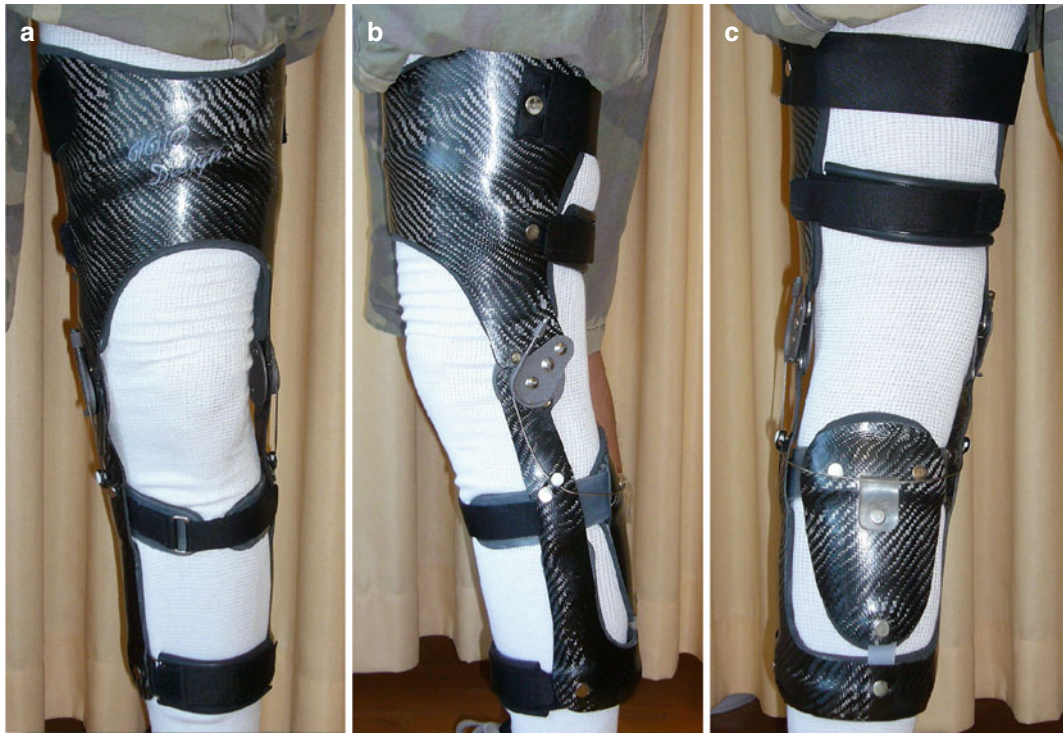


Fig. 4 Dynamic customized PCL-brace is used from the sixth week to 6 months post-operatively. (**a**) Front view; (**b**) Side view; (**c**) Back view

and/or posterolateral lesions. Patients are non-weight-bearing or just "toe touching" for a period of 6 weeks. The mobilization of the knee can start in the second week in the prone position with a flexion initially limited to 30°. The flexion angle will be progressively increased by about 30° every 2 weeks. From the sixth week, the patient will progress to full weight-bearing and will start his muscle reconditioning focusing first on the quadriceps muscle. At the same time, the patient is put in a PCL dynamic brace (Fig. 4) that will protect the PCL graft from untimely posterior drawer. The flexion angle will be progressively open to full range of motion. After 3–4 months, it will be critical to work on the dynamic stability of the injured limb.

Surgical Treatment

Surgical treatment represents the best option in young and active patients or in patients with high physical demands. This is a complex surgery that should be performed by an experienced team.

Timing of Surgery

Reconstructive surgery should be performed in one-stage in the so-call "therapeutic window" from the first to the third week after the trauma. The timing depends upon the soft tissue status. Bruising, swelling and skin condition should permit several approaches around the knee. The correlation between early surgery and stiffness is still a matter of debate. We know that the incidence of stiffness increases with the repair of the MCL and a prolonged limited motion in the post-operative period. We also know that results are better when the surgery is performed at the sub-acute phase (<3 weeks) compared to the chronic one [15]. However, if acute or sub-acute surgery has a higher incidence of stiffness, surgery at the chronic phase has higher incidence of residual laxity. This information should be part of the discussion with the patient when the strategy of treatment is discussed.

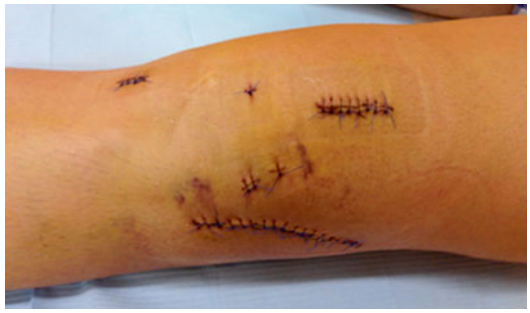


Fig. 5 Longitudinal incision for the harvesting of the quadriceps tendon, one incision for the PCL and ACL tibial tunnels, and one lateral approach for the lateral compartment

Techniques

Surgical technique can be arthroscopically-assisted or open, the surgeon may utilize autografts and/or allografts. Advantages of allografts in this surgery are a decreased tourniquet time, a strong graft, fewer skin incisions and less dissection, and no graft site morbidity. The aim is to minimize the iatrogenic insult of this extensive surgery. The surgeon should perform the techniques with which he has the most experienced, and a technique that is well adapted to the injury pattern and to the grafts available.

In our institution, we favour a quadriceps tendon autograft for the PCL, a BPTB allograft for the ACL, and a semi-tendinosus tendon autograft and/or allograft for the lateral compartment.

We do also prefer several limited incisions rather than a long centralized one (Fig. 5).

We usually "fix all that is torn" in one-stage, beginning with the PCL and ACL, and following with peripheral lesions. PCL and ACL reconstructions are carried out arthroscopically while peripheral lesions are treated through open approaches. The use of a fluoroscopic control to ensure a proper placement of the different tunnels is recommended especially in chronic lesions (Fig. 6). Lesions of menisci and/or cartilage are addressed at the same time, with the preservation of the meniscal tissue and the stimulation of the intrinsic repair capacity of the cartilage. In most of the cases, avulsion injuries of the medial compartment can be repaired using sutures, sutures anchors, screws and washers. For mid-substances injuries, an augmentation procedure can be required and we usually use a semi-tendinous or gracilis tendons allograft. Lesions of the lateral compartment need to be finely analyzed in order to determine the proper technique between re-insertion of a distal avulsion upon the fibular head, reconstruction of mid-substances injuries of the LCL, arcuate complex, popliteofibular ligament and popliteus tendon, as well as eventual repair-re-insertion of the proximal attachment upon the femur. Lesions at the musculoskeletal junction of the popliteus muscle can be repaired, but the functional recovery of such a repair is limited. Repair of the posterolateral corner and lateral collateral ligament has shown a significantly higher failure rate in comparison with reconstruction, and a lower rate of return to sports activities [15, 16].

Post-operative Rehabilitation

After the operation, the knee is immobilized in a brace locked in extension. The treatment should be adjusted to the injury pattern and aiming at the protection of the PCL graft. Patients are usually non-weight-bearing or just "toe-touching" for a period of 6 weeks. The mobilization of the knee can start on the second post-operative day in the prone position with initial flexion limited to 30°. The brace is then unlocked and the mobilization can be made with the support of the brace. The flexion angle will be progressively increase by about 30° each 2 weeks. From the sixth week, the patient will progress to full weight-bearing and will start his muscle reconditioning focusing on the quadriceps muscle recovery. At the same time, the patient is put in a mobile PCL dynamic brace (Fig. 3) that will protect the PCL graft from untimely posterior drawer. The flexion angle will be progressively open to full range of motion. From the third to fourth month, exercises aiming at the recovery of the static stability are begun. Then, from the fifth month, the rehabilitation focuses on the recovery of the dynamic stability of the injured limb. Return to activity is usually slow and gradual return to physical work and sporting activities at 9–12 months at earliest [9].

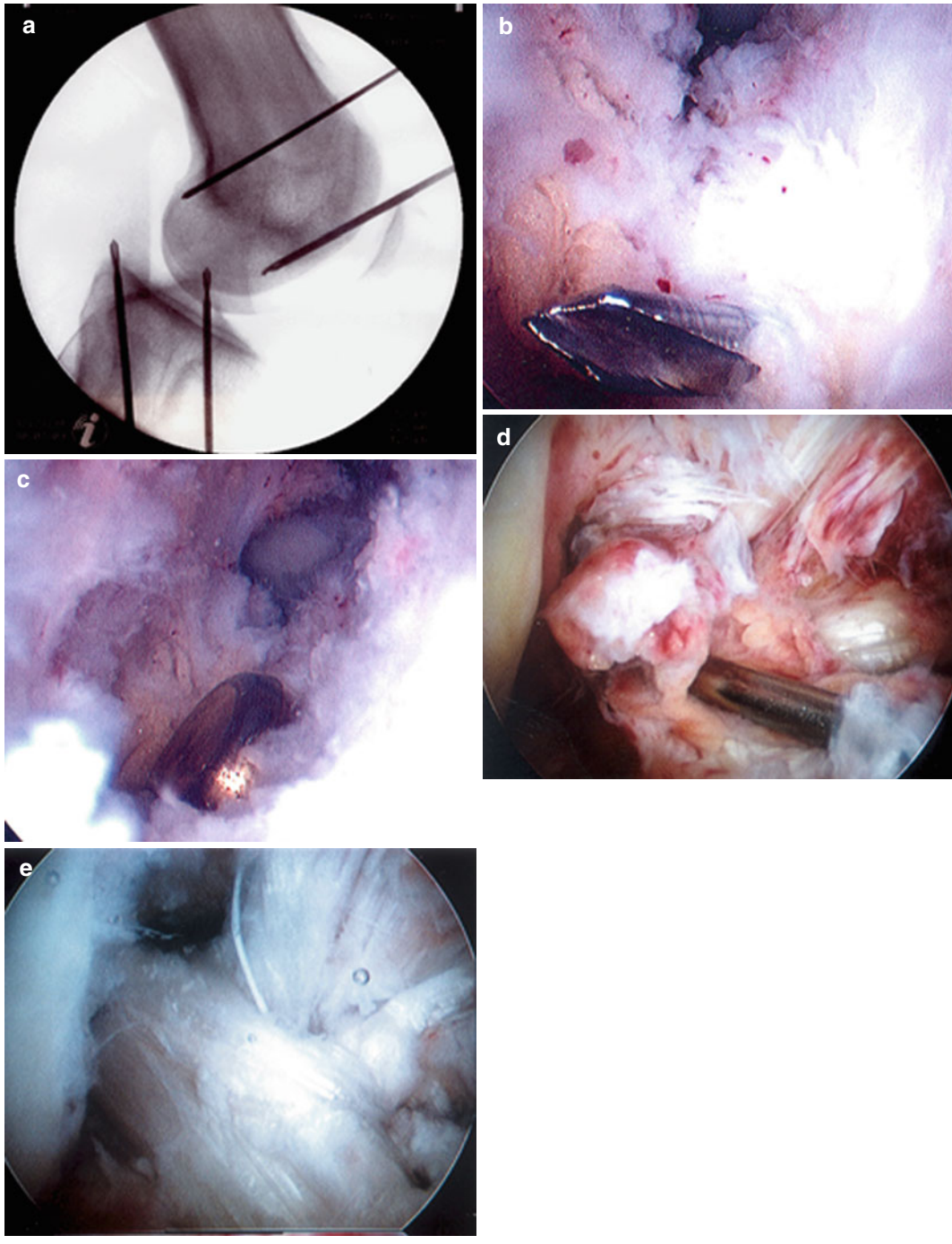


Fig. 6 (**a**) Fluoroscopic control of the proper placement of the ACL and PCL tibial and femoral tunnels. (**b**, **c**) Arthroscopic view of the PCL tibial tunnel position from the posteromedial portal. (**d**) ACL and PCL post-injury. (**e**) ACL and PCL graft after reconstructions

Sports and physical activities can be extended in the absence of knee effusion, an almost complete range of motion, good knee stability, and an excellent muscle strength and control.

Results

Most of the studies related to multi-ligament-injured knee are retrospective case series with a level of evidence of grade IV, but recently some studies of level II and meta-analysis have been published.

According to Dedmond et al. [2] meta-analysis (n = 205 patients) of operative and non-operative treatment of knee dislocation, the surgical treatment group resulted in consistently higher mean Lysholm scores (85 vs 67) than the non-operative one.

In 1999, Mariani et al. [17] made a comparison between reconstruction and direct repair of knee ligaments. They found that direct repair of knee ligaments had higher rate of posterior sag sign and lower rate of return to pre-injury activity level ($p < 0.05$). However, Frosch et al. [4], in a recent meta-analysis, have examined suture versus reconstruction of cruciate ligaments with respect to injury pattern. They found no significant difference between suture repair and reconstruction of the ACL and PCL. Both showed good clinical results and they concluded that suture repair of cruciate ligament can serve as an alternative option for multi-ligament knee injury [4].

Harner et al. [6] reported on 31 patients who underwent surgery following knee dislocation, including 19 patients treated <3 weeks after injury (acute) and 12 patients treated >3 weeks after injury (chronic). Mean follow-up was 44 months. Patients treated in the acute period had a higher Knee Outcome Score, Survey Sports Activity score (89 versus 69), less positive Lachman test at the post-operative physical examination, and a better final Lysholm score (91 versus 80). Final knee range of motion was similar regardless of time to treatment, although four acutely reconstructed patients required manipulation under anaesthesia for arthrofibrosis (21 %) [14]. In a recent study, Tzurbakis et al. [37] reported about 44 knee dislocations, including 35 patients operated in the acute (<3 weeks) and 9 patients in a chronic setting. Mean follow-up was 51 months. A statistically greater percentage of patients treated in the acute period rated their outcome as normal (A) or near-normal (B) on the IKDC knee subjective form (86 % versus 56 %) and symptom (85 % versus 56 %) subgroups. Overall IKDC normal or near-normal rating (77 % versus 55 %), mean Lysholm score (88 versus 82), and final ROM were not significantly different. Levy et al. [15] realized a systematic review in 2009 and demonstrated that an acute surgical treatment (<3 weeks) showed better functional and clinical results than a delayed treatment, with higher Lysholm and IKDC scores and better sports activity scores using the Knee Outcome Survey.

Recently, a large prospective series of knee dislocation with a minimum 2-year follow-up has demonstrated that patients could achieve a good Lysholm score (median 83) and show good functional level (83 % of hop test comparable to the other knee) and level of general activities [3]. They also found that high-energy knee dislocations have less favourable results than low-energy dislocations. In addition, those who injured all four ligaments (KD-IV) had worse outcomes in comparison to those who injured two or three ligaments (KD-II, KD-III) [3]. Finally, open dislocations have worse outcomes with a reported 43 % infection and 17 % amputation rate [9].

The most common problems of these knee dislocations are stiffness or failure of repaired and/or reconstructed ligaments. In the long-term, more than 50 % of patients may develop post-operative osteoarthritis [41].

Conclusions

Knee dislocation is a devastating injury that necessitates a prompt diagnosis. Associated vascular injury must be diagnosed and treated urgently. A precise anatomical definition of all lesions should be determined by thorough clinical examination and imaging. Then, the treatment has to be tailored according to the injury pattern and the patient profile. In young active patients, all ligaments and associated injuries should be fixed in a one-stage procedure when possible. Reconstruction of the multi-ligament-injured knee provides satisfactory subjective

functional assessment, range of motion and stability while the ability of patients to return to high demand sports and heavy manual labour is less predictable.

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Meniscal Repair

Romain Seil, Alexander Hoffmann, Torsten Gerich, and Dietrich Pape

Abstract

In the last 30 years, meniscal repair has shown to be effective over the medium and long term in 70–80 % of cases. Despite these excellent results, this procedure represents, on an annual basis, no more than 2 % of meniscal surgery as a whole, suggesting that meniscal repair enjoys considerable potential for the years to come. Specific lesion types are becoming better known while at the same time surgical techniques are getting simpler. The trend is to less invasive surgery, with improved safety and greater technical precision. This article presents an overview of existing techniques, new surgical trends and established data.

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Introduction

In the last 30 years, meniscal repair has shown to be effective over the medium and long term in 70–80 % of cases. Despite these excellent results, this procedure represents, on an annual basis, no more than 2 % of meniscal surgery as a whole [27], suggesting that meniscal repair enjoys considerable potential for the years to come. Specific lesion types are becoming better known while at the same time surgical techniques are getting simpler. The trend is to less invasive surgery, with improved safety and greater technical precision [104].

Indications and Surgical Prognostic Factors

Indications for meniscal repair may be distinguished in terms of associated lesions, and notably of knee ligament status and lesion morphology.

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A meniscus tear should be considered for repair if its size is at least 10 mm, if it can be dislocated over the equator of the femoral condyle and if degeneration of meniscus tissue is not too advanced. The ideal patient for a meniscal repair is under the age of 40, free of associated degenerative lesions, with a vertical lesion in the peripheral third of the meniscus (red-red zone) which is preferably associated to anterior cruciate ligament (ACL) lesion. Several factors can be identified in the better results found with meniscal repair associated to ACL reconstruction: apart from more favourable biological conditions, with increased vascularization after knee trauma and hematogenous effusion supplying growth factors needed for meniscal healing, there is also a selection bias: the lesions are generally traumatic, whereas lesions in stable knees concern menisci that are presumably symptomatic and affected in some way by tissue degeneration. Peripheral lesions have a greater healing potential [25, 98], confirming the initial anatomical work by Arnoczky and Warren [9] which showed meniscal vascularization to be confined to the periphery of the meniscus. The effect of age on meniscus repair is highly controversial. Meniscal tissue was shown to contain fewer fibrochondrocytes in patients over the age of 40, with consequently reduced healing capacity [74]. This theory was borne out by Eggli et al. [34], who found more recurrent tears in subjects over the age of 30. In contrast, Bach et al. [11] found re-tearing to occur mainly in younger patients, and Accadbled et al. [1] found the re-tear rate in children and adolescents to be comparable to that in adults. Other large series showed no age-related influences [15, 25, 26, 54, 78, 79, 98, 108]. The issue thus remains disputed, and current data suggest that age is not a contra-indication for meniscal repair: it merely reduces the probability of finding meniscal tissue of sufficient quality to enable repair.

The various clinical situations for which meniscal repair may be indicated are detailed below.

Meniscal Lesions in Unstable Knees

Large-scale data from international registries show that ACL injuries are associated with meniscus injuries in 9–44 % for the lateral (LM) and 19–40 % for the medial meniscus (MM) [31, 44, 64, 68]. In a series of 1,000 ACL reconstructions with varying accident-to-surgery delays, only 43 % of the ACL tears were isolated, whereas 29 % were associated with MM lesions, 18 % with LM lesions and 10 % with lesions of both menisci [18]. With respect to this high number of associated meniscus lesions and their good healing potential if combined with ACL reconstruction, meniscal repair is recommended whenever possible. Considering the knee trauma cascade [88], meniscus injuries in relation with knee ligament injuries can be present either at the initial traumatic event or appear secondarily due to chronic instability. In an acute setting, indications for meniscal repair are rare and should be considered in the presence of a dislocated bucket-handle or, more exceptionally, a complete radial tear [118]. In such cases, concomitant ACL reconstruction can only be recommended in the first hours after injury. Once swelling and synovitis have occurred, ACL surgery should be postponed to approximately 6 weeks after initial meniscus repair. In most other documented ACL injuries with meniscus lesions, an initial non-operative treatment is recommended to obtain favorable conditions of knee motion and swelling before performing meniscus repair in association with ACL reconstruction. In chronic instabilities, the indication for meniscal repair in association with ACL surgery is less dependent on individual timing. Meniscectomy should be avoided, especially on the lateral side, where it is known to worsen the clinical results of ACL reconstruction [33, 59, 61, 106], due to the onset of pain and swelling.

Posterior subluxation of the femur during the injury mechanism explains why most of the lesions occur in the area of the posterior horn. Whereas the frequency of LM injuries remains stable, MM injuries become more frequent over time in unstable knees [16, 37, 48, 52, 55, 77, 80, 89, 121]. This difference is due to biomechanical and kinematic factors. With increased anterior laxity, the less mobile MM has been shown to act as a secondary stabilizer of the knee [52, 55, 62, 84]. The LM, in contrast, is more mobile and has an inferior stabilizing effect [62, 63]. In terms of knee kinematics,

the posterior horn of the LM subluxates behind the tibial plateau in deep knee flexion, whereas its medial counterpart is compressed between the tibial plateau and the femoral condyle in this situation [70]. It is therefore recommended that medial meniscal lesions associated with ACL tears should be stabilized [91], and particularly any vertical lesion exceeding 10 mm in length, with associated ligament stabilization. Consequently, it would seem that certain LM lesions associated with ACL injuries may be left in situ [91], as they are capable of spontaneous cicatrization [50, 118].

In recent years, the typology of meniscus lesions associated with ACL tear has been refined [22, 117]. On the lateral side, Ahn et al. [3, 120] has reported first results of meniscal repair for radial split tears, whereas on the medial side, increased attention has been given to menisco-synovial tears of the posterior compartment, which is associated to approximately 20 % of ACL injuries [21, 66, 113].

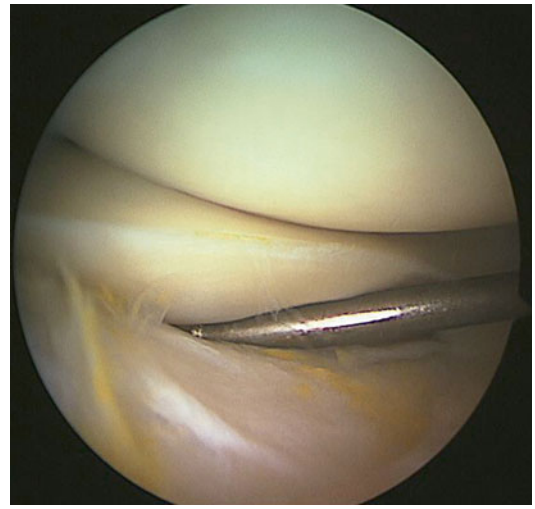

Fig. 1 Example of recurrent subluxation of the lateral meniscus of a patient presenting with posterolateral knee pain. Arthroscopic probing revealed an unstable posterior horn which needed to be stabilized arthroscopically using intra articular and outside-in repair techniques

Meniscal Lesions in Stable Knees

Meniscal lesions in stable knees differ significantly according to age at onset which is one of the main criteria for surgical decision-making. In a large study of some 1,500 meniscal lesions in stable knees, Metcalf and Barrett [75] found a greater number of complex, degenerative and horizontal lesions in patients over 40; whereas potentially repairable lesions (bucket-handle and vertical lesions) as well as radial lesions were more frequent in the under-40s. They also reported differences between the medial and lateral menisci: 98 % of MM lesions involved the posterior horn only while the anterior horn was almost never affected. However, in LM lesions, the middle segment and posterior horn showed equal involvement and the anterior horn were affected in 25 % of the cases. Similar findings were reported by Servien et al. [105]. These baseline figures must be kept in mind when considering an isolated meniscal repair.

LM Posterior Horn Instability

A specific subcategory is that of LM posterior horn instability causing recurrent subluxation of the posterior horn of the lateral meniscus (RSLM) (Fig. 1). RSLM is rare and mainly found in teenage and young patients. It can mimic patellar subluxations [8] and is to be borne in mind in case of painful knee locking in flexion or lateral knee pain with no immediately obvious structural lesion on arthroscopy. In such cases, meniscal stability should be checked by hook palpator. Posterior horn subluxation beyond the femoral condyle equator is to be considered pathological.

The literature on this subject is not abundant. Simonian et al. [109] and Suganuma et al. [114] described the specific anatomy of the posterior LM attachment, with popliteomeniscal fibres and their MRI aspect. George and Wall [39] reported the case of a 9-year-old patient presenting with symptomatic instability of the posterior horn of the LM, repaired by inside-out suture. A similar case was reported by Garofalo et al. [38] in a 19-year-old soccer player.

Horizontal Meniscus Delamination

Symptomatic horizontal delaminations can be amenable to repair either for posterior horn lesions of the MM or middle segment lesions of the LM [92]. Especially on the lateral side, they are frequently associated with the presence of a meniscal

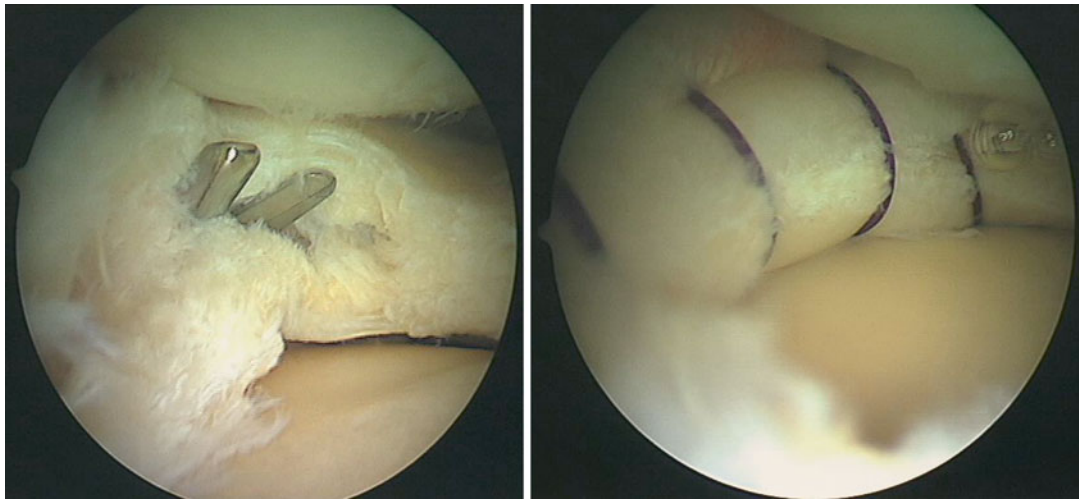

Fig. 2 Horizontal delamination of the middle segment of a LM, associated with a meniscus cyst in a 55-year-old patient (*right knee*). After intra- and extra-articular debridement and partial resection of the 2 meniscal layers, meniscal repair was performed with an "outside-in" technique, using absorbable PDS-O suture

cyst (Fig. 2). Surgery is required in cases with pain associated either to the intra-articular lesion or to the cyst. Cyst-related symptoms range from local swelling to peroneal nerve compression on the lateral side. These lesions may evolve with little symptoms over time and therefore indications for surgery must not be systematic and should be made with caution. We shall not attempt here to deal with the full range of LM cysts, but rather focus on the associated horizontal lesions, which almost always involve the middle segment and often extend to either the posterior or the anterior horn or both. The two superficial meniscal layers are often more or less intact while the conjunctive layer has been destroyed. An innovative attitude has therefore recently developed, seeking to conserve as much meniscal capital as possible [67, 92]. After intra- or extra-articular debridement of the cyst and degenerative meniscal tissue, the remaining two layers of meniscal tissue can be repaired by outside-in sutures or even by open meniscal repair. Initial findings are encouraging.

Discoid Meniscus

This section will seek not to deal exhaustively with the problems posed by discoid meniscus, but rather to provide an update on recent developments in knowledge (Fig. 3). It is now well established that symptomatology triggered by discoid meniscus is absolutely not to be managed by total meniscectomy. Most authors currently recommend partial meniscectomy in the affected area and restoring a normal meniscal form (saucerization). Recent studies have shown most pathological discoid menisci to be associated with peripheral instability due to an absence of meniscocapsular attachment. This is found in 28–77 % of cases ([43], and [58], respectively) and is more frequent in complete discoid meniscus and in the anterior horn (47–53 %) than in the posterior horn (39 %) or body segment (11 %) [43, 58].

Medial Meniscal Root Lesions

Root lesions of the MM were first described in the early 1990s by Berg [20] and Pagnani et al. [83], then forgotten about, only to be "rediscovered" recently. They consist of either bony or ligamentous avulsion of the posterior horn menisco-tibial insertion. Bone avulsion would seem to be the same pathological entity as the previously described meniscal ossicles [65, 95, 119]. The posterior detachment robs the meniscus of all biomechanical capacity, resulting in an increase in pressure and reduction in tibiofemoral bearing surface equivalent

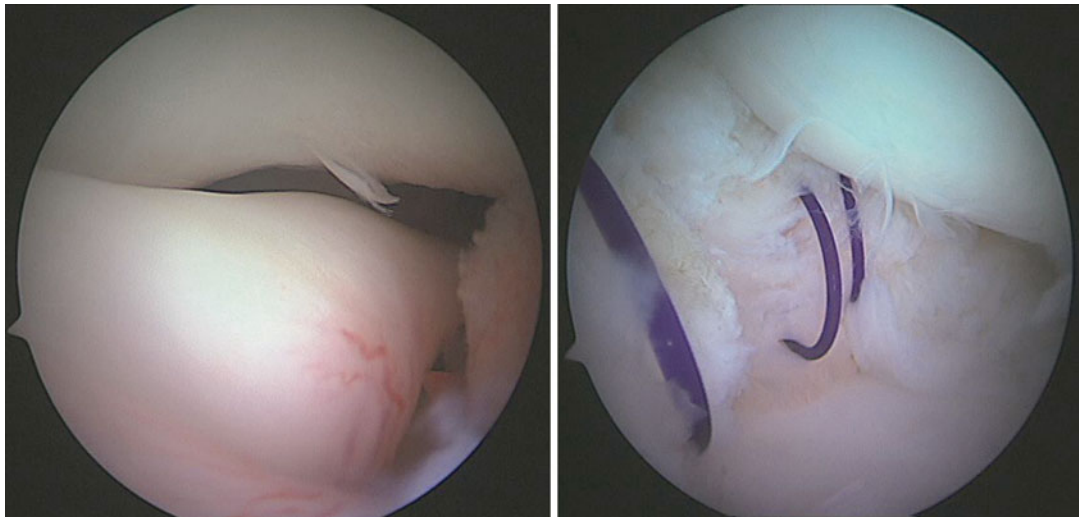

Fig. 3 Complete discoid meniscus in a 6-year-old girl (*right knee*). She presented with a flexion contracture. Saucerization and meniscocapsular repair were performed, using all-inside and outside-in sutures

to total meniscectomy [5, 71]. In young patients, the lesion is traumatic, occurring in a stable knee, and can be managed either by anchorage [29] or by transtibial tunnelling [2, 35, 45, 67, 87, 93]. Partial meniscectomy, as initially recommended by Pagnani et al. [83], incurs a risk of rapid joint degeneration. Apart from such purely traumatic lesions in young patients, a series of 67 radial meniscus root lesions in stable knees in older patients (mean age, 56 years) was recently reported by Ozkoc et al. [82]; unlike in the lesions previously discussed, partial meniscectomy was performed here to prevent locking symptoms in these menisci that had probably already lost any biomechanical function. Most medial detachments have been reported in stable knees. Engelsohn et al. [35] described posteromedial meniscal root detachment in severe knee trauma with associated multi-ligament lesions (Fig. 4). These medial lesions are to be distinguished from LM root lesions, which are usually associated with ACL tear. It emerges from the above that meniscal root lesions deserve greater attention in future. Diagnosis is still imprecise, differential management needs refining, and it remains to be demonstrated that results justify the effort of repair.

Surgical Techniques

Biological Healing Enhancement

Stimulating the Surrounding Meniscal and Synovial Tissue

In order to trigger the biological processes of tissue repair, the 1st step of meniscus repair should generally consist in stimulating the surrounding meniscal and synovial tissue using a shaver or dedicated rasp [10, 40, 41, 47, 57, 107]. Especially in long-standing lesions, it is essential to refresh the scar tissue, which tends to be fairly bradytrophic and vascularized only in the peripheral third.

Piercing Vascular Input Channels

Several authors have also described the so-called "needling" technique, which consists in piercing vascular input channels from the base to the avascular centre of the meniscus, using an 18G needle. Although Zhang et al. [122] demonstrated the effectiveness of the technique in an animal model, there is little scientific evidence for it from a clinical point of view, apart from one study by Fox et al. [36].

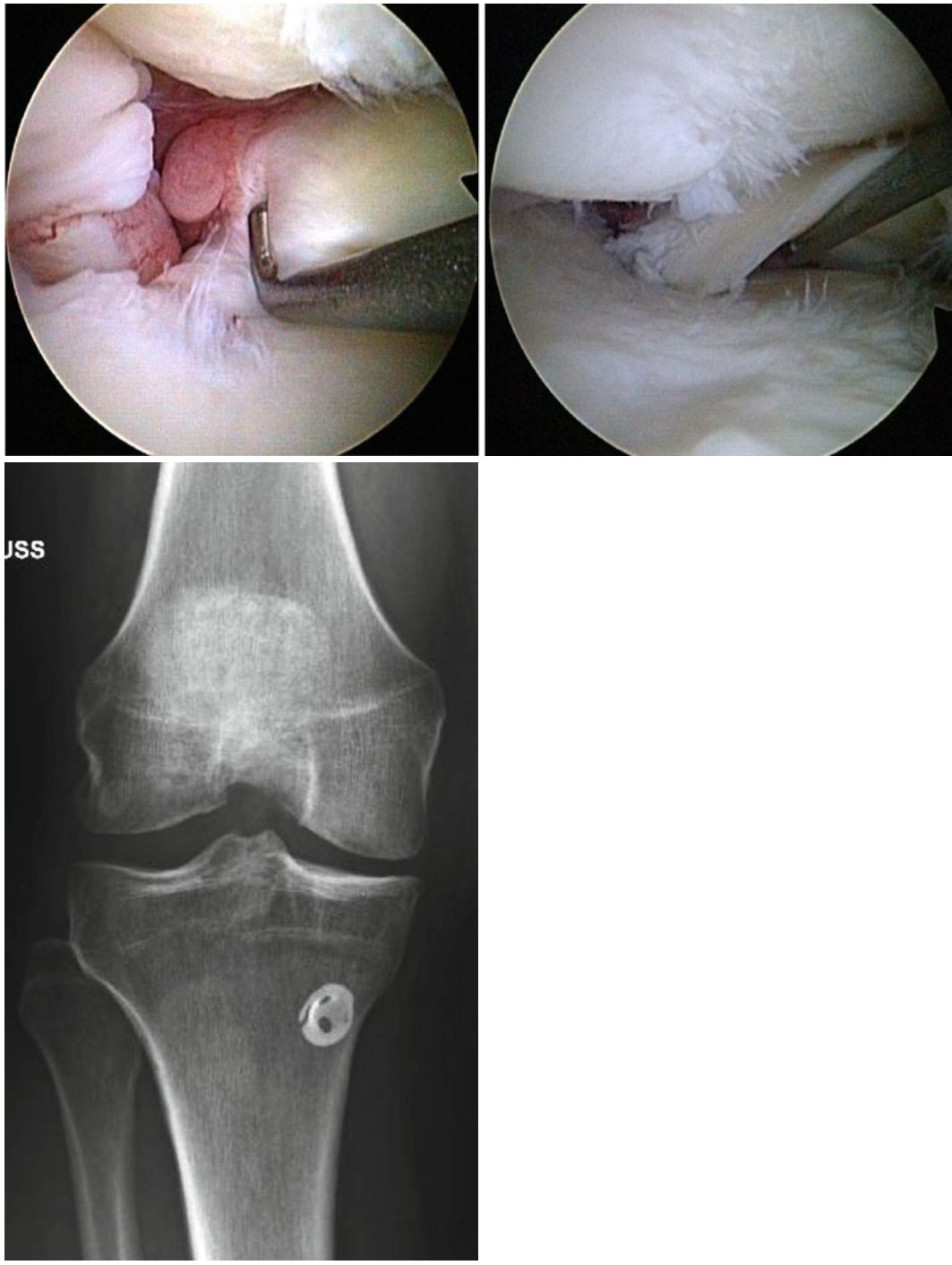

Fig. 4 Repair of the posterior root of the medial meniscus in a 42 years-old patient consulting for medial femorotibial mechanical pain in the right knee. Arthroscopy showed a found grade 2 medial condyle cartilage lesions associated with posterior horn detachment of the medial meniscus. A transosseous fixation was performed

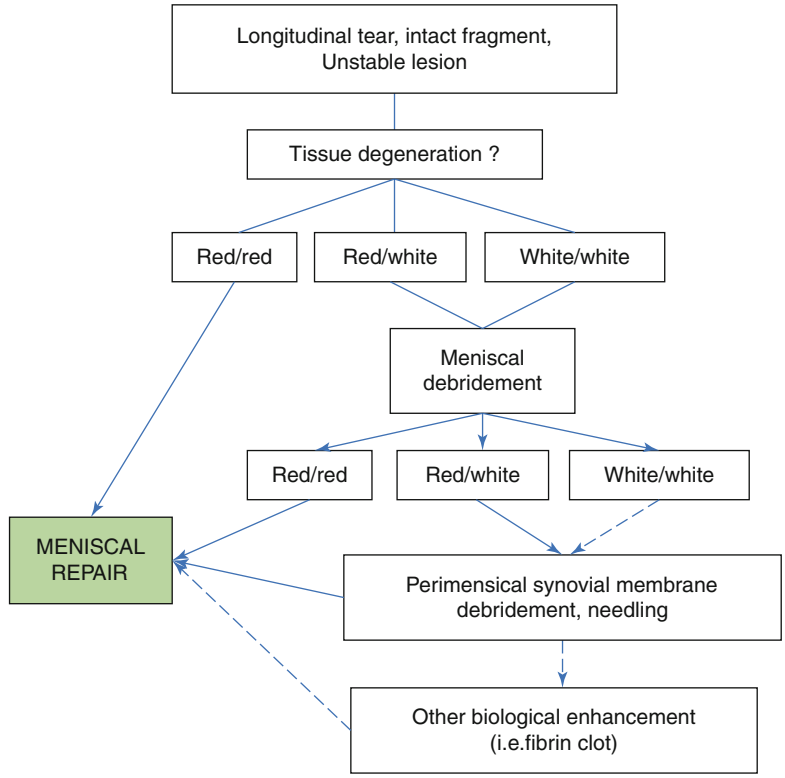

Fig. 5 Meniscal repair decision algorithm according to the tear zone (white/white, white/red, red/red) (Modified from Seil et al. [104])

Suturing an Autologous Venous Blood Clot

The third "biological" option presently available consists in suturing an autologous venous blood clot into the meniscal lesion in order to supply the growth factors needed for healing [10]. Despite promising experimental results, this technique does so far not seem to have been given large-scale application.

The current surgical attitude is presented as a decision algorithm in Fig. 5.

Meniscal repair as such may involve three different types of technique: meniscal suture, rigid implants, and combined suture and implantation (Table 1).

Table 1 Review of main meniscal repair methods

Suture systems	Rigid implants	Hybrid techniques
In-out (Needles & flexible cannulas	Meniscus arrow (Conmed Linvatec)	FasT-Fix (Smith & Nephew)
Out-in (standard IV needles & shuttle relays – micro lassos)	Meniscal dart (Arthrex)	MaxFire (Biomet)
All-inside Meniscal Viper (Arthrex)	BioStinger (Conmed Linvatec)	Meniscal Cinch (Arthrex)
All-inside (posterior compartment) Spectrum II (Conmed-Linvatec)	Meniscal screw (Biomet)	RapidLoc (DePuy Mitek)

Meniscal Sutures

Several techniques are presently available:

Outside-in Technique

This is a simple and cost-efficient technique which can be applied in the anterior horn and in the middle segment of the meniscus.

Percutaneous needles transport the sutures which are passed from outside the joint through the lesion and shuttled again through the outside, where they are sutured to the knee capsule.

Inside-Out Technique

Until a few years ago, this was still the most widespread meniscal repair technique. It is suitable for posterior horn lesions, and uses zone-specific cannulae to pass long needles through the meniscal tissue. Exiting the needles from the joint requires a posterolateral or posteromedial approach. Through the required additional approach, this technique bears the risk of iatrogenic damage to the saphenous nerve posteromedially and the peroneal nerve posterolaterally and to the main vasculonervous structures in the center of the popliteal space. Both for in-out and out-in techniques absorbable and non-absorbable repair materials are available. None of them has shown any superiority in terms of meniscal healing. Non-absorbable materials carry the potential of damaging the overlying cartilage, especially in the absence of healing at the repair site.

All-Inside Suture Technique

Two types of techniques are to be distinguished. Both require the surgeon to be skilled in arthroscopic knot tying. For menisco-synovial lesions (Fig. 6) of the capsular attachment of posterior horns that are hard to repair by other techniques, meniscal suturing may be performed using a curved hook (i.e. Spectrum; Conmed Linvatec) through a posterolateral or posteromedial arthroscopic approach. The method was developed from one of the earliest meniscal repair techniques, described by Morgan in 1991. It is difficult to perform, as it requires an additional posterior approach and the surgeon needs to be proficient in arthroscopic knot techniques.

The second purely articular technique was developed by Arthrex Inc., with a dedicated instrument called the "Meniscal Viper". It is especially useful for LM lesions facing the popliteal hiatus. In the medial femorotibial compartment, the size of the instrument often requires superficial medial collateral ligament release by percutaneous micro-incision using a needle; this provides 2–3 mm greater joint opening [85] and reduces the risk of iatrogenic cartilage lesions.

Meniscal Implants

Several biodegradable meniscus implants have been developed at the beginning of the 1990's. These repair techniques were intended for longitudinal lesions in the peripheral third of the meniscus, and especially in the posterior horn. Some of them have proved comparable to classical meniscus sutures in terms of clinical result. They were very popular at the turn of the century, but are now giving way to hybrid techniques.

Hybrid Techniques

Hybrid techniques combine implants and sutures. They are quick and relatively easy to perform in simple longitudinal lesions, and are currently very popular despite their cost and the fact that the implants are not biodegradable. This raises the risk of the implant becoming a free body in the joint in case of detachment, causing subcutaneous or intra-articular irritation.

Results

In reporting meniscal repair results, it is important to distinguish anatomical and clinical recovery rates. Anatomical healing criteria include three categories of healing: complete, incomplete and absent [46]. This method of assessment can only be made after invasive diagnosis such as by second look arthroscopy, arthroscan or arthro-MRI imaging. Figure 7 presents them according to three clinical categories: unstable knee, stable knee and repair associated to ACL reconstruction. Healing rates vary greatly with the clinical context, as can be seen at a glance from this graph. Pujol et al. [90] showed that repair which was limited to the posterior horn healed less well than lesions extending to the middle segment and

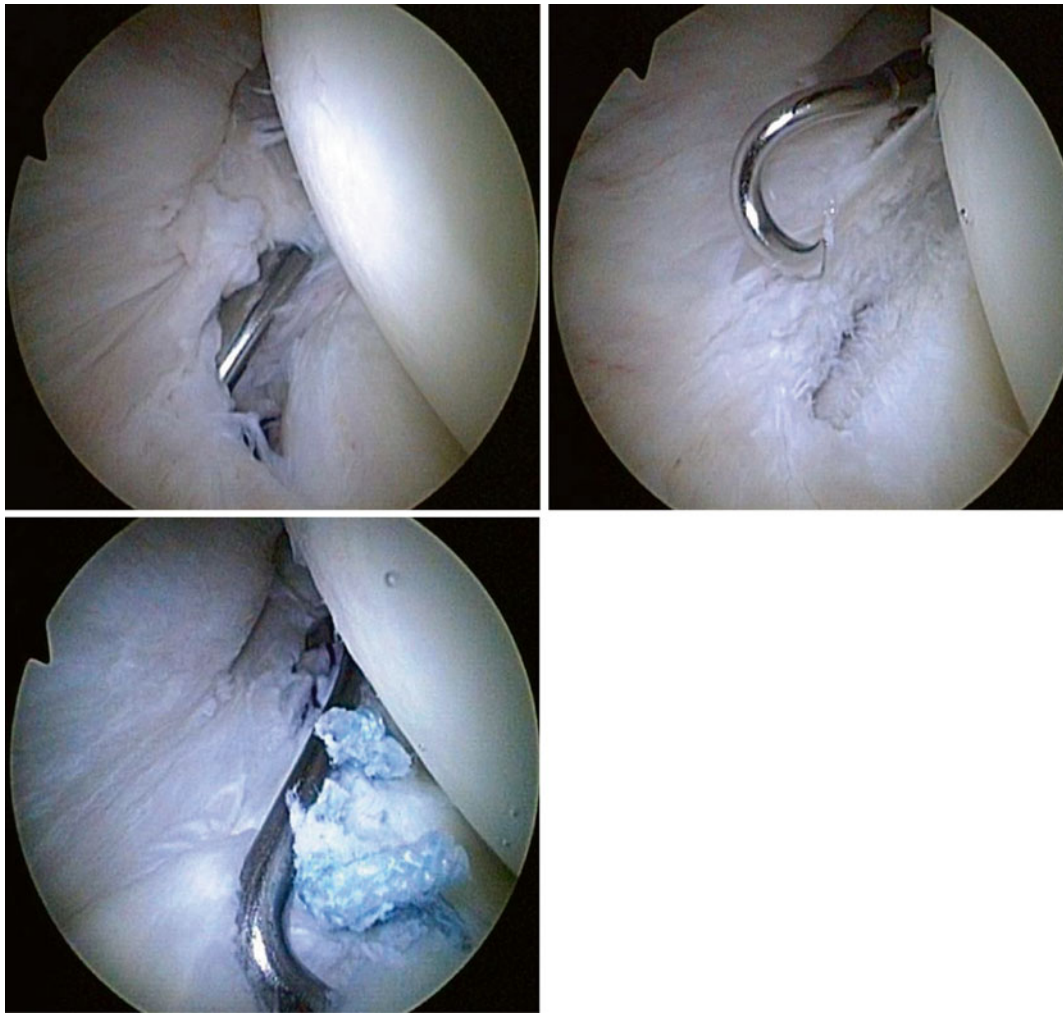

Fig. 6 Right medial meniscosynovial lesion in association with an ACL tear. The lesion is visualised from the intercondylar notch with a 30° scope, a posteromedial working portal was applied. The lesion was repaired with a suture hook used as shuttle-relay. Final probing of the repaired area with strong non-absorbable sutures

the anterior horn; they further reported that healing induced a narrowing of the meniscus, probably due to shortening caused by cicatrization.

On the contrary, clinical recovery criteria concern pain, associated or not with intra-articular effusion. They tend to overestimate healing as compared to anatomical criteria, due to clinically silent cases of partial healing [4, 25, 101]. Meniscal repair healing rates vary from 50 to 91 % [103], and depend on lesion type, associated ligament reconstruction, knee stability and alignment, and accident-to-surgery interval. Recent findings confirmed two essential clinical impressions: (1) In comparison with partial meniscectomy, meniscal repair resulted in superior clinical and radiological long-term outcomes, although higher re-operation rates were noted with repairs. (2) Meniscal repairs at the time of ACL reconstruction had lower failure rates than isolated repairs [86, 116].

Medium-to-long-term results are analyzed on the following three criteria: recurrence rate, radiographic signs of osteoarthritis, and joint function. Recurrent tearing ranges from 7 to 36 % (mean, 21 %) at 7.5 to 12.9 years' FU after primary surgery (Fig. 8). Its incidence is maximal during the first

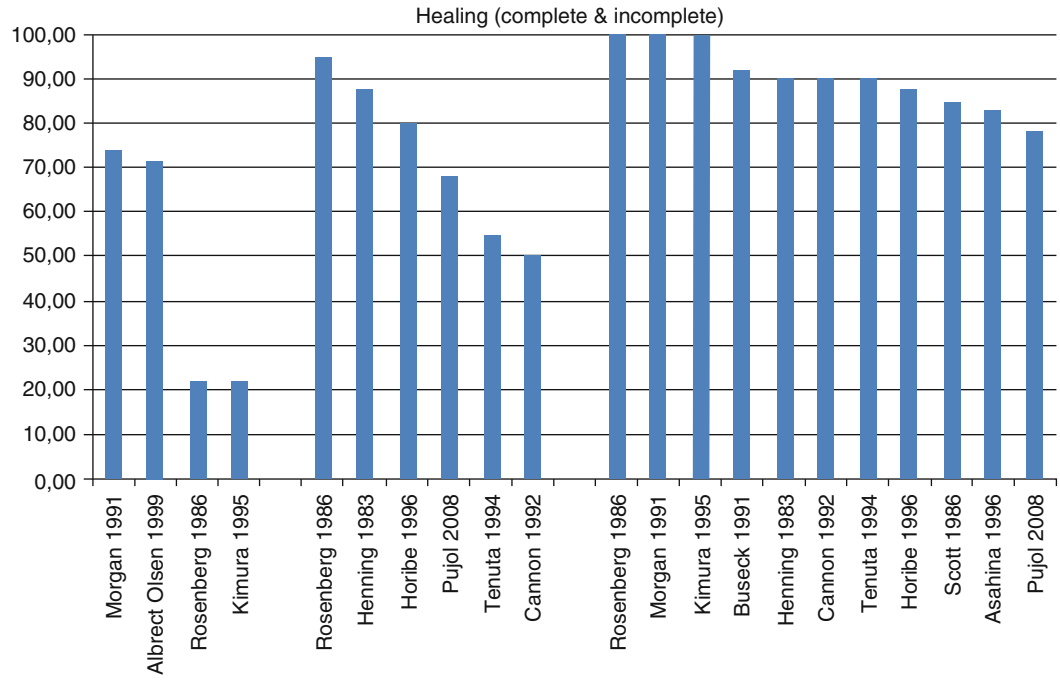

Fig. 7 Anatomic healing rates (%) for meniscal repair in various studies, according to three clinical categories: unstable knees (*left*), stable knees (*middle*), and repair associated to ACL reconstruction (*right*) (Modified from Seil et al. [104])

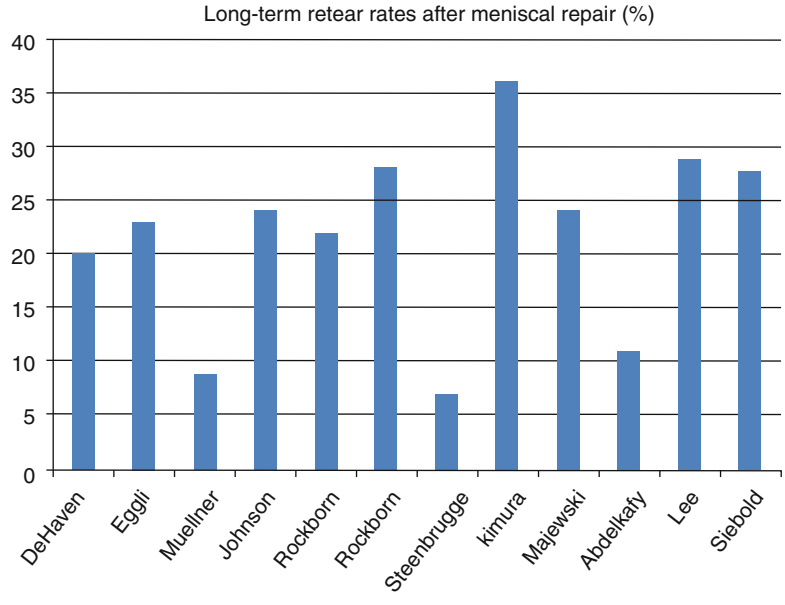

Fig. 8 Recurrent tear rates (%) after meniscal repair in studies with long-term FU (≥7.5 years) (Modified from Seil et al. [104])

3 years following repair. It is more frequent in cases of persisting knee instability, which is why it is no longer recommended to repair menisci in unstable knees. Radiographic signs of osteoarthritis were found to be more frequent in cases of recurrent tears than where meniscal repair was effective: 57 % vs 15 % [32], and 57 % vs 13 % [96, 97]. There seems to be a lower risk of radiographic osteoarthritis development in cases with meniscal healing.

Complications

Complication rates after meniscal repair are low [110, 111]. The most frequent complications were related to saphenous nerve lesions caused by a posteromedial approach in the inside-out repair technique [19, 24, 56, 76, 99, 100]. In such cases, lesions of the main branch of the saphenous nerve induce paresthesia or pain in the nerve territory on the medial side of the limb. They are generally caused by a compression of the retractor or the suture equipment. The infrapatellar branch of the saphenous nerve leaves the main nerve trunk in the distal part of the posteromedial approach, and extends laterally and distally. Compression or sectioning of this fine nerve network induces hyperaesthesia or paraesthesia of a territory the size of the palm of the hand below the patella. Other authors reported peroneal nerve lesions after LM repair [6, 53] as well as medial meniscal cysts following suture repairs [28, 56].

Several complications have been reported following the use of biodegradable implants. Broken implant migration in subcutaneous tissue, synovial irritation, prolonged intra-articular effusion and sometimes very severe cartilage lesions have been observed [7, 14, 42, 60, 72, 73, 81, 102]. Nor are hybrid implants problem-free. Their non-resorbable part has been incriminated in intra-articular damage [112].

Rehabilitation

Currently, there is no universally consensual validated program of rehabilitation after meniscal repair [12, 13, 23, 30, 69]. Programmes are based on biomechanical evidence [17, 94] and vary according to the type and location of meniscus and associated lesions. The parameters which influence rehabilitation are weight-bearing and knee range of motion. It is known that compression of the posterior horns increases with knee flexion. In deep flexion the meniscus shifts posteriorly, with the LM slipping behind the tibial plateau and the MM being compressed between tibial plateau and femoral condyle [17, 51]. In order to avoid these critical situations, we limit knee flexion to 90° within the first 6 weeks and do not recommend deep squatting for 4–6 months after surgery.

Weight-bearing is allowed from the beginning with the knee blocked in full extension in a brace for 6 weeks. This avoids shear forces and allows compression of the repair site in those lesions without a radial component. In the rare lesions where the integrity of the meniscal circumference is endangered (either a radial tear or a root tear), we do not allow weight- bearing for the first 6 weeks. Pivot, and especially pivot-contact, activity as well as squat exercises involving maximum flexion of the knee under weight-bearing are not to be resumed for 4–6 months.

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Revision Anterior Cruciate Ligament Reconstruction

Matteo Denti, P. Randelli, C. Bait, and P. Volpi

Anterior Cruciate Ligament (ACL) reconstruction is a successful operation with satisfactory outcomes; an overall clinical failure rate of 10–25 % has been reported.

Therefore, an increasing number of patients are requiring revision ACL reconstruction.

Revision of ACL reconstruction is a complicated and delicate clinical procedure whose results are theoretically less satisfactory than those of the first operation because further intervention is required in an area where anatomical landmarks may have been altered by previous procedures.

The number of revision ACL reconstructions has almost doubled during the past 10 years according to National Registries.

Post-operative complications, such as infection, arthrofibrosis (motion loss), extensor mechanism dysfunction, and a painful knee because of cartilage deterioration can lead to unsatisfactory outcomes.

However, the vast majority of a second procedures are for recurrent knee instability.

Diagnosis of recurrent knee instability after ACL reconstruction is based on history, clinical examination, and imaging.

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Usually, patients have a subjective sensation of instability, giving way, and they have functional limitations that affect daily or sports activities. Instability may be accompanied by knee pain and swelling in some patients.

Knee stability and graft function is assessed by physical examination using both the Lachman and the pivot-shift test which may demonstrate excessive laxity. In addition, objective laxity can be measured using the KT-1000 arthrometer. A side-to-side difference of more than 5 mm between the two knees is not acceptable and is correlated with poor functional results.

Causes of graft failure and recurrent instability are:

1. technical errors
2. biological failure of graft incorporation
3. a new trauma to the knee and the graft and
4. failure to recognize and treat concomitant laxity (usually postero-lateral instability).

The most common technical error is improper tunnel placement. A non-anatomical graft placement (failure to place the graft in the native femoral and tibial footprints) will result in graft impingement, stretching of the graft, and laxity. A common scenario of poor graft placement, is a vertically-oriented graft in the coronal plane. In this way, anteroposterior stability may be restored, but not the rotational stability. Poor graft quality, inadequate graft tensioning and failure of graft fixation may also be causes of a poor surgical result due to technical errors.

Imaging of the knee using plain x-rays, which are the most simple and useful investigations,

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will contribute to diagnosis and help to define the cause of failure, as well as, planning the revision. Pre-operative radiographs will show tunnel position and widening, and the presence of metal hardware. The necessity for removal of metallic hardware, options for graft fixation, and if a single or two-stage procedure is required (because of tunnel expansion) can be decided by the surgeon by using simple x-rays, in most cases. Finally, a CT scan or an MRI can be obtained if additional information regarding tunnel placement and expansion are needed.

In our experience the two types of subject at risk after an ACL reconstruction are the adolescents and females due to their biology and constitutional anatomy.

It is always important to check the personal motivation of the patient before proposing a revision of a ACL reconstruction.

The type of graft is usually related to the previous surgery.

Our favourite grafts for revision of ACL reconstruction are the hamstring, the patellar tendon autograft and the Achillis tendon allograft.

It is much easier to revise a hamstring tendon ACL reconstruction with a patellar tendon than vice versa.

The use of the allograft allows us a better reconstruction in cases of enlargement of the bone tunnels.

In many cases you can also leave the previous fixation devices.

It is always better to understand the technical cause of failure before creating new bone tunnels.

We usually prefer the one-stage surgery because it is one operation and one rehabilitation for the patient.

If there are signs of tunnel widening we have to consider a two-stage procedure with bone grafting. A two-staged procedure can also be necessary if there are large fixations devices.

During the period September 2000 and September 2004 we performed 66 arthroscopically-assisted revision Anterior Cruciate Ligament (ACL) reconstructions. In this clinical revision we did not include patients with associated instability or axial deformity.

Pre-operatively all the 66 pts. had a failure of the ACL reconstruction with a positive Lachman and Pivot-shift tests and were symptomatic in daily living and in sport activities.

Of the 66 ACL revisions we were able to review 50 patients at a follow-up of 1–5 years (mean 29.9 months) using clinical evaluation, IKDC score including KT1000 and Lysholm scores.

Six patients were lost to follow-up and ten were contacted by telephone due to their inability to attend. In this group of ten patients we used only the Lysholm score.

The causes of failure were: surgical in 37, traumatic in 21 and biological in 2.

The revision was performed by a one-incision technique in the majority of patients and an accelerated rehabilitation program was followed.

A one-stage technique was performed in 55 patients whilst a two-stage technique was used in 5 (4 for recovery of ROM and 1 for tunnel re-filling).

The graft utilized for the revision ACL reconstruction was: BPTB in 11, contralateral BPTB in 12, double semitendinosus and gracilis in 35 and Achilles allograft in 2 patients.

Associated lesions (meniscal, articular cartilage) were present and treated in 31 cases on 24 patients.

At follow-up, using the IKDC, there were 18 patients (36 %) with A 23 pts (46 %) with B, 9 pts (18 %) with C and no pts with D.

With the KT1000 we obtained 28 (56 %) with A, 17 pts (34 %) with B and 5 pts (10 %) with C, and no pts with D.

The Lachman test was negative in 34 pts, 1+ with a firm stop in 10 pts, 1+ with a soft stop in 5 pts and 2+ in 1 pt.

The Lysholm score was: excellent in 34 pts (57 %), good in 8 (13 %), fair in 13 (22 %) and poor in 5 (8 %). This score included also the 10 pts contacted telephonically.

39 pts resumed sport at the same level that before the ACL lesion, 7 reduced the sport activity level and 4 gave up with sport.

The revision ACL reconstruction produced 90 % of excellent or good results (KT1000) in

terms of stability while 18 % of this group of pts. (IKDC) complained of knee pain due to arthritis.

10 pts (20 %) resumed sport at a higher level than after ACL reconstruction.

We were surprised at the considerable number of patients (78 %) who, after ACL reconstruction revision, returned to perform the same level of sport as *before their initial* knee injury compared to the only 58 % who returned to the same sport at the same level after the primary reconstruction. This could be explained by the fact that, in our opinion, a large number among these patients did not have good knee stability after the first reconstruction. Therefore, as a consequence of the revision surgery, 20 % more of the patients have been able to return to sport. This result is in conflict with the underlying belief that an ACL revision is a salvage operation meant to improve quality of life (activities of daily living) rather than to secure a return to sport, which is more likely to happen with professional athletes who achieve a good result. Obviously, when satisfactory knee stability is reached, most patients return to perform their favourite sport as before their initial injury.

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Part IX

Foot and Ankle

Treatment of Chronic Achilles Tendinopathies

Jon Karlsson, Annelie Brorsson,
and Karin Grävare Silbernagel

Abstract

Achilles tendinopathy is a common and often difficult to treat problem. The best known and best researched treatment is rehabilitation exercises either concentric or concentric-eccentric exercises. To experience a favourable outcome from exercise, the exercises are allowed to cause pain. Therefore, the use of a pain-monitoring model together with a training log help the patient and the clinician to balance between overloading and loading enough to achieve a positive response to the exercises. The exercise programme needs to continue for at least 12 weeks, and often it needs to be continued for up to a year. It might also be beneficial to combine the exercise treatment with other treatments, such as shockwave therapy, laser therapy and the use of orthotics. Surgery is considered as the last option. Patients with insertional Achilles tendinopathy are more likely to need surgery compared with patients with mid-portion Achilles tendinopathy

Achilles Tendinopathy

The *overuse type* of injury to the Achilles tendon is the painful type of injury that occurs when the body's reparative capability is exceeded by repetitive microtrauma [1]. The injury can be in an acute or chronic phase. The exact time criteria that are used to classify the injury as acute or chronic are arbitrary. In the literature, definitions for the injury to be chronic range from 4 weeks to 3 months or pain on and off for more than 6 months [2–5]. The acute phase injury consists of partial ruptures, bursitis or paratendonitis. The chronic phase injury can be divided into distal Achilles tendinopathy and midportion Achilles tendinopathy depending on the location of the pain.

In 163 patients with chronic Achilles tendinopathy, surgical and histopathological findings showed that 90 % had degenerative changes, so-called tendinosis [6]. On the other hand, degenerative changes were also found in 20 % of non-symptomatic tendons. Another finding was

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that 19 % of the patients had partial ruptures that always occurred in the tendinosis area. There was also a lack of inflammatory cells and poor healing response in the biopsies. Åström and Rausing [6] describe the surgical findings in an Achilles tendon with tendinopathy as a loss of the normally glistening white appearance of the tendon; it becomes grey and the tendon thickens.

The degenerative changes in the tendon can be divided into several subcategories such as hypoxic, mucoid, hyaline, lipoid, fibrinoid, calcific or a combination of these [7, 8]. The degenerative changes can be the result of a variety of causes such as aging, microtrauma, vascular compromise or other reasons and they may vary from tendon to tendon [7]. The histopathological findings of tendinosis are collagen disorientation, disorganization and fiber separation. Tendinosis might also occur together with the involvement of the paratenon. This can present itself as crepitation due to adhesions between the tendon and the paratenon.

Achilles tendinopathy is a clinical diagnosis for the clinical syndrome, characterized by a combination of pain, swelling (diffuse or localized) and impaired performance of the Achilles tendon. Clinically, a distinction between mid-portion (2–6 cm proximal to tendon insertion) and distal (insertion to the calcaneus) Achilles tendinopathy can be made on the basis of the location of the pain. The typical symptoms of Achilles tendinopathy are pain during and after physical activity, tenderness on palpation and morning stiffness [9–11]. With increased severity, patients may also have pain during daily functional activities [10, 11].

Mid-portion Achilles Tendinopathy

Mid-portion Achilles tendinopathy is reported to account for 55–65 % of all Achilles tendon injuries [12–15]. Patients usually describe a gradual onset of pain. However, they occasionally report a single incident that starts the symptoms. Many patients have had pain for many months or on and off for many years. Initially, the symptoms occur after heavy physical activity, but as the injury progresses some patients develop pain during physical activity. Patients may also have pain with daily activities, such as walking. Morning stiffness and/or stiffness after sitting for longer periods of time are also common. Correlation between pain level, morning stiffness and severity of disease are reported in the literature [10, 11, 16, 17]. Clinically, the patients report pain on palpation in the middle part of the tendon (2–6 cm proximal to the tendon insertion) and sometimes there is a palpable thickening in the same area, usually in the more chronic stages (Fig. 1). Noticeable crepitation can be indicative of adhesions of the paratenon and paratendinopathy in more acute stages. A thorough physical examination is important in order to rule out any other causes of the pain.

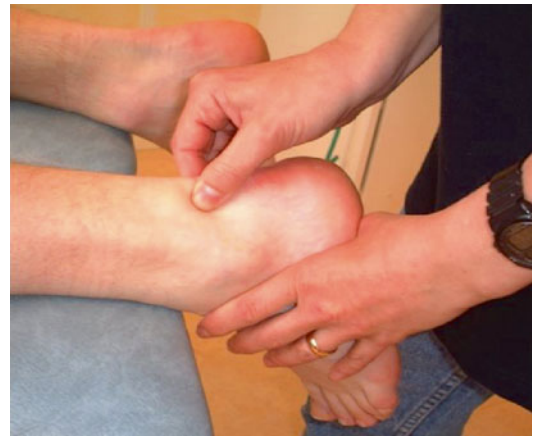

Fig. 1 Palpation of mid-portion Achilles tendinopathy

Distal Achilles Tendinopathy

Approximately 20–25 % of all Achilles tendon injuries are reported to be distal. This condition is also called “insertional” Achilles tendinopathy [12–15]. In a study of patients with Achilles tendon injury during the years 1976–1986, 23 % had pain distally and, of these, 61 % were diagnosed as insertion tendinitis, 21 % as retrocalcaneal bursitis and 18 % as both [15]. These patients report the same complaints as in mid-portion injury and/or pain related to the type of shoe/athletic wear. In this case the pain can occur due to

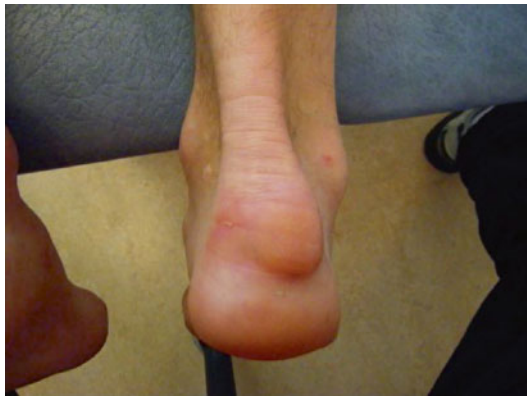

Fig. 2 Typical prominent superior projection of the calcaneus occurring together with distal Achilles tendinopathy

external compression on the tendon insertion. Swelling around the Achilles tendon insertion to the calcaneus, with redness and warmth, can also be present and might be related to active bursitis. The patients sometimes also report pain after having run uphill, standing on a ladder or walking barefoot on sand. Clinically, there is pain when the tendon insertion is palpated. This type of injury can also be caused by compression injury of the tendon and the bursa onto the calcaneus, so-called posterior impingement. A prominent superior projection of the calcaneus, i.e. Haglund's deformity, can be the cause of the posterior impingement (Fig. 2).

Treatment

In the literature various types of treatments such as ultrasound, deep friction massage, anti-inflammatory medication, surgery, sclerosing injection, shock wave therapy, low level laser therapy and exercise are described to be used for Achilles tendinopathy. Systematic reviews indicate that exercise, especially eccentric exercise, have the most evidence of effectiveness but has been less successful in the patients with insertional Achilles tendinopathy compared to those with midportion injury [18, 19]. Today the consensus is that Achilles tendinopathy should initially be treated with exercise for at least 3–6 months. Even with other types of treatments some type of exercise is recommended.

Therapeutic Exercise

The basis of exercise as treatment for Achilles tendinopathy is to address possible impairments and deficiencies in strength, range of motion, balance, proprioception and function and to promote healing of the tendon. Since the tendon is subjected to the highest loads eccentrically, eccentric training has always been an important part of the prescribed exercise. Increased speed of movement also increases the load of the tendon during the eccentric muscle activation and, to increase the load on the tendon during exercise, both the external load and the speed of movement can be increased.

Current Rehabilitation Protocols

There are currently two exercise programs that have been used in various studies evaluating treatment in patients with Achilles tendinopathy. One of the protocols, the so-called Eccentric only protocol [20], uses eccentric loading only whereas the other protocol, the so-called Comprehensive Treatment Protocol [21], includes both concentric and eccentric strengthening. Both protocols have been shown to have good short-term results in patients with midportion tendinopathy. When evaluating the long-term outcome of these two treatment protocols, it was found that with the Eccentric-only protocol 38 % of the patients were completely pain-free at 5 years, and with the Comprehensive Treatment Protocol 80 % were fully recovered after 5 years [22, 23].

The Eccentric-only protocol has also been evaluated in patients with distal Achilles tendinopathy. It was found that this exercise programme was more successful in patients with distal Achilles tendinopathy if the amount of dorsiflexion was limited. It is therefore recommended, with both of the different treatment protocols, that patients with distal Achilles tendinopathy should be standing flat on the ground instead of standing at the edge of a step.

Eccentric-Only Exercise Protocol

Alfredson and co-workers published in 1998 a non-randomized study using a protocol with only eccentric heel-rises with both the knee straight

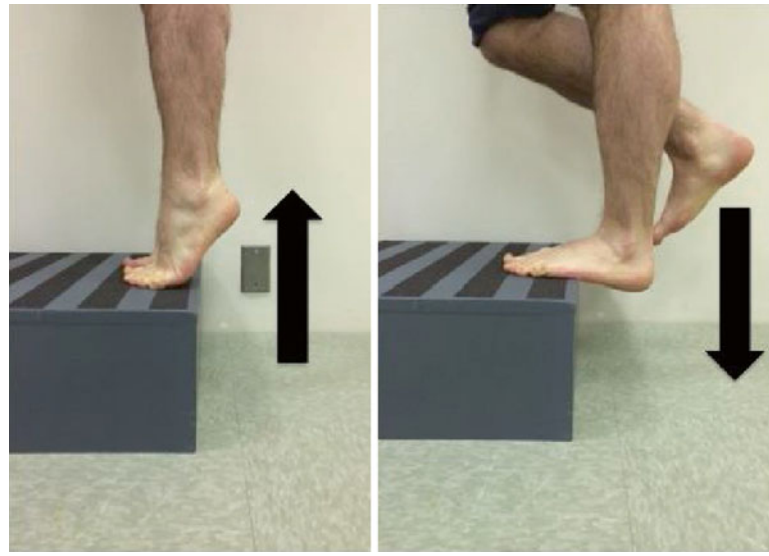

Fig. 3 Eccentric heel-rise with the knee straight

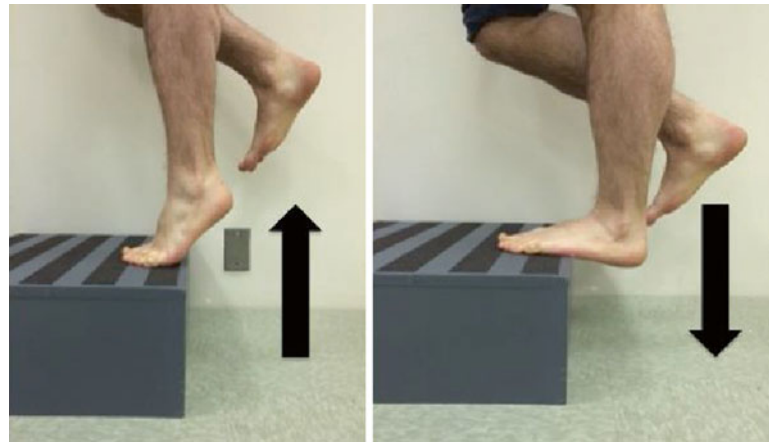

Fig. 4 Single leg standing heel-rise

and the knee bent. The patients are instructed to use the uninjured side to get up on the toes and then place the weight on the injured sided and then lower the heel all the way down (Fig. 3). The patient performs three sets of 15 repetitions of the two exercises, twice a day for a total of 12 weeks. The treatment programme is also supposed to be painful, and if the exercises could be performed without experiencing any minor pain or discomfort, the patients were instructed to increase the load by wearing a backpack with added weights.

A Comprehensive Treatment Protocol

This protocol includes both concentric and eccentric exercises of the calf muscles. The reason for this is that both concentric and eccentric activations are included in all physical activities and it has been shown that patients with Achilles tendinopathy have both concentric and eccentric strength deficits [24]. The programme consists of single (Fig. 4) and double-legged standing heel rises (Fig. 5), seated heel rises, eccentric heel rises and quick rebounding heel rises. There are four different phases of the programme with gradually increasing strength-demands, and what phase the patient is in is dependent on their symptoms and function (Fig. 6). This treatment protocol allows the patient to experience pain during and after exercise. The pain-monitoring model is used to facilitate the patients' understanding of the amount of pain allowed during and after exercise (Fig. 7). The model was initially developed

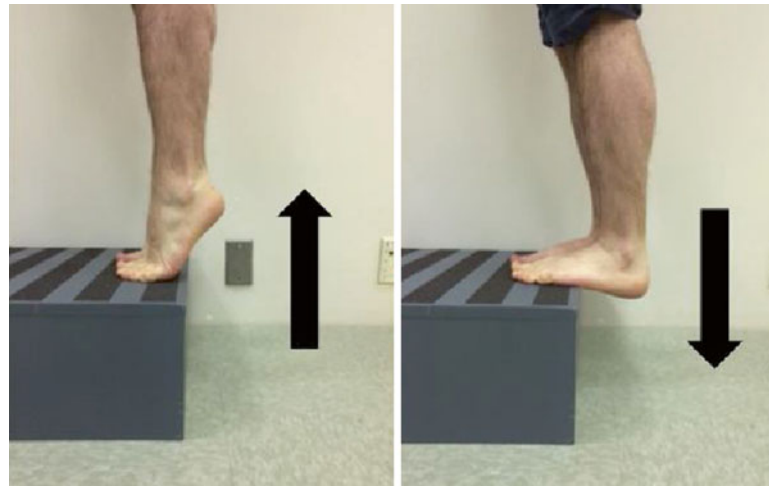

Fig. 5 Double-legged standing heel rise

The Comprehensive Treatment Protocol

Phase 1: Week 1–2 **Patient status:** Pain and difficulty with all activities, difficulty performing 10 single-leg heel-rises
Goal: Start to exercise, understanding nature of their injury and of **pain monitoring model** **Treatment program:** Perform exercises every day • Pain monitoring model information and advice on exercise activity • Circulation exercises (foot up/down) • Double-leg heel-rises standing on the floor (3x10–15) • Single-leg heel-rises standing on the floor (3x10) • Sitting heel-rises (3x10) • Eccentric heel-rises standing on the floor (3x10)
Phase 2: Week 2–5 *(If pain distally continue standing on the floor)* **Patient status:** Pain with exercise, morning stiffness, pain when performing heel-rises
Goal: Start strengthening **Treatment program:** Perform exercises every day • Double-leg heel-rises standing on edge of stair (3x15) • Single-leg heel-rises standing on edge of stair (3x15) • Sitting heel-rises (3x15) • Eccentric heel- rises standing on edge of stair (3x15) • Quick rebounding heel-rises (3x20)
Phase 3: Week 3–12 (or longer if needed) *(If pain distally continue standing on the floor)* **Patient status:** Handle the phase 2 exercise program, no pain distally in tendon insertion, Possibly decreased or increased morning stiffness
Goal: Heavier strength training, increase or start running and / or jumping activity **Treatment program**: Perform exercises every day and with heavier load 2–3 times per week • Single-leg heel-rises standing on edge of stair with added weight (3x15) • Sitting heel-rises (3x15) • Eccentric heel-rises standing on edge of stair with added weight (3x15) • Quick rebounding heel-rises (3x20) • Plyometrics training
Phase 4: 3–6 months (or longer if needed) *(If pain distally continue standing on the floor)* **Patient status:** Minimal symptoms, not morning stiffness every day, can participate in sports without difficulty
Goal: Maintenance exercise, No symptoms **Treatment program:** Perform exercises 2–3 times per week • Single-leg heel-rises standing on edge of stair with added weight (3x15) • Eccentric heel-rises standing on edge of stair with added weight (3x15) • Quick rebounding heel-rises(3x20)

Fig. 6 The comprehensive treatment protocol

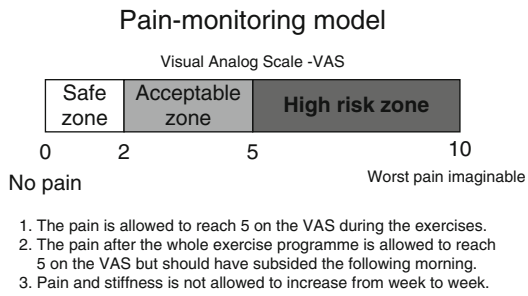

Fig. 7 The pain-monitoring model

by Thomeé and presented in a randomized controlled trial in 1997 for patients with patellofemoral pain syndrome [25]. The pain-monitoring model together with a training log are tools that also helps the clinician and patient to determine how the exercise programme should progress and also how much is the optimal amount of exercise overall. The exercise programme, complemented with the pain-monitoring model, has been evaluated in two randomized controlled trials and led to significant improvements in patients with mid-portion Achilles tendinopathy [21, 26].

Non-steroidal Anti-inflammatory Drugs (NSAID's)

Since Achilles tendinopathy is mainly a non-inflammatory condition, apart from a possible short initial inflammatory phase, the use of NSAIDs will have no major therapeutic effect [6, 27, 28]. NSAIDs might, however, have an analgesic effect for the patient. Åström and Westlin [29] found no beneficial effect from NSAIDs in patients with Achilles tendinopathy. In a review of the literature, the investigators report insufficient evidence for determining the efficacy of NSAIDs in chronic tendon injury [30].

Corticosteroids

Corticosteriods are commonly used for their anti-inflammatory action. In a review of the use of corticosteroids in chronic tendon injuries, it was found that they might provide some initial pain relief but that their beneficial effect on the outcome remained uncertain [30]. Corticosteroid injections in and/or around tendons have also been associated with tendon ruptures, even though this still remains controversial, and is mostly described in case reports [10, 30–32]. A recent systematic review reported that cortocosteriod injections for tendinopathy may show positive short-term results but this treatment was found to be worse then other options in the intermediate and long terms [33]. The effects might also vary depending on the site for tendinopathy and due to the heavy load on the Achilles tendon and the potential increased risk for Achilles tendon rupture it is not recommended as an option.

Nitric Oxide

Nitric oxide (NO) is a small free radical generated by a family of enzymes, the nitric oxide synthase (NOSs). In the animal model tendon healing was found to be enhanced when additional NO was added [34]. Clinical trials have reported that treatment with NO delivered via a transdermal patch enhances the subjective and objective recovery in patients with tendinopathy [35, 36]. It is important to note however that the results have not been found to be superior to exercise and side effects such as severe headaches are reported with this treatment.

Extracorporal Shockwave Therapy

Extracorporal shockwave therapy (ESWT) is used for pain relief and to promote tendon healing however the underlying mechanism is not clear. The published trials for the use of ESWT in tendinopathy also vary in intensity, frequency and duration [37–41]. ESWT has been found to be more efficacious then rest but similar to placebo ESWT for tendinopathy [19]. The general recommendation is that it might be beneficial to use ESWT in conjunction with optimal therapeutic exercise and patients with distal Achilles tendinopathy might benefit more than patients with mid-portion injury.

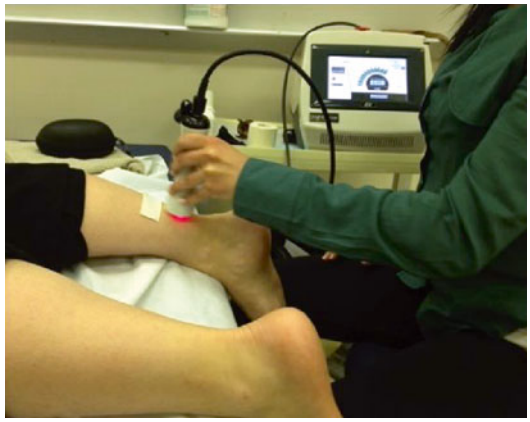

Fig. 8 Treatment with laser

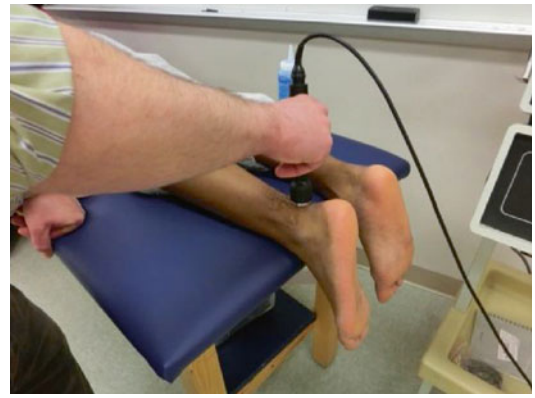

Fig. 9 Treatment with ultrasound

Laser

The photobiostimulation that occurs when treating the tissue with laser has been reported to reduce inflammation [42] and have positive effects on angiogenesis [43] and collagen synthesis [44]. Controversy exists over dosage recommendations, and consensus does not exist of the most efficacious dose [45]. A systematic review evaluating the effect of Low-level laser therapy (LLLT) on tendinopathy indicated favourable outcome with this treatment but the results varies between different studies [45]. In general this treatment has been combined with eccentric exercise, and it has been found to be more beneficial then eccentric exercise alone [46]. However, none of the studies has evaluated the effect of LLLT on patients with the distal type injury. Recent published clinical guidelines recommended based on moderate evidence that clinicians should consider the use of LLLT to decrease pain and stiffness in patients with Achilles tendinopathy [47] (Fig. 8).

Therapeutic Ultrasound

In animal studies therapeutic ultrasound has been found to enhance tendon healing [48] but few clinical studies show positive results. For Achilles tendinopathy therapeutic ultrasound has been shown to be inferior to eccentric exercise [49] (Fig. 9). Systematic reviews and meta-analyses have failed to show that active ultrasound is more effective then placebo [50].

Deep Friction Massage

In the clinical setting manual techniques such as soft tissue massage are often used. Deep friction massage is proposed to relieve pain and/or release scar tissue. Clinically deep friction massage is often used in combination with other treatments such as exercise (Fig. 10).

A Cochrane review only found two randomized trials that evaluated the effect of this treatment and concluded that no consistent benefit could be found.

Orthotics

It has been suggested that biomechanical malalignments are risk factors for Achilles tendinopathy. Corrective orthotics are therefore often prescribed for patients with Achilles tendinopathy. There is one double-blind study which showed no benefit from using visco-elastic heel pads for Achilles tendinopathy [51]. Clinically, some patients report no effects with orthotics, whereas others report significant improvements with its use. Until there is research showing that corrective orthotics is effective in relieving symptoms, its use should be based on clinical judgement.

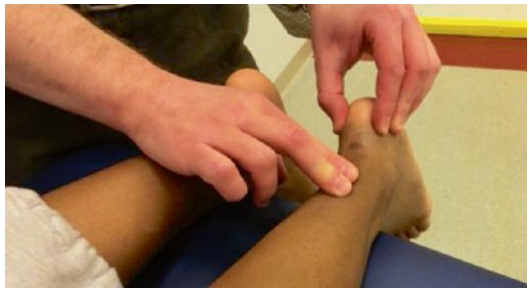

Fig. 10 Treatment with deep friction massage

Surgery

There appears to be consensus in the literature that surgery should only be performed after patients have been treated unsuccessfully with a treatment protocol involving exercise for a minimum of 6 months [10, 11, 27, 52]. The surgical techniques vary but usually include removing abnormal tendon tissue and releasing adhesion and scarring [10, 11, 52]. It is not clear why surgery sometimes helps and the post-operative rehabilitation may be as important as the actual surgery [27]. The success rates for surgery are reported to be approximately 70–80 % [11, 53–58]. In a review of the outcome of surgery for chronic Achilles tendinopathy, a negative correlation was found between reported success rates and overall method scores [58]. Complications after surgery also need to be considered and, in a study of 432 consecutive patients, there were 46 (11 %) complications from treatment [59]. With improvements in non-surgical treatment, there will, however, be fewer requirements for surgery.

"Wait-And-See"

It has been shown that a 4 months "wait-and-see" strategy was ineffective compared with eccentric training and low energy shockwave therapy (SWT) when treating patients with mid-portion Achilles tendinopathy [38].

Conclusions

The treatment with the highest level of evidence is rehabilitation exercises. To experience a favourable outcome from exercise, the exercises are allowed to cause pain. The use of a pain-monitoring model, together with a training log, help the patient and the clinician in the balance between overloading and loading enough to achieve a positive response to the exercises. The exercise programme needs to continue for at least 12 weeks, but more often it needs to be continued for up to a year. It might also be beneficial to combine the exercise treatment with other treatments, such as shockwave therapy, laser therapy and the use of orthotics. Surgery is to be considered as the last option. Patients with insertional Achilles tendinopathy are more likely to need surgery compared to patients with mid-portion Achilles tendinopathy.

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Persistent Pain After Ankle Sprain

Donald J. McBride

Abstract

Persistent pain after an ankle sprain remains a frequent cause of disability across all age groups. Ankle injuries are very common. They account for a significant number of lost working days and interfere with individual enjoyment of sporting and leisure pursuits. When chronic symptoms occur after these apparently simple sprains a methodical approach to their diagnosis and management will alleviate unnecessary incapacity and provide good symptom relief. This paper describes an anatomical and regional approach to the history, examination, investigation and management of this difficult problem.

Introduction

Ankle injuries are common. The overall incidence of sprains has been calculated as 1/10,000 persons per day with 25,000 ankle sprains occurring in the USA every day [1]. Forty to forty-five percent of ankle injuries are sports related, 85 % are sprains and 85 % are due to inversion affecting the lateral ligament. Lateral injuries usually affect the ATFL (anterior talo-fibular ligament) (40 %), ATFL and CFL (calcaneo-fibular ligament) (58 %) and, rarely, the ATFL, CFL and PTFL (posterior talo-fibular ligament) (2 %). Medial (deltoid) ligament injuries usually occur with lateral fractures and are rare in isolation. However, persistent pain may occur laterally, medially, anteriorly and posteriorly affecting a wide variety of extra-articular structures and may also arise from damage to the intra-articular surfaces, either chondral or osteochondral with or without synovitis and impingement. In addition, the inferior tibio-fibular joint, interosseous membrane, proximal fibula and superior tibio-fibular joint may occasionally be affected.

History

The history as always is very important in determining the diagnosis of persisting ankle pain after a sprain. Clearly, a thorough appraisal of the initial injury and the relevant current symptoms

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is mandatory. The main presenting symptoms in the ankle will be pain, instability, stiffness, swelling and locking. However, it is helpful to categorise the symptoms based on anatomical site; namely, anterior, posterior, medial and lateral.

Anterior

This will usually indicate chondral or osteochondral surface injury [2], most commonly to the talus rather than the tibia, and anterior impingement in the ankle [3].

With the former, pain usually occurs with walking, running and jumping and tends to be more problematic when climbing or descending stairs, slopes or steps or on uneven ground. Start-up pain may occur with standing, walking or the initial phase of running but tends to improve when the activity continues. There may be swelling indicating synovitis. Although, in the vast majority the lesion may be identified as medial or lateral by the patient, this lateralisation is not always reliable.

Impingement affecting the anterior aspect of the ankle usually results in pain, which is worse with walking or running up slopes or stairs. Landing at the end of a jump or squatting may aggravate the pain. Lateralisation is more unreliable with anterior impingement. Anterior distal tibial osteophytes, rarely, talar osteophytes or both are the usual cause of anterior impingement (Fig. 1). It is thought that they may arise as a result of minor repetitive injuries. In Europe, the condition may be referred to as "footballer's ankle" but it frequently occurs in other athletes.

Rarely, anterior ankle pain may occur with tibialis anterior tendinopathy or rupture.

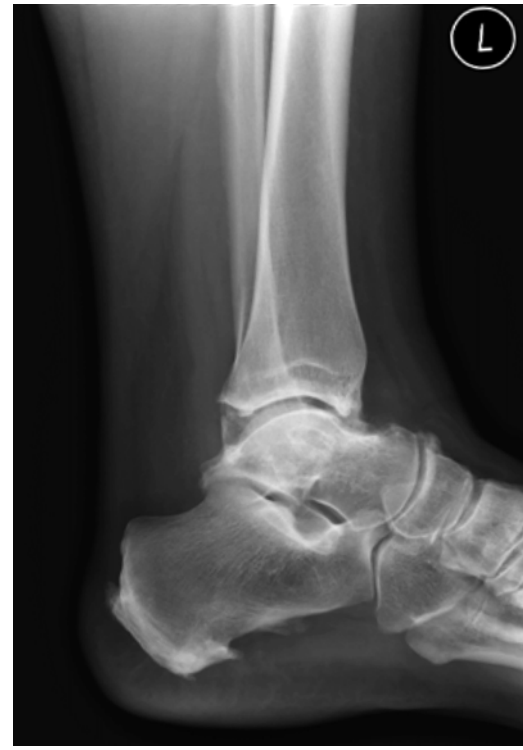

Fig. 1 Osteophytic anterior ankle impingement

Posterior

This normally occurs as a result of posterior ankle impingement [4]. It is common in Ballet dancers but may result from an inversion injury in other athletes. The commonest cause is the presence of an os trigonum with or without a fracture (Fig. 2). This occurs in 10 % of adults but if present 50 % of individuals will have the same condition on the contralateral side. Pain may arise as a result of disruption of the ligamentous attachment between the os trigonum and the postero-lateral process of the talus. However, pain is more common when degeneration is also present within the articulation. Usually, the complaint is of pain in the posterior aspect of the heel or deep in the ankle. Clearly, in Ballet aggravation of this pain occurs with the Pointe position but it may happen in any activity involving standing on tip-toe. Alternatively, and rarely, this may occur with injuries, including fractures, of the posteromedial process of Stieda, to the posterolateral ligaments and rarely with anomalous muscles [5].

Other potential causes include tendon injuries or tendinopathy (Achilles tendon, FHL), Haglund's disease or, rarely, tarsal tunnel syndrome.

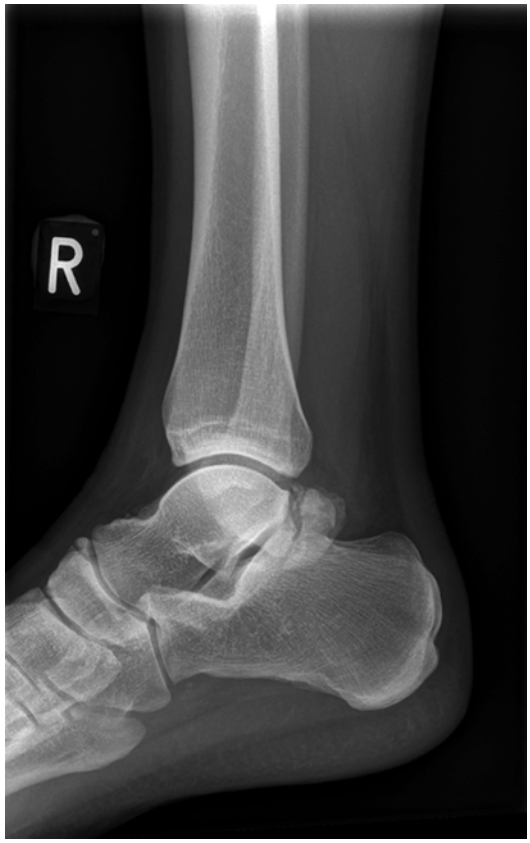

Fig. 2 Posterior talar process

Lateral

This may arise from unrecognised fractures, peroneal tendon tears or dislocation [6] or a recent sprain. There is usually quite marked anterolateral synovitis.

Unrecognised fractures affect the anterior process of the calcaneus [7], the lateral process of the talus [8] and the tuberosity of the fifth metatarsal. They are commonly associated with lateral ligament strains caused by inversion injuries. In each case they may involve a not insignificant part of the calcaneo-cuboid joint, posterior subtalar joint and fifth tarso-metatarsal joint respectively. In this regard they may lead to significant on-going lateral ankle and foot pain if there is a delay to diagnosis with the risk of premature osteoarthritis in the affected joints.

Ankle synovitis will normally cause anterolateral swelling with pain adjacent to the lateral malleolus, aggravated by going up and down stairs and running, and relieved by rest.

Peroneal tendon tears may or may not be associated with anterolateral instability. Peroneus brevis is more commonly torn than peroneus longus. The tear occurs at the tip of the fibula. Most patients do not present acutely but later with postero-lateral ankle pain and swelling along the tendon and its sheath. Increased activity will aggravate the discomfort especially traversing uneven ground.

Peroneal tendon dislocation may happen spontaneously but commonly occurs with lateral ankle sprains. It may be seen in skiers acutely, as they make a forceful turn in the snow but often occurs in other athletes with a similar mechanism. Usually, a "click or pop" may be heard or felt. Often the tendon spontaneously reduces and constantly redislocates or it may remain dislocated and be felt over the distal fibula. However, there is usually postero-lateral ankle pain with swelling and there may be recurrent "clicking and popping" with recurrent dislocation episodes. The condition tends to be worse when walking or running over uneven ground. Peroneal tubercle syndrome, usually in high performance athletes is a rare cause of lateral ankle pain [9].

Lateral "ankle" pain may also occur with injuries to the inferior tibio-fibular joint or interosseous membrane with or without associated fractures. The pain may be associated with instability, swelling and rotational discomfort usually external. Rarely, it may be associated with sinus tarsi syndrome and nerve entrapment [10].

Medial

Medial sprains to the superficial or deep deltoid ligaments, particularly the latter, very rarely occur without associated ankle fractures, usually on the lateral side. Occasionally, a tear or sprain of the tibialis posterior tendon may occur in isolation or be associated with deltoid ligament sprains. They usually follow an eversion strain but are somewhat dependent on the pre-existing morphology of the foot, particularly, pes planovalgus. In younger adults there may be an associated accessory navicular.

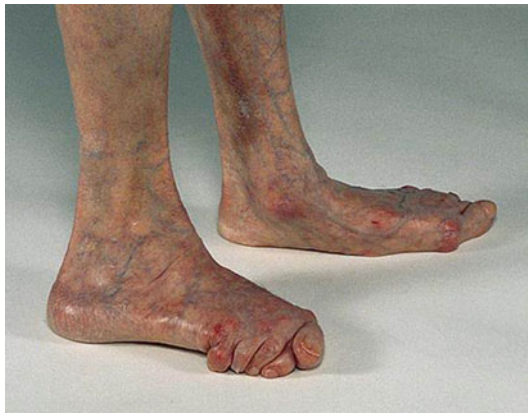

Fig. 3 Rheumatoid arthritis in the ankle

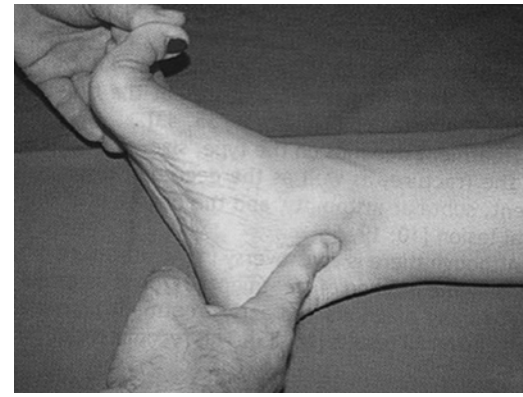

Fig. 4 Painful dorsiflexion of the great toe by stretching FHL

Rarely, FHL tendinopathy or tarsal tunnel syndrome may result in chronic medial ankle pain.

General

Finally, there are a number of other conditions, which may cause chronic ankle pain. In these cases it is not unusual for the patient to recall a history of injury potentially misleading the attending clinician. These include CRPS (Chronic Regional Pain Syndrome) type 1, and inflammatory disorders such as gout, pseudogout, reactive arthritis, septic arthritis and rheumatoid arthritis (Fig. 3).

Examination

A thorough examination of the patient including a general assessment, a neurological and vascular assessment of the lower limbs and a specific examination of the foot and ankle is mandatory bearing in mind the history from the patient. Routine assessment of the foot and ankle includes examination of the patient's shoewear and orthotics, followed by observation of the patient standing, walking and recumbent. Passive and active range of joint motion is recorded with an assessment of heel strike, midstance and toe-off when weight-bearing. The features of CRPS type 1 and inflammatory disorders should be sought.

Anterior

Anterior ankle pain is usually associated with synovitis, although the exact location may vary. With articular surface injuries there may be no other significant clinical features. However, anterior chondral or osteochondral talar dome injuries may provoke tenderness with the ankle plantar-flexed.

Anterior ankle impingement is usually associated with poor anterior tibial progression during the midstance phase of weight bearing and a block to dorsiflexion of varying degrees usually associated with anterior ankle tenderness and pain. Occasionally, ankle plantar-flexion may be painful.

Tibialis anterior tendinopathy is rare but usually typical with diffuse tendon thickening, crepitus with synovitis and pain on stressed dorsiflexion. Tibialis anterior rupture occasionally occurs in this situation.

Posterior

With posterior ankle impingement there is usually posteromedial or posterolateral point tenderness with swelling and marked pain on full plantar-flexion of the ankle. With a large os trigonum involving the subtalar joint there may be subtalar irritability or, rarely, instability. With posteromedial impingement dorsiflexion of the great toe stretching FHL may be particularly painful (Fig. 4).

Tendinopathy involving the Achilles tendon or FHL and Haglund's disease have characteristic local findings but the features of tarsal tunnel syndrome are more variable.

Lateral

Unrecognised fractures of the anterior process of the calcaneum, lateral process of the talus and tuberosity of the fifth metatarsal may be confirmed clinically by specific palpation directly over the anatomical site. Bruising and swelling may or may not be evident depending on the time from the injury.

Anterolateral or lateral synovitis may be evident, the latter usually with peroneal tendon tears. A dislocated peroneal tendon is easily felt over the distal fibula but the tendon may also be "dislocatable" and frequently demonstrated by the patient. It is sometimes bilateral but asymptomatic on the opposite side. A hypertrophic peroneal tubercle may be evident in peroneal tubercle syndrome with more distal swelling and tenderness over the peroneal tendons.

Inferior tibio-fibular joint injuries are usually characterised by tenderness over the anterior surface of the joint although this may extend more proximally and by pain on external rotation of the foot. In more severe cases the distal fibula may be obviously mobile. The features of associated fractures or other ankle and foot injuries may be evident.

Sinus tarsi syndrome reveals specific tenderness over the sinus tarsi often with localised tenderness and quite severe pain on full dorsiflexion and eversion of the foot and ankle. Nerve entrapment syndromes may have a positive Tinel's sign with sensory impairment distally.

Medial

There will normally be the features of associated fractures usually on the lateral side of the ankle. However, there may be specific tenderness with swelling over the deep deltoid ligament, the calcaneo-navicular ligament and tibialis posterior in patients with pes planovalgus. There may be tenderness and swelling over an accessory navicular.

Investigation

Radiographs

AP and lateral weight bearing views of the ankle and foot with oblique views of the foot will confirm the diagnosis in the vast majority of cases. Special views including those of Broden and Cobey are helpful in clarifying unrecognised fractures (Figs. 5 and 6). Stress X-rays may be useful in instability (Fig. 7).

Ultrasound

Ultrasound has become increasingly applied in the clinical setting, and is particularly helpful with tendinopathy. Previously, the remit of musculoskeletal radiologists this technique may be available in the clinic or office for foot and ankle surgeons trained in the many musculoskeletal ultrasound courses now available.

CT Scanning

This is generally more accepted in the trauma setting for calcaneal and talar fractures and Pilon fractures. Recent studies have supported its routine use in the clarification of posterior malleolar fractures. However, it is particularly useful for identifying the extent of fractures of the anterior process of the calcaneum and lateral process fractures of the talus (Fig. 8). It is helpful in determining fracture healing.

MRI Scanning

Most static abnormalities may be diagnosed by MRI scanning. However, it is particularly useful with intra-articular abnormalities such as chondral or osteochondral defects in the talus (Fig. 9), soft tissue abnormalities such as synovitis and tendinopathy. It is not as reliable when determining

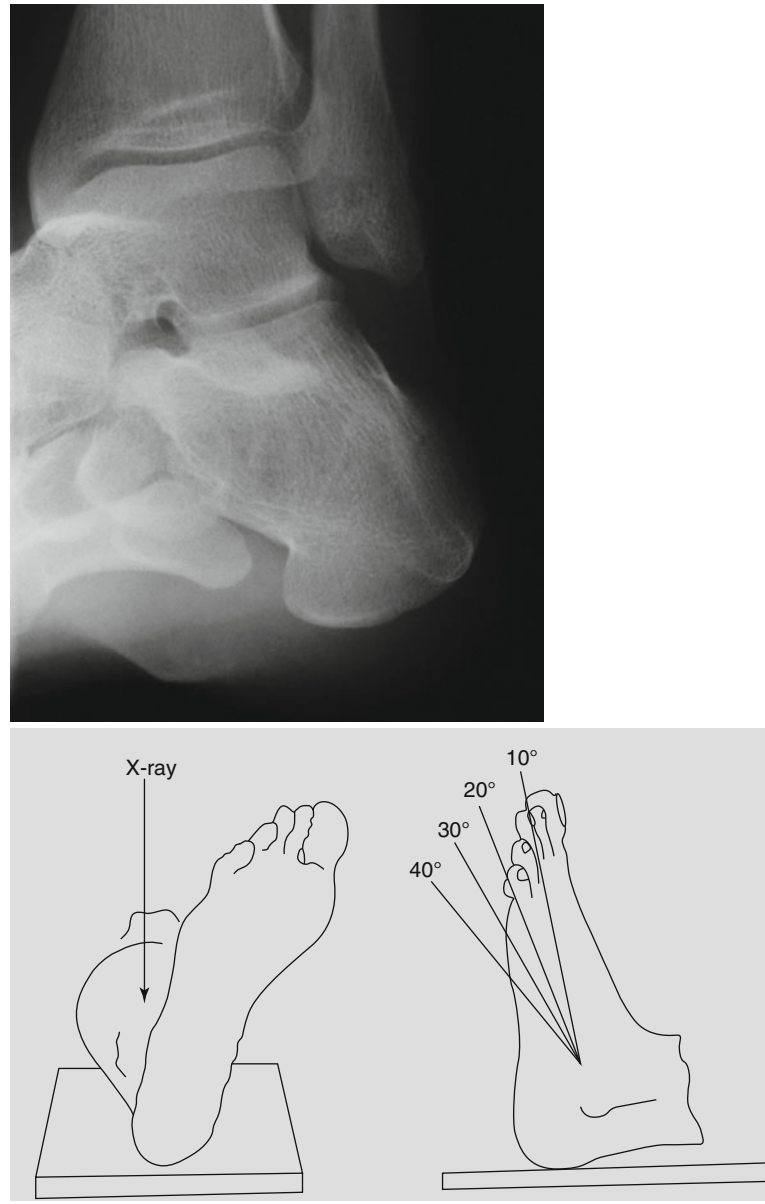

Fig. 5 Broden view

structural dynamic stability, for example, of the lateral ligament complex.

Nuclear Scanning

Standard bone scans may be helpful in clarifying more diffuse disease either locally or generally and may occasionally help with the localisation of particular joint abnormalities but their use is limited. Indium labelled scans may help clarify regarding infection. However, SPECT scanning is much more specific and is gaining popularity in assisting with the localisation of mainly degenerative disorders.

Management

Conservative management will usually have been commenced in the primary care setting prior to referral including analgesia, anti-inflammatory

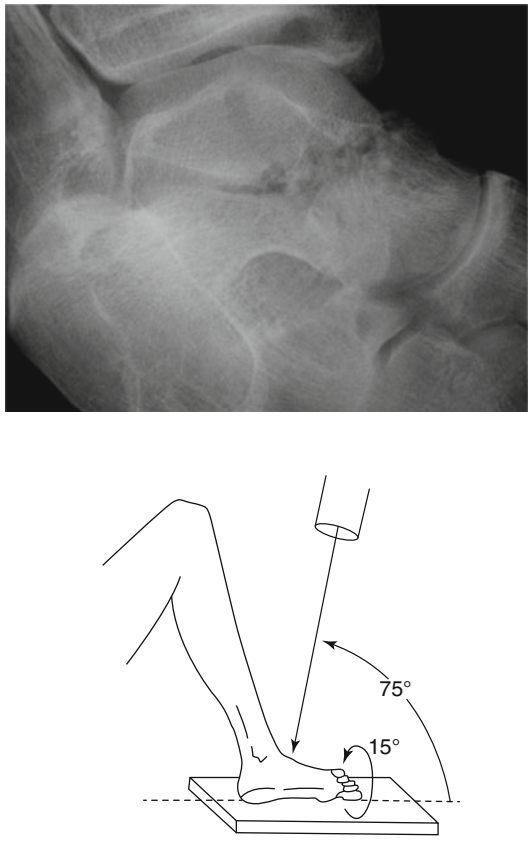

Fig. 6 Cobey view

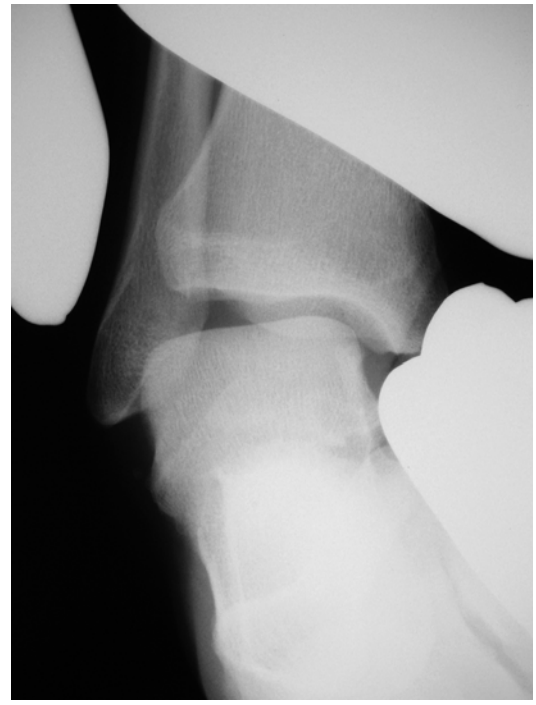

Fig. 7 Stress AP view of the ankle

gels or tablets, supports, orthotics and shoewear adjustments. A proportion will have been referred to physiotherapy. Most "simple" ankle injuries will resolve with this process. CRPS type 1 and inflammatory disorders should be referred to the appropriate speciality.

General

Following the history, examination and use of selective and specific investigation, the diagnosis will usually be apparent. However, in a proportion of cases there will be a place for diagnostic and often therapeutic injections under x-ray control with the use of confirmatory contrast injection. Therefore, this may be part of the investigative and management plan.

Recently, extracorporeal shock therapy [11] and autologous blood injection [12] has become popular for tendinopathies and other intractable conditions around the hindfoot such as plantar fasciopathy. Although preliminary results are encouraging their exact role remains uncertain. In general terms local anaesthetic and steroid injections for tendinopathy have lost favour because of the risk of tendon rupture.

Anterior

Persisting anterior ankle pain either from chondral or osteochondral lesions is an indication for ankle arthroscopy usually anterior but occasionally posterior when the surface lesion lies on the posterior half of the talus. Anterior synovitis will respond to synovectomy and anterior impingement with anterior cheilectomy. Open surgery for the latter should only rarely be required. However, it is useful to obtain an intra-operative radiograph to confirm adequate removal of the osteophytes. The treatment of chondral or more usually osteochondral lesions depends on the grade of the lesion but may include debridement, drilling, micro-fracture, bone graft and subsequently articular cartilage implantation in a proportion [2].

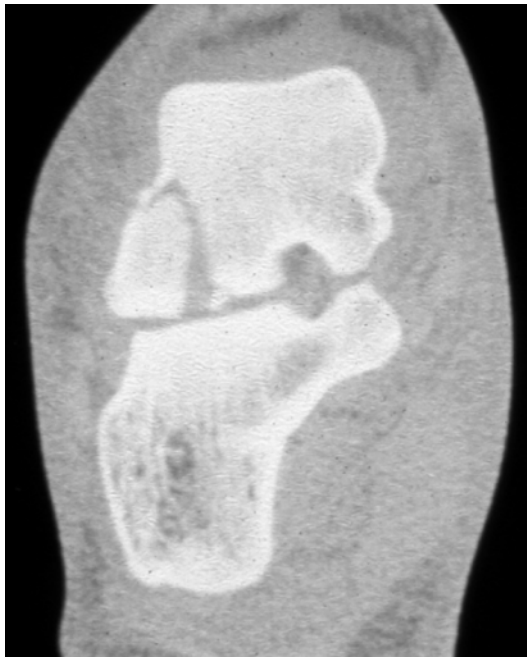

Fig. 8 CT scan lateral process fracture talus

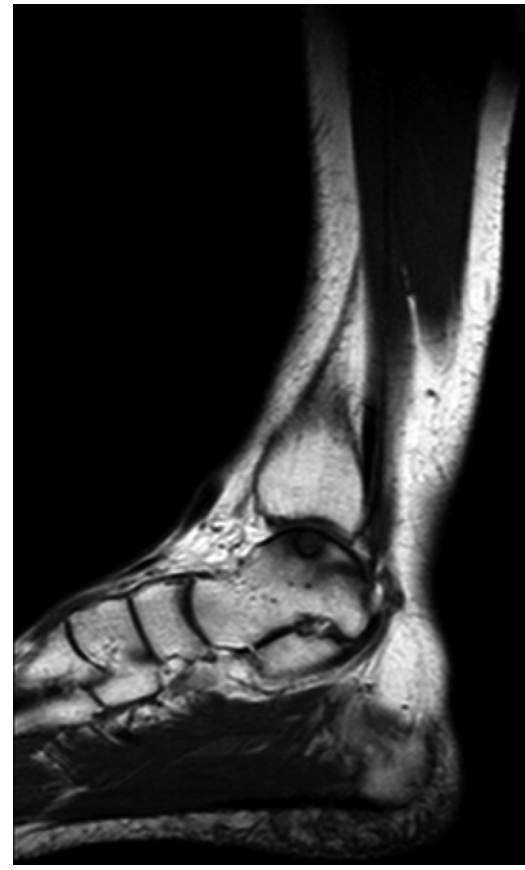

Fig. 9 Talar OCD

Posterior

The management of central Achilles tendinopathy, Haglund's disease and tarsal tunnel syndrome should be discussed elsewhere.

FHL tendinopathy may be treated endoscopically in isolation or as part of a posterior arthroscopic excision of an os trigonum or prominent and painful Stieda's process. FHL tendinopathy may specifically occur with the latter. Care should be exercised in relation to the extent of a posterior process lesion as some may include a sizeable portion of the posterior facet of the subtalar joint. This may be best assessed on a CT scan. Internal fixation in this situation may be preferred for unhealed posterior fractures as excision may lead to subtalar instability and premature osteoarthritis.

Lateral

The management of unrecognised fractures depends on their extent, the level of healing and the time from the initial causative injury. In general terms, if the fractures are small and have healed expectant treatment would be appropriate. Occasionally, small unhealed symptomatic fragments may be excised. However, if they are sizeable, involving the adjacent joint, and have not healed then open reduction and internal fixation may be appropriate. If there has been a significant delay to diagnosis then the patient should be warned about a potentially poor outcome.

Peroneal tendon tears and synovitis are more commonly treated by endoscopic means if refractory to conservative treatment. Peroneal tendon dislocation or subluxation may be accepted by the patient but operative treatment may be preferred in particularly painful cases. The surgery may be performed endoscopically [13] but is usually, and more simply, carried out using a small postero-lateral incision. The tendon or tendons may be reduced, the groove

deepened and the peroneal retinaculum repaired and secured to the distal fibula by a variety of techniques. Mitek anchors are commonly used, for example.

The management of refractory inferior tibiofibular joint pain depends on the extent of instability. If stable it may respond to a diagnostic and therapeutic injection with local anaesthetic and steroid injection alone. In the early stages after injury stabilisation by screw fixation or anchor and, usually, anterior ligament repair may prevent progression of the condition. Rarely, stabilisation by fusion may be required with intractable chronic pain arising from this joint. If persistent talar shift has occurred then appropriate management of the ensuing ankle osteoarthritis will be necessary.

Sinus tarsi syndrome often responds to a selective injection of local anaesthetic and steroid and rarely requires surgical decompression [14] but nerve entrapment will more usually benefit from surgery.

Medial

Isolated deltoid ligament tears with or without associated fractures with persisting pain may be treated by local anaesthetic and steroid injection. Rarely, with associated instability it is appropriate to repair the ligament and secure it with an anchor (Mitek) more frequently to the medial malleolus. This will normally resolve matters [15].

The treatment of tibialis posterior tendinopathy, accessory navicular, calcaneo-navicular ligament tears and pes plano-valgus, tarsal tunnel syndrome and FHL tendinopathy should be discussed elsewhere.

Conclusions

Unfortunately, persistent pain after ankle sprain remains common. However, a sensible and systematic approach to the history of the initial injury, the current symptoms, a thorough examination, the appropriate use of the relevant investigations and a methodical management plan will alleviate the symptoms and disability in the vast majority and reduce the risk of complications in the longer term.

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