Volume 48 Supplement 1 June 2017 ISSN 0020-1383

ELSEVIER

Decade of Action for Road Safety 2011-2020 Supported by *Injury*

Official Journal of the British Trauma Society

Gerhard Küntscher Society

Italian Society of Orthopaedics & Traumatology

Official Journal of the Saudi Orthopaedic Association

Official Journal of the Australasian Trauma Society

AOTrauma

European Society of Tissue Regeneration in Orthopaedics and Traumatology

Groupe d'Etude en Traumatologie Ostéoarticulaire

Croatian Trauma Society

Brazilian Association of Orthopedic Trauma

Club Italiano Osteosintesi

Turkish Orthopaedic Trauma Society

Spanish Society of Orthopaedic Surgery and Traumatology (SECOT)

BOTA British Orthopaedic Trainees Association

Hungarian Trauma Society

Trauma Society of India

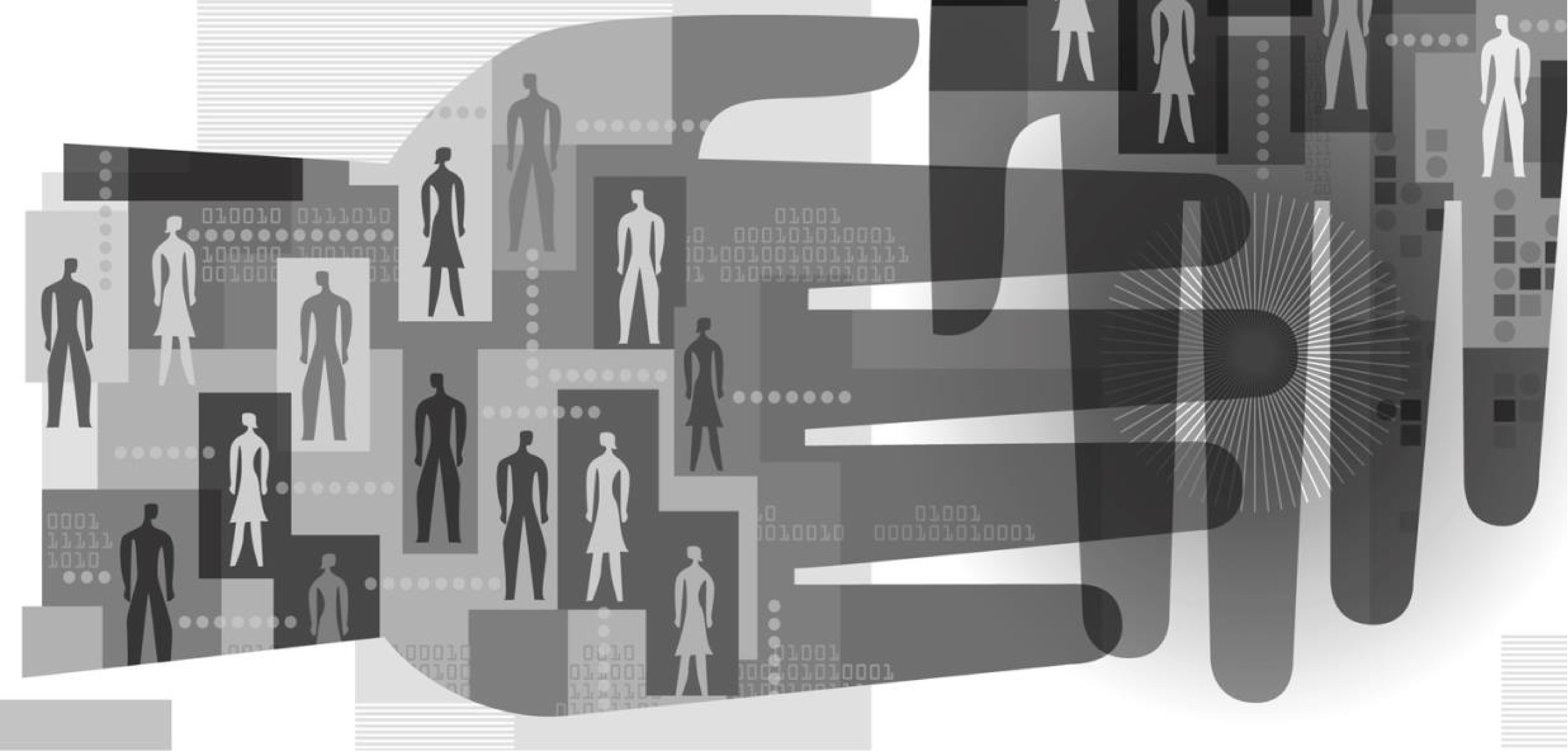
Osteosynthesis & Trauma Care Foundation

Injury

International Journal of the Care of the Injured

Complications of intramedullary nailing - Evolution of treatment

Guest Editors: Volker Alt, Hamish Simpson and Theodore Miclau



INJURY

International Journal of the Care of the Injured

Official Journal of the British Trauma Society, the Australasian Trauma Society and the Saudi Orthopaedic Association in Trauma and affiliated with the Italian Society of Orthopaedics and Traumatology, the Gerhard Küntscher Society, the Spanish Society of Orthopaedic Surgery and Traumatology (SECOT), the Turkish Orthopaedic Trauma Society, AOTrauma, Group d'Etude en Traumatologie Ostéoarticulaire, the Croatian Trauma Society, the Brazilian Association of Orthopedic Trauma, the Club Italiano Osteosintesi and the European Society of Tissue Regeneration in Orthopaedics and Trauma.

Complications of intramedullary nailing - Evolution of treatment

Guest Editors:

Volker Alt, Hamish Simpson and Theodore Miclau

OTC

Osteosynthesis & Trauma Care Foundation

Support for the 2015 workshop entitled "Intramedullary Nailing – Evolution of Treatment" and this subsequent supplement was provided by the Osteosynthesis and Trauma Care Foundation (OTC) sponsored by a research grant from Stryker

INJURY

International Journal of the Care of the Injured

Author inquiries: You can track your submitted article at http://www.elsevier.com/track-submission. You can track your accepted article at http://www.elsevier.com/trackarticle. You are also welcome to contact Customer Support via http://support.elsevier.com

For a full and complete Guide for Authors, please go to: http://www.elsevier.com/locate/injury.

Publication information: *Injury* (ISSN 0020-1383). For 2017, volume 48 (12 issues) is scheduled for publication. Subscription prices are available upon request from the Publisher or from the Elsevier Customer Service Department nearest you or from this journal's website (http://www.elsevier.com/locate/injury). Further information is available on this journal and other Elsevier products through Elsevier's website (http://www.elsevier.com). Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by standard mail (surface within Europe, air delivery outside Europe). Priority rates are available upon request. Claims for missing issues should be made within six months of the date of dispatch.

Orders, claims, and journal enquiries: please contact the Elsevier Customer Service Department nearest you: **St. Louis:** Elsevier Customer Service Department, 3251 Riverport Lane, Maryland Heights, MO 63043, USA; phone: (800) 6542452 [toll free within the USA]; (+1) (314) 4478871 [outside the USA]; fax: (+1) (314) 4478029; e-mail: JournalsCustomerService-usa@elsevier.com **Oxford:** Elsevier Customer Service Department, The Boulevard, Langford Lane, Kidlington OX5 1GB, UK; phone: (+44) (1865) 843434; fax: (+44) (1865) 843970; e-mail: JournalsCustomerServiceEMEA@elsevier.com **Tokyo:** Elsevier Customer Service Department, 4F Higashi-Azabu, 1-Chome Bldg, 1-9-15 Higashi-Azabu, Minato-ku, Tokyo 106-0044, Japan; phone: (+81) (3) 5561 5037; fax: (+81) (3) 5561 5047; e-mail: JournalsCustomerService Japan@elsevier.com **Singapore:** Elsevier Customer Service Department, 3 Killiney Road, #08-01 Winsland House I, Singapore 239519; phone: (+65) 63490222; fax: (+65) 67331510; e-mail: JournalsCustomerServiceAPAC@elsevier.com

Injury has no page charges.

Printed by Henry Ling Ltd., The Dorset Press, Dorchester, UK

INJURY

International Journal of the Care of the Injured

Official Journal of the British Trauma Society, the Australasian Trauma Society and the Saudi Orthopaedic Association in Trauma and affiliated with the Societa' Italiana Di Ortopedia e Traumatologia, The Gerhard Kuentscher Society, the Spanish Society of Orthopaedic Surgery and Traumatology (SECOT), the Turkish Orthopaedic Trauma Society, AOTrauma, the Group d'Etude en Traumatologie Ostéoarticulaire, the Croatian Trauma Society, the Brazilian Association of Orthopedic Trauma, the Trauma Society of India, the Club Italiano Dell'Osteosintesi (CIO) and the European Society of Tissue Regeneration in Orthopaedics and Trauma (ESTROT).

Volume 48 Supplement 1, June 2017

Contents

Complications of intramedullary nailing - Evolution of treatment
Guest Editors: Volker Alt, Hamish Simpson and Theodore Miclau

0020-1383(201706)48:S1;1-U

Injury is abstracted/indexed by: Current Contents, Science Citation Indexed Expanded, Index Medicus, Pubmed/Medline and EMBASE. Also covered in the abstract and citation database SCOPUS®.

Section V: Non-unions

USA mailing notice: *Injury* (ISSN 0020-1383) is published monthly by Elsevier Ltd. (P.O. Box 211, 1000 AE Amsterdam, The Netherlands). Periodicals postage paid at Jamaica, NY 11431 and additional mailing offices.
USA POSTMASTER: Send change of address to *Injury*, Elsevier Customer Service Department, 3251 Riverport Lane, Maryland Heights, MO 63043, USA.
AIRFREIGHT AND MAILING in USA by Air Business Ltd., c/o Worldnet Shipping Inc., 156-15, 146th Avenue, 2nd Floor, Jamaica, NY 11434, USA.

∞ The paper used in this publication meets the requirements of ANSI/NISO Z 39.48–1992 (Permanence of Paper)

Injury, Int. J. Care Injured 48S (2017) S1–S2

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Editorial

Intramedullary nailing—Evolution of treatment

Intramedullary nailing has become one of the most important internal fixation procedures in modern orthopaedic trauma surgery. After first attempts to use wooden sticks as intramedullary stabilizers by Maya doctors and further experiments with intramedullary implants made from tusks, antlers or cow bone from European and Americans surgeons before the 20th century, the first "modern" intramedullary nailing procedure was performed by Gerhard Küntscher in 1939 [1,2]. He introduced three key concepts, which were the insertion of nails from an entrance point at a distance to the fracture site without disrupting the fracture hematoma, the use of a sufficient calibre of the implant, and of the full length of the intramedullary canal for sufficient biomechanical stabilization of the fractured extremity [2]. Küntscher reported on 13 cases treated with intramedullary nailing at the Annual Meeting of the German Surgical Society in March 1940 [3]. World War II and post-war turmoil brought the concept of intramedullary nailing to the United States as formerly captured US soldiers were treated with this method in Germany. TIME magazine reported on one of the first repatriated nailing cases in its issue of March 12, 1945: "At England General Hospital in Atlantic City last week was a wounded soldier with a strangely mended femur (thighbone). The man had been treated by the Germans, his captors. When the broken bone failed to heal, after weeks of conventional treatment, the soldier was operated on. He was mystified to find that his only new wound was a $2^1/_2$-in. incision above the hipbone. Two days later, the German surgeons told him to move his leg; a few days after that, they told him to walk. He did. He has walked ever since." [4]. Klaus Klemm and Dieter Schellmann introduced the idea of putting bone screws in small holes of the nail and called this construct an "interlocking nail" [5], which remains the basic principle of modern intramedullary treatment of long bone shaft fractures today.

Despite these indisputable achievements, surgeons and researchers are still faced with open questions on how to further improve clinical outcome after nailing, specifically by avoiding complications and optimizing basic principles. Inclusion of relevant related technologies and a deeper understanding of biological and mechanical aspects are cornerstones in this regard and were the focus of a workshop entitled "Intramedullary Nailing – Evolution of Treatment," sponsored by the Orthopaedic Trauma Care (OTC) Foundation in Zurich from November 2–3, 2015.

The OTC is a global network of surgeons and scientists, dedicated to the advancement of osteosynthesis and trauma care, which has addressed several "hot topics" in orthopaedic trauma care, e.g. biological and biomechanical aspects of osteoporotic fractures, in previous workshops. The proceedings of these workshops have been published as Supplement issues in Injury [6–8].

The current Supplement intends to provide 18 "mini reviews" on essential topics linked to the aforementioned workshop in Zurich on intramedullary nailing from experts and key opinion leaders in the field. In this issue, central theme topics include (1) the systemic response after trauma and nailing, (2) reduction techniques and (3) technique-related complications, such as insertion site pain or compartment syndrome. Furthermore, recent developments including locking solutions and intramedullary lengthening techniques are comprehensively presented.

We hope that a wide range of colleagues will benefit from the information provided and that next the next-generation improvements in intramedullary nailing will further improve patient outcomes.

Acknowledgements

The Guest Editors and all other authors of this Supplement express their thanks to the Orthopaedic Trauma Care Foundation (OTCF) and the grantor Stryker® for the sponsorship of the workshop in Zurich 2015 and of this Supplement in Injury.

References

[1] Farill J. Orthopedics in Mexico. J Bone Joint Surg Am 1952;24:506–12.
[2] Seligson D. History of intramedullary nailing. In: Rommens PM, Hessmann MH, editors. Intramedullary nailing. London, Heidelberg, New York, Dordrecht: Springer; 2015. p. 3–12.
[3] Küntscher G. Die Marknagelung von Knochenbrüchen. Langenbecks Arch Chir 1940;200:443–55.
[4] Medicine: Amazing Thighbone. The Time Magazine. March 12, 1945.
[5] Klemm K, Schellmann WD. Dynamische und statische Verriegelung des Marknagels. Unfallheilkunde 1972;75:568–75.
[6] Bottlang M, Augat P. The bottleneck of evidence-based fracture care. Injury 2014;45(Suppl. 2):S1–2.
[7] Alt V, Miclau T. Osteoporotic fractures—the biological perspective. Injury 2016;47(Suppl. 1):S1–2.
[8] Augat P, Goldhahn J. Osteoporotic fracture fixation—a biomechanical perspective. Injury 2016;47(Suppl. 2):S1–2.

Volker Alt*
Hamish Simpson
Theodore Miclau
Department of Trauma, Hand and Reconstructive Surgery, Giessen University Hospital Giessen-Marburg, Campus Giessen, Rudolf-Buchheim-Str. 7, 35385 Giessen, Germany

http://dx.doi.org/10.1016/j.injury.2017.04.034

Department of Trauma and Orthopaedics, University of Edinburgh, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh, EH16 4SA, UK

Orthopaedic Trauma Institute, UCSF, San Francisco General Hospital, 2550 23rd Street Building 9, 2nd Floor, San Francisco, CA 94110, USA

* Corresponding author at: Department of Trauma Surgery, University Hospital Giessen-Marburg, Campus Giesen, Rudolf-Buchheim-Str. 7, 35392 Giessen, Germany.
E-mail address: volker.alt@chiru.med.uni-giessen.de (V. Alt).

Injury, Int. J. Care Injured 48S (2017) S3–S6

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Timing of definitive fixation of major long bone fractures: Can fat embolism syndrome be prevented?

Taco J. Blokhuis[a,*], Hans-Christoph Pape[b], Jan-Paul Frölke[c]

[a] Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands
[b] Department of Orthopaedics and Traumatology, University Hospital RWTH Aachen, Germany
[c] Department of Surgery, Universitair Medisch Centrum Radboud, Nijmegen, The Netherlands

A R T I C L E I N F O

Keywords:
Fat embolism
Fat embolism syndrome
Safe Definitive Surgery (SDS)
Damage control orthopaedics
Femur fracture

A B S T R A C T

Fat embolism is common in patients with major fractures, but leads to devastating consequences, named fat embolism syndrome (FES) in some. Despite advances in treatment strategies regarding the timing of definitive fixation of major fractures, FES still occurs in patients. In this overview, current literature is reviewed and optimal treatment strategies for patients with multiple traumatic injuries, including major fractures, are discussed. Considering the multifactorial etiology of FES, including mechanical and biochemical pathways, FES cannot be prevented in all patients. However, screening for symptoms of FES should be standard in the pre-operative work-up of these patients, prior to definitive fixation of major fractures.

Introduction

Fat embolism is very common in femoral shaft fractures, with an incidence of 95% [1]. In some patients this results in fat embolism syndrome (FES), a severe complication that occurs in 1–10% of patients in isolated femoral fractures and even more frequently in bilateral fractures [2]. The exact etiology of FES remains controversial. A mechanical explanation describes that FES results from fat and intramedullary contents that are released from the fracture and entered into the circulation. Due to embolisation of these particles respiratory dysfunction and severe neurological complications can occur [3]. Some authors claim that the emboli can be released from the medullary cavity directly from the fracture, whereas others suggest a relation with increased intramedullary pressure during reaming or insertion of an intramedullary nail [4]. A biochemical theory states that FES results from a proinflammatory state. This, in turn, is evoked by products from bone marrow fat, leading to end-organ dysfunction [3,5]. The combination of mechanical and biochemical phenomena is likely to occur, and explains the diverse onset of symptoms as well as the combination of venous and arterial symptoms [6].

Timing of definitive intramedullary fracture fixation in the context of FES remains a controversial subject. Especially in patients with multiple traumatic injuries the discussion focusses on early total care versus damage control orthopaedics. The arguments in this discussion are the advantages of early fixation (less blood loss, fat embolism) versus the risk of serious complications in early definitive fixation (the ‘second hit’). Especially the intramedullary fixation of femur fractures is subject of discussion, as these fractures are associated with high energy trauma as well as with a relatively high rate of systemic complications. This overview aims to describe trends in timing of fixation over the last decades and to illustrate the contemporary state of the art. The focus will be on the relation between timing of definitive fixation and incidence of systemic complications, in particular the fat embolism syndrome.

Historical perspective

In the beginning of intramedullary fixation, early nailing of long bone fractures in multitrauma patients was associated with mortality rates up to 50%. For this reason early definitive fixation was abandoned and replaced by delayed fixation at day 10–14. Following these insights it was Küntscher himself [7] who recommended to delay nailing as long as symptoms of fat embolization are present, and to wait a few days in any definitive major fracture fixation. However, delayed fixation leads to prolonged immobilization, which is associated with complications

* Corresponding author at:.Department of Surgery, Maastricht University Medical Center +, Postbus 5800, 6202 AZ Maastricht, the Netherlands
E-mail address: Taco.Blokhuis@mumc.nl (T.J. Blokhuis).

http://dx.doi.org/10.1016/j.injury.2017.04.015
0020-1383/© 2017 Published by Elsevier Ltd.

such as decubitus and pneumonia. In fact, delayed fracture fixation was shown to induce longer ICU admissions [8].

In the early 1980s the treatment protocols began to change. Following several well-documented prospective studies on early fracture fixation [9,10] general practice changed into fixation of fractures in the first days after trauma, both for major and minor fractures. Early mobilization and a decrease of ARDS incidence were achieved, but the more aggressive approach resulted in a shift towards very early fixation of all fractures, in the first 24 h after injury. This, in turn, evoked a higher incidence of complications, due to increased blood loss and the phenomenon we now know as the second hit; a challenge to the patient's physiology by aggravating the inflammatory response to trauma [11,12]. Specifically, in the multitrauma patients the very early definitive fixation of major fractures resulted in life threatening complications; ARDS and multiple organ failure.

The introduction of damage control orthopedics followed the insights obtained from analysis of the aggressive approach. In selected patients, life-saving procedures are performed timely and as minimally invasive as possible, followed by resuscitation in the intensive care unit and definitive fracture fixation when the patient's physiology allows. This damage control orthopedics strategy has now been widely adopted and several publications show improvement of patient outcome parameters, especially in inflammatory parameters, in this staged approach [10,13–15]. Other studies, however, have not been able to reproduce these results [16] and show limited effectiveness. Still, the staged approach has not shown the high incidence of complications associated with early definitive fixation of fractures that was observed previously. Demonstrating the effectiveness of damage control orthopedics may therefore well be limited by the acute and urgent nature of the patient population.

State of the art: timing of definitive fixation

In 2014, the Eastern Association for the Surgery of Trauma published their guidelines on timing of fracture stabilization in polytrauma patients [17]. For this guideline a critical review of all available literature was performed according to the GRADE criteria. Although the quality of the retrieved studies was rated as limited by these criteria, this guideline addresses the discussion on timing of fixation of femur fractures by analyzing the outcome parameters mortality, infection, venous thromboembolism (VTE), nonunion or malunion and amputation. For mortality, infection and VTE early internal fixation, within 24 h after injury, showed better results than delayed internal fixation. The authors concluded from their extensive literature review that early internal fixation should be considered in all femur fractures in the absence of clear contraindication to surgery or anesthesia. However, their conclusions are conditional, with specific recommendations to use the guideline to inform the decision-making process only. In selecting the studies used for review, studies on damage-control orthopedics were left out as external fixation was not a subject of their analysis. Also, no conclusions can be drawn on other outcomes such as fat embolism and compartment syndrome.

Prevention of fat embolism syndrome?

Most studies, as described above, focus on systemic complications related to major fractures and the fixation of major fractures. The incidence of fat embolism syndrome is often not taken into account, as the number of patients is too low. In the literature most descriptions regarding fat embolism syndrome are given based upon a specific case, such as in a recent overview on fat embolism syndrome by Kosova et al. [6]. The cases often illustrate the onset of symptoms, but more importantly, the relation between treatment and onset of symptoms. Unfortunately, many cases describe the onset of symptoms prior to intramedullary instrumentation [1,18,19]. This phenomenon is consistent with a combined mechanical and biochemical etiology of fat embolism syndrome [3,6], and it means indirectly that the incidence of fat embolism syndrome should not be an argument in the discussion on timing of definitive fixation of fractures. In other words, the cases in the literature support the idea that the fat embolism syndrome will occur in some patients, irrespective of the definitive treatment, and can therefore not be prevented by changing the timing of definitive fixation of major fractures. On the other hand, the presence of clinical signs of fat embolism syndrome should always lead to the decision to delay intramedullary instrumentation in a patient. Fortunately the general prognosis of fat embolism syndrome is good. Mortality has decreased to less than 10% [20], and in patients who survive most symptoms will resolve [21].

Practical consequences

In patients with multiple traumatic injuries the decision on timing of intervention with respect to the fracture care is part of a process called Safe Definitive Orthopaedic Surgery (SDS) [22]. The decision making within the SDS process depends largely on the physiological condition of the patient, but also on other clinical and environmental parameters. For example, has the patient been transferred from a rural area with considerable delay, or did the patient get injured in an urban environment with rapid rescue? The latter patient is expected to deteriorate further within the first hours after presentation, whereas the delayed patient may have reached a more stable physiology. The process is therefore dynamic, including repeated assessment of the patient. Four categories of patients can be used in the decision making [15]; patients can be stable, borderline, unstable or in extremis. For stable patients and patients in extremis the optimal strategy is quite simple; respectively early total care and resuscitation should be initiated. In stable patients with a serious brain injury [23] or borderline patients their condition should be reassessed in the operating room and if the patient remains stable, intramedullary nailing can be performed directly. An unstable patient must be properly stabilized first (correction of acidosis and life-saving operations such as laparotomy or embolization) and then assessed how soon definitive internal fixation is justified [24]. A temporary traction splint can be used to perform definitive fixation the next day. An external fixator is indicated for prolonged immobilization. In patients in extremis life-saving measures are crucial, followed by a damage control approach to their other injuries. Again, this decision making process is dynamic, meaning that repeated assessment of the patient should take place constantly during the first days after trauma (Fig. 1).

Using the SDS approach in severely injured patients helps in restoring the patient's physiology and to improve survival. Whether it can help in preventing FES is another question. Considering the etiology of FES, based on a combination of mechanical and biochemical causes, it is even unlikely that FES can be prevented in all patients irrespective of the chosen strategy. This is underlined by the onset of symptoms of FES as described throughout the literature. Once symptoms have started, however, it appears logical to delay intramedullary instrumentation in these patients, and therefore ruling out FES should be a part of the preoperative workup.

Conflict of interest

None.

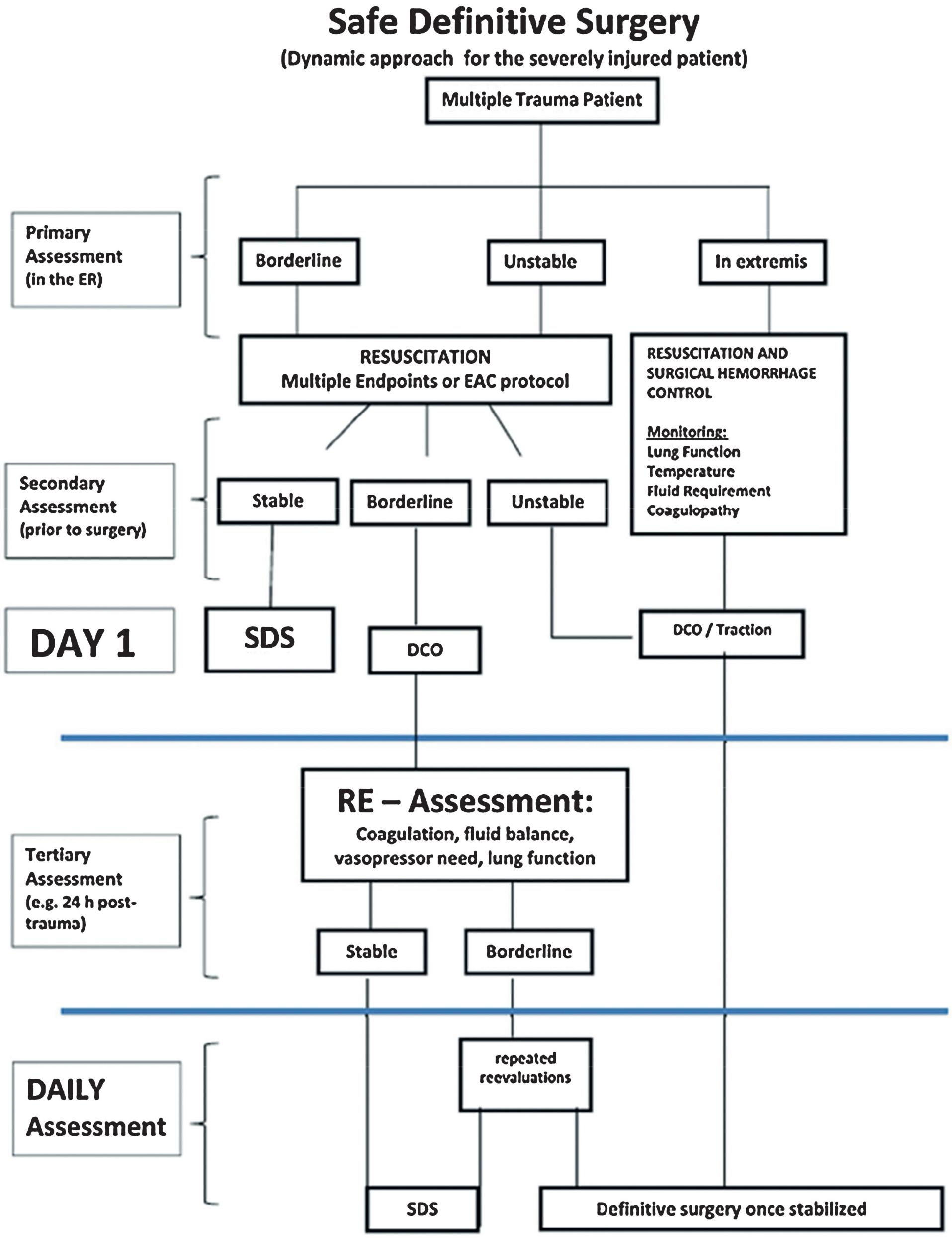


Fig. 1. Flow chart for Safe Definitive Surgery (SDS) (22).

References

[1] Randelli F, Capitani P, Pace F, Favilla S, Galante C, Randelli P. Bilateral femoral shaft fractures complicated by fat and pulmonary embolism: a case report. Injury 2015;46(Suppl. 7):S28–30.
[2] Stein PD, Yaekoub AY, Matta F, Kleerekoper M. Fat embolism syndrome. Am J Med Sci 2008;336(6):472–7.
[3] Husebye EE, Lyberg T, Roise O. Bone marrow fat in the circulation: clinical entities and pathophysiological mechanisms. Injury 2006;37(Suppl. 4):S8–18.
[4] Giannoudis PV, Tzioupis C, Pape HC. Fat embolism: the reaming controversy. Injury 2006;37(Suppl. 4):S50–8.
[5] Prakash S, Sen RK, Tripathy SK, Sen IM, Sharma RR, Sharma S. Role of interleukin-6 as an early marker of fat embolism syndrome: a clinical study. Clin Orthop Relat Res 2013;471(7):2340–6.
[6] Kosova E, Bergmark B, Piazza G. Fat embolism syndrome. Circulation 2015;131 (3):317–20.
[7] Küntscher G. Practice of intramedullary nailing. Springfield, IL: Charles Thomas; 1967.
[8] Seibel R, LaDuca J, Hassett JM, Babikian G, Mills B, Border DO, et al. Blunt multiple trauma (ISS 36), femur traction, and the pulmonary failure-septic state. Ann Surg 1985;202(3):283–95.
[9] Bone LB, Johnson KD, Weigelt J, Scheinberg R. Early versus delayed stabilization of femoral fractures: a prospective randomized study. J Bone Joint Surg Am 1989;71(3):336–40.
[10] Nahm NJ, Vallier HA. Timing of definitive treatment of femoral shaft fractures in patients with multiple injuries: a systematic review of randomized and nonrandomized trials. J Trauma Acute Care Surg 2012;73(5):1046–63.
[11] Giannoudis PV, Abbott C, Stone M, Bellamy MC, Smith RM. Fatal systemic inflammatory response syndrome following early bilateral femoral nailing. Intensive Care Med 1998;24(6):641–2.
[12] Scalea TM, Boswell SA, Scott JD, Mitchell KA, Kramer ME, Pollak AN. External fixation as a bridge to intramedullary nailing for patients with multiple injuries and with femur fractures: damage control orthopedics. J Trauma 2000;48(4):613–23.
[13] O'Toole RV, O'Brien M, Scalea TM, Habashi N, Pollak AN, Turen CH. Resuscitation before stabilization of femoral fractures limits acute respiratory distress syndrome in patients with multiple traumatic injuries despite low use of damage control orthopedics. J Trauma 2009;67(5):1013–21.
[14] Pape HC, Grimme K, Van GM, Sott AH, Giannoudis P, Morley J, et al. Impact of intramedullary instrumentation versus damage control for femoral fractures on immunoinflammatory parameters: prospective randomized analysis by the EPOFF Study Group. J Trauma 2003;55(1):7–13.

[15] Pape HC, Tornetta III P, Tarkin I, Tzioupis C, Sabeson V, Olson SA. Timing of fracture fixation in multitrauma patients: the role of early total care and damage control surgery. J Am Acad Orthop Surg 2009;17(9):541–9.
[16] Tuttle MS, Smith WR, Williams AE, Agudelo JF, Hartshorn CJ, Moore EE, et al. Safety and efficacy of damage control external fixation versus early definitive stabilization for femoral shaft fractures in the multiple-injured patient. J Trauma 2009;67(3):602–5.
[17] Gandhi RR, Overton TL, Haut ER, Lau B, Vallier HA, Rohs T, et al. Optimal timing of femur fracture stabilization in polytrauma patients: a practice management guideline from the Eastern Association for the Surgery of Trauma. J Trauma Acute Care Surg 2014;77(5):787–95.
[18] Aggarwal R, Pal S, Soni KD, Gamangatti S. Massive cerebral fat embolism leading to brain death: a rare presentation. Indian J Crit Care Med 2015;19 (11):687–9.
[19] Eriksson EA, Schultz SE, Cohle SD, Post KW. Cerebral fat embolism without intracardiac shunt: a novel presentation. J Emerg Trauma Shock 2011;4 (2):309–12.
[20] Talbot M, Schemitsch EH. Fat embolism syndrome: history, definition, epidemiology. Injury 2006;37(Suppl. 4):S3–7.
[21] Habashi NM, Andrews PL, Scalea TM. Therapeutic aspects of fat embolism syndrome. Injury 2006;37(Suppl. 4):S68–73.
[22] Pape HC, Pfeifer R. Safe definitive orthopaedic surgery (SDS): repeated assessment for tapered application of Early Definitive Care and Damage Control?: an inclusive view of recent advances in polytrauma management. Injury 2015;46(1):1–3.
[23] Giannoudis PV, Veysi VT, Pape HC, Krettek C, Smith MR. When should we operate on major fractures in patients with severe head injuries? Am J Surg 2002;183(3):261–7.
[24] Vallier HA, Wang X, Moore TA, Wilber JH, Como JJ. Timing of orthopaedic surgery in multiple trauma patients: development of a protocol for early appropriate care. J Orthop Trauma 2013;27(10):543–51.

Injury, Int. J. Care Injured 48S (2017) S7–S9

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Damage control and intramedullary nailing for long bone fractures in polytrauma patients

Peter Patka

Department of Trauma Surgery and Emergency Medicine; Nc017, Erasmus MC, University Medical, Center Rotterdam, P.O. Box 2040, Rotterdam, 3000 CA, The Netherlands

ARTICLE INFO

Keywords:
Long bone fracture
Intramedullary nail
Polytrauma
Fracture treatment
Damage control

ABSTRACT

The early fracture treatment in patients with multiple injuries should be focused on damage control. The fracture type and its location, local soft tissue condition as well as the patient's physiological condition shall determine the time and type of fracture treatment. Prevention of local and systemic complications must be immediately considered and included in the treatment planning. The use of external fixator (ExFix), which will be replaced by IM-implants in most cases at a later stage, provides adequate temporary fracture stabilization with less collateral damage.

Good clinical results can be expected in patients with long bone fractures if the principles of damage control surgery are applied and local complications are prevented through proper reduction, firm fixation, early soft tissue reconstruction, and early rehabilitation.

Introduction

Fractures of long bones are not infrequently associated with a wide range of additional trauma, such as soft tissue, vascular, neurological and systemic/organ injuries. Therefore, the ‘damage control concept’ for long bone fractures should focus on restoration/preservation of the patient’s physiological state, safe management of solid organ injuries and adequate temporarily fracture stabilization of the affected extremities [1].

The ultimate rule of damage control for long bone fractures is “Life over limb”! [2–4] This means that the therapeutic approach for long bone fractures may be substantially different from a single fracture treatment. In extreme situations, in some severe trauma cases, amputation may be the only chance for a patient’s survival and recovery [5]. The optimal sequencing of therapeutic procedures for trauma patients with long bone fractures is:

- save life (get patient out of the Death Triangle).
- save the extremity (Vascularity, Ischemia, Compartment Syndrome).
- secure neurology (Sensibility, Paresis/paralysis).
- prevent complications (Local & systemic).

This all should be done in order to allow an optimal treatment including nursing and advanced diagnostic procedures and additional therapeutic procedures. In the longer term, this policy prevents complications and allows prompt rehabilitation [6].

Decision process

In the physiologically unstable polytrauma patient, the initial Trauma protocol includes immediate damage control of all life threatening injuries (wounds, soft tissue, organs, vascular & neurological damage) and primary diagnostic procedures (CT scans- standard Radiographs). This, more or less “universal”, Trauma protocol should be leading in the first few hours after injury has occurred and must be respected by all personnel providing treatment.

In most cases of long bone fractures, the diagnosis leads to treatment of a complex injury. The fracture type and location as well as the patient's condition and local soft tissue condition must determine the time and type of fracture treatment.

Clinical judgment based on the assessment of the patient’s overall physiological condition is of vital importance not only for the purposes of damage control but also to assure the best outcome. Therefore, damage control should be seen as a complex injury treatment in which the motto is: see the patient first, save his live, save his extremity and prevent complications. For instance, the presence of bilateral femur shaft fractures should be directly recognized as an increased risk for systemic complications [1].

E-mail address: p.patka@erasmusmc.nl (P. Patka).

http://dx.doi.org/10.1016/j.injury.2017.04.016
0020-1383/

The choice of local therapeutic procedure for a long bone fracture determines not only the local outcome (fracture healing and restoration of extremity function) but is also an important determinant in total recovery outcome [6]. Therefore, the prevention of local and systemic complications which could be induced by local long bone fracture treatment is an important issue. The approach for a successful fracture reduction and stabilization should be the least invasive possible. Initially, in a patient with compromised physiology, temporary fracture stabilization can be better achieved with the use of an external fixator (Fig. 1a and b). For definitive stabilization, Intramedullary nailing (IM nailing) continues to be the optimal choice of fixation. The less invasive stabilization plate (LISS) due to its insufficient mechanical properties is less recommended for long bone fracture stabilization [6,7].

Intramedullary nailing

Fracture stabilization with IM nailing is a delicate process with potential pitfalls. However, when all technical procedures are performed in a correct manner, the fracture nailing effort should end successfully, at least in most cases. Conditions that should be present and which contribute to the success of the nailing procedure include: protection of vascularity of the affected extremity; avoidance of fracture (over)distraction and careful handling of the soft tissue envelope amongst others. In addition, the nail entry point should be well chosen as well as the preferable nail diameter. The nail type, length and especially the nail diameter should depend on the type of long bone (upper- or lower extremity) and on the implant provider instruction. The introduction of a guide wire is a delicate procedure [8]. Its correct introduction and position within the long bone medullar cavity prevents the occurrence of false route or extra-anatomical placement of a reamer. It has already been shown that guide wire introduction is connected to an intramedullary pressure increase. Therefore, an anatomically correct and slow speed wire introduction is needed in order to avoid fat embolism by intramedullary pressure increase. These precautions must also be applied during the reaming of long bone cavity. To drill a pressure reducing hole in the distal part of a fractured bone cortex is not necessary in all cases. However, in long bones with long undamaged shaft due to fracture location in their epiphysis, the distance to the opposite metaphysis may be long and, in these situations, the reamer creates a substantial increase of intramedullary pressure with a sub consequent introduction of fat embolism. Introducing a unicortical hole located in the opposite metaphyseal region will reduce the intramedullary pressure and minimize the risk of fat embolism in these situations. The use of reamers with a suction system is expensive and not common yet. The use of a low speed sharp cutting reamer with a stepwise, small (0.5 mm) subsequent diameter increase avoids tissue damage by friction heat. To make the implant introduction easy "over reaming" of the bone cavity can be used, of up to 1.0–1.5 mm more than the chosen nail diameter. This is an important condition for an undisturbed, smooth nail introduction. This procedure also prevents the appearance of mal-reduction during the nail introduction and will support optimal fracture healing. In two-level fractures of tibia and ulna, safety measures to prevent rotation of an intermediate fracture fragment during the reaming procedure should be applied in order to prevent an avascular necrosis by stripping soft tissue which could harm the vascularity of this bone fragment. The use of forceps with a claw head, embedded in the intermediate fragment percutaneously and held firmly during the passage of the reamer head through the medullar cavity of this fracture fragment, prevents the fragment rotation and soft tissue striping. Two-level fractures of the humerus and femur tend to rotate less when the reamer head is passing through the medullary cavity because of the firm soft tissue anchoring of these fragments.

The interlocking screws prevent unexpected shortening or malrotation in fracture side and allow an early postoperative mobilization and patient rehabilitation. However, there must be close cooperation between the surgeon and the physiotherapist concerning the weight bearing capacity of interlocking screws in relation to the actual weight bearing ability of the patient and fracture consolidation degree in the rehab process. The therapeutic guidance should be closely coordinated by the surgeon and the rehab therapist to prevent any unnecessary impairment to fracture healing and to prevent failure of hardware.

a)

b)

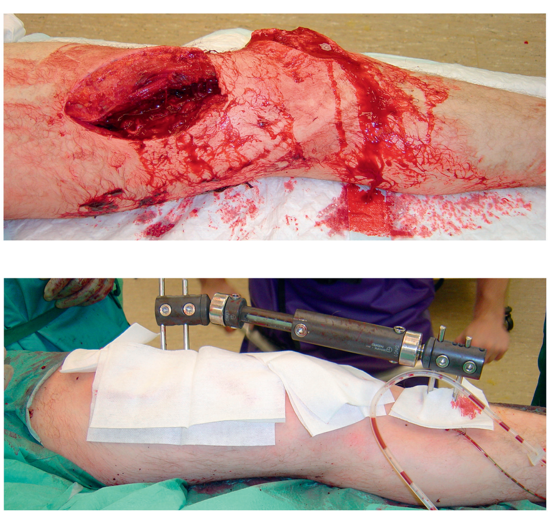


Fig. 1. Open Femur & Tibia fracture damage control: a. initial situation, b. stabilization of fractures with an ExFix and soft tissue treatment.

Complications in fracture healing

In patients where impairment in the fracture healing process has been established, appropriate adequate measures should be taken in order to improve the conditions for bone healing. The type of intervention depends on the reason for a delayed union/ nonunion in a particular patient [9–12]. These interventions can be related to the improvement of mechanics or biology of fracture healing. In cases with small or no-fracture gaps, dynamization of a statically interlocked nail is the first step for an uneventful fracture healing response. In fractures with large bone defect, autologous bone grafting should be considered. Recombinant bone morphogenetic protein-7 (rhBM-7) (Osigraft®) was demonstrated to be equivalent to autologous bone graft for the treatment of tibial nonunions. The use of rhBM-7 when compared to autograft was associated with lower intraoperative blood loss and shorter operative times in different studies [13–15]. However, the use of growth is not a standard method in treatment of delayed union/ non-union and should be reserved for difficult cases of non-union where other therapeutic procedures fail.

Damage control for long bone fractures also includes the prevention and treatment of infection. The avoidance of an infected fracture site is obviously better and much easier to deal than infected fractured bone. In particular, open tibia fractures are at risk of infection which makes the clinical treatment outcome less optimal [16,17]. Infection prevention in all cases of closed fractures requires, the administration of prophylactic antibiotics, with units having developed their own local protocols. In open fractures, the antibiotic therapy should be continued for a longer period, generally for 5 days. Once an infection appears the therapy must be extended to more complex procedures. Removal of the IM-nail followed by another type of fracture stabilization will only be exceptionally necessary in some severe infections.

Conclusions

Damage control for long bone fractures needs skilled surgeons with an experience in management of trauma. The surgeon should be supported by a trauma-dedicated team and sufficient equipment.

Good clinical results can be expected in patients with long bone fractures if the principals of damage control are applied and complications are prevented through proper reduction, firm fixation, early soft tissue reconstruction, and early rehabilitation.

Conflict of interest

The authors declare no conflict of interest with regards to the content of this manuscript.

References

[1] Kobbe P, Micansky F, Lichte P, Sellei RM, Pfeifer R, Dombroski D, et al. TraumaRegister DGU. Increased morbidity and mortality after bilateral femoral shaft fractures: myth or reality in the era of damage control. Injury 2013;44:221–5.

[2] van Dongen TT, Idenburg FJ, Tan EC, Rasmussen TE, Hamming JF, Leenen LP, et al. Combat related vascular injuries: dutch experiences from a role 2 MTF in Afghanistan. Injury 2016 Jan;47(1):94–8.

[3] Kataoka Y, Minehara H, Kashimi F, Hanajima T, Yamaya T, Nishimaki H, et al. treatment combining emergency surgery and intraoperative interventional radiology for severe trauma. Injury 2016 Jan;47(1):59–63.

[4] Boutefnouchet T, Gregg R, Tidman J, Isaac J, Doughty H. Emergency red cells first: rapid response or speed bump? The evolution of a massive transfusion protocol for trauma in a single UK centre. Injury 2015 Sep;46(9):1772–8.

[5] Bosse MJ, MacKenzie EJ, Kellam FJ, a.o. An Analysis of Outcomes of Reconstruction or Amputation after Leg-Threatening Injuries. N Engl J Med 2002;374:1924–31.

[6] Xue XH, Yan SG, Cai XZ, Shi MM, Lin T. Intramedullary nailing versus plating for extra-articular distal tibial metaphyseal fracture: a systematic review and meta-analysis. Injury 2013;45:667–76.

[7] Dunbar RP, Nork SE, Barei DP, Mills WJ. Provisional plating of type III open tibia fractures prior to intramedullary nailing. J Orthop Trauma 2005;19:412–4.

[8] Ansari Moein LM, Duis ten HJ, Oey PL, Kort de GAP, Meulen van der W, van der Chr Werken. Intramedullary femoral nailing through the trochanteric fossa versus greater trochanter tip: a randomized controlled study with in-depth functional outcome results. Eur J Trauma Emerg Surg 2011;37:615–22.

[9] Metsemakers WJ, Roels N, Belmans A, Reynders P, Nijs S. Risk factors for nonunion after intramedullary nailing of femoral shaft fractures: remaining controversies. Injury 2015;46(August (8)):1601–7.

[10] Stavrou PZ, Ciriello V, Theocharakis S, Gudipati S, Tosounidis TH, Kanakaris NK, et al. Prevalence and risk factors for re-interventions following reamed intramedullary tibia nailing. Injury 2016;47(Suppl. 7)S49–52 Dec.

[11] Giannoudis PV, Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury 2016;47(Suppl. 6)S53–61 Dec.

[12] Giannoudis PV, Gudipati S, Harwood P, Kanakaris NK. Long bone non-unions treated with the diamond concept: a case series of 64 patients. Injury 2015;46 (Suppl 8)S48–54 Dec.

[13] Calori GM, Colombo M, Bucci M, Mazza EL, Fadigati P, Mazzola S. Clinical effectiveness of Osigraft in long-bones non-unions. Injury 2015;46 S8:55–64.

[14] Singh R, Bleibleh S, Kanakaris NK, Giannoudis PV. Upper limb non-unions treated with BMP-7: efficacy and clinical results. Injury 2016;47(Suppl. 6)S33–9 Dec.

[15] Alt V, Borgman B, Eicher A, Heiss C, Kanakaris NK, Giannoudis PV, et al. Effects of recombinant human Bone Morphogenetic Protein-2 (rhBMP-2) in grade III open tibia fractures treated with unreamed nails-A clinical and health-economic analysis. Injury 2015;46(November (11)):2267–72.

[16] Cho JH, Lee IJ, Bang JY, Song HK. Factors affecting clinical outcomes after treatment of extra-articular open tibial fractures. J Orthop Sci 2016;21:63–7.

[17] Otchwemah R, Grams V, Tjardes T, Shafizadeh S, Bäthis H, Maegele M, et al. Bacterial contamination of open fractures – pathogens, antibiotic resistances and therapeutic regimes in four hospitals of the trauma network Cologne, Germany. Injury 2015;46(Suppl. 4)S104–8 October.

Injury, Int. J. Care Injured 48S (2017) S10–S14

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Inflammatory response after nailing

Nikolaos K. Kanakaris[a,*], Christopher Anthony[b], Antonios Papasotiriou[c], Peter V. Giannoudis[d]

[a] Clinical Lead of Major Trauma Services, Leeds General Infirmary, Clarendon Wing, Level D, LS13EX, Leeds, West Yorkshire, UK
[b] Trauma and Orthopaedics Yorkshire and Humber Deanery, Leeds Teaching Hospitals NHS Trust, UK
[c] Department of Trauma and Orthopaedics, Leeds Teaching Hospitals NHS Trust, UK
[d] Academic Department of Trauma and Orthopaedics, School of Medicine, University of Leeds, UK

ARTICLE INFO

Keywords:
Intramedullary nailing
Reaming
Immune response
Cytokines
SIRS
CARS

ABSTRACT

Intramedullary nailing, as the gold standard stabilisation method of most long bones, has been tailed by its extensive use as the basic tool of investigating the immune response to trauma in many large and small animal models, as well as at the clinical setting.

Over the last few decades a complex map of interactions between pro and anti-inflammatory pathways has been the result of these significant global research efforts.

Parallel to the evolution of modern nailing and reaming techniques, significant developments at the fields of other disciplines relevant to trauma care, has improved the contemporary management of injured patients, challenging previous concepts and altering clinical barriers.

The current article aims to summarise the current understanding of the effect of instrumenting the medullary canal after trauma, and hint on potential future directions.

Introduction

The instrumentation of the medullary canal of long bones was conceived even before the 16th century, since anthropologists in Mexico witnessed such a procedure of Aztec surgeons, inserting wooden sticks into long bone fractures [1]. Intramedullary instrumentation at the developed world was further recorded in the late 19th century by different surgeons describing the concept of interlocking devices from metal, autogenous or bovine bone, or ivory. At that point of time, long before the era of antibiotics and the evolution of medical metallurgy, all these were heavily criticized, as they were associated with early failures due to high rates of infection, instability, metal electrolysis and fatigue failure [2].

Only after the end of World War II and the wider acknowledgement of “marrow nailing” as that described by Gerhard Küntscher, this type of procedures started building their reputation as an effective and safe fixation method of long bones. Since then, intramedullary nailing has evolved extensively, including mainly the introduction of flexible reaming of the medullary canal, which allowed the increase of the contact area between the nail and the endosteum, and the incorporation of the interlocking screws, which increased the control of rotational and length deforming forces. More recent advances include the mechanical characteristics of newer alloys, the anatomic design of the modern nails, the incorporation of interfragmentary compression options, angular stability of the interlocking screws, antibiotic coating of the nails, as well as reaming irrigating and aspirating systems.

Immune response to trauma

The contemporary understanding of the physiologic response to trauma is that this includes a complex network of interactions, regulated by mediators of inflammation and coagulation. Basic objectives of this response is to dispose the damaged tissues, initiate tissue repair, and protect against infection, (Fig. 1). The dominating effect of the magnitude and of the nature of the “first

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; CARS, compensatory anti-inflammatory response syndrome; CD-11, cluster of differentiation molecule 11; CRP, c-reactive protein; DAMPs, damage-associated molecular patterns; FES, fat embolism syndrome; HLA-DR, human leucocyte antigens – antigen D related; IL, interleukin; LBP, lipopolysaccharide binding protein; MODS, multiple organ distress syndrome; MOF, multiple organ failure; PAMPs, pathogen associated molecular patterns; PCT, procalcitonin; s-ICAM-1, soluble intercellular adhesion molecule- 1; SIRS, systemic inflammatory response syndrome; TNF, tumor necrosis factor.

* Corresponding author.
E-mail addresses: n.kanakaris@nhs.net (N.K. Kanakaris), christopher.anthony@doctors.org.uk (C. Anthony), antpapas@hotmail.com (A. Papasotiriou), pgiannoudi@aol.com (P.V. Giannoudis).

http://dx.doi.org/10.1016/j.injury.2017.04.017
0020-1383/

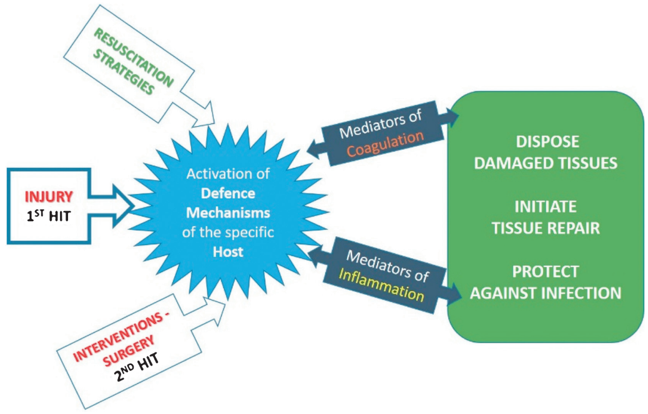


Fig. 1. Schematic representation of the network of interactions following an injury, including the effect of administered resuscitation and surgical interventions, regulated by mediators of the immune and coagulation systems, with main goals the clearance of the damaged tissues, initiate tissue repair, and protect against infection.

hit" on the defence mechanisms of the host, is also associated to the exaggerated response to any secondary physiologic insults – second hits/interventions.

As far as the timeline of the immune response, this is currently assumed to include the early innate phase of hyper-inflammation, the delayed adaptive, and late adaptive phases, (Fig. 2). The initial tissue damage and haemorrhage, via the activation of coagulation, tissue hypoperfusion and neuroendocrine stress response pathways, ignite the pro-inflammatory stage [3]. The extracellular release of damage-associated molecular patterns (DAMPs) and the resultant stimulation of the immune cells (polymorphonuclear leukocytes, monocytes, macrophages, natural killer cells) via chemokines, as the IL-8 and the complement fragment C5a, and initial stage mediators as the IL-6, TNF-a and the IL-1, lead to the activation of endothelial cells. The role of the endothelial system dominates the complications of these early days post trauma via the increased vascular permeability, tissue oedema, loss of

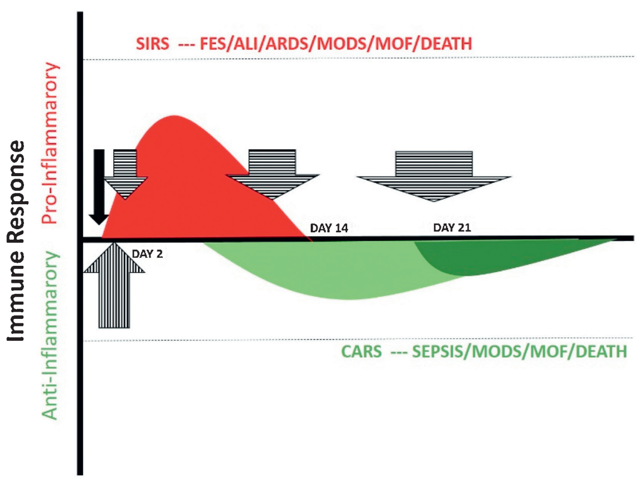


Fig. 2. Schematic representation of the understanding of the timeline of the immune response following a traumatic event ("first hit" – black dense arrow), the initial resuscitation effort (arrow with vertical lines), the surgical interventions ("second hits" – arrows with horizontal). The hyper-inflammatory phase in red (innate immune response) is followed by the delayed adaptive anti-inflammatory phase in light green and the late adaptive phase in darker green. Exacerbation of the hyper inflammatory state may lead to manifestations of SIRS, and subsequent ALI, ARDS, MODS, MOF or even death. The same adverse outcome may be reached when the anti-inflammatory state prevails leading to immune paralysis of the patient – CARS and sepsis.

endothelial integrity, and the clinical manifestations of FES, ALI/ARDS, MODS, and MOF (respectively, fatty embolism syndrome, acute lung injury/acute respiratory distress syndrome, multiple organ distress syndrome, and multiple organ failure) [4].

The delayed adaptive phase is characterised by immune-suppression, where endogenous triggers – alarmins and CD5+ B cells, part of the delayed DAMPs, lead to an autoimmune regulated tissue destruction after the first ten days from trauma. The subsequent late adaptive phase is characterised by immune-proliferation, where pathogen associated molecular patterns (PAMPs), via T- and B- lymphocyte mediators and the production of conventional antibodies, gradually restore the equilibrium of the immune response [5,6].

The immune response following an injury, fluctuates between two extremes conditions. That of the systemic inflammatory response syndrome (SIRS) of the acute phase, and subsequently the compensatory anti-inflammatory response syndrome (CARS), influenced by a number of factors including the initial injury, the physiologic reserves of the individual, the timing and nature of secondary interventions, and the effectiveness of the delivered resuscitation [3].

Role of intramedullary nailing

From the era of Gerhard Küntscher, it was recognised that the intramedullary instrumentation of the long bones was a surgical technique that influenced gravely the outcome of patients under special conditions. Back in the early 50s, he was clearly recommending extra caution when "marrow nailing" was performed in the presence of multiple other associated injuries, or at the early period after the traumatic event, or in the presence of an expressed fatty embolism [7]. Thereafter, remarkable scientific effort has been made to expand our understanding on the significance of the magnitude and nature of the initial trauma or else called "first hit", together with that of the additional burden of comorbidities and of the physiological age of the patient, as well as the importance of all resuscitative and restorative interventions, or else called "second hit", to the outcome of injured patients [8,9].

The great clinical significance of intramedullary nailing as the gold standard method of stabilisation of most long bones, has been tailed by its extensive use as the example of the "second hit" phenomenon to most "in vivo" studies in large and small animal models [10], as well as in many clinical studies exploring the physiologic response to trauma [11]. These studies over the last decades include the assessment of both physical and biological adverse effects of intramedullary nailing to the patients physiology. The current article aims to summarise the current understanding of this important aspect of the effect of intramedullary instrumentation of the medullary canal and hint on its potential future directions.

Intramedullary pressure and fat intravasation

The early studies of the physiologic response to the instrumentation of the canal of long bones identified the increase of the intramedullary pressures, as well as that of embolic showers and fat intravasation, during the different stages of nailing (entry point preparation, insertion of guide wire, insertion of series of flexible reamers, insertion of the nail, insertion of interlocking screws) [12,13]. Evidence supports that even subtle manoeuvres of the canal, as opening of the canal or insertion of the guide wire [14], or even simple bone endoscopy [15] lead to increased pressures. The range of values of these pressures is relevant to a number of parameters as the anatomical site, the size of the long bone, the reaming technique, and the specific features of the reaming system. Whilst an increase of just 40 mmHg [16] is associated to intravasation of canal contents, this phenomenon becomes clinically important with measurable embolic showers after the intramedullary pressure surpasses the 200 mmHg [17]. Studies comparing the intramedullary pressure effect, as well as the resultant embolic showers between reamed and unreamed nails often contradict to their results, concluding mostly that the careful technique of reaming is a factor in order to minimise such adverse effects, which are however present in both methods of nailing [18–20]. Echocardiographic monitoring of the intraoperative embolic showers identified higher volume during a reamed intramedullary nailing, especially if it happens after 48 h from the injury [21,22].

The reamer aspiration irrigation (RIA) was invented in order to minimise the increase of intramedullary pressures during canal preparation, and subsequently minimise the volume of fat infiltration through the transcortical vessels, the resultant embolic showers, and their cardiopulmonary, central nervous system and immune implications [23]. Earlier evidence supported this concept, as instrumenting the medullary canal after emptying it from its contents [24]. More recent in vivo and clinical studies demonstrated superior results after using the new RIA system in comparison to other reaming techniques or even unreamed nailing [25–29].

Generation of heat

The process of reaming, this mostly necessary stage of modern intramedullary nailing, has been also associated with another adverse effect; that of heat generation locally. A threshold of 56 °C has been defined as critical for bony thermal injury [30], at which level the cellular enzymes are destroyed and bone necrosis is evident. Together with the number of stages of reaming [31], and its duration [32], they have been all linked to the risk of heat necrosis of the canal, whilst other authors advocated in favour of reaming if careful technique is applied [33], if the reamer heads are sharp, and the correct stepwise increase of their diameter, by 0.5 mm increments, is used [34–36]. Furthermore, the RIA system has also been proven to decrease the overheating phenomena, as the measured maximum temperatures were statistically significantly lower from those of standard reamers at the model of cadaveric tibias of Higgins et al. [37].

Defining the “Second hit” of nailing

The effect of intramedullary nailing to the patients physiology as a “second hit”, besides the above mentioned causation – i.e. from the increased pressures of the intramedullary canal, the intravasation of fat particles and the resultant activation of coagulation, the marrow embolization of the lungs and/or of the brain, and the overheating of the endosteum, it has been also attributed to the increased blood loss especially after reaming. Mostly in regards to femoral reaming, it has been associated with measurable additional bleeding from the fractured extremity [36,38,39].

Several biomarkers of the cumulative effect of all these factors, or else the “second hit” effect during intramedullary nailing, have been explored at the clinical setting (Table 1); either from sampling of peripheral blood at different time points, or even locally from the canal [4,10,11,40]. From all these, the IL-6 has been identified to correlate remarkably to the early post-traumatic immune response for both the first and the second hit. Reamed and unreamed nailing were found to be associated with elevation of the serum IL-6 [11], with no statistical significant at least differences between the two types of nailing [41,42]. The profile of release of a number of inflammatory mediators using the RIA system during femoral intramedullary nailing was recorded at a recent clinical study [43]. The IL-6 was again identified as the most reliable biomarker of the immune response to the first and second hit. Within the methodological limitations of the study no statistically

Table 1
Evidence on main biomarkers-mediators of the immune response after intramedullary nailing of long bones.

Biomarkers	Function	Key Studies
Markers of Mediators Activity		
IL-6 Interleukin 6	Released by secreted by T cells and monocytes. Main pro-Inflammatory cytokine.	[40,45,46,48,57]
IL-8 Interleukin 8	Released by monocytes/macrophages, epithelial cells, and endothelial cells. Pro-inflammatory cytokine.	[40,48,58]
IL-10 Interleukin 10	Released by activated monocytes/macrophages, and by lymphocytes. Pleiotropic cytokine.	[40,48,58]
TNF-a Tumor Necrosis Factor	Released by activated monocytes/macrophages, as well as many other cell types such as lymphocytes, NK cells, neutrophils, et al. Pro-inflammatory mediator.	[40,48,57–59]
Acute Phase Reactants		
CRP C-reactive protein	Mainly of hepatic origin. Non-specific acute phase protein.	[60–63]
PCT Procalcitonin	Mainly from C-cells of the thyroid and probably hepatic cells. Correlates with first hit, as well as the severity of secondary sepsis during late SIRS.	[62,64]
LBP Lipopolysaccharide binding protein	Mainly of hepatic origin. Non-specific marker of trauma and sepsis.	[62,65,66]
Markers of Cellular activity		
s-ICAM-1 soluble Intercellular Adhesion Molecule- 1	Present at the surface of leukocytes and endothelial cells.	[41,62]
s-E-selectin soluble cell adhesion molecule	Present at the surface of leukocytes and endothelial cells. Relevant to the magnitude of “first hit”.	[41,62]
CD11b cluster of differentiation molecule 11B	Present at the surface of leukocytes, including monocytes, granulocytes, macrophages, and natural killer cells.	[41,62]
Elastase	Marker of neutrophil cellular activity. Corresponds with acute lung injury and ARDS.	[41,62]
HLA-DR expression Human leucocyte antigens	Expression of cell-surface antigens on leucocytes, monocytes, neutrophils. Decreased expression after trauma (indicating immune suppression).	[45,46,67]

significant differences as far as the IL-6 levels peri-operatively were noted using a control group of standard reamers [43].

Most recent studies have identified as more significant factor to the type of surgical procedure, the initial burden of trauma, as this is expressed with the overall injury severity, as well as the presence of specific injury combinations [44–46]. These include severe chest injuries/lung contusions, traumatic brain injuries, also multiple long bone fractures i.e. bilateral femurs [47–49].

Furthermore, the factor of timing of the surgical intervention, as well as that of the effectiveness of the inbetween administered resuscitation [11,50,51], have been both explored and identified also, as more important than the effect of canal instrumentation [9,51–54]. Following the priming of the immune system of polytrauma patients from the initial trauma, a number of studies have hinted that the period after the first 48 h till the 5th day are suboptimal for major surgeries including intramedullary nailing [55,56]. A "second hit" during that period, is associated with increased release of pro-inflammatory mediators, amplifying the risk of SIRS, and complications [9,51].

Future directions

As evident from a series of studies [9–11], intramedullary nailing of major long bones produces a measurable response to the already activated immune system of the patient. The effort to explore all dimensions of the complex pathophysiology of trauma continues to use nailing as an essential tool for research at the in vivo, also at the clinical set up. This is explained mostly due to the fact that nailing still represents the gold standard fixation technique for a number of common fractures in the polytrauma population. Also because it has been used extensively to the existing relevant literature, thus it allows comparative analysis of any new findings, building on the existing knowledge.

Still, contemporary trauma management has evolved significantly over the last few decades, in large because of this type of research. Do the findings and conclusions of clinical studies of different eras apply today? Has the epidemiology and the demographic characteristics of modern trauma victims changed? What is the influence of the evolution of all different disciplines that are involved in trauma management? Contemporary concepts of early appropriate care, damage control resuscitation, as well as the great improvements of laboratory resources and techniques pave the future on this field.

Between many other, open questions remain the influence of timing of the second hit to the immune response of the polytrauma patient; the role of the genomic profile of our patients to their outcome after trauma; the effect of the nailing/second hit to the development of infections during the immunosuppressive phases besides its effect at the initial hyper-inflammatory stage; together with the careful translation of the evidence between the lab and the clinical practice, as well as between different health systems and patient cohorts.

Conflict of interest

All authors declare no existing conflict of interests.

References

[1] Farill J. Orthopedics in Mexico. J Bone Joint Surg Am 1952;24 A:506–12.
[2] Gakuu LN. Comprehensive global evolution of intramedullary nailing of diaphyseal fractures. East Afr Orthop J 2009;3:36–9.
[3] Lord JM, Midwinter MJ, Chen YF, Belli A, Brohi K, Kovacs EJ, et al. The systemic immune response to trauma: an overview of pathophysiology and treatment. Lancet 2014;384:1455–65.
[4] Giannoudis PV, Tosounidis TI, Kanakaris NK, Kontakis G. Quantification and characterisation of endothelial injury after trauma. Injury 2007;38:1373–81.
[5] Kasten KR, Goetzman HS, Reid MR, Rasper AM, Adediran SG, Robinson CT, et al. Divergent adaptive and innate immunological responses are observed in humans following blunt trauma. BMC Immunol 2010;11:4.
[6] Xu PB, Lou JS, Ren Y, Miao CH, Deng XM. Gene expression profiling reveals the defining features of monocytes from septic patients with compensatory anti-inflammatory response syndrome. J Infect 2012;65:380–91.
[7] Kuentscher G. Intrmedullary surgical technique and its place in orthopaedic surgery: my present concept. J Bone Joint Surg Am 1965;47:809–18.
[8] Roberts CS, Pape HC, Jones AL, Malkani AL, Rodriguez JL, Giannoudis PV. Damage control orthopaedics: evolving concepts in the treatment of patients who have sustained orthopaedic trauma. Instr Course Lect 2005;54:447–62.
[9] Easton R, Balogh ZJ. Peri-operative changes in serum immune markers after trauma: a systematic review. Injury 2014;45:934–41.
[10] Lasanianos NG, Kanakaris NK, Giannoudis PV. Intramedullary nailing as a 'second hit' phenomenon in experimental research: lessons learned and future directions. Clin Orthop Relat Res 2010;468:2514–29.
[11] Lasanianos NG, Kanakaris NK, Dimitriou R, Pape HC, Giannoudis PV. Second hit phenomenon: existing evidence of clinical implications. Injury 2011;42:617–29.
[12] Neudeck F, Obertacke U, Wozasek G, Thurnher M, Schlag G, Schmit-Neuerburg KP. Pathophysiologic consequences of various osteosynthesis procedures in polytrauma patients. Part I: experimental studies of intramedullary pressure development in reamed and unreamed intramedullary nailing and plate osteosynthesis of the femur. Aktuelle Traumatol 1994;24:114–20.
[13] Wozasek GE, Simon P, Redl H, Schlag G. Intramedullary pressure changes and fat intravasation during intramedullary nailing: an experimental study in sheep. J Trauma 1994;36:202–7.
[14] Smith PN, Leditschke A, McMahon D, Sample RR, Perriman D, Prins A, et al. Monitoring and controlling intramedullary pressure increase in long bone instrumentation: a study on sheep. J Orthop Res 2008;26:1327–33.
[15] Oberst M, Herget G, Riede U, Kreim SY, Konrad G, Suedkamp NP, et al. Fat marrow embolism during intramedullary bone endoscopy: an experimental study in sheep. J Orthop Res 2009;27:1060–6.
[16] Wenda K, Ritter G, Ahlers J, von Issendorff WD. Detection and effects of bone marrow intravasations in operations in the area of the femoral marrow cavity. Unfallchirurg 1990;93:56–61.
[17] Wenda K, Runkel M, Degreif J, Ritter G. Pathogenesis and clinical relevance of bone marrow embolism in medullary nailing–demonstrated by intraoperative echocardiography. Injury 1993;24(Suppl. 3):S73–81.
[18] Heim D, Regazzoni P, Tsakiris DA, Aebi T, Schlegel U, Marbet GA, et al. Intramedullary nailing and pulmonary embolism: does unreamed nailing prevent embolization? An in vivo study in rabbits. J Trauma 1995;38:899–906.
[19] Kropfl A, Berger U, Neureiter H, Hertz H, Schlag G. Intramedullary pressure and bone marrow fat intravasation in unreamed femoral nailing. J Trauma 1997;42:946–54.
[20] Hogel F, Gerlach UV, Sudkamp NP, Muller CA. Pulmonary fat embolism after reamed and unreamed nailing of femoral fractures. Injury 2010;41:1317–22.
[21] Riska EB, Myllynen P. Fat embolism in patients with multiple injuries. J Trauma 1982;22:891–4.
[22] Robinson CM, Ludlam CA, Ray DC, Swann DG, Christie J. The coagulative and cardiorespiratory responses to reamed intramedullary nailing of isolated fractures. J Bone Joint Surg Br 2001;83:963–73.
[23] Green J. History and development of suction-irrigation-reaming. Injury 2010;41(Suppl. 2):S24–31.
[24] Mueller CA, Rahn BA. Intramedullary pressure increase and increase in cortical temperature during reaming of the femoral medullary cavity: the effect of draining the medullary contents before reaming. J Trauma 2003;55:495–503 discussion.
[25] Wang RY, Li R, Zdero R, Bell D, Blankstein M, Schemitsch EH. The physiologic and pathologic effects of the reamer irrigator aspirator on fat embolism outcome: an animal study. J Orthop Trauma 2012;26:e132–7.
[26] Pape HC, Zelle BA, Hildebrand F, Giannoudis PV, Krettek C, van Griensven M. Reamed femoral nailing in sheep: does irrigation and aspiration of intramedullary contents alter the systemic response. J Bone Joint Surg Am 2005;87:2515–22.
[27] Husebye EE, Lyberg T, Opdahl H, Roise O. Intravasation of bone marrow content. Can its magnitude and effects be modulated by low pressure reaming in a porcine model? Injury 2010;41(Suppl. 2):S9–S15.
[28] Van Gorp CC, Falk JV, Kmiec Jr. SJ, Siston RA. The reamer/irrigator/aspirator reduces femoral canal pressure in simulated TKA. Clin Orthop Relat Res 2009;467:805–9.
[29] Klein C, Sprecher C, Rahn BA, Green J, Muller CA. Unreamed or RIA reamed nailing: an experimental sheep study using comparative histological assessment of affected bone tissue in an acute fracture model. Injury 2010;41 (Suppl. 2):S32–7.
[30] Matthews LS, Hirsch C. Temperatures measured in human cortical bone when drilling. J Bone Joint Surg Am 1972;54:297–308.
[31] Ochsner PE, Baumgart F, Kohler G. Heat-induced segmental necrosis after reaming of one humeral and two tibial fractures with a narrow medullary canal. Injury 1998;29(Suppl. 2):B1–B10.
[32] Eriksson RA, Albrektsson T. The effect of heat on bone regeneration: an experimental study in the rabbit using the bone growth chamber. J Oral Maxillofac Surg 1984;42:705–11.
[33] Giannoudis PV, Snowden S, Matthews SJ, Smye SW, Smith RM. Temperature rise during reamed tibial nailing. Clin Orthop Relat Res 2002;25:5–61.

[34] Muller C, Rahn BA, Pfister U, Weller S. Extent of bluntness and damage to reamers from hospitals. Injury 1993;24(Suppl. 3):S31–5.
[35] Muller CA, Baumgart F, Wahl D, Perren SM, Pfister U. Technical innovations in medullary reaming: reamer design and intramedullary pressure increase. J Trauma 2000;49:440–5.
[36] Giannoudis PV, Snowden S, Matthews SJ, Smye SW, Smith RM. Friction burns within the tibia during reaming. Are they affected by the use of a tourniquet? J Bone Joint Surg Br 2002;84:492–6.
[37] Higgins TF, Casey V, Bachus K. Cortical heat generation using an irrigating/aspirating single-pass reaming vs conventional stepwise reaming. J Orthop Trauma 2007;21:192–7.
[38] Forster MC, Aster AS, Ahmed S. Reaming during anterograde femoral nailing: is it worth it. Injury 2005;36:445–9.
[39] Shepherd LE, Shean CJ, Gelalis ID, Lee J, Carter VS. Prospective randomized study of reamed versus unreamed femoral intramedullary nailing: an assessment of procedures. J Orthop Trauma 2001;15:28–32 discussion −3.
[40] van Griensven M. Cytokines as biomarkers in polytraumatized patients. Unfallchirurg 2014;117:699–702.
[41] Giannoudis PV, Smith RM, Bellamy MC, Morrison JF, Dickson RA, Guillou PJ. Stimulation of the inflammatory system by reamed and unreamed nailing of femoral fractures. An analysis of the second hit. J Bone Joint Surg Br 1999;81:356–61.
[42] Morley JR, Smith RM, Pape HC, MacDonald DA, Trejdosiewitz LK, Giannoudis PV. Stimulation of the local femoral inflammatory response to fracture and intramedullary reaming: a preliminary study of the source of the second hit phenomenon. J Bone Joint Surg Br 2008;90:393–9.
[43] Giannoudis PV, Tan HB, Perry S, Tzioupis C, Kanakaris NK. The systemic inflammatory response following femoral canal reaming using the reamer-irrigator-aspirator (RIA) device. Injury 2010;41(Suppl. 2):S57–61.
[44] Pfeifer R, Sellei R, Pape HC. The biology of intramedullary reaming. Injury 2010;41(Suppl. 2):S4–8.
[45] Hietbrink F, Koenderman L, Leenen LP. Intramedullary nailing of the femur and the systemic activation of monocytes and neutrophils. World J Emerg Surg 2011;6:34.
[46] Hietbrink F, Koenderman L, van Wessem KJ, Leenen LP. The impact of intramedullary nailing of tibia fractures on the innate immune system. Shock 2015;44:209–14.
[47] Pape HC, Griensven MV, Hildebrand FF, Tzioupis CT, Sommer KL, Krettek CC, et al. Systemic inflammatory response after extremity or truncal fracture operations. J Trauma 2008;65:1379–84.
[48] Pape HC, Grimme K, Van Griensven M, Sott AH, Giannoudis P, Morley J, et al. Impact of intramedullary instrumentation versus damage control for femoral fractures on immunoinflammatory parameters: prospective randomized analysis by the EPOFF Study Group. J Trauma 2003;55:7–13.
[49] Bone LB, Giannoudis P. Femoral shaft fracture fixation and chest injury after polytrauma. J Bone Joint Surg Am 2011;93:311–7.
[50] Morshed S, Miclau 3rd T, Bembom O, Cohen M, Knudson MM, Colford Jr. JM. Delayed internal fixation of femoral shaft fracture reduces mortality among patients with multisystem trauma. J Bone Joint Surg Am 2009;91:3–13.
[51] Vallier HA, Moore TA, Como JJ, Wilczewski PA, Steinmetz MP, Wagner KG, et al. Complications are reduced with a protocol to standardize timing of fixation based on response to resuscitation. J Orthop Surg Res 2015;10:155.
[52] Rixen D, Steinhausen E, Sauerland S, Lefering R, Maegele MG, Bouillon B, et al. Randomized, controlled, two-arm, interventional, multicenter study on risk-adapted damage control orthopedic surgery of femur shaft fractures in multiple-trauma patients. Trials 2016;17:47.
[53] O'Toole RV, O'Brien M, Scalea TM, Habashi N, Pollak AN, Turen CH. Resuscitation before stabilization of femoral fractures limits acute respiratory distress syndrome in patients with multiple traumatic injuries despite low use of damage control orthopedics. J Trauma 2009;67:1013–21.
[54] Crist BD, Ferguson T, Murtha YM, Lee MA. Surgical timing of treating injured extremities: an evolving concept of urgency. Instr Course Lect 2013;62:17–28.
[55] Brundage SI, McGhan R, Jurkovich GJ, Mack CD, Maier RV. Timing of femur fracture fixation: effect on outcome in patients with thoracic and head injuries. J Trauma 2002;52:299–307.
[56] Pape HC, van Griensven M, Rice J, Gansslen A, Hildebrand F, Zech S, et al. Major secondary surgery in blunt trauma patients and perioperative cytokine liberation: determination of the clinical relevance of biochemical markers. J Trauma 2001;50:989–1000.
[57] Hartsock LA, Barfield WR, Kokko KP, Liles LL, Wind T, Green J, et al. Randomized prospective clinical trial comparing reamer irrigator aspirator (RIA) to standard reaming (SR) in both minimally injured and multiply injured patients with closed femoral shaft fractures treated with reamed intramedullary nailing (IMN). Injury 2010;41(Suppl. 2):S94–8.
[58] Tschoeke SK, Hellmuth M, Hostmann A, Ertel W, Oberholzer A. The early second hit in trauma management augments the proinflammatory immune response to multiple injuries. J Trauma 2007;62:1396–403 discussion 403-4.
[59] Pape HC, Schmidt RE, Rice J, van Griensven M, das Gupta R, Krettek C, et al. Biochemical changes after trauma and skeletal surgery of the lower extremity: quantification of the operative burden. Crit Care Med 2000;28:3441–8.
[60] Garnavos C, Xirou ST, Nikolatos A, Kanakaris N, Tzortzi P, Balbouzis T, et al. Alteration of body temperature, erythrocyte sedimentation rate, and C-reactive protein after reamed intramedullary nailing: a prospective study. J Orthop Trauma 2005;19:323–8.
[61] Gosling P, Dickson GR. Serum c-reactive protein in patients with serious trauma. Injury 1992;23:483–6.
[62] Giannoudis PV, Hildebrand F, Pape HC. Inflammatory serum markers in patients with multiple trauma. Can they predict outcome? J Bone Joint Surg Br 2004;86:313–23.
[63] Waydhas C, Nast-Kolb D, Trupka A, Zettl R, Kick M, Wiesholler J, et al. Posttraumatic inflammatory response, secondary operations, and late multiple organ failure. J Trauma 1996;40:624–30 discussion 30-1.
[64] Maier B, Lefering R, Lehnert M, Laurer HL, Steudel WI, Neugebauer EA, et al. Early versus late onset of multiple organ failure is associated with differing patterns of plasma cytokine biomarker expression and outcome after severe trauma. Shock 2007;28:668–74.
[65] Meisner M, Adina H, Schmidt J. Correlation of procalcitonin and C-reactive protein to inflammation, complications, and outcome during the intensive care unit course of multiple-trauma patients. Crit Care 2006;10:R1.
[66] Miyaoka K, Iwase M, Suzuki R, Kondo G, Watanabe H, Ito D, et al. Clinical evaluation of circulating interleukin-6 and interleukin-10 levels after surgery-induced inflammation. J Surg Res 2005;125:144–50.
[67] Smith RM, Giannoudis PV, Bellamy MC, Perry SL, Dickson RA, Guillou PJ. Interleukin-10 release and monocyte human leukocyte antigen-DR expression during femoral nailing. Clin Orthop Relat Res 2000;23:3–40.

Injury, Int. J. Care Injured 48S (2017) S15–S17

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Medication management after intramedullary nailing of atypical fractures

Jean-Marc Feron*, Adeline Cambon-Binder

Orthopaedic and Trauma Department, Saint Antoine Hospital, UPMC- Sorbonne Universities, Paris, France

ARTICLE INFO

Keywords:
Osteoporosis
Atypical femoral fracture
Fatigue fracture
Bisphosphonates
PTH

ABSTRACT

Long term use of bisphosphonates (BPs) in osteoporotic patients may be associated with stress fractures of the sub-trochanteric and shaft area of the femur, so called "atypical" femoral fractures (AFF). Specific diagnosis criteria have been defined with 5 major features; the presence of four of them characterizes the AFF. Once a complete fracture occurred, the best surgical treatment is closed reduction and intra medullary nailing. The BPs treatment should be stopped immediately after an AFF occurred. Dietary calcium and vitamin D status should be assessed, and adequate supplementation prescribed. Principle of combination of a systematic bone anabolic treatment is strongly debated. The recombinant parathyroid hormone 1–34 or Teriparatide ® (TPTD) has an anabolic effect on bone and prevent osteoporotic fractures. Available preclinical and clinical data have also demonstrated the role played by TPTD to enhance bone fracture healing and the potential beneficial effect in impaired fracture healing or specific clinical condition like AFFs. Some authors have proposed in incomplete BP use stress fractures different medical management according the MRI findings. Bone anabolic agents may be promising both to prevent healing complications in AFFs and to promote healing in conservative treatment of incomplete AFFs. More clinical studies are needed to confirm this hypothesis.

Introduction

Bisphosphonates (BPs) are the first-line and most commonly prescribed drugs for the treatment of osteoporosis to prevent fragility fractures. Strong evidence is supported by several randomized clinical trials in lowering the risk of initial fragility fracture (vertebral and non-vertebral fracture) by 41% to 70% [1]. Bisphosphonates are effective in osteoporosis treatment by inhibiting the osteoclastic bone resorption and increasing the bone mineral density. Long term use of BPs may be associated with stress fractures of the sub-trochanteric and shaft area of the femur, so called "atypical" femoral fractures (AFFs).

The first relationship between BPs and AFFs was reported by Odvina in 2005 [2], since the number of cases is in augmentation due to the growing use of BPs. Despite a relative risk of AFFs in patients using BPs, ranging from 2.1 to 128, the absolute risk remains very low ranging from 3.2 to 50 cases per 100,000 person-years [3]. The last 10 years several reports have linked the duration of bisphosphonates use to low energy sub-trochanteric femoral fracture [4]. The risk was higher for a long duration of treatment over 5 years [5] and decreased after drug withdrawal by 70% per year since the last use [6]. Although the pathogenesis is not well understood, these "atypical" femoral fractures (AFFs) are considered as fatigue fractures, resulting of bone remodeling suppression would cause a bone microarchitecture deterioration, impair the repair process and lead to an accumulation micro-cracks [7].

Cases definition of AFFs were revised in the second report of the task force of the American Society of Bone and Mineral Research (ASBMR) [3]: the fracture must be located from just distal to the lesser trochanter to just proximal from the supracondylar flare and at least 4 of 5 major features must be present and none of the minor features is required but have sometimes been associated with these fractures. (Table 1).

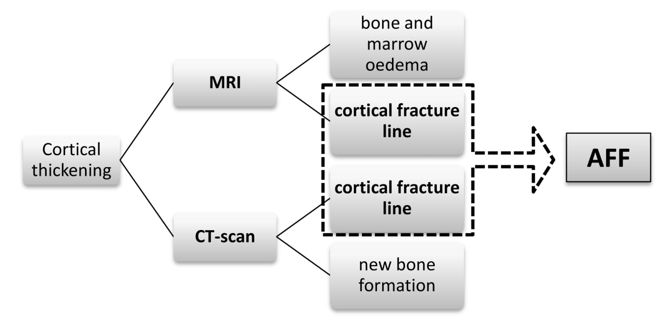
* Corresponding author at: 184 Rue du Faubourg St Antoine, 75571 Paris Cedex, France.
E-mail address: jean-marc.feron@aphp.fr (J.-M. Feron).

http://dx.doi.org/10.1016/j.injury.2017.04.030
0020-1383/

Table 1
ASBMR Task Force 2013 Revised Case Definition of AFFs.

Major features	• The fracture is associated with minimal or no trauma, as in a fall from a standing height or less • The fracture line originates at the lateral cortex and is substantially transverse in its orientation, although it may become oblique as it progresses medially across the femur • Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex • The fracture is non-comminuted or minimally comminuted • Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site ("breaking" or "flaring")
Minor features	• Generalized increase in cortical thickness of the femoral diaphyses • Unilateral or bilateral prodromal symptoms such as dull or aching pain in the groin or thigh • Bilateral incomplete or complete femoral diaphysis fractures • Delayed fracture healing

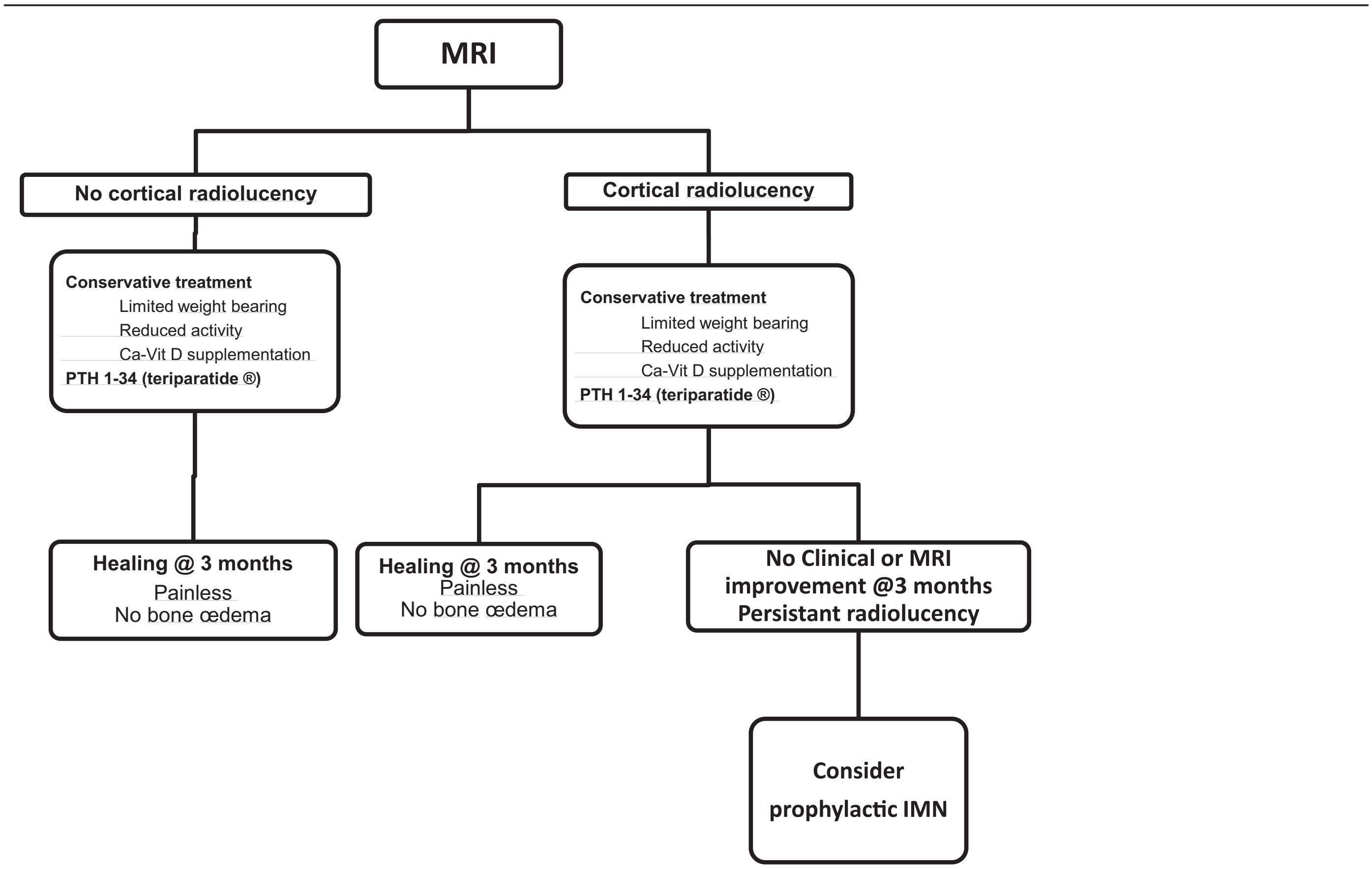
Table 2
Imaging diagnosis criteria of an incomplete AFF.



Surgical management of AFFs

Once the complete fracture occurs to the femur surgical reduction and fixation is necessary. The best treatment options are closed methods of intra-medullary nailing (IMN) or bridging plating to promote secondary healing process. Rigid plate fixation should be avoided due to the inhibition by BPs of the osteoclast function playing a major role in the primary healing process [8]. The current literature suggests an increase of the healing time and a significant higher rate of major complications (delayed and non-unions, implant failure) after fixation of AFFs [9,10]. Bilateral AFFs have also been reported in 28% of cases [11] occurring few months or years after the initial fracture. In some patients having prodromal contralateral thigh or groin pain and suspicion patterns of a stress fracture on X-ray or on an isotope bone scan a

Table 3
Management algorithm of incomplete AFFs.



prophylactic fixation has been proposed to prevent further complete fracture [12,13].

Medication management of AFFs

There is a consensus to stop the BPs treatment immediately after a AFFs occurred. Dietary calcium and vitamin D status should be assessed, and adequate supplementation prescribed. [3,14]. A daily calcium supplementation of 1200 mg/day after 50 years is recommended and vitamin D supplementation is needed to maintain an optimal level of 25-hydroxyvit D $\geq$ 30 ng/mL (or 75 nmol/L).

Although there is insufficient evidence to recommend a systematic bone anabolic treatment, it is still strongly debated in both situations of complete and incomplete AFFs. There is strong evidence that recombinant parathyroid hormone 1–34 or Teriparatide ® (TPTD) has an anabolic effect on bone and prevent osteoporotic fractures. TPTD is currently approved for this indication worldwide. Available preclinical and clinical data have also demonstrated the important role played by TPTD to enhance bone fracture healing and the potential beneficial effect in impaired fracture healing or specific clinical condition like AFFs [15–18]. Patients under BP therapy with the presence of a focal or diffuse periosteal thickening of the lateral cortex of the femoral shaft may or not progress to a complete AFF. Koh et al. demonstrated the presence of prodromal symptoms of thigh pain and of a “dread black line” within the cortical stress reaction were highly predictive of progression to a complete fracture [19]. This fracture line is not always radiologically easily identifiable and MRI or CT-scan is contributing to better visualize the fracture line. (Table 2). Based on the presence or absence of a radiolucent line, Saleh et al. [20] have proposed a different management of the BP use stress fractures in a small retrospective series of 14 patients. Five patients without fracture line were conservatively treated with an additional treatment of a 2-year course of TPTD. None of these cases progressed to complete displaced fracture. Nine patients with a radiolucent line received a trial conservative treatment as described above and were reassessed at 3 months. Only 2 of them presented both clinical and radiological healing and continued the conservative therapy. 7 patients with persistence of the fracture line were elected for prophylactic surgery. This series suggest that TPTD treatment can be successful in fractures without a radiolucent line, but may not achieve healing after 3 months in fracture with a radiographic “dread black line”. The authors proposed a management algorithm to the incomplete AFFs to prevent progression of the fracture and help to decide surgical intervention (Table 3).

Conclusion

The AFFs remains a topic of great interest to both clinicians and scientists [21–26]. These fractures are rare entity and the risk–benefit ratio still remains favorable for use of bisphosphonates to prevent fragility fractures. Discontinuation of bisphosphonates, calcium and vitamin D supplementation, and fracture fixation by IMN are the recommended treatment in patients with a stress fracture in a setting of a long-term use of BPs. So far there is insufficient evidence to recommend a systemic treatment by bone anabolic agent, but the recombinant 1–34 PTH (teriparatide®) may be promising both to prevent healing complications in AFFs and to promote healing in conservative treatment of incomplete AFFs. More clinical studies are needed to confirm this hypothesis.

Conflict of interest

None declared by the authors related to this article.

References

[1] Bawa HS, Weick J, Dirschl DR. Anti-osteoporotic therapy after fragility fracture lowers rate of subsequent fracture: analysis of a large population sample. J Bone Joint Surg Am 2015;97(October (19)):1555–62.
[2] Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, Pak CY. Severely suppressed bone turnover: a potential complication of alendronate therapy. J Clin Endocrinol Metab 2005;90(March (3)):1294–301.
[3] Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American society for bone and mineral research. J Bone Miner Res 2014;29(January (1)):1–23.
[4] Schilcher J, Koeppen V, Aspenberg P, Michaelsson K. Risk of atypical femoral fracture during and after bisphosphonate use. N Engl J Med 2014;371 (September (10)):974–6.
[5] Dell RM, Adams AL, Greene DF, Funahashi TT, Silverman SL, Eisemon EO, et al. Incidence of atypical nontraumatic diaphyseal fractures of the femur. J Bone Miner Res 2012;27(December (12)):2544–50.
[6] Schilcher J, Michaelsson K, Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. N Engl J Med 2011;364(May (18)):1728–37.
[7] Saita Y, Ishijima M, Kaneko K. Atypical femoral fractures and bisphosphonate use: current evidence and clinical implications. Ther Adv Chronic Dis 2015;6 (July (4)):185–93.
[8] Teo BJ, Koh JS, Goh SK, Png MA, Chua DT, Howe TS. Post-operative outcomes of atypical femoral subtrochanteric fracture in patients on bisphosphonate therapy. Bone Joint J 2014;96-B(May (5)):658–64.
[9] Bogdan Y, Tornetta 3rd P, Einhorn TA, Guy P, Leveille L, Robinson J, et al. Healing time and complications in operatively treated atypical femur fractures associated with bisphosphonate use: a multicenter retrospective cohort. J Orthop Trauma 2016;30(April (4)):177–81.
[10] Weil YA, Rivkin G, Safran O, Liebergall M, Foldes AJ. The outcome of surgically treated femur fractures associated with long-term bisphosphonate use. J Trauma 2011;71(July (1)):186–90.
[11] Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American society for bone and mineral research. J Bone Miner Res 2010;25 (November (11)):2267–94.
[12] Das De S, Setiobudi T, Shen L, Das De S. A rational approach to management of alendronate-related subtrochanteric fractures. J Bone Joint Surg Br 2010;92 (May (5)):679–86.
[13] Capeci CM, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. J Bone Joint Surg Am 2009;91(November (11)):2556–61.
[14] Yang KH, Min BW. Atypical femoral fracture: 2015 position statement of the Korean society for bone and mineral research. J Bone Metab 2015;22(August (3)):87–91.
[15] Campbell EJ, Campbell GM, Hanley DA. The effect of parathyroid hormone and teriparatide on fracture healing. Expert Opin Biol Ther 2015;15(January (1)):119–29.
[16] Goldhahn J, Feron JM, Kanis J, Papapoulos S, Reginster JY, Rizzoli R, et al. Implications for fracture healing of current and new osteoporosis treatments: an ESCEO consensus paper. Calcif Tissue Int 2012;90(May (5)):343–53.
[17] Hegde V, Jo JE, Andreopoulou P, Lane JM. Effect of osteoporosis medications on fracture healing. Osteoporos Int 2016;27(March (3)):861–71.
[18] Fukuda F, Kurinomaru N, Hijioka A. Weekly teriparatide for delayed unions of atypical subtrochanteric femur fractures. Biol Ther 2014;4(December (1–2)):73–9.
[19] Koh JS, Goh SK, Png MA, Kwek EB, Howe TS. Femoral cortical stress lesions in long-term bisphosphonate therapy: a herald of impending fracture? J Orthop Trauma 2010;24(February (2)):75–81.
[20] Saleh A, Hegde VV, Potty AG, Schneider R, Cornell CN, Lane JM. Management strategy for symptomatic bisphosphonate-associated incomplete atypical femoral fractures. Hss J 2012;8(July (2)):103–10.
[21] Khow KS, Paterson F, Shibu P, Yu SC, Chehade MJ, Visvanathan R. Outcomes between older adults with atypical and typical femoral fractures are comparable. Injury 2017;48(February (2)):394–8.
[22] Iizuka Y, Iizuka H, Kaneko T, Mieda T, Takechi R, Suzuki H, et al. Bone turnover markers and the factors associated with atypical femur fractures among Japanese patients. Injury 2016;47(November (11)):2484–9.
[23] Park JH, Lee Y, Shon OJ, Shon HC, Kim JW. Surgical tips of intramedullary nailing in severely bowed femurs in atypical femur fractures: simulation with 3D printed model. Injury 2016;47(June (6)):1318–24.
[24] Collinge C, Favela J. Use of teriparatide in osteoporotic fracture patients. Injury 2016;47(January (Suppl 1)):S36–8.
[25] Aspenberg P. Atypical fractures, a biased perspective. Injury 2016;47(January (Suppl 1)):S28–30.
[26] Schilcher J. High revision rate but good healing capacity of atypical femoral fractures: a comparison with common shaft fractures. Injury 2015;46 (December (12)):2468–73.

Injury, Int. J. Care Injured 48S (2017) S18–S21

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Insertion-related pain with intramedullary nailing

Yohan Jang[a,*], Laurence B. Kempton[b], Todd O. Mckinley[b], Anthony T. Sorkin[b]

[a] Department of Orthopaedic Surgery, Beaumont Health Botsford, Farmington Hills,MI, USA
[b] Department of Orthopaedics & Sports Medicine, Indiana University Health Methodist Hospital, Indianapolis, IN, USA

A R T I C L E I N F O

Keywords:
Intramedullary nail
Insertional pain
Etiology
Incidence

A B S T R A C T

The use of intramedullary nails for the treatment of long bone fractures has become increasingly frequent over the last decade with gradually expanding indications and technological advances. Improved biomechanics relative to plates and less direct fracture exposure are some of the potential benefits of intramedullary nails. However, persistent insertion-related pain is common and may limit satisfactory long term outcomes. The etiologies of this phenomenon remain unclear. Proposed theories for which there is a growing body of supporting evidence include hardware prominence, suboptimal nail entry points leading to soft tissue irritation and structural compromise, local heterotrophic ossification, implant instability with persistent fracture micromotion, and poorly defined insertional strain. Many factors that lead to insertion-related pain are iatrogenic, and careful attention to detail and refined surgical techniques will optimize outcomes.

Introduction

Intramedullary nail fixation of long bone fractures has increased dramatically in recent years [1]. This shift is largely due to advances in implant technology and the recognition of mechanical advantages of intramedullary versus extramedullary fixation. Additional clinical benefits include increased opportunity for biologic-friendly reduction techniques with less direct fracture exposure and load sharing properties of nails leading to earlier weight-bearing and faster rehabilitation [2–13].

Despite the many advantages of intramedullary fixation, post-operative or insertional nail pain after fixation of femur, tibia, and humeral fractures remains a common and poorly understood problem. Obremskey et al. reported that 11% of 437 patients with tibial shaft fractures treated with infrapatellar intramedullary nailing had significant knee pain at 1 year, including 25% of patients that were unable to kneel and 30% of patients that could not climb stairs without difficulty or at all [14]. A retrospective review by El Moumni et al. found that 23% of 75 patients treated with a retrograde femoral nail for diaphyseal fractures had persistent knee pain after 18 months [15]. Baltov at al reported outcomes of 111 patients treated with intramedullary nails for humerus fractures; 16% complained of significant shoulder pain with a mean follow up of 3.5 years [16]. The complexity of insertional pain has been described often with a combination of theories and anecdote but with little supporting evidence. In contrast to common beliefs that all “long term” insertion site pain is permanent, recent studies have revealed that certain causes may be linked to transient rather than permanent pain. The purposes of this review are to summarize the literature supporting causes of intramedullary nail insertional pain and delineate the surgical techniques that can help to avoid or address this problem.

Hardware prominence

The causal relationship between prominent hardware and insertional pain remains disputed. Lefaivre, et al. followed 56 patients for an average of 14 years and found self-reported knee pain and knee tenderness in physical examination were not correlated with nail prominence in radiographic images [4]. Similarly, Keating et al. found no correlation between knee pain and nail prominence in 107 patients [17]. In contrast Tahririan, et al. demonstrated that anterior or superior protrusion of the nail resulted in higher risk of developing knee pain [18]. Song et al. in their retrospective study of 45 patients found anterior nail prominence did not correlate with knee pain while superior nail prominence did [19]. Darabos et al. found in a similar retrospective review of 50 patients that those without insertional pain all had nails positioned at least 6 mm below the tibial plateau [20]. The abundance of retrospective literature on this topic has revealed no clear causal relationships between nail position and knee pain.

* Corresponding author at: Department of Orthopaedic Surgery, Beaumont Health Botsford, 28050 Grand River Ave, Farmington Hills, MI 48336, USA.
E-mail address: Yohan.Jang@beaumont.org (Y. Jang).

http://dx.doi.org/10.1016/j.injury.2017.04.029
0020-1383/

Correlation between femoral nail hardware prominence and pain has also been examined retrospectively. Regardless of technique used in femoral nailing (antegrade piriformis, antegrade trochanteric, or retrograde), pain from hardware prominence is most commonly attributed to proximal and distal interlocking screws. Dodenhoff et al. found no significant relationship between antegrade nail tip prominence and pain in femoral nailing; however, pain from prominent proximal interlocking screws resolved with screw removal [21]. In retrograde femoral nailing, a prominent nail tip can impinge on the patellar tendon and the patellar articular surface. The incidence of retrograde femoral nail prominence has decreased with advances in surgical technique and improved implant technology. Similar to antegrade femoral nailing, protrusion of interlocking screws is the most common cause of knee pain related to retrograde femoral nailing [22].

Humeral nails are most commonly inserted using an antegrade technique. Common causes of insertion site pain at the shoulder are lateral migration of the nail, loss of fixation of proximal interlocking screws, and prominence of the nail under (or through) the rotator cuff. [23–27].

Treatment of symptomatic prominent hardware is generally elective implant removal if the patient decides their pain is substantial enough to warrant the procedure. Pain relief following hardware removal is inconsistent [17,28–31], and causation between prominent hardware and pain remains unclear [4]. Therefore, patients should be made aware preoperatively of the variable success with pain relief after removal.

Heterotopic ossification

Formation of heterotopic bone near the nail insertion site can also contribute to persistent pain. Dodenhoff et al., reported a 30% incidence of heterotopic ossification in antegrade femoral nailing, and of those patients, 88% had pain [21]. Other groups have reported incidences of heterotopic ossification in antegrade femoral nailing ranging from 48 to 60% [32,33]. Heterotopic ossification following tibial nailing is less common [17,34–36]. Insertion-related heterotopic ossification has been described in the patellar tendon of patients treated with a transtendinous approach. Antegrade humeral nailing is rarely associated with the development of heterotopic ossification, but it has been reported. [37]. Bone morphogenetic protein invokes heterotopic bone formation by in regional mesenchymal stem cells (MSCs) [38]. Similarly, reaming debris containing MSCs left in soft tissues may increase the risk of heterotopic ossification. Furlong et al. found that heterotopic ossification occurred in 35.7% cases with reamed antegrade femoral nailing, compared to 9.4% in the unreamed group [39]. In contrast, Brumback et el found no differences in the severity of heterotopic ossification after focused irrigation in surrounding tissues after nailing [33]. It is possible that debris is further embedded by high pressure irrigation [40,41]. It is likely that soft tissue injury from surgical dissection and osteogenic reaming debris both contribute to formation of heterotopic ossification in long bone IM nailing. Therefore, we recommend a meticulous surgical approach, utilization of soft tissue protectors including appropriate trocars, and removal of as much reaming debris as possible before it spread throughout the wound and embedded in the soft tissues.

Poor starting point/Soft tissue irritation

The location of intramedullary nail insertion point is critical because of the potential deleterious effects on the surrounding local tissue. A cadaveric study by Tornetta et al. demonstrated that the safe zone for the tibial nail starting point is located 4.4 mm lateral to the midline of the plateau and has a footprint from 12.6 to 22.9 mm in width [42]. Keeping the starting point within the described safe zone avoids injury to the menisci and intermeniscal ligament. Injury to these structures may result in persistent pain after intramedullary nailing. Ellman et al. reported a case of an anterior medial meniscal root tear after intramedullary tibial nailing and resulting persistent knee pain until the tear was repaired [43]. We believe iatrogenic meniscal injuries are under-reported as recently reviewed in a cadaveric study by Tornetta et al. They reported 20% intra-articular structural damage and 30% subjacent location of nail in relation to one of the menisci [42]. Many different surgical techniques have been described for tibial nailing and conflicting evidence exists regarding whether there is an advantage among different surgical approaches in regard to minimizing insertion-related knee pain. The transtendinous approach was thought to be the cause of knee pain from the development of fibrous scar tissue; however multiple studies have refuted this [17]. More recent evidence has cast doubt on the causal link between different approaches and knee pain [18,30,44]. Iatrogenic injury to the infrapatellar fat pad and the infrapatellar branch of the saphenous nerve in the medial parapatellar or the transtendinous approach may be a cause of knee pain. Weil et al. performed a retrospective review of 78 patients with tibia fractures treated with a reamed intramedullary nail using a modified lateral approach and found 19% of patients still had anterior knee pain [45]. A prospective study of 37 fractures treated with a suprapatellar approach by Sanders et al. reported no anterior knee pain [10]. The effect of instrumentation on the articular cartilage of the patellofemoral joint is still under investigation. Chan et al. recently reported the results of a randomized controlled pilot study comparing infrapatellar and suprapatellar approaches for tibial nail insertion. Of the 25 patients that completed the 12 month follow-up, 11 were treated with the suprapatellar approach, which included pre- and post-nail patellofemoral arthroscopy and a MRI at one year. There were no significant differences in knee pain or function between the two groups. In addition, there was a lack of correlation between the three patients with post-nail articular cartilage changes and patellofemoral pain at one year [46].

It is unusual for a poor starting point in antegrade femoral nailing to cause insertional pain, but there may be a correlation with poor fracture reduction, especially in proximal fractures. In retrograde femoral nailing, a poor starting point with sagittal plane malposition can damage the cruciate ligaments or trochlear side of the patellofemoral joint. Combined with an incompletely seated nail, this can lead to impingement on the patellar articular surface in knee flexion [47,48]. The traditional starting point for antegrade humeral nails is located at the medial edge of the greater tuberosity. This location is near the hypovascular zone of the rotator cuff insertion and may lead to injury and fibrosis of the supraspinatus tendon, contributing to shoulder pain [23,49]. Recently, a relatively medial starting point was proposed and demonstrated improved outcomes [50–52]. Clearly, locating the appropriate nail starting point while remain mindful of the local anatomy can minimize iatrogenic insertional pain.

Implant instability/Persistent fracture micromotion

Activities of daily living exert forces leading to elastic strains in the femur and tibia. IM implants affect elastic strain and may contribute to hardware pain [53,54]. For example, cementless femoral prostheses have been causally linked to thigh pain secondary to changes in proximal femur strain. In patients with proximal femur fractures, Li et al. found that patients treated with long cephalmedullary nails had significantly less hip pain than those with short nails in a study involving 156 patients [55]. That finding further supports the notion that an increase in flexural rigidity and cortical stress at the stem tip can cause hip and thigh pain [56]. Fractures treated with intramedullary nails are subject to relative stability and secondary healing. In the early period of fracture healing, intramedullary nails should facilitate micromotion at the fracture site if secondary healing and callus formation are desired [57]. However, it is possible that insertional pain from intramedullary nailing could result from the construct micromotion translated proximally or distally through cortical contact. Ryan et al. retrospectively reviewed 443 patients with tibial shaft fractures that were treated with an intramedullary nail [58]. They identified a statistically significant inverse relationship between fracture union and insertional knee pain. The potential causality between pathologic motion from incomplete fracture union and insertional pain requires further investigation.

Insertional strain

IM nailing invariably leads to radial hoop stresses primarily located near the insertion site. These stresses could theoretically contribute to insertional pain. Finite element modeling has shown insertional hoop stresses are primarily affected by location of the starting point and implant geometry. The presence of an intramedullary nail also affects the biomechanics of the surrounding bone. Finite element analysis comparing intact tibia, a tibia with a nail inserted and a tibia after nail removal in 3 loading situations (standing, walking and single-limb kneeling) by Mir et al. demonstrated an increase in strain from 350 to 550% at the nail insertion zone for all three loading situations. The difference between the loading situations was magnified in the area of bone loss at the insertion zone [59]. The presence of an intramedullary nail results in the highest strain value and removal of nail did not normalize the elevated strain values. There is, however, an unclear correlation between insertional strain and pain. Tupis et al. used finite element analysis to compare the strain magnitude between piriformis and greater trochanteric starting points and found significantly higher strains that exceeded the yield level of bone with greater trochanteric insertion [60]. A prospective, randomized study of 34 patients with subtrochanteric femur fractures treated through either a trochanteric or piriformis nail by Starr et al. found no difference in the Harris Hip Scores or complication rates at 14 months [61]. In contrast, Stannard et al. found slightly better functional outcomes and analog pain scales in patients with greater trochanteric starting points in their prospective, randomized study of 110 patients [62]. This finding was only transient and equalized at 12 months. Despite the transient clinical linkage between insertional strain and insertional pain, we do understand there is an increase in strain at the starting point, and this may translate into intra-operative fracture or post-operative pain. We recommend that caution should be taken during insertion of intramedullary nails.

Conclusion

Persistent implant-related pain can be frustrating for both the surgeon and patient. Future investigations may help to differentiate more accurately between true nail insertion-related pain and incidental radiographic findings and also determine whether theoretical causes of insertion site pain are clinically significant. Surgeons should minimize potential iatrogenic causes of insertional pain such as limiting prominent hardware and avoiding soft-tissue injury at the starting point.

Conflict of interest

None.

References

[1] Anglen JO, Weinstein JN. Nail or plate fixation of intertrochanteric hip fractures: changing pattern of practice: a review of the American Board of Orthopaedic Surgery Database. J Bone Joint Surg Am 2008;90:700–7.
[2] Bohl DD, Basques BA, Golinvaux NS, Miller CP, Baumgartner MR, Grauer JN. Extramedullary compared with intramedullary implants for intertrochanteric hip fractures. J Bone Joint Surg Am 2014;96:1871–7.
[3] Tornetta III P, Egol KA, Ertl JP, Mullis B, Collinge CA, Ostrum RF. Locked plating versus retrograde nailing for distal femur fractures: a multicenter randomized trial. Presented at the Annual Meeting of the Orthopaedic Trauma Association. .
[4] Lefaivre KA, Guy P, Chan H, Blachut PA. Long term follow up of tibial shaft fractures treated with intramedullary nailing. J Orthop Trauma 2008;22:525–9.
[5] Kwok CS, Crossman PT, Loizou CL. Plate versus nail for distal tibial fractures: a systematic review and meta analysis. J Orthop Trauma 2014;28:542–8.
[6] Lang GJ, Cohen BE, Bosse MJ, Kellam JF. Proximal third tibial shaft fractures: should they be nailed? Clin Orthop Rela Res 1995;315:64–74.
[7] Freedman EL, Johnson EE. Radiographic analysis of tibial fracture malalignment following intramedullary nailing. Clin Orthop Relat Res 1995;315:23–33.
[8] Krettek C, Stephan C, Schandelmaier P, Richter M, Pap HC, Miclau T. The use of poller screws as blocking screws in stabilizing tibial fractures with small diameter intramedullary nails. J Bone Joint Surg Br 1999;81B:963–8.
[9] Ryan SP, Steen B, Tornetta III P. Semi extended nailing of metaphyseal tibial fractures: alignment and incidence of postoperative knee pain. J Orthop Trauma 2014;28:263–9.
[10] Sanders RW, Dipasquale TG, Jordan CJ, Arrington JA, Sagi HC. Semiextended intramedullary nailing of the tibiausing a suprapatellar approach: radiographic results and clinical outcomes at a minimum of 12 months follow up. J Orthop Trauma 2014;28:245–55.
[11] Changulani M, Jain UK, Keswani T. Comparison of the use of the humerus intramedullary nail and dynamic compression plate for management of diaphyseal fractures of the humerus. A randomized controlled study. Int Orthop 2007;31:391–5.
[12] McCormack RG, Brien D, Buckley RE, McKee MD, Powell J, Schemitsch EH. Fixation of fractures of the shaft of the humerus by dynamic compression plate or intramedullary nail: a prospective, randomized trial. J Bone Joint Surg Br 2000;82:336–9.
[13] Putti AB, Uppin RB, Putti BB. Locked intramedullary nailing versus dynamic compression plating for humerus shaft fractures. J Orthop Surg 2009;17:139–41.
[14] Obremskey W, Agel J, Archer K, To P, Tornetta III P, SPRINT Investigators. Character, incidence, and predictors of knee pain and activity after infrapatellar intramedullary nailing of an isolated tibia fracture. J Orthop Trauma 2016;20:135–41.
[15] El Moumni M, Schraven P, Ten Duis HJ, Wendt K. Persistent knee complaints after retrograde undreamed nailing of femoal shaft fractures. Acta Orthop Belg 2010;76:219–25.
[16] Baltov A, Mihail R, Dian E. Complications after interlocking intramedullary nailing of humeral nailing of humeral shaft fractures. Injury 2014;45(Suppl. 1): S9–15.
[17] Keating JF, Orfaly R, O'Brien PJ. Knee pain after tibial nailing. J Orthop Trauma 1997;11:10–3.
[18] Tahririan MA, Ziaei E, Osanloo R. Significance of the position of the proximal tip of the tibial nail: an important factor related to anterior knee pain. Adv Biomed Res 2014;3:119.
[19] Song SY, Chang HG, Byun JC, Kim TY. Anterior knee pain after tibial intramedullary nailing using a medial paratendinous approach. J Orthop Trauma 2012;26:172–7.
[20] Darabos N, Bajs ID, Rutic Z, Darabos A, Poljak D, Dobsa J. Nail position has an influence on anterior knee pain after tibial intramedullary nailing. Coll Antropol 2011;3:873–7.
[21] Dodenhoff RM, Dainton JN, Hutchins PM. Proximal thigh pain after femoral nailing. J Bone Joint Surg Br 1997;79:738–41.
[22] Katsoulis E, Court-Brown C, Giannoudis PV. Incidence and aetiology of anterior knee pain after intramedullary nailing of the femur and tibia. J Bone Joint Surg Br 2006;88:576–80.
[23] Cox MA, Dolan M, Synnott K, McElwain JP. Closed interlocking nailing of humerus shaft fractures with the Russell–Taylor nail. J Orthop Trauma 2000;14:349–53.
[24] Giannoudis PV, Xypnitos FN, Dimitriou R, Manidakis N, Hackney R. Internal fixation of proximal humeral fractures using the polarus intramedullary nail: our institutional experience and review of the literature. J Orthop Surg Res 2012;7:39.
[25] Kuma V, Datir S, Venkateswaran B. Intramedullary nailing for displaced proximal humeral fractures. J Orthop Surg 2010;18:324–7.
[26] Bhandari M, Devereaux PJ, McKee MD, Schemitz EH. Compression plating versus intramedullary nailing of humeral shaft fractures. A meta analysis. Acta Orthop 2006;72:279–84.
[27] Kurup H, Hossain M, Andrew JG. Dynamic compression plating versus locked intramedullary nailing for humeral shaft fractures in adults. Cochrane Database Syst Rev 2011(6), doi:http://dx.doi.org/10.1002/14651858.CD005959.pub2 Art. No.: CD005959.

[28] Toivanen JA, Honkonen SE, Koivisto AM, Jarvinen MJ. Treatment of low energy tibial shaft fractures: plaster cast compared with intramedullary nailing. Int Orthop 2001;25:110–3.
[29] Court-Brown CM, Gustilo T, Shaw AD. Knee pain after intramedullary tibial nailing: its incidence, etiology, and outcome. J Ortho Trauma 1997;11:103–5.
[30] Toivanen JA, Vaisto O, Kannus P, Latvala K, Honkonen SE, Jarvien MJ. Anterior knee pain after intramedullary nailing of fractures of the tibial shaft A prospective, randomized study comparing two different nail-insertion techniques. J Bone Joint Surg Am 2002;84:580–5.
[31] Karachalios T, Babis G, Tsarouchas J, Sapkas G, Pantazpoulos T. The clinical performance of a small diameter tibial nailing system with a mechanical distal aiming device. Injury 2000;31:451–9.
[32] Marks PH, Paley D, Kellam JF. Heterotopic ossification around the hip with intramedullary nailing of the femur. J Trauma 1988;28:1207–13.
[33] Brumback RJ, Wells JD, Lakatos R, Poka A, Bathon GH, Burgess AR. Heterotopic ossification about the hip after intramedullary nailing for fractures of the femur. J Bone Joint Surg Am 1990;72:1067–73.
[34] Gosselin RA, Belzer JP, Contreras DM. Heterotopic ossification of the patellar tendon following intramedullary nailing of the tibia: report of two cases. J Trauma 1993;34:161–3.
[35] Howell RD, Park JH, Egol KA. Late symptomatic heterotopic ossification of the patellar tendon after medial parapatellar intramedullary nailing of the tibia. Orthopedics 2011;34:226.
[36] Tornetta III P, Barbera C. Severe heterotopic bone formation in the knee after tibial intramedullary nailing. J Orthop Trauma 1992;6:113–5.
[37] Schmidt AH, Templeman DC, Grabowski CM. Antegrade intramedullary nailing of the humerus complicated by heterotopic ossification of the deltoid: a case report. J Orthop Trauma 2001;15:69–73.
[38] Urist MR, Nakagawa M, Nakata N, Nogami H. Experimental myositis ossificans: cartilage and bone formation in muscle in response to diffusible bone matrix derived morphogen. Arch Pathol Lab Med 1978;102:312–6.
[39] Furlong AJ, Giannoudis PV, Smith RM. Heterotopic ossification: a comparison between reamed and undreamed femoral nailing. Injury 1997;28:9–14.
[40] Owens BD, White DW, Wenke JC. Comparison of irrigation solution and devices in a contaminated musculoskeletal wound survival model. J Bone Joint Surg Am 2009;91:92–8.
[41] Hassinger SM, Hardin G, Wongworawat MD. High-pressure pulsatile lavage propagates bacteria into soft tissue. Clin Orthop Relat Res 2005;439:27–31.
[42] Tornetta III P, Riina J, Geller J, Purban W. Intraarticular anatomic risks of tibial nailing. J Orthop Trauma 1999;12:247–51.
[43] Ellman MB, James EW, LaPrade CM, Laprade RF. Anterior meniscus root avulsion following intramedullary nailing for a tibial shaft fracture. Knee Surg Sports Traumatol Arthosc 2015;23:1188–91.
[44] Vaisto O, Toivanen JA, Kannus P, Jarvinen MJ. Anterior knee pain after intramedullary nailing of fractures of the tibial shaft. An eight year follow up of a prospective, randomized study comparing two different nail insertion techniques. J Trauma 2008;64:1511–6.
[45] Weil YA, Gardner MJ, Boraiah S, Helfet DL, Lorich DG. Anterior knee pain following the lateral parapatellar approach for tibial nailing. Arch Orthop Trauma Surg 2009;129:773–7.
[46] Chan DS, Serrano-Riera R, Griffing R, Steverson B, Infante A, Watson D, et al. Suprapatellar versus infrapatellar tibial nail insertion: a prospective randomized control pilot study. J Orthop Trauma 2016;30:130–4.
[47] Krupp RJ, Malkani AL, Goodin RA, Voor MJ. Optimal entry point for retrograde femoral nailing. J Orthop Trauma 2003;17:100–5.
[48] Carmack DB, Moed BR, Kingston C, Zmurko M, Watson JT, Richardson M. Identification of the optimal intercondylar starting point for retrograde femoral nailing: an anatomic study. J Trauma Acute Care Surg 2005;55:692–5.
[49] Riemer BL, D'Ambrosia R, Kellam JF, Butterfield SL, Burke 3rd CJ. The anterior acromial approach for antegrade intramedullary nailing of the humeral diaphysis. Orthopedics 1993;16:1219–23.
[50] Park J, Pandler DS, Chun J, Lee ST. Antegrade humeral nailing through the rotator cuff interval: a new entry portal. J Orthop Trauma 2008;22:419–25.
[51] Knierim AE, Bollinger AJ, Wirth MA, Fehringer EV. Short, locked humeral nailing via neviaser portal: an anatomic study. J Orthop Trauma 2013; 27:63–7.
[52] Lopiz Y, Gacia-Coiradas J, Garcia-Fernandez C, Marco F. Proximal humerus nailing: a randomized clinical trial between curvilinear and straight nails. J Shoulder Elbow Surg 2014;23:369–76.
[53] Hussain A, Pollak AN, Moehrin HD, Olson SA, Chapman MW. Removal of intramedullary nails from the femur, review of 45 cases. J Orthop Trauma 1996;10:560–2.
[54] Hernigou P, Cohen D. Proximal entry for intramedullary nailing of the tibia: the risk of unrecognized articular damage. J Bone Joint Surg Br 2000;82:33–41.
[55] Li Z, Liu Y, Liang Y, Zhao C, Zhang Y. Short versus long intramedullary nails for the treatment of intertrochanteric hip fractures in patients older than 65 years. Int J Clin Exp Med 2015;8:6299–302.
[56] Nambe RS, Keyak JH, Agnes S, Louis P, Skinner HB. Cementless implant composition and femoral stress: a finite element analysis. Clin Orthop Relat Res 1998;347:261–7.
[57] Jagodzinski M, Krettek C. Effect of mechanical stability on fracture healing- an update. Injury 2007;38(March (Suppl. 1)):S3–10.
[58] Ryan SP, Tornetta III P, Dielwart C, Kaye-Krall E. Knee pain correlates with union after tibial nailing. J Orthop Trauma 2011;25:731–5.
[59] Mir H, Ruxi M, Harden J, Thomas R. Biomechanical effects of the nail entry zone and anterior cortical bone loss on the proximal tibia. J Orthop Trauma 2013;27:34–41.
[60] Tupis TM, Altman GT, Altman DT, Cook HA, Miller MC. Femoral bone strains during antegrade nailing: a comparison of two entry points with identical nails using finite element analysis. Clin Biomech (Bristol Avon) 2012;27:354–9.
[61] Starr AJ, Hay MT, Reinert CM, Borer DS, Christensen KC. Cephalomedullary nails in the treatment of high-energy proximal femur fractures in young patients: a prospective, randomized comparison of trochanteric versus piriformis fossa entry portal. J Orthop Trauma 2006;20:240–6.
[62] Stannard JP, Bankston L, Futch LA, McGwin G, Volgas DA. Functional outcome following intramedullary nailing of the femur. J Bone Joint Surg Am 2011;93:1385–91.

Injury, Int. J. Care Injured 48S (2017) S22–S25

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Acute compartment syndrome

Andrew H. Schmidt

Department of Orthopaedic Surgery, Hennepin County Medical Center, University of Minnesota, 701 Park Ave. South, Mailcode G2, Minneapolis, MN, USA

ARTICLE INFO

Keywords:
Compartment syndrome
Fasciotomy
Intramuscular pressure
Tibia fracture
Perfusion pressure

ABSTRACT

Acute compartment syndrome is a well-known complication of tibial fractures, yet it remains difficult to diagnose and the only effective treatment is surgical fasciotomy. Delayed fasciotomy is the most important factor contributing to poor outcomes, and as a result, treatment is biased towards performing early fasciotomy. Current diagnosis of ACS is based on clinical findings and intramuscular pressure (IMP) measurement, and is targeted at identifying safe thresholds for when fasciotomy can be avoided. Since clinical findings are variable and difficult to quantify, measurement of IMP – ideally continuously – is the cornerstone of surgical decision – making. Numerous investigators are searching for less invasive and more direct measurements of tissue ischemia, including measurement of oxygenation, biomarkers, and even neurologic monitoring. This article provides a brief but thorough review of the current state of the art in compartment syndrome diagnosis and treatment.

Introduction

Acute compartment syndrome (ACS) is a complication of trauma or other conditions that cause bleeding, edema, or that compromises perfusion to an extremity. Fracture or a crush injury to the limb are the most common cause of ACS [1]. The progressive limb swelling that occurs following fracture, a crush injury, or limb ischemia increases mass within the myofascial compartment due to accumulation of blood and fluid. Since muscle fascia and other connective tissues are inelastic, this increased mass causes increased pressure within the compartment, which is transmitted to the thin-walled veins causing venous hypertension [2], and progressive tissue ischemia. With the onset of cellular death, cell-membrane lysis releases osmotically active cellular contents into the interstitial space, causing further accumulation of fluid and further increase in intracompartment pressure. Arteriolar perfusion can also be compromised, leading to microvascular collapse [3]. Myonecrosis may occur within 2 h of injury in patients with ACS [4]. After 6–8 h of circulatory failure, irreversible ischemic injury has occurred to the myoneural tissues within the compartment.

Incidence in tibia fractures

Tibia fractures are the most common injury associated with ACS, and age, mechanism of injury, and fracture pattern and location all influence the risk of ACS (Table 1). Young men up to age 29 are the highest risk for ACS [5]. In terms of fracture pattern, segmental tibia fractures, bicondylar tibial plateau fractures and medial knee fracture-dislocations are very high risk [6,7]. Automobile versus pedestrian injuries, ballistic injuries to the proximal tibia and fibula [8], and tibia fractures occurring during soccer or football [5,9] are examples of mechanisms of injury associated with a high risk of ACS.

With regards to tibia fractures, Park et al. evaluated 414 acute tibial fractures, evaluating the rate of fasciotomy according to fracture location (Park 2009). ACS was most common in diaphyseal tibia fractures, occurring in 8% of cases, compared to less than 2% in proximal and distal metaphyseal fractures, respectively. Among the diaphyseal fractures, younger age was the only risk factor that was independently associated with the incidence of ACS. Several series report an appreciable incidence of compartment syndrome in patients with tibial plateau fractures [7,10] and these fractures must also be considered in the high-risk category.

Since ACS evolves after injury, one must be aware of the potential for ACS to develop if one is considering transferring a patient to another center for definitive care, and fasciotomy should be done prior to transfer if there is significant time involved before the patient arrives at the second institution [11,12].

Problems in diagnosis

Although the existence of ACS is well-known and most clinicians understand the potential limb-threatening nature of ACS, there is no clear definition of when compartment is actually

E-mail address: schmi115@umn.edu (A.H. Schmidt).

http://dx.doi.org/10.1016/j.injury.2017.04.024
0020-1383/

Table 1
Summary of the reported incidence of acute compartment syndrome related to various patterns and mechanism of injury and presence of clinical examination findings.

Risk Factor/Clinical Finding	Risk of CS
Fracture Pattern	
Segmental tibia Fracture	48% [6]
Bicondylar Tibial Plateau Fracture	18% [7]
Medial Knee Fracture-Dislocation	53% [7]
Mechanism of Injury	
Tibia fracture during sport	20% [5]
Soccer	55% [9]
Football	27% [9]
Ballistic Injury Proximal-third tibia or fibula	21% [8]
Clinical Exam Findings (pain, paresthesias, pain with passive stretch, paresis) [17]	
One clinical finding	
Pain	25%
Paresthesias	26%
Pain with passive stretch	25%
Paresis	19%
Two clinical findings	
Pain and pain with passive stretch	68%
Three clinical findings	
Pain, pain with passive stretch, paresis	93%
All four clinical findings	98%

present. Thus, there is considerable variation in the clinical management of compartment syndrome [13–15]. The consequences of missed diagnosis are severe for both the patient and the physician and hospital [16]. The generally accepted clinical signs of ACS are worsening pain that is out of proportion to what is otherwise expected, pain with passive stretch of the involved muscle, and paresthesia in the distribution of any sensory nerves within the compartment. It has been established that the clinical signs and symptoms of ACS are poor as a screening test, with low sensitivity [17] (Table 1). Many of these clinical findings also occur in patients without ACS, perhaps due to direct tissue injury. For example, Robinson et al. reviewed 208 consecutive patients who underwent reamed nailing of a tibia fracture, and 5 percent of them developed dysfunction of the common or deep peroneal nerve [18]. Many of them exhibited isolated weakness of the extensor hallucis longus associated with numbness in the first web space. Interestingly, all of these patients had continuous compartment pressure monitoring and none developed compartment syndrome [18].

Early diagnosis of ACS is critical for avoiding morbidity [19–23]. Unfortunately, despite the common teaching that compartment syndrome is an ‘orthopedic emergency’, there are frequent delays in the time from initial assessment to diagnosis and in the time from diagnosis to surgery in patients with ACS [22]. The incidence of late diagnosis can be diminished by frequent or continuous measurement of intramuscular pressure (IMP) [23,24]. Whenever the clinical examination is not reliable, measurement of IMP in one or more compartments in an at-risk patient is mandatory. Many investigators recommend routine measurement of IMP in all patients [25–28]. However, the need for IMP monitoring has been quite controversial, and there are also well-done studies that the refute the value of pressure monitoring [29–31]. However, the studies questioning the value of IMP measurement employed clinical protocols that employed very frequent and detailed clinical assessment. For example, Al-Dadah et al. reported similar rates of fasciotomy and time to diagnosis of compartment syndrome both before and after adopting a protocol of continuous monitoring of anterior compartment pressure [31]. However, patients in both groups were assessed by trained nurses every hour [31]. These results may not be generalizable to institutions that cannot offer that level of care.

The difficulty in using specific pressure thresholds for diagnosing ACS and deciding when fasciotomy should be done is highlighted by Prayson et al. who carefully followed blood pressure and compartment pressure in 19 patients with isolated lower extremity fractures who did not have compartment syndrome by clinical criteria, or at follow-up [29]. In their series, 84% of the patients had at least one measurement in which their perfusion pressure less than 30 mmHg, and 58% had were less than 20 mm Hg [29]. Thus, single pressure measurements alone may not be representative and do not establish trends with time. In contrast, serial or continuous measurements demonstrate rising IMP or falling perfusion pressure more clearly, and are likely to be more specific for patients that truly have ACS. Consistent with this, McQueen et al. recently reported data suggesting that continuous pressure monitoring should be the gold standard for diagnosis of ACS; using a threshold for fasciotomy related to the perfusion pressure (intramuscular pressure within 30 mm Hg of the diastolic blood pressure for 2 consecutive hours or more), they demonstrated a sensitivity for diagnosis of ACS of 94% [32].

Clinicians should be aware of potential pitfalls with use of pressure measurements for decision-making in patients at-risk of ACS. First, there is spacial variation in the pressure within a given compartment, with pressures being highest within 5 cm of the fracture [33] and more centrally in the muscle [34]. It has never been established whether one should obtain pressures near the fracture to obtain the highest pressure, or measure further away (outside the zone of injury) to obtain a pressure that may be more representative of the majority of the compartment [30]. Secondly, there may be uncertainty and/or variability in measured values of IMP. Using a cadaver model, Large et al. documented significant variability in the technique of IMP measurement, and showed that only 60% of measurements done correctly were within 5 mm Hg of the known IMP [35]. Another potential source of uncertainty when calculating perfusion pressure is what blood pressure value to use, especially if the patient is under general anesthesia. Tornetta et al. recorded preoperative, intraoperative, and postoperative blood pressures in patients undergoing tibial nailing [36]. Their conclusion was that use of intraoperative diastolic blood pressure measurements for calculation of perfusion pressure may give a spuriously low perfusion pressure and lead to unnecessary fasciotomy. These authors recommend using preoperative blood pressure values when calculating perfusion pressure in a patient under general anesthesia, except when the patient is going to remain under anesthesia for several more hours [36].

There is significant effort being done to improve the diagnosis of ACS. Promising modalities include near-infrared spectroscopy, measurement of pH, and use of biomarkers. Lower tissue oxygenation levels correlate with increase IMP [37]. Near-infrared spectroscopy (NIRS) has been shown to demonstrate a sudden decrease in tissue oxygenation in patients with ACS [38], but the reliability of NIRS in an injured leg remains uncertain and its role in the diagnosis of ACS has not been defined. Biomarkers, including measurement of pH and intramuscular glucose have been reported to identify patients with impaired muscle metabolism due to ACS. In an animal model, Doro et al. showed that glucose concentration and oxygen tension were significantly lower within 15 min of creating compartment syndrome [39]. Finally, in a study of 61 patients at-risk for extremity ACS, continuous monitoring of pH performed better than continuous measurement of IMP (Personal communication, A Johnstone, 2016).

Problems in treatment

The only effective treatment for ACS is immediate surgical fasciotomy, releasing the skin and muscle fascia in order to increase the volume of the affected muscle compartment and immediately reduce compartment pressure. Fasciotomy must be done before irreversible tissue necrosis occurs, thus there is a strong clinic bias towards doing fasciotomy in patients who are considered to be at high risk and/or who have concerning clinical findings. Numerous clinical series document the efficacy of early fasciotomy [21,40–42] and the potential complications of late fasciotomy [20,41]. It is generally accepted that performing an unnecessary fasciotomy is better than performing a fasciotomy too late, or missing a true case of compartment syndrome, given the potential systemic risks (rhabdomyolysis and myonecrosis) and functional loss associated with untreated ACS.

Fasciotomy, despite being definitive management for ACS, is associated with its own set of complications. These include the need for further surgery for delayed wound closure or skin grafting, cosmetic problems, pain and nerve injury, permanent muscle weakness, and chronic venous insufficiency [12,24,43]. Further, fasciotomy increases the cost of care [44,45].

With the morbidity and expense of fasciotomy, numerous investigators are trying to identify less invasive approaches to treating ACS. Odland et al. have reported on the potential use of tissue ultrafiltration for both diagnosing ACS on the basis of biomarker measurement, as well as decreasing IMP by removal of interstitial fluid [46,47]. Lawendy and colleagues have shown that the inflammatory response to injury may play a significant role in the pathophysiology of ACS [48]. Attenuation of the inflammatory response by indomethacin reduced tissue injury and compartment pressures in an animal model [49].

Summary

Acute compartment syndrome remains a vexing complication of tibial shaft fractures. Although clinicians understand the clinical presentation, pathophysiology, and potential morbidity, ACS remains difficult to diagnose, with clinical intuition (also referred to as a “high index of suspicion”) remaining a cornerstone of decision-making. The clinical exam is excellent for ruling out ACS [17], but positive clinical findings do not accurately indicate which patient has ACS [17]. Similarly, current thresholds for fasciotomy based on measurement of intramuscular pressure and calculation of perfusion pressure are based on avoiding missed ACS (minimizing false negative diagnoses) rather than avoiding unnecessary fasciotomy (false positive diagnoses). Thus, there is a current need for more precise methods of diagnosis, as well as identification of less invasive means of preventing or treating ACS in its early stages, before irreversible muscle ischemia has occurred.

Conflict of interest

The author owns stock in Twin Star Medical and has received research support from the United States Dept. of Defense.

References

[1] McQueen MM, Gaston P, Court-Brown CM. Acute compartment syndrome. Who is at risk? J Bone Joint Surg Br 2000;82-B:200–3.
[2] Matsen FA. Compartment syndrome. An unified concept. Clin Orthop Rel Res 1975;113:8–14.
[3] Heppenstall RB, Sapega AA, Izant T, Fallon R, Shenton D, Park YS. Compartment syndrome: a quantitative study of high-energy phosphorus compounds using 31P-magnetic resonance spectroscopy. J Trauma 1989;29(8):1113–9.
[4] Vaillancourt C, Shrier I, Vandal A, Falk M, Rossignol M, Vernec A, et al. Acute compartment syndrome: how long before muscle necrosis occurs? Can J Emerg Med 2004;6(3):147–54.
[5] McQueen MM, Duckworth AD, Aitken SA, Sharma RA. Court-Brown CM: Predictors of compartment syndrome after tibial fracture. J Orthop Trauma 2015;29:451–5.
[6] Woll TS, Duwelius PJ. The segmental tibial fracture. Clin Orthop Rel Res 1992;281:204–7.
[7] Stark E, Stucken C, Trainer G, Tornetta III P. Compartment syndrome in Schatzker type VI plateau fractures and medial condylar fracture-dislocations treated with temporary external fixation. J Orthop Trauma 2009;23:502–6.
[8] Meskey T, Hardcastle J, O'Toole RV. Are certain fractures at increased risk for compartment syndrome after civilian ballistic injury? J Trauma 2011;71:1385–9.
[9] Wind TC, Saunders SM, Barfield WR, Mooney III JF, Hartsock LA. Compartment syndrome after low-energy tibia fractures sustained during athletic competition. J Orthop Trauma 2012;26:33–6.
[10] Chang YH, Tu YK, Yeh WL, Hsu RW. Tibial plateau fracture with compartment syndrome: a complication of higher incidence in Taiwan. Chang Gung Med J 2000;23(3):149–55.
[11] Prasarn ML, Ahn J, Achor TS, Paul O, Lorich DG, Helfet DL. Acute compartment syndrome in patients with tibia fractures transferred for definitive fracture care. Am J Orthop 2014;43:173–7.
[12] Ritenour AE, Dorlac WC, Fang R, Woods T, Jenkins DH, Flaherty SF, et al. Complications after fasciotomy revision and delayed compartment release in combat patients. J Trauma 2008;64:S153–62.
[13] Davis ET, Harris A, Keene D, Porter K, Manji M. The use of regional anaesthesia in patients at risk of acute compartment syndrome. Injury 2006;37:128–33.
[14] O'Toole RV, Whitney A, Merchant N, Hui E, Higgins J, Kim TT, et al. Variation in diagnosis of compartment syndrome by surgeons treating tibial shaft fractures. J Trauma 2009;67:735–41.
[15] Wall CJ, Richardson MD, Lowe AJ, Brand C, Lynch J, de Steiger RN. Survey of management of acute, traumatic compartment syndrome of the leg in Australia. J Trauma 2007;63:268–75.
[16] Bhattacharyya T, Vrahas MS. The medical-legal aspects of compartment syndrome. J Bone Joint Surg Am 2004;86-A:864–8.
[17] Ulmer T. The clinical diagnosis of compartment syndrome of the lower leg: are clinical findings predictive of the disorder? J Orthop Trauma 2002;16:572–7.
[18] Robinson CM, O'Donnell J, Will E, Keating JF. Dropped hallux after the intramedullary nailing of tibial fractures. J Bone Joint Surg Br 1999;81-B:481–4.
[19] Finkelstein JA, Hunter GA, Hu RW. Lower limb compartment syndrome: course after delayed fasciotomy. J Trauma 1996;40:342–4.
[20] Hope MJ, McQueen MM. Acute compartment syndrome in the absence of fracture. J Orthop Trauma 2004;18:220–4.
[21] Prasarn ML, Ouellette EA, Livingstone A, Giuffrida AY. Acute pediatric upper extremity compartment syndrome in the absence of fracture. J Pediatr Orthop 2009;29:263–8.
[22] Vaillancourt C, Shrier I, Falk M, Rossignol M, Vernec A, Somogyi D. Quantifying delays in the recognition and management of acute compartment syndrome. Can J Emerg Med 2001;3:26–30.
[23] McQueen MM, Christie J, Court-Brown CM. Acute compartment syndrome in tibial diaphyseal fractures. J Bone Joint Surg Br 1996;78(1):95–8.
[24] Kashuk JL, Moore EE, Pinski S, Johnson JL, Moore JB, Morgan S, et al. Lower extremity compartment syndrome in the acute care surgery paradigm: safety lessons learned. Patient Saf Surg 2009;3:11–6.
[25] White TO, Howell GED, Will EM, Court-Brown CM, McQueen MM. Elevated intramuscular pressures do not influence outcome after tibial fracture. J Trauma 2003;55:1133–8.
[26] McQueen MM, Court-Brown CM. Compartment monitoring in tibial fractures. The pressure threshold for decompression. J Bone Joint Surg Br 1996;78(1):99–104.

[27] Allen MJ, Stirling AJ, Crawshaw CV, Barnes MR. Intracompartmental pressure monitoring of leg injuries. An aid to management. J Bone Joint Surg Br 1985;67-B:53–7.
[28] Ozkayin N, Aktuglu K. Absolute compartment pressure versus differential pressure for the diagnosis of compartment syndrome in tibial fractures. Int Orthop 2005;29:396–401.
[29] Prayson MJ, Chen JL, Hampers D, Vogt M, Fenwick J, Meredick R. Baseline compartment pressure measurements in isolated lower extremity fractures without clinical compartment syndrome. J Trauma 2006;60:1037–40.
[30] Harris IA, Kadir A, Donald G. Continuous compartment pressure monitoring for tibia fractures: does it influence outcome? J Trauma 2006;60:1330–5.
[31] Al-Dadah OQ, Darrah C, Cooper A, Donell ST, Patel AD. Continuous compartment pressure monitoring vs: clinical monitoring in tibial diaphyseal fracture. Injury 2008;39:1204–9.
[32] McQueen MM, Duckworth AD, Aitken SA, Court-Brown CM. The estimated sensitivity and specificity of compartment pressure monitoring for acute compartment syndrome. J Bone Joint Surg Am 2013;95-A:673–7.
[33] Heckman MM, Whitesides TE, Grewe SR, Rooks MD. Compartment pressure in association with closed tibial fractures: the relationship between tissue pressure, compartment, and the distance from the site of the fracture. J Bone Joint Surg Am 1994;76-A:1285–92.
[34] Nakhostine M, Styf JR, van Leuven S, Hargens AR, Gershuni DH. Intramuscular pressure varies with depth: the tibialis anterior muscle studied in 12 volunteers. Acta Orthop Scand 1993;64:377–81.
[35] Large TM, Agel J, Holtzman DJ, Benirschke SK, Krieg JC. Interobserver variability in the measurement of lower leg compartment pressures. J Orthop Trauma 2015;29:316–21.
[36] Kakar S, Firoozabadi R, McKean J, Tornetta III P. Diastolic blood pressure in patients with tibia fractures under anesthesia: implications for the diagnosis of compartment syndrome. J Orthop Trauma 2007;21:99–103.
[37] Shuler MS, Reisman WM, Kinsey TL, Whitesides Jr TE, Hammerberg EM, Davila MG, et al. Correlation between muscle oxygenation and compartment pressures in acute compartment syndrome of the leg. J Bone Joint Surg Am 2010;92-A:863–70.
[38] Shuler MS, Reisman WM, Cole AL, Whitesides TE, Moore TJ. Near infrared spectroscopy in acute compartment syndrome: case report. Injury 2011;42:1506–8.
[39] Doro CJ, Sitzman TJ, O'Toole RV. Can intramuscular glucose levels diagnose compartment syndrome? J Trauma Acute Care Surg 2014;76:474–8.
[40] Rorabeck CH. The treatment of compartment syndromes of the leg. J Bone Joint Surg Br 1984;66B:93–7.
[41] Sheridan GW, Matsen FA. Fasciotomy in the treatment of the acute compartment syndrome. J Bone Joint Surg Am 1976;b:112–5.
[42] Lagerstrom CF, Reed II RL, Rowlands BJ, Fischer RP. Early fasciotomy for acute clinically evident posttraumatic compartment syndrome. Am J Surg 1989;158:36–9.
[43] Frink M, Klaus AK, Kuther G, Probst C, Gosling T, Kobbe P, et al. Long term results of compartment syndrome of the lower limb in polytraumatised patients. Injury 2007;38:607–13.
[44] Crespo AM, Manoli III A, Konda SR, Egol KA. Development of compartment syndrome negatively impacts length of stay and cost after tibia fracture. J Orthop Trauma 2015;29:312–5.
[45] Schmidt AH. The impact of compartment syndrome on hospital length of stay and charges among adult patients admitted with a fracture of the tibia. J Orthop Trauma 2011;25:355–7.
[46] Odland R, Schmidt AH, Hunter B, Kidder L, Bechtold JE, Linzie BM, et al. Use of tissue ultrafiltration for treatment of compartment syndrome: a pilot study using porcine hindlimbs. J Orthop Trauma 2005;19:267–75.
[47] Odland RM, Schmidt AH. Compartment syndrome ultrafiltration catheters: report of a clinical pilot study of a novel method for managing patients at risk of compartment syndrome. J Orthop Trauma 2011;25:358–65.
[48] Lawendy A-R, Bihari A, Sanders DW, McGarr G, Badhwar A, Cepinskas G. Contribution of inflammation to cellular injury in compartment syndrome in an experimental rodent model. Bone Joint J 2015;97-B:539–43.
[49] Manjoo A, Sanders D, Lawendy A, Gladwell M, Gray D, Parry N, et al. Indomethacin reduces cell damage: shedding new light on compartment syndrome. J Orthop Trauma 2010;24:526–9.

Injury, Int. J. Care Injured 48S (2017) S26–S29

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Radiation exposure during intramedullary nailing

David J. Hak

Orthopedic Surgery, University of Colorado, Denver Health Medical Center, Denver CO, USA

ARTICLE INFO

Keywords:
Fluoroscopy
Radiation safety
Radiation exposure protection

ABSTRACT

Surgeons should aim to keep radiation exposure “As Low As Reasonably Achievable (ALARA)” during intramedullary nailing and other minimally invasive surgical procedures. This requires understanding the principles of ionizing radiation and methods for minimizing exposure risk. The main source of radiation exposure to surgical personnel during fluoroscopy is from scattered radiation. Since radiation scatter is mainly directed towards the fluoroscopy source, the best configuration during surgery to reduce radiation dose to the surgeon is to position the fluoroscopic source below the operating room table and the image collector above the table. During cross table imaging, the surgeon should stand on the side with the image collector to minimize their exposure to radiation scatter. To reduce scattered radiation the patient must be placed as close to the image collector and as far away from the x-ray tube as possible. Standing farther away from the patient can exponentially reduce radiation exposure. The hands usually have the greatest dose exposure to radiation during surgical procedures, but they are far less radiosensitive than the eyes or thyroid. To minimize exposure to the hands, a surgeon should use the hands-off technique taking fluoroscopic images only when his or her hands are farthest from the radiographic field. Lead gowns, lead thyroid shields, and lead glasses, further reduces an individual’s exposure to radiation.

Introduction

Intraoperative fluoroscopy is being increasingly used during orthopedic trauma surgery due to the expansion of minimally invasive techniques and expanding indications for intramedullary nailing. As such, it is important for Orthopedic surgeons to understand the principles of ionizing radiation and methods for minimizing exposure risk to themselves, their patients, and the operating room team. The goal should be to follow the ALARA principle, which means radiation exposure that is “As Low As Reasonably Achievable.”

Radiation is defined as energy from a source that travels through space and may be able to penetrate various materials. Radiation may be nonionizing, such as light, radio, and microwaves. Ionizing radiation refers to radiation produced by unstable atoms, or by a high-voltage device such as an x-ray machine.

Units of measurement

The energy produced by x-rays is measured in Roentgen equivalents in men (Rems). Energy deposited in a material is measured in Gray (Gy) and reflects the physical effects of the radiation. Energy deposited in biologic material is expressed as a dose equivalent called Sievert (Sv) and reflects the biological effect of the radiation.

Radiation exposure

Everyone is exposed to a baseline level of radiation. In the United States the level of exposure from cosmic radiation is 0.27 mSv/year. Medical exposure through receiving a chest x-ray equals 0.1 mSv, while a head CT results in 1.5 mSv, and 9.9 mSv with a whole body CT scan. The dose of radiation required to produce radiation sickness is between 500 and 1000 mSv, which is equal to the amount that the citizens of Hiroshima were exposed to in 1945.

Adverse effects of radiation on the body can be due to either somatic effects or stochastic effects. Somatic effects are directly related to the radiation dose. Early somatic effects include radiation sickness, while late somatic effects include leukemia, thyroid cancer, and radiation induced cataracts. Levels of radiation below the calculated threshold levels for these injuries do not result in an increased risk of illness. In contrast stochastic effects occur by chance. There is no safe threshold for stochastic effects, and damage is cumulative with multiple exposures to radiation. Stochastic effects typically exhibit a latent period prior to effects

E-mail address: David.hak@dhha.org (D.J. Hak).

http://dx.doi.org/10.1016/j.injury.2017.04.023
0020-1383/

development that can exceed 25 years. Late stochastic effects include thyroid cancer and leukemia.

Maximum allowable thresholds

The International Commission on Radiological Protection (ICRP) sets maximum allowable thresholds for radiation exposure. In 2012 they recommended a new lower annual limits for radiation dose to the eye. Threshold levels for the eye are 20 mSv per year averaged over 5 years or a maximum of 50 mSv in any single year [1]. The lens of the eye is particularly sensitive to radiation and high levels of exposure can cause radiation induced cataracts. Threshold levels for the thyroid are 300 mSV and for the hand are 500 mSv. Papillary thyroid cancer is the predominant cancer type seen in patients who have had previous radiation to the head and neck.

The hands usually have the greatest dose exposure to radiation during surgical procedures, but they are far less radiosensitive than the eyes or thyroid. The hands-off technique, which requires the surgeon to take fluoroscopic images when his or her hands are farthest from the radiographic field, is suggested for minimizing exposure to the hands.

Radiation exposure during intramedullary nailing

Radiation exposure during 8 closed interlocking intramedullary femoral nailings was monitored using high sensitive thermoluminescent dosimeters [2]. The average radiation dose received by the eye was 19.0 μSv, by thyroid gland was 35.4 μSv and by the hands was 41.7 μSv. The values reported in this study are μSv (10^{-6}) whereas threshold values are in mSv (10^{-3}), therefore they are far below the recommended threshold levels for even a very busy surgeon.

Radiation dose to primary surgeon's and the first assistant‘s hands was monitored during 41 intramedullary nailing of femoral and tibial fractures using ring dosimeters worn on their dominant index fingers [3]. The average radiation dose to the primary surgeon's dominant hand was 1.27 mSv, and that for the first assistant was 1.29 mSv. The authors calculated that the annual threshold level for the hand of 500 mSV would be exceeded only if a surgeon performed more than 407 intramedullary nailing procedures per year.

The researchers also performed in-vitro measurements during operative procedures of the lower leg simulating different intraoperative situations to assess the surface doses to the primary surgeon's thyroid gland with and without wearing a lead shield. The average radiation dose without a thyroid shield was approximately 70 times higher than with thyroid lead protection. Using an average fluoroscopy time of 4.6 min for intramedullary nailing, the authors extrapolated that if 1000 intramedullary nailings were performed without wearing a thyroid shield the surgeon would only reach 13% of the annual thyroid threshold level, and if wearing a thyroid shield they would only reach 0.2% of the annual threshold value.

A study comparing 12 senior surgeons with a group of 10 junior surgeons performing 23 long bone IM nailing procedures found that the junior group used statistically more fluoroscopic time and had significantly greater radiation exposure to their hands [4].

A study of 107 consecutive orthopaedic trauma operations found that the assistant, who commonly was performing the reduction, was approximately 10 cm from the fluoroscopy beam while the surgeon was always more than 90 cm from the beam [5]. As a result, the primary surgeon's dosimeter readings outside their lead gown averaged 3.3 mREM monthly, while the assistant closer to the beam averaged 20.22 mREM monthly. Dosimeter readings beneath their lead gown for the primary surgeon was zero, while the assistant still received a monthly average of 6 mREM.

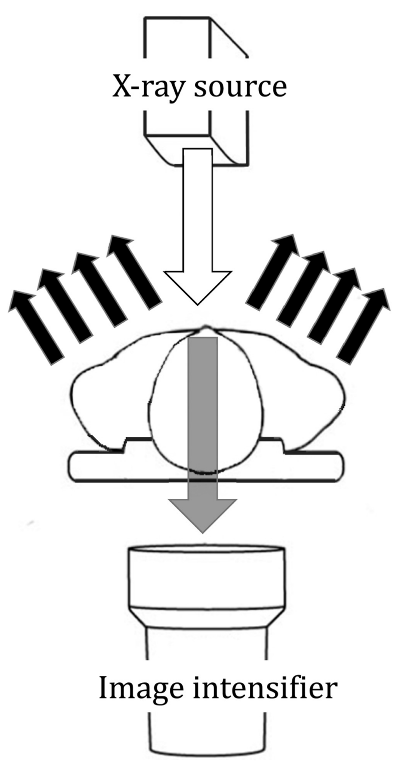


Fig. 1. Radiation not absorbed by the patient is scattered (solid arrows) and is mainly directed towards the x-ray source.

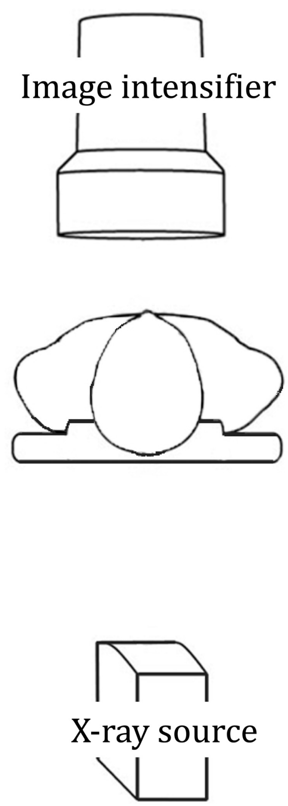


Fig. 2. The fluoroscopic beam source should be positioned below the table with the image intensifier placed above the table to minimize the surgical teams exposure to scatter radiation.

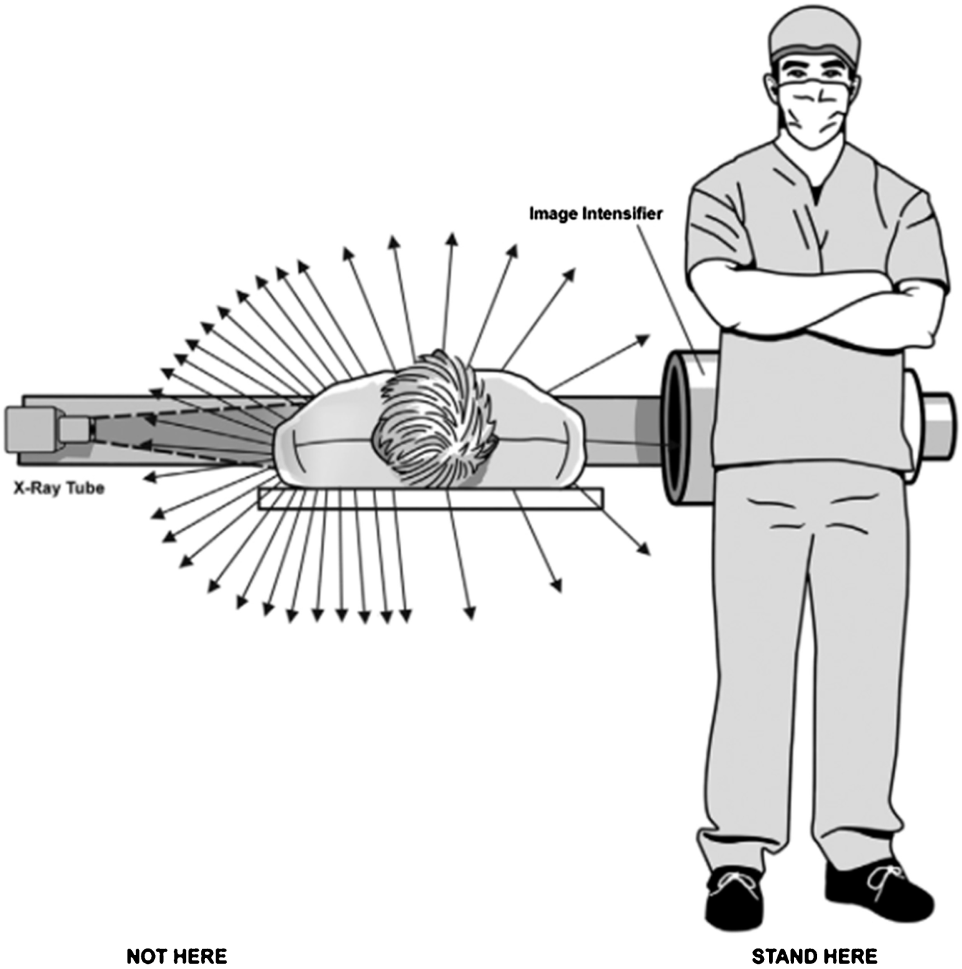


Fig. 3. Illustration of proper physician positioning relative to the beam source during lateral fluoroscopic imaging.
Reprinted with permission from Srinivan D, et al. World Neurosurgery. 82: 1337–1343.

The amount of radiation required to perform free-hand placement of interlocking screws has also been studied and compared to radiation free techniques. In a study of free-hand placement of 41 interlocking screws investigators found it took an average of 10 s of fluoroscopy producing 9.2 mrads of radiation during set-up to achieve "perfect circles" and an average of 18 s of fluoroscopy producing 32.9 mrads of radiation to insert each interlocking screw [6]. In another study, the average fluoroscopy time for placing two distal locking screws during 43 antegrade femoral nailing procedures was 10 s with an average radiation dose was 690.27 μGy (range, 200–2310 μGy) [7].

Protecting yourself and your team from radiation exposure

The main source of radiation exposure to surgical personnel during fluoroscopy is from scattered radiation. For every 1000 photons delivered by the fluoroscopy machine, only about 20 actually reach the image detector. Between 100 and 200 photons bounce off the patient as scattered radiation. Radiation scatter is mainly directed towards the fluoroscopy source. The remaining photons are absorbed by the patient (radiation dose to the patient) (Fig. 1).

Methods to reduce radiation exposure during intra-operative fluoroscopy can be categorized into 1) fluoroscopy tube position, 2) position and distance from fluoroscopy tube, and 3) use of various protection equipment.

Since radiation scatter is mainly directed towards the fluoroscopy source, the best configuration during surgery to reduce radiation dose to the surgeon is to position the fluoroscopic source below the operating room table and the image collector above the table (Fig. 2). Since scatter radiation follows Newton's inverse-square law, that is the radiation intensity is inversely proportional to the square of the distance from the source, exposure can be exponentially reduced by standing farther away from the patient.

During cross table imaging, the surgeon should stand on the side with the image collector to minimize their exposure to radiation scatter (Fig. 3). Surgeons standing on the side of the fluoroscopic source receive 3–4 times more radiation to their thyroid than they would if the stood on the side of the image collector [8].

Most fluoroscopy systems allow the operator to reduce the field size through the use of lead shutters or collimators. Collimation can markedly reduce the amount of radiation exposure because it reduces the size of the primary beam and the amount of scatter exposure to the surgeon. In comparison, the use of magnification increases scattered radiation to surgeon because it requires a higher relative patient entrance dose, and therefore there is greater scattered radiation. Depending on the design of the machine, selecting the magnification option may increase the radiation dose by a factor of 2–4. To minimize scattered radiation avoid using the magnification option and use collimation whenever feasible.

Another important factor to reduce scattered radiation is the distance of the fluoroscopic source in relation to the patient. To reduce scattered radiation the patient must be placed as close to the image collector and as far away from the x-ray tube as possible.

Proper positioning of the fluoroscopic imaging device can be aided with the use of a laser target. Alternatively, adhesive tape can be used to mark the correct floor position of the fluoroscopic machine. Both of these methods can minimize unnecessary images that are not properly positioned at the area of interest.

The use of pulsed fluoroscopy mode is an important tool for fluoroscopic dose reduction. Historically, fluoroscopy was performed in the continuous mode such that when the unit was activated a continuous x-ray beam was produced. Modern fluoroscopic equipment offers an alternative to continuous fluoroscopy in which the x-ray beam is pulsed by the machine, or turned on and off at a selected pulse rate. This pulsed technique both improves the image quality and significantly lowers the radiation dose to the patient [9].

Personal radiographic protection equipment reduces an individual's exposure to radiation. The use of lead glasses (0.75 mm lead-equivalent) on average provides a 90% reduction in radiation exposure to the surgeon's eye [10]. Thyroid shields decrease the scattered radiation exposure to the thyroid by at least 85% [11]. A lead apron decreases radiation exposure 16-fold in the AP plate and 4-fold in the lateral plane. Wearing a lead apron (0.25 mm thickness) will attenuate 90% of radiation [12].

Conclusion

Since intraoperative fluoroscopy is being increasingly used during orthopedic trauma surgery it is important for surgeons to understand the principles of ionizing radiation and methods for minimizing exposure risk to themselves, their patients, and the operating room team. Surgeons should aim to keep radiation exposure "As Low As Reasonably Achievable (ALARA)" during intramedullary nailing and other minimally invasive surgical procedures. Since the main source of radiation exposure to surgical personnel during fluoroscopy is from scattered radiation, the surgeon should understand methods for minimizing this exposure through appropriate positioning of the fluoroscopy tube with respect to the patient and the members of the operating team.

Conflict of interest

None.

References

[1] ICRP. ICRP Statement on tissue reactions/early and late effects of radiation in normal tissues and organs – threshold doses for tissue reactions in a radiation protection context. ICRP Publication 118. Ann. ICRP 41(1/2).

[2] Fuchs M, Schmid A, Eiteljörge T, Modler M, Stürmer KM. Exposure of the surgeon to radiation during surgery. Int Orthop 1988;22(3):153–6.

[3] Müller LP, Suffner J, Wenda K, Mohr W, Rommens PM. Radiation exposure to the hands and the thyroid of the surgeon during intramedullary nailing. Injury 1998 Jul;29(6):461–8.

[4] Blattert TR, Fill UA, Kunz E, Panzer W, Weckbach A, Regulla DF. Skill dependence of radiation exposure for the orthopaedic surgeon during interlocking nailing of long-bone shaft fractures. Arch Orthop Trauma Surg 2004;24(10):659–64.

[5] Tasbas BA, Yagmurlu MF, Bayrakci K, Ucaner A, Heybeli M. Which one is at risk in intraoperative fluoroscopy? Assistant surgeon or orthopaedic surgeon?. Arch Orthop Trauma Surg 2003;123(5):242–4.

[6] Chan DS, Burris RB, Erfogan M, Sagi HC. The insertion of intramedullary nail locking screws without fluoroscopy: a faster and safer technique. J Orthop Trauma 2013;27(7):363–6.

[7] Maqungo S, Horn A, Bernstein B, Keel M, Roche S. Distal interlocking screw placement in the femur: free-hand versus electromagnetic assisted technique (Sureshot). J Orthop Trauma 2014;28(12):e281–3.

[8] Rampersaud YR, Foley KT, Shen AC, Williams S, Solomito M. Radiation exposure to the spine surgeon during fluoroscopically assisted pedicle screw insertion. Spine 2000;25(20):2637–45.

[9] Hernanz-Schulman M, Goske MJ, Bercha IH, Strauss KJ. Pause and pulse: ten steps that help manage radiation dose during pediatric fluoros- copy. AJR Am J Roentgenol 2011;197:475–81.

[10] Burns S, Thornton R, Dauer LT, Quinn B, Miodownik D, Hak DJ. Leaded eyeglasses substantially reduce radiation exposure of the surgeon's eyes during acquisition of typical fluoroscopic views of the hip and pelvis. J Bone Joint Surg Am 2013;95(July (14)):1307–11.

[11] Lee SY, Min E, Bae J, Chung CY, Lee KM, Kwon SS, et al. Types and arrangement of thyroid shields to reduce exposure of surgeons to ionizing radiation during intraoperative use of C-arm fluoroscopy. Spine (Phila Pa 1976) 2013;38 (November (24)):2108–12.

[12] Singer G. Occupational radiation exposure to the surgeon. J Am Acad Orthop Surg 2005;13(January-February (1)):69–76.

Injury, Int. J. Care Injured 48S (2017) S30–S34

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Malalignment in intramedullary nailing. How to achieve and to maintain correct reduction?

Enrique Guerado*, Maria Luisa Bertrand

Department of Orthopaedic Surgery and Traumatology, Hospital Costa del Sol, University of Malaga, Malaga, Autovia A-7 Km. 187, 29603 Marbella, Spain

ARTICLE INFO

Keywords:
Nailing
Fracture treatment
Fracture management
Fracture surgery
Malalignment
Less invasive surgery
Osteosynthesis

ABSTRACT

Intramedullary nailing has become the standard for the treatment of long bones diaphyseal fractures. Modern techniques of locking have further enlarged the primary indications to more proximal and distal fractures relying upon a former correct alignment. Nevertheless, residual deformities are not rare as once the nail has left the narrow diaphyseal canal and comes into the wider metaphysis, it may follow an unwished trajectory. There is also a chance for malreduction in diapyhseal fractures. The more complex the fracture is, the more difficult its reduction, not only for the alignment of the proximal or the distal part of bone in relation to the diaphysis, but also correct rotation and length. In this paper, we analyze recommended techniques to achieve accurate bone fracture reduction, to avoid post-operative deformities combined with correct implant insertion.

Introduction

Since the introduction, in the forties of the last century, of reaming by Gerard Kuntscher, and of locking by Grosse and Kempf in the seventies, intramedullary nailing has become the standard for the treatment of long bones diaphyseal fractures [1–3]. Modern techniques of locking have further enlarged the primary indications to more proximal and distal fractures [4,5].

Proximal and distal fractures reduction and osteosynthesis of long bones by intramedullary nailing relies upon a former correct alignment of the implant into the diaphyseal canal. Nevertheless, flexion, extension, varus or valgus residual deformities are not rare as once the nail leaves the narrow diaphyseal canal and comes into the wider metaphysis, it may follow an unwished trajectory. There is also a chance for malreduction in diapyhseal fractures. The more complex the fracture is, the more difficult its reduction, not only for the alignment of the proximal or the distal part of bone in relation to the diaphysis, but also correct rotation and length.

As these deformities may be severe even in younger patients (Fig. 1), new techniques have been developed for trying to avoid deformities and to achieve accurate bone fracture reduction and correct implant insertion [6]. These techniques are either implant-related or non-implant related (Fig. 2).

Non-related to implant techniques

Accurate fracture reduction is a guarantee for correct alignment, proper implant insertion, and better prognosis for fracture healing. Hence, fracture reduction is the desirable aim that any surgeon has planned while surgically treating a long bone fracture. Fracture reduction may be very difficult, mainly if displacement requires aggressive reduction techniques. Surgeons always try to preserve tissues viability and vascularization of fracture site by atraumatic manipulation of bone fragments. For that purpose, indirect reduction techniques are preferable. However, open reduction should definitely be performed if closed techniques fail.

Indirect reduction

Non-invasive

Indirect reduction preserves bone ends and causes little damage to the surrounding tissues. Indirect reduction includes non-invasive and invasive approaches.

The most classical indirect reduction method by a non-invasive approach is the use of a traction operating table. Traction tables provide continuous excellent traction in the diaphyseal axis achieving correct alignment and maintaining the proper position of bone fragment while the guide penetrates for nailing and actual implant insertion. Traction by operating tables has the advantage that no person needs to do any efforts, avoiding fatigue. Nonetheless, combination of this axial traction with varus, valgus, flexion, extension or even rotation maneuvers, may become a quite

* Corresponding author.
E-mail address: eguerado@hcs.es (E. Guerado).

http://dx.doi.org/10.1016/j.injury.2017.04.027
0020-1383/

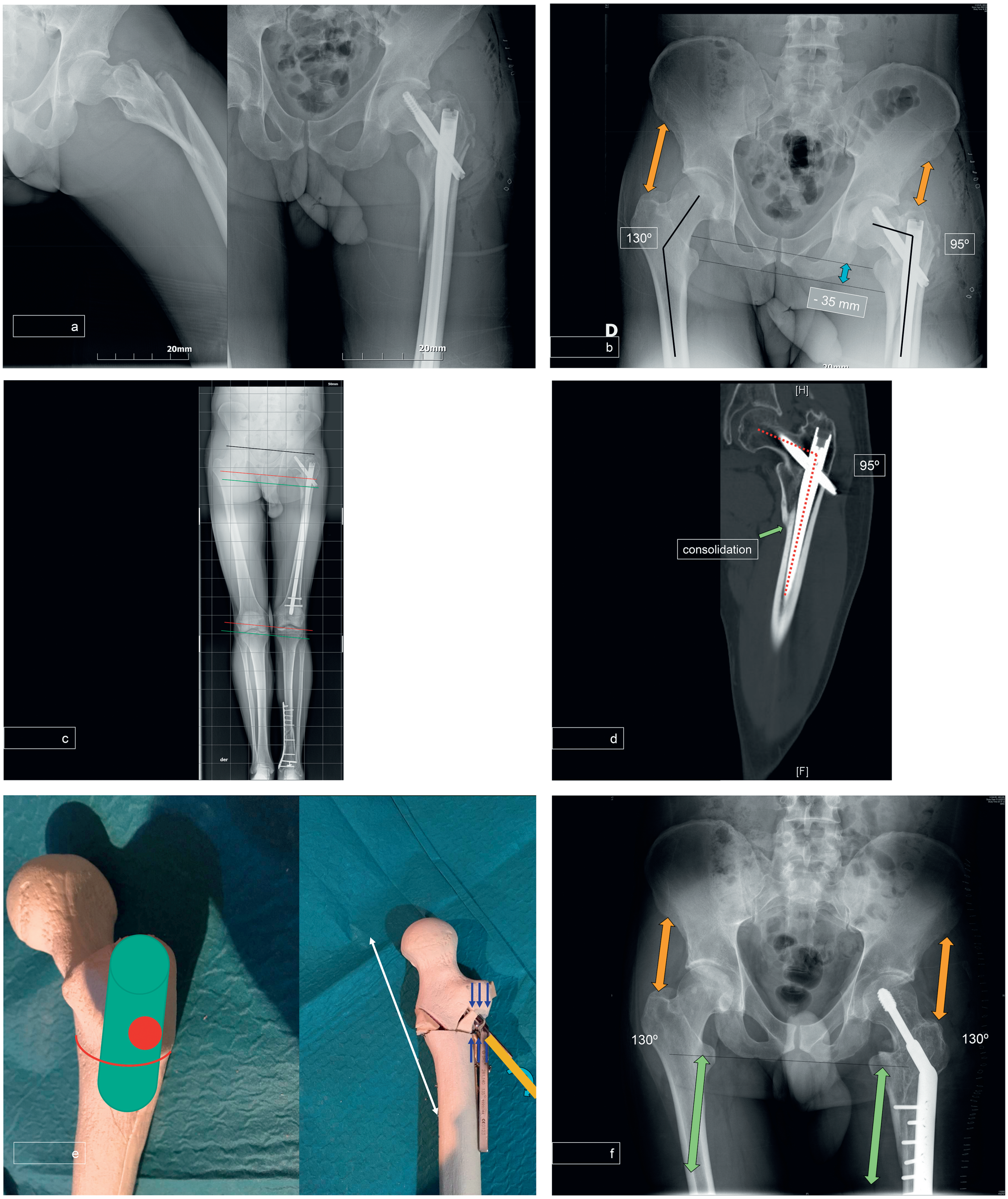


Fig. 1. Incorrect reduction and osteosynthesis of a proximal femoral fracture treated with nailing.
a. A 35 year old patient suffered a car crash sustaining a left trochantero-diaphyseal fracture. He was treated at the emergency trauma department with closed reduction and nailing.
b. The patient recovered well but presented a residual left coxa vara of 35° (130−95° = 35°), provoking limb shortening of 35 mm and as the tip of the greater trochanter was closer the pelvis bone, also a gluteus medius and minor insufficiency with limp.
c. Apart from the deformities described, left extremity looked normal.
d. Consolidation was fully achieved 5 months later as assured by CT-scan.
e. Plans for coxa vara correction were made. Valgus osteotomy was a challenge as the tip of the greater trochanter presented a hole as a consequence of the entry point for nailing. In fact the whole greater trochanter was already very weak because of the former nailing, together with further weakness expected to have in its lateral part because of the new osteosynthesis device for osteotomy synthesis entry point.
f. Finally valgus osteotomy was successfully performed although osteosynthesis was thought not to be as robust as in a normal case. The patient was kept without weight bearing for 4 months.

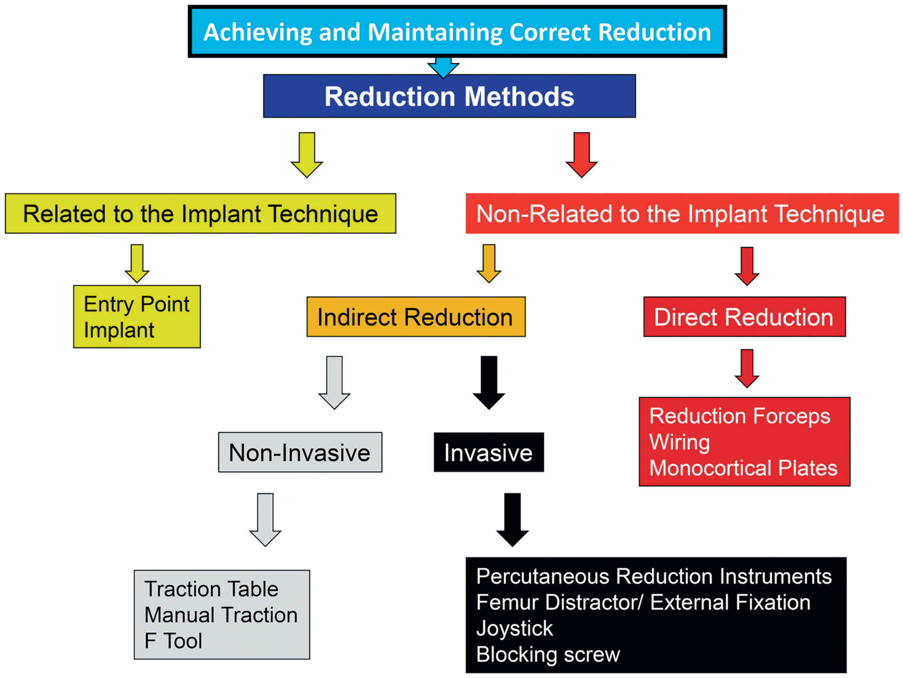


Fig. 2. Algorithm of methods for achieving and maintaining correct reduction of fractures.

an impossible task. Therefore traction by operating tables may become appropriate for diaphyseal long bone fractures, but for more proximal or distal fracture lines, mainly in tibia bone, requiring further reduction movements, traction applied by operating tables may be a burden for fracture reduction [7].

Manual traction allows any reduction maneuver in whichever anatomical axis. The problem with this traction applied by a surgical assistant is that in case of heavy and strong patients, particularly with femur bone fractures, fatigue may be a major problem even under deep anesthesia with muscle relaxation [8]. Consequently, manual traction is preserved for some distal tibia fractures. Diaphyseal femur or tibia fractures [9], as well as distal femur of proximal tibia fractures, can be treated in a hanging position of the leg; in this way the own extremity weight applies enough traction for correct fracture reduction [10]. Some other devices for indirect non-invasive reduction such as F-tools are now out of use.

Invasive

Indirect invasive reduction methods violate the skin barrier, and penetrate into soft tissues; they may also push or pull from bone fragments but still indirect invasive reduction has two advantages over direct reduction: they do not affect vascularization of bone fragments and soft tissues are minimally damaged.

Percutaneous introduction of instruments include “king-tongue” pushers, hooks, joystick-pins, external fixation, and blocking screws. AO femur distractor may also be classified as an invasive indirect reduction method.

Pushers, joystick-pins, hooks, and external fixation usually purchase themselves in only one cortex as blocking of intramedullary canal would correct prevent guide wire and nail placement. They commonly anchor in the lateral cortex whereas bone hooks pull to lateral from the medial cortex [11–15].

AO femur distractor device for closed indirect reduction was introduced in the 1980s [16,17]. Pins positioning and rod preparation can however be time consuming and has prevented its frequent use.

Blocking screws are worldwide known as “poller” screws because of its similarity with some cone-shaped traffic signs, creating an obligatory narrower way in streets and roads. Poller screws were first described by Krettek et al. [18] and have been very popular so far. Its principles consist of creating a non-passing zone for the nail by creating a narrower corridor by the use of some bicortical screws in the metaphyseal bone. Poller screws can be used for femur and also for tibia bones, either proximally, distally or in both locations [4,19,20]. They can also be used for guide introduction. Depending on the fracture pattern, the number of poller screws may vary from only one to several, and they can be removed once the nail has been inserted or can be left for reduction maintenance [21,22]. Since poller screws are bicorticallly introduced and its removal might be troublesome, an alternative to poller screws are the use of temporary bicortical pins or even wires, which will be removed once the surgical operation is over [23,24].

Direct reduction

Direct reduction techniques are constituted by invasive surgical methods. The fracture site is entirely opened and maneuvers are addressed to bone fragments next to or within the fracture site.

Direct reduction techniques have the advantage of achieving the best possible reduction, particularly in complex fracture situations. Direct reduction is usually less technically demanding than indirect reduction and in many instances less time consuming. Nonetheless, direct reduction maneuvers largely interfere with bone ends vascularization and with soft tissues vitality.

Direct reduction tools include forceps, wires and reducing plates. In order to minimize tissue lesion by direct reduction, many new devices have been developed for that purpose but the main damage is made by the time of surgical approach in a field already injured [25].

The fact of reduction maintenance in intramedullary nailing

Much has been written about achieving fracture reduction, but less about its maintenance. Keeping what has been achieved by reduction maneuvers depend more on fracture pattern and bone host condition than on implants or external devices.

There are two main issues when discussing about techniques for fracture reduction maintenance: osteosynthesis principles and implants.

Osteosynthesis principles

In general, there are four main principles for osteosynthesis: Compression forces, neutralization –also called protection-buttressing and tension band.

Compression is the golden standard for fracture stability. However, compression forces are absorbed by the compressed bone ends interface a few weeks after operation, before consolidation takes place. Consequently, compression principle needs to be complemented by neutralization. Compression principle can only be applied into a pure simple fracture pattern, being possible in intramedullary nailing only if almost anatomical reduction of the fracture has been achieved. Then the nail fills well the femoral or tibia canal, avoiding varus, valgus, flexion, extension or rotation movements. Therefore, compression principle in intramedullary nailing is uniquely achieved in case of simple diaphyseal fracture osteosynthesis, whereas more proximal or distal nailed fractures can hardly be submitted to compression forces.

Neutralization is the biomechanical complement for compression, buttressing or tension band forces. Neutralization controls rotation and shearing forces, and conducts compression forces into the appropriate inverse to each other force vector. In intramedullary nailing, neutralization can be achieved either at the fracture site in case of reaming nailing or from both bone ends in case of locking nailing. The nearer the neutralization is made to the fracture site, the more stable the construct is. Therefore, when the fracture pattern is simple and transverse, reaming until an intimate contact to the inner diaphyseal cortex at the fracture represents best conditions for a robust neutralization situation. In this case, the use of neutralization as a complement for the compression principle makes the fixation more stable. Further compression can be applied and maintained until consolidation by early weight bearing if monoaxial compression forces are going to be within the long bone vertical axis.

When this stability is not possible due to a more complex fracture pattern or location, neutralization must be accomplished by blocking the nail with bolts either proximally, distally, or at both sites bone-implant location. In this case, a buttressing principle is applied as the nails avoid the fracture to collapse, which can be considered as the opposite of compression. Should the fracture pattern be more complex, fracture stability may be compromised. Buttresing is a clear principle to be applied in case of fracture patterns tending to move in an undesirable manner, particularly tending to collapse. Therefore the actions of bolts in locking intramedullary nailing are two folds: neutralization and buttressing. Both are applied far away from the fracture site. No rigid stability of dynamic monaxial compressive construct can be achieved when neutralization is applied by the insertion of proximal and distal bolts.

The last of the four principle enunciated above is tension band. By definition tension band cannot be applied in intramedullary nailing as, under this principle, medial cortex is under compression whereas distracting forces are absorbed by the implant located on the outer part of more lateral cortex.

By mistake some other biomechanical principles, apart from the four discussed, of osteosynthesis are defined for intramedullary nailing, such as bridging, which is usually a buttressing construct aimed not to a biomechanical action but to a biological one together with a biomechanics buttressing and neutralization principles [26].

Technical devices for maintaining fracture reduction

Mainly, reduction maintenance relies upon fracture pattern and host bone quality, otherwise implants frequently break. Osteosynthesis devices contribute to this, by means of the principles discussed above. New devices and designs have come out to improve the role of osteosynthesis in fracture reduction.

New nails generation allow more bolts for further stability, and helices and new locking screws are aimed to provide proximal and distal more efficient purchase. Biomechanics studies have shown that stability is further gained by using these devices, but apparently inference to the clinical setting is otherwise. Ramos et al. in a randomized prospective study of diaphyseal tibia fractures treated by unreamed intramedullary nailing locked distally with either two or three bolts, found no differences in angular deviation or rotation in either group, conversely time to union became significantly reduced when using two bolts instead of three. Radiation time, surgical time, and expenses were also increased while using three bolts [27].

Nowadays, it is possible to achieve more biomechanical stability in fractures treated by intramedullary nailing, but whether stability means stiffness or a burden for consolidation, remains still unknown [28].

Implant related techniques

Since more proximal fractures of tibia bone, because of the quadriceps muscle and pes anserinus muscles traction, usually present a proximal fragment deformity in hyperextension, the entry point for canal preparation of nailing tends to be made too anteriorly. This common displacement results in an anterior fracture gap and an anterior nail trajectory. Solution for this, apart from correct reduction before nailing, which may become a difficult task, consist of more posterior nail entry point, and a more proximally curved implant – the so called Herzog curve. Therefore, taking into account the described fracture deformity, entry point as well as implant design becomes of overwhelming importance [4,5].

New tibia nails generation pay attention to this design and to a more posterior entry point, as the prolongation of the diaphyseal axis; therefore suprapatellar approach to the proximal tibia has gained interest [6].

Suprapatellar approach is a quite recent technique. It has two biomechanical advantages: on the one hand, for its performance the knee must be semiextended, minimizing the muscle actions provoking extension deformity in the more proximal fragment, on the other, retropatellar approach is aligned to the proximal prolongation of the diaphyseal axis. However, further validation is needed for suprapatellar approach as patellar and femur trochlear cartilage damage is quite possible. No knowledge of residual pain, technical errors and some other important issues, such as iatrogenic soft tissue lesions has been largely published yet [4,6].

Conflict of interest

None.

References

[1] Jones MD, Carpenter C, Mitchell SR, Whitehouse M, Mehendale S. Retrograde femoral nailing of periprosthetic fractures around total knee replacements. Injury 2016;47(February (2)):460–4.

[2] Yoo JH, Kim SW, Kwak YH, Kim HJ. Overlapping intramedullary nailing after failed minimally invasive locked plating for osteoporotic distal femur fractures–Report of 2 cases. Injury 2015;46(6):1174–7.
[3] Stavrou PZ, Ciriello V, Theocharakis S, Gudipati S, Tosounidis TH, Kanakaris NK, et al. Prevalence and risk factors for re-interventions following reamed intramedullary tibia nailing. Injury 2016;(Suppl (7))S49–52 December (47).
[4] Kuhn S, Hansen M, Rommens PM. Extending the indication of intramedullary nailing of tibial fractures. Eur J Trauma Emerg Surg 2007;33:159–69.
[5] Hiesterman TG, Shafiq BX, Cole PA. Intramedullary nailing of extraarticular proximal tibia fractures. J Am Acad Orthop Surg 2011;19:690–700.
[6] Rothberg DL, Holt DC, Horwitz DS, Kubiak EN. Tibial nailing with the knee semi-extended: review of techniques and indications. J Bone Joint Surg Am 2013;95:1–8 e116.
[7] Flierl MA, Stahel PF, Hak DJ, Morgan SJ, Smith WR. Traction table-related complications in orthopaedic surgery. J Am Acad Orthop Surg 2010;18:668–75.
[8] Stephen DJ, Kreder HJ, Schemitsch EH, Conlan LB, Wild L, McKee MD. Femoral intramedullary nailing: comparison of fracture-table and manual traction. J Bone Joint Surg Am 2002;84:1514–21.
[9] Kim KJ, Choy WS, Lee SK, Park HJ. Closed femoral intramedullary nailing in the lateral decubitus position with the aid of intraoperative skeletal traction. Eur J Orthop Surg Traumatol 2012;22:481–5.
[10] Beazley JC, Hull P. Temporary intra-operative reduction techniques for tibial fracture fixation: a review of the literature. Injury 2010;41:1228–33.
[11] Chen CY, Lin KC, Yang SW, Tarng YW, Hsu CJ, Renn JH. Use of the Schanz screw as a joystick and the Poller screw in intramedullary nailing for subtrochanteric or proximal femoral fracture. Eur J Orthop Surg Traumatol 2013;23:241–2.
[12] Rohilla R, Singh R, Magu NK, Devgan A, Siwach R, Sangwan SS. Simultaneous use of cannulated reamer and schanz screw for closed intramedullary femoral nailing. ISRN Surgery 2011;2011:1–8 ID 502408.
[13] Schlickewei CW, Rueger JM, Ruecker AH. Nailing of displaced intertrochanteric hip fractures. Tech Orthop 2015;30:70–86.
[14] Wood GW. Intramedullary nailing of femoral and tibial shaft fractures. J Orthop Sci 2006;11:657–69.
[15] Zheng ZL, Yu X, Xu GQ, Chen W, Zhang YZ, Jiao ZQ. Four pins assisted reduction of complex segmental femoral fractures: a technique for closed reduction. J Huazhong Univ Sci Technol Med Sci 2014;34:912–6.
[16] Baumgaertel F, Dahlen C, Stiletto R, Gotzen L. Technique of using the AO-femoral distractor for femoral intramedullary nailing. J Orthop Trauma 1994;8:315–21.
[17] McFerran MA, Johnson KD. Intramedullary nailing of acute femoral shaft fractures without a fracture table: technique of using a femoral distractor. J Orthop Trauma 1992;6:271–8.
[18] Krettek C, Miclau T, Schandelmaier P, Stephan C, Möhlmann U, Tscherne H. The mechanical effect of blocking screws (“poller screws”) in stabilizing tibia fractures with short proximal or distal fragments after insertion of small diameter intramedullary nails. J Orthop Trauma 1999;13:550–3.
[19] Nork SE, Tornetta P. Extreme nailing of the tibia. Oper Tech Orthop 2003;13:104–12.
[20] Wood GW. Intramedullary nailing of femoral and tibial shaft fractures. J Orthop Sci 2006;11:657–69.
[21] Chan DS, Nayak AN, Blaisdell G, James CR, Denard A, Miles J, et al. Effect of distal interlocking screw number and position after intramedullary nailing of distal tibial fractures: a biomechanical study simulating immediate weight-bearing. J Orthop Trauma 2015;29:98–104.
[22] Stedtfeld HW, Mittlmeier T, Landgraf P, Ewert A. The logic and clinical applications of blocking screws. J Bone Joint Surg Am 2004;86(Suppl 2):17–25.
[23] Tonogai I, Hamada D, Goto T, Takasago T, Tsutsui T, Suzue N, et al. Retrograde intramedullary nailing with a blocking pin technique for reduction of periprosthetic supracondylar femoral fracture after total knee arthroplasty: technical note with a compatibility chart of the nail to femoral component. Case Rep Orthop 2014;2014:1–5 ID 856853.
[24] Biewener A, Grass R, Holch M, Zwipp H. Intramedullary nail placement with percutaneous Kirschner wires: illustration of method and clinical examples. Unfallchirurg 2002;105:65–70.
[25] Afsari A, Liporace F, Lindvall E, Infante A, Sagi HC, Haidukewych GJ. Clamp-assisted reduction of high subtrochanteric fractures of the femur. J Bone Joint Surg Am 2009;91:1913–8.
[26] Weller S, Kuner E, Schweikert CH. Medullary nailing according to Swiss study group principles. Clin Orthop Relat Res 1979;138:45–55.
[27] Ramos L, Bertrand ML, Benitez-Parejo N, Guerado E. How many distal bolts should be used in unreamed intramedullary nailing for diaphyseal tibial fractures. Injury 2012;43:S59–62.
[28] Chan DS, Nayak AN, Blaisdell G, James CR, Denard A, Miles J, et al. Effect of distal interlocking screw number and position after intramedullary nailing of distal tibial fractures: a biomechanical study simulating immediate weight-bearing. J Orthop Trauma 2015;29:98–104.

Injury, Int. J. Care Injured 48S (2017) S35–S40

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Computer-assisted surgery: The use of stored intraoperative images for accurate restoration of femoral length and rotational alignment after fracture

David M. Kahler

Orthopaedic Surgery, University of Virginia, Box 800159, Charlottesville, VA, 22908-0159, USA

ARTICLE INFO

Keywords:
Femoral fractures
C-arm fluoroscopy
Computer assisted surgery
Navigation
Image-guided surgery
Fracture reduction
Long bone fracture
Malrotation

ABSTRACT

Most femoral fractures are now managed with minimally invasive internal fixation. In the absence of formal exposure of the fracture lines, these procedures make heavy use of C-arm fluoroscopy to allow both fracture reduction and placement of implants, at the expense of measurable radiation exposure to both patient and surgeon. Although this technology has been commercially available for over a decade, it has not yet been widely accepted by the Orthopaedic community.

Introduction

Orthopaedic surgeons are experienced in using two-dimensional image data from arthroscopy or fluoroscopy during minimally invasive surgery. CAS takes this a step further, by providing access to multiple simultaneously-displayed stored two-dimensional (2D) fluoroscopic images. Synonyms for this particular type of CAS are surgical navigation, image-guided surgery (IGS), C-arm navigation, virtual fluoroscopy, and 2D fluoroscopic navigation. The surgeon may store multiple 2D images of each area of interest, allowing accurate assessment of fracture reduction and alignment in three dimensions. Most current systems use an optical tracking system to follow both the position of the patient and special surgical instruments during the course of the procedure. These optical systems offer a large effective working distance, and appear to be best suited for trauma applications. In all types of IGS systems, the predicted position of the surgical instruments and fracture fragments are displayed on a computer monitor relative to the position of the patient's skeletal anatomy on the stored images.

Surgical navigation in the treatment of long bone fractures

Nearly all femoral fractures, from the femoral neck to the distal metaphysis, are now managed with minimally invasive techniques that do not require direct exposure of the fracture. Closed antegrade or retrograde intramedullary nailing of diaphyseal femoral fractures (OTA 32-A–C) allows minimally invasive stabilization of these injuries at the expense of significant ionizing radiation exposure to both the patient and the operative team. The procedure typically requires several minutes of fluoroscopy time. Most surgeons feel very comfortable performing this procedure using C-arm guidance alone, without the use of navigation. As navigation may add time to the surgical procedure, it is probably not necessary for all femoral fractures, although early experience suggests great decreases in radiation exposure when using navigation. The biggest advantage of navigation is the ability to accurately restore not only axial alignment, but also anatomic length and rotational alignment to match the injured femur to the uninjured side[1,2]. In comminuted fractures, this is otherwise difficult to do using standard non-navigated technique (Fig. 1). Although a variety of techniques have been described to compare anteversion of the femur to the contralateral side using intraoperative imaging, these techniques are not entirely reliable, and length remains particularly difficult to judge [3]. Femoral malrotation is an underappreciated problem in trauma care. While rotational variation up to 10° is common in uninjured femora, a rotational difference of 15° or more is considered malreduction [4]. When femoral rotation (version) is critically assessed with computed tomography (CT) following locked nailing of femoral fractures, it appears that surgeons leave the injured femur malrotated by over 15° in 20–30% of cases [5]. According to the AAOS Closed Claims survey (1985–1998), femoral fractures

E-mail address: Dmk7y@virginia.edu (D.M. Kahler).

http://dx.doi.org/10.1016/j.injury.2017.04.031
0020-1383/

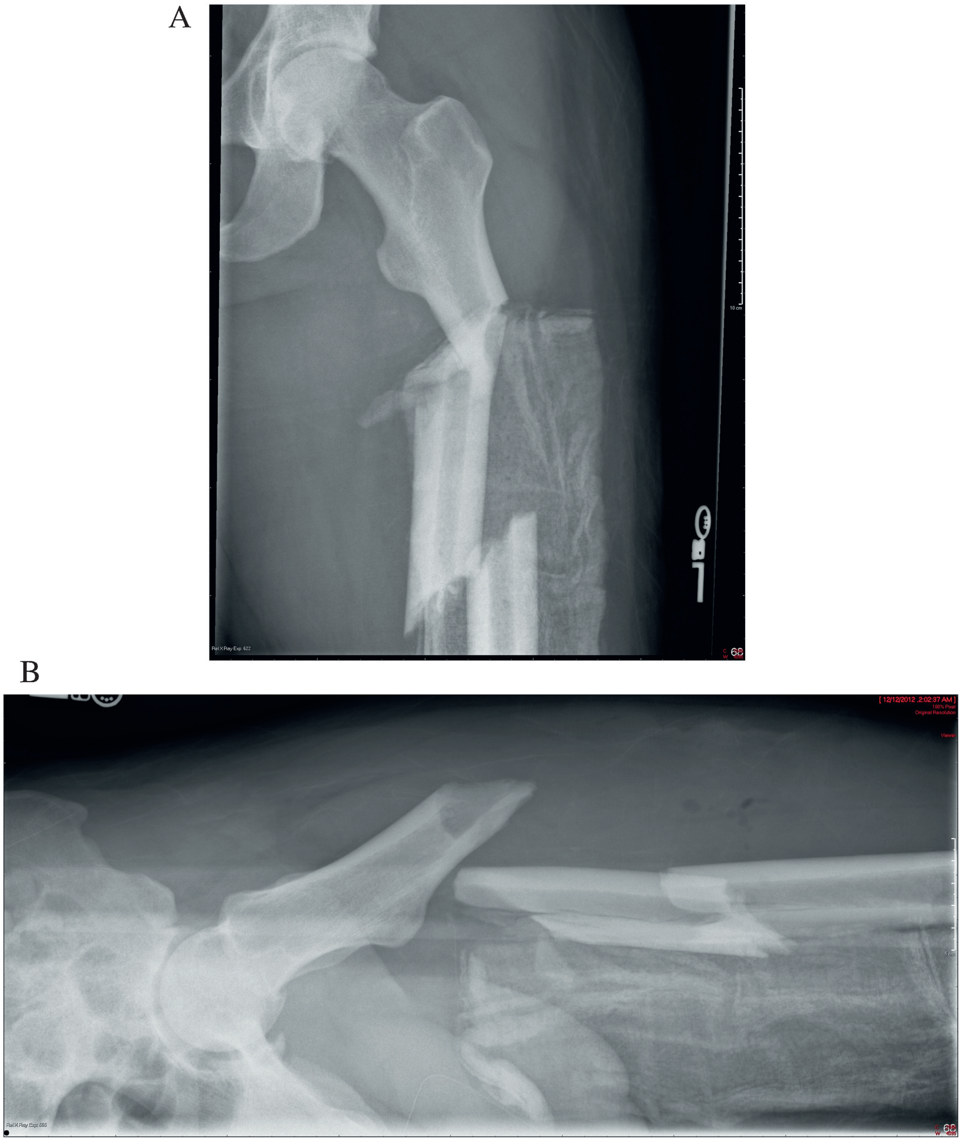


Fig. 1. A and B depict an example of a femoral fracture in which it may be difficult to restore anatomic length and alignment without using the contralateral normal side as a model.

accounted for more malpractice claims than any other diagnosis [6].

Multiple C-arm images are usually obtained during the critical portions of the femoral nailing procedure:

- Identification of the proper skin incision site, and the insertion site for the femoral nail in the proximal femur.
- Reduction of the fracture, followed by passage of a reduction rod and/or guide wire across the fracture.
- After axial alignment is corrected by passage of the intramedullary device, the final reduction involves restoration of normal length and rotational alignment. This step in particular is difficult without navigation.
- Interlocking of the nail.

The total radiation exposure has historically been approximately four minutes of fluoroscopy time during these steps, and over one hundred individual images are often obtained. Many of these images must be obtained with the surgeon's hands in the radiation field, particularly during starting point preparation, reduction and guide wire passage, and freehand locking. Virtual fluoroscopy allows the performance of the critical portions of the femoral nailing procedure with as few as 12 individual stored images, and only a few seconds of fluoroscopy time [7]. As both the C-arm and the patient are tracked during the navigated procedure, the computer can accurately determine femoral length and rotational alignment on the uninjured side, and the surgeon can then match the anatomy of the injured to the uninjured side prior to definitive locking [8]. The surgeon may be well away from the radiation beam during imaging, and no additional imaging is required during the procedure, although several confirmatory images are usually obtained. A fluoroscopic CAS technique for femoral nailing, including fracture reduction, is described below.

Surgical technique

Preoperative CT is not required when using the 2D navigation workflow; all of the images are obtained intraoperatively, and normal femoral length and rotation is calculated using C-arm images of the uninjured extremity. A standard C-arm unit is retrofitted with a calibration target to allow tracking of the unit by the computer system, and optical correction of any distortion in the C-arm images. A non-invasive reference array is attached to the patient's uninjured leg. Four images are obtained of the well leg to determine the neck axis (anteversion) and length of the femur. The surgeon defines the center of the femoral head, the axis of the femoral neck, and the posterior condylar axis of the distal femur on the computer workstation. The computer then calculates and stores the length and antetorsion of the intact femur. After prepping, draping, and attachment of reference frames to the proximal and distal fracture fragments, six standard images are obtained of the injured femur: AP and lateral of femoral neck; AP and lateral of fracture site; and AP and true lateral of the distal femur. It may require several minutes and several attempts to obtain the optimal images; once these images have been stored, however, the C-arm may be taken out of the field and the surgeon

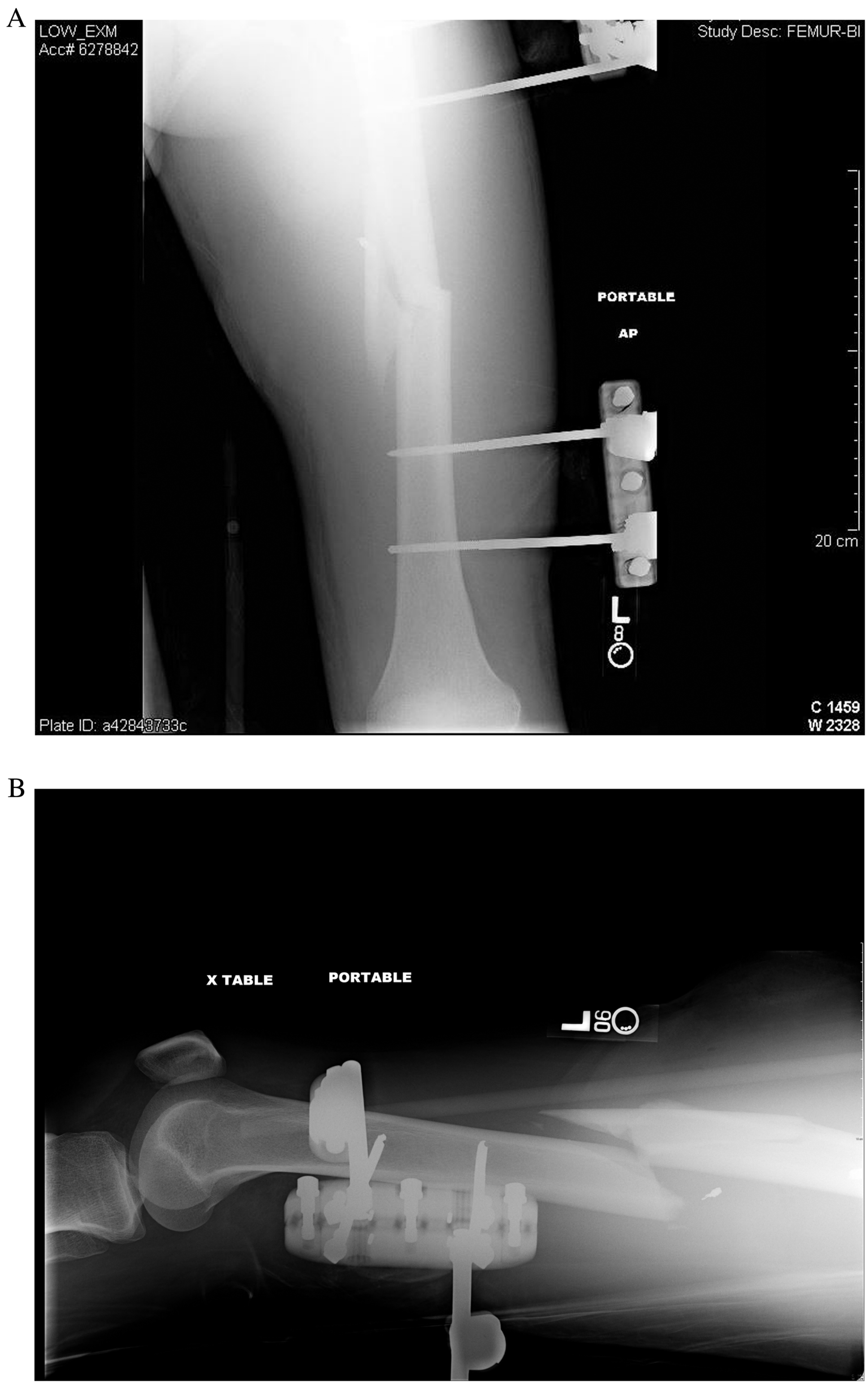


Fig. 2. A and B shows views of a left femoral shaft fracture following damage control external fixation; although length may be restored radiographically, rotation will rely on the surgeon's best judgement, unless navigation is utilized. This is the case shown in Fig. 3.

may proceed with navigation. In practice, the attachment of the reference frames and obtaining all images takes about 20 min. The real time position of surgical instruments, such as a drill guide or reduction rod, may be overlaid onto the stored images. The virtual images are updated several times per second, allowing real-time feedback as the instruments are moved. This allows the critical portions of the femoral nailing procedure to be performed using only two stored images of the relevant anatomy during each step, without the need for constantly reacquiring fluoroscopic images during the surgical procedure.

The antegrade femoral nailing procedure is generally performed with the patient supine on a fracture table. The patient's legs are scissored, with the injured leg placed in traction with slight flexion and adduction at the hip. The starting point for nail insertion is identified using virtual fluoroscopic guidance. A trajectory "look ahead" feature is used to align the drill guide with the femoral canal in both views, and a 2.8 mm guide wire is inserted through the piriformis fossa into the center of the intramedullary canal. The wire is then over drilled with a rigid compound reamer to open a working channel in the proximal femur.

The next step is initial fracture reduction, aligning the proximal and distal diaphyses to correct translational and angulatory displacement. If desired, the surgeon may manual align the fractured bone ends and axes using feedback from the navigation system. A guide wire or reduction rod is then placed across the fracture. The final step in reduction is restoration of length and rotational alignment to match the uninjured side, by applying traction and rotation through the fracture table to accurately reduce the fracture. Recent studies suggest that rotational malalignment is common following closed intramedullary nailing of femoral fractures, and while difficult to detect on physical exam, may profoundly affect functional outcome. Femoral fracture reduction software allows not only accurate reduction in the sagittal and coronal planes, but also accurate restoration of normal femoral anteversion and length compared to the contralateral uninjured femur. The surgeon may leave the operating room with a printout confirming that femoral rotation and length has been accurately restored (Fig. 2).

Following insertion of the femoral nail and final reduction, the distal locking screws are inserted to provide rotational stability. An additional perfect lateral view of the locking screw holes in the nail must be obtained for adequate guidance. An AP image is also helpful for length. The universal drill guide is then used to drill the holes for the locking screws under virtual fluoroscopic guidance. A trajectory length feature of the system acts as a virtual depth gauge for selection of the proper screw length.

Fixation of distal fractures using femoral locking plate (LCP)

Locking plates for distal femoral fractures are typically inserted with the aid of traditional fluoroscopic guidance, and sometimes with a targeting arm for percutaneous insertion of the proximal locking screws. These devices are well suited for minimally invasive insertion, without actually exposing either the fracture site or the proximal segment. Although the plate is generally affixed to the distal fragment with direct visualization through a small incision, the proximal segment must be accurately reduced and fixed to the plate using fluoroscopy alone. This requires the surgeon to control six degrees of freedom at once. Even if the plate

A

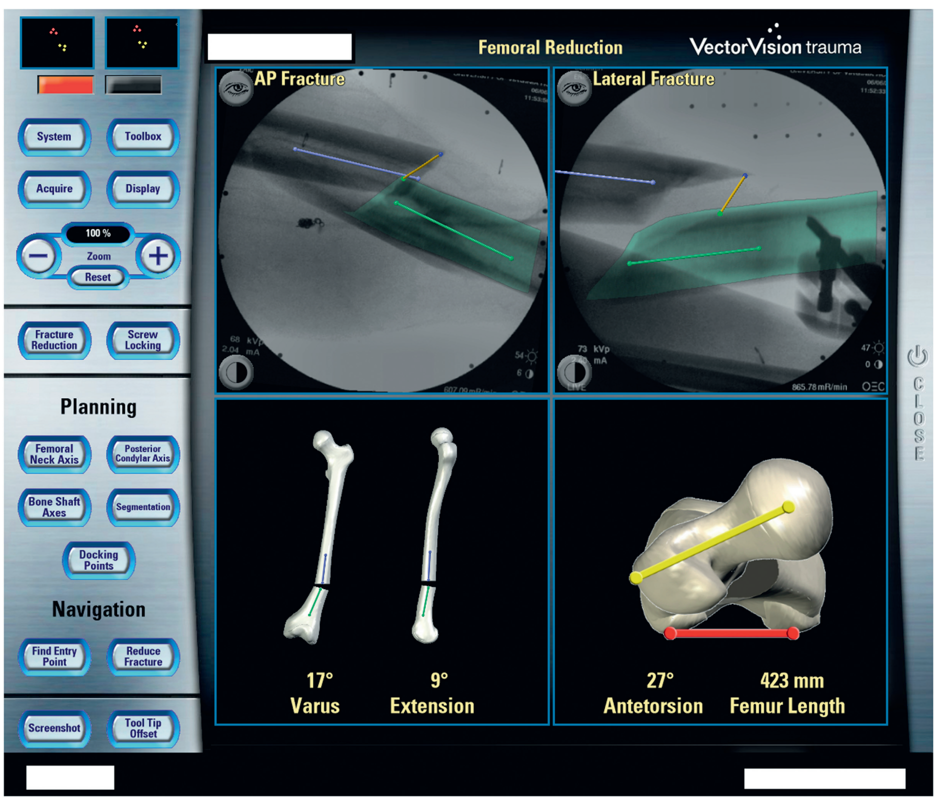


Fig. 3. Intraoperative navigated screenshots following placement of navigation trackers and intraoperative fluoroscopic imaging.
3A. In the first frame, the external fixator has been removed; the femur is short and internally rotated. Imaging of the contralateral side determined anatomic length and anteversion to be 445 mm and 7° antetorsion.
3B. Screenshot following nail insertion, and final reduction on the fracture table prior to locking. Length, version, and overall alignment have been restored to closely match the contralateral femur, based on intraoperative fluoroscopic images of the well leg.

B

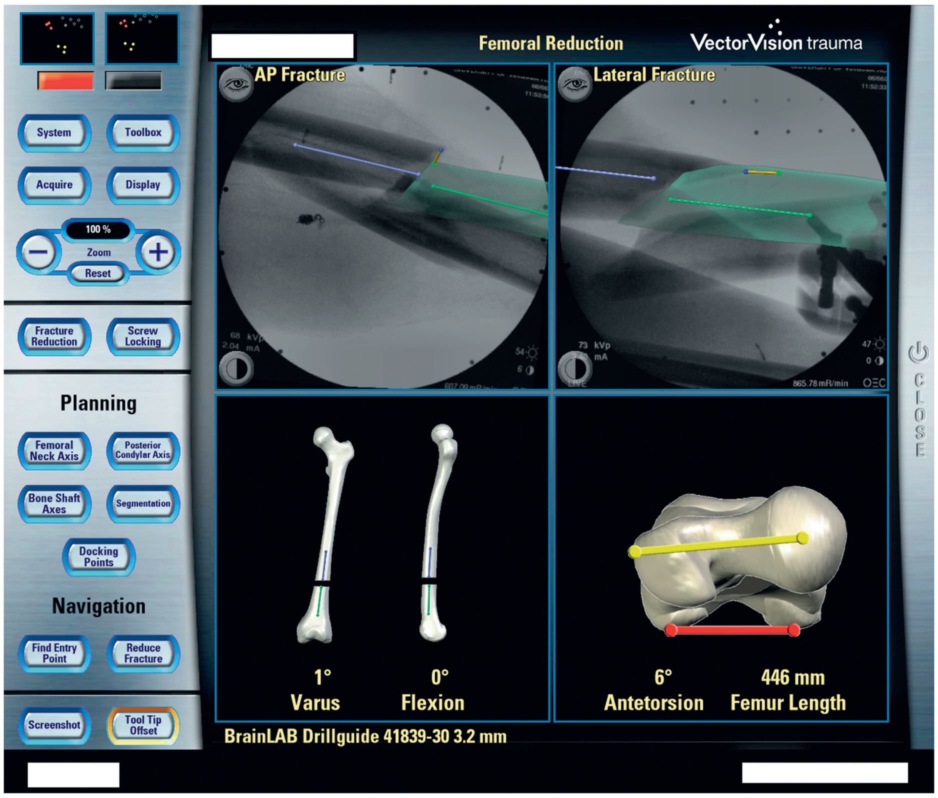


Fig. 3. (Continued)

is well aligned with the proximal fragment, the surgeon must still achieve proper reduction of femoral length and rotational alignment, as in the nailing procedure.

Surgical navigation first allows accurate fixation of the plate to the distal fracture fragment, with respect to the distal condylar axis, posterior condylar axis, and trochlear axis. The distal fragment/plate construct and the proximal fragment are then tracked independently in two planes during reduction of the fracture. In the past, navigation system manufacturers and implant companies have provided a library of nails and plates that can be directly superimposed on the virtual fluoroscopic images during implant insertion and final reduction, prior to placement of any locking screws. This type of implant-specific software may improve the appeal of image guided surgery in the eyes of the trauma surgeon [8].

Discussion and conclusion

Despite the obvious potential applications of CAS technology in fracture care, this technology was first embraced by the arthroplasty and spine communities. Although IGS has seen growth in Europe and parts of Asia, the use of IGS techniques has declined in the United States. There are several potential reasons for the lack of adoption: initial cost of the system, additional time required for setup at the start of the procedure, and the fact that training programs for this technology are not readily available.

All three critical portions of the femoral nailing procedure have been performed using virtual fluoroscopic guidance. Hand radiation exposure and additional imaging during reduction can be eliminated using this technique. Early clinical experience suggests that intraoperative radiation exposure during femoral nailing may be decreased by as much as an order of magnitude when compared to standard fluoroscopic technique. The additional 20 min setup time necessary for IGS, performed at the start of the case, seems to be offset by operative time savings during implant placement.

Femoral malreduction is probably an underreported problem in fracture care. Residual femoral malrotation causes measurable gait disturbance and abnormal hip joint contact pressures [9–11]. Residual leg length discrepancy may cause similar problems. While navigation is certainly not necessary in the treatment of every femoral fracture, surgeons should consider the use of navigation, if available, during the treatment of severely comminuted fractures where there are no anatomic cues for restoring length and rotation.

Fluoroscopic navigation is now a mature technology that has numerous potential applications in the field of Orthopaedic trauma. Using this technique, it is possible to perform the femoral nailing procedure using well less than one minute of fluoroscopy time. Despite the need for specialized equipment and instruments, this technology has the potential to greatly decrease the Orthopaedic surgeon's reliance on intraoperative ionizing radiation during the performance of minimally invasive surgery, while improving the accuracy of reduction.

Conflict of interest

None.

References

[1] Kendoff D, Citak M, Gardner MJ, Gosling T, Krettek C, Hufner T. Navigated femoral nailing using noninvasive registration of the contralateral intact femur to restore anteversion. Technique and clinical use. J Orthop Trauma 2007;21:725–30.
[2] Weil YA, Gardner MJ, Helfet DL, Pearle AD. Computer navigation allows for accurate reduction of femoral fractures. Clin Orthop Relat Res 2007;460:185–91.

[3] Hak DJ. Getting the rotation right: techniques for assessing rotation in intramedullary tibial and femoral nailing. Orthopedics 2011;34:36.
[4] Jaarsma RL, Van Kampen A. Aspects of current management: rotational malalignment after fractures of the femur. J Bone Joint Surg (Br) 2004;86:1100–4.
[5] Jaarsma RL, Pakvis DF, Verdonschot N, Biert J, van Kampen A. Rotational malalignment after intramedullary nailing of femoral fractures. J Orthop Trauma 2004;18(7):403–9.
[6] Bhattacharyya T. Evidence-based approaches to minimizing malpractice risk in orthopedic surgery. Orthopedics 2005;28:378–81.
[7] Kahler DM. Image guidance: fluoroscopic navigation. Clin Orthop Relat Res 2004;421:70–6.
[8] Kahler DM. Navigated long-bone fracture reduction. J Bone Joint Surg Am 2009;91:102–7.
[9] Jaarsma RL, Ongkiehong BF, Gruneberg C, Verdonschot N, Duysens J, van Kampen A. Compensation for rotational malalignment after intramedullary nailing for femoral shaft fractures: an analysis by plantar pressure measurements during gait. Injury 2004;35(12):1270–8.
[10] Gugenheim J, Probe RA, Brinker MR. The effects of femoral shaft malrotation on lower extremity anatomy. J Orthop Trauma 2004;18(10):658–64.
[11] Salem KH, Maier D, Keppler P, Kinzl L, Gebhard F. Limb malalignment and functional outcome after antegrade versus retrograde intramedullary nailing in distal femoral fractures. J Trauma 2006;61:375–81.

Injury, Int. J. Care Injured 48S (2017) S41–S46

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Intramedullary nail fixation of non-traditional fractures: Clavicle, forearm, fibula

Niloofar Dehghan[a,c], Emil H. Schemitsch[b,*]

[a] Li Ka Shing Institute,St. Michael's Hospital, Toronto, Canada
[b] Division of Orthopaedics, Department of Surgery, Western University, London, Canada
[c] Orthopaedic surgeon - The CORE Institute, Banner University Medical Center, Phoenix, Arizona, USA

ARTICLE INFO

Keywords:
Intramedullary nail fixation
clavicle fixation
forearm fixation
ankle fixation

ABSTRACT

Locked intramedullary fixation is a well-established technique for managing long-bone fractures. While intramedullary nail fixation of diaphyseal fractures in the femur, tibia, and humerus is well established, the same is not true for other fractures. Surgical fixations of clavicle, forearm and ankle are traditionally treated with plate and screw fixation. In some cases, fixation with an intramedullary device is possible, and may be advantageous. However, there is however a concern regarding a lack of rotational stability and fracture shortening. While new generation of locked intramedullary devices for fractures of clavicle, forearm and fibula are recently available, the outcomes are not as reliable as fixation with plates and screws. Further research in this area is warranted with high quality comparative studies, to investigate the outcomes and indication of these fractures treated with intramedullary nail devices compared to intramedullary nail fixation.

CLAVICLE FRACTURES

Surgical fixation of clavicle fractures has been traditionally performed with use of plates and screws, utilizing Arbeitsgemeinschaft fur Osteosynthesefragen (AO) techniques of anatomic reduction and stable fixation. However, intramedullary fixation is also possible, and different types of devices have been used for intramedullary fixation of the clavicle throughout the years, including smooth K-wires, Hagie pins (Smith & Nephew) [1], Knowles pins (Zimmer) [2], Rockwood Clavicle Pins (DePuy) [3,4] and titanium elastic nails (TEN) (Synthes) [5]. To our knowledge, the only modern nail with interlocking capability is the Sonoma CRx clavicle pin (Sonoma Orthopedic Products Inc, Santa Rosa, CA, USA) [6,7] (Fig. 1).

Intramedullary fixation is thought to allow for a smaller incision, which can be more cosmetically appealing. It may also decrease soft tissue dissection and hardware prominence associated with plates, and may allow for easier hardware removal [4,8]. Contraindications to use of intramedullary fixation include significant comminution, small canal diameter, and lateral third clavicle fractures [4].

Biomechanical studies have shown that intramedullary nails are inferior to plates in resisting displacement with regards to maximal load and cyclical stress testing [9]. The majority of available clavicular intramedullary devices have no locking capability, and are unable to control for length and rotation at the fracture site [8]. The lack of control for length causes fracture shortening, malunion, as well as implant prominence and soft tissue irritation. One randomized controlled trial reported a 23% rate of nail protrusion due to cut-out or fracture shortening. Implant failure and breakage have also been reported [10,11].

Intramedullary devices can also migrate, especially smooth Kirschner wires [12–14], which have been reported to migrate to the thorax or aorta. Thus the use of Kirschner wires should be avoided in the shoulder girdle. A study utilizing titanium elastic nails for fixation of clavicle fractures reported a 30% rate of hardware migration [15]. Pin migration has also been reported with other intramedullary devices [3,11].

Intramedullary devices can cause local irritation and prominence at the insertion site [3,11]. One randomized study reported implant-related irritation in 31% of patients treated with the Hagie Pin [1]. Other studies have reported medial protrusion of the Titanium Elastic Nails with local irritation requiring removal [10,16,17]. Many intramedullary devices necessitate routine

* Correspondence to: 339 Windermere Road, Room C9−116, London, N6A 5A5 Ontario, Canada.
E-mail address: schemitsch@lhsc.on.ca (E.H. Schemitsch).

http://dx.doi.org/10.1016/j.injury.2017.04.018
0020-1383/

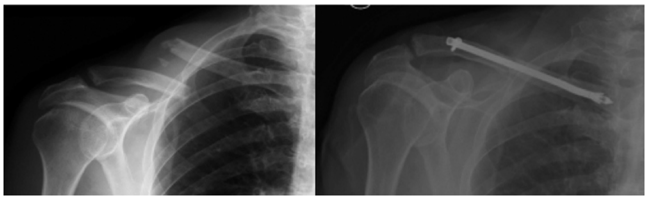


Fig. 1. Clavicle shaft fracture treated with Sonoma CRx clavicle pin.

removal after fracture union, which requires another surgical procedure [1,3,4,18]. A randomized controlled trial comparing the Rockwood pin to compression plating reported 100% rate of hardware removal for the Rockwood pin, compared to 53% in the plating group.

A meta analysis investigating the complications of clavicle fractures treated with intramedullary nails noted a low risk of major complications such as additional surgery for nonunion ($<7\%$). However, wound infections and implant irritation were as high as 31%. Most implants required routine removal, rendering patients to undergo an additional surgical procedure [19].

Evidence in the literature

Numerous studies have reported use of intramedullary devices for fixation of clavicle fractures, including several randomized controlled trials. In general, studies show that compared to non-operative treatment, intramedullary fixation leads to better outcomes, and lower rates of nonunion and malunion [1,5,20]. However, the results were concerning regarding nail protrusion, and implant irritation requiring removal.

Several randomized controlled trials have also reported the results of intramedullary nails compared to plate fixation [2,4,7,17,21–24]. A recent meta-analysis [25] identified seven randomized controlled trials comparing intramedullary nails to plate fixation for treatment of clavicle fractures [2,4,7,17,21–23]. This meta-analysis reported no differences regarding functional outcomes, nonunion, symptomatic hardware, or fixation failure. However, infection was higher in the plate groups (8/117) compared to nails (1/125) ($P = 0.05$). The authors concluded that intramedullary fixation had potential advantages, such as decreased soft tissue dissection, blood loss, and more cosmetic satisfaction. However, they also noted that disadvantages included skin irritation, implant migration, and frequent need for implant removal.

This meta-analysis was fraught with multiple shortcomings. The indications for surgery were not uniform across the studies included, some studies were based on elderly patients, or a combination of acute fractures and nonunions [2]. The studies also utilized different types of nails (Knowles pins, Rockwood pin, TEN, Sonoma CRx clavicle pin) and in general out-dated plating systems. Only two studies reported the use of pre-contoured clavicular plates, which are the recommended plate for fixation of clavicle fractures. Several studies utilized pelvic reconstruction plates, which have higher rates of fixation failure [21,23], and compression plates, which have higher rates of implant irritation [26].

Technical considerations

In general, intramedullary nail fixation of clavicle fractures is performed with open reduction techniques. Many authors report routine "opening of the fracture site", to assist in reduction and nail placement [4]. The nail can be inserted in a retrograde or antegrade manner, depending on the type of device used. Alternatively, some intramedullary devices can also be inserted through the fracture site, especially if the fracture site is opened to aid with reduction [4]. Intraoperative fluoroscopy must be utilized to aid with positioning of the device. The nail must be cut short, to prevent soft tissue irritation.

Conclusions

In general, studies report good outcomes with intramedullary nail fixation of clavicle fractures compared to non-operative treatment. Clavicular nails may be used as an alternative in patients with simple clavicle fractures with a large canal, and should be avoided in comminuted fractures. However, there are still concerns regarding implant migration, implant irritation, routine hardware removal, and lack of stability causing shortening [3,11]. Although it remains controversial, in general intramedullary fixation has inconsistent results compared with plate fixation, and thus is not as commonly used in North America [1,27–29]. There is a need for large randomized controlled trials, comparing new modern nails to modern clavicle specific plates, to assess if there is a difference regarding outcomes and complications between these two modes of fixation.

FOREARM FRACTURES

Single and both bone forearm fractures in adults are routinely treated surgically, due to high rates of complications with non-operative treatment (except for minimally displaced ulnar "night stick" fractures) [30,31]. In general, surgical fixation of forearm fractures in adults is performed with open reduction and compression plating, utilizing AO techniques of fixation. While intramedullary (IM) nailing of forearm fractures is commonly performed in children, plate fixation is still considered as the gold standard for the treatment of adults, and use of intramedullary devices is rare [32].

Intramedullary nail fixation of forearm fractures has the potential advantages of smaller incisions, decreased periosteal stripping and hardware irritation [31]. Another potential advantage is lower risk of re-fracture after hardware removal, which is a concern with plate fixation [30,31,33]. Currently, indications for intramedullary nail fixation of forearm fractures are limited. Intramedullary devices may be advantageous in treatment of mangled extremities and burns (to minimize soft tissue stripping), segmental fractures, and pathologic fractures (to span the entire length of bone) [30,34]. Contraindications include canal diameter smaller than 3 mm, (may differ based on type of implant used) [30,32], fracture extension to the metaphysis or articular surface, comminuted fractures, and Monteggia and Galeazzi fractures that require anatomic restoration of length [32,33,35,36]. In such cases, plate fixation should be performed.

Disadvantages/complications

Intramedullary nails do not allow for anatomic fixation, and restoration of length and rotation are difficult, especially in severely comminuted fractures. Biomechanical studies have shown that the ulna contributes more to forearm stability in bending and torsion than the radius. Therefore, in single bone forearm fractures, IM nailing of the ulna provides significantly less torsional stability, compared to IM nailing of the radius. Intramedullary nail fixation of both bone forearm fractures has significantly lower torsional stiffness compared to plate fixation (2% vs. 83% of intact forearm), as well as lower resistance to distraction and compression [37]. Due to this biomechanical inferiority, unlike plate fixation, fixation of forearm fractures with unlocked intramedullary nails requires a period of immobilization post-operatively [30]. Even with the use of locked intramedullary devices, some authors routinely immobilize patients with an above elbow cast or brace for several weeks [33,36,38].

If the fractures are not reducible in a closed manner, an open reduction may be required, which has been shown to increase the time to union [38]. Complications of forearm intramedullary nail fixation include radio-ulnar synostosis [39], posterior interosseous nerve palsy (from proximal radial interlocking screws), nail migration, iatrogenic fractures, nonunions and delayed unions [30].

Types of nails

Early nailing techniques of forearm fractures included various non-locked implants, such as Rush rods, Kirschner wires, and elastic intramedullary nails [40], which lacked rotational and axial stability, and had high rates of nonunion (up to 21%) [30]. The new generation of forearm nails allow for interlocking capability, and several types of nails are currently available for use (Fig. 2).

The Foresight nail (Smith & Nephew) is a stainless steel nail that has interlocking capability both proximally and distally. They are straight, and require intraoperative contouring. The Acumed radius and ulna nails are titanium, pre-contoured, and have interlocking capability only at the insertion end (proximally in the ulna, distally in the radius). The other end of the nails is fluted and has a paddle-blade tip, which is driven into the metaphysis to provide rotational stability [30,36]. The TST intramedullary forearm nails (TST Rakor Tıbbi Aletler San. ve Tic. Ltd. Sti., Istanbul, Turkey) are made of titanium alloy. The radial nails allow for distal interlocking only, and a proximal 10° bend provides proximal stability. The ulnar nails have distal and proximal interlocking capability.

Evidence in the literature

Several case series have reported on the use of locked intramedullary forearm nails for fixation of single bone and both bone forearm fractures [32,36,38,39]. Most studies include a heterogeneous group of fractures. In general, good results have been reported, with a DASH score of 5–15 (mild-moderate disability), and time to union of 3–4 months. Comparative and randomized studies are limited, with only one RCT published to date [33].

Lee et al. [33] recently reported on a randomized controlled trial of 67 patients with both bone forearm fractures, 35 treated with the Acumed nail and 32 with plate fixation. Monteggia, Galeazzi as well as osteoporotic and comminuted segmental fractures were excluded. Closed reduction was performed in all closed fractures treated with a nail. Patients in the nail group were treated with long arm cast immobilization for two weeks, and a hinged elbow brace for another four weeks. Time to union was significantly shorter in the plate group compared to the nail group (10 vs. 14 weeks, $p = 0.048$). The presence of a butterfly fragment and severe displacement were factors associated with increased time to union in the nail group. Rate of hardware removal, infection and synostosis was similar between both groups. Plate fixation had significantly improved radial bow restoration (95%) compared to the nail group (90%). However, this did not affect clinical outcomes such as DASH scores or rotation. The authors concluded that with proper patient selection, intramedullary nailing can be an acceptable and effective treatment option for both bone forearm fractures in adults.

Techniques

Nail length and diameter must be carefully determined from preoperative radiographs of the unaffected side [32]. Intra-operative fluoroscopy aids in reduction, identification of the start points and nail insertion. Given the small diameter of bones, most nails are not cannulated, and a guide wire is not required [30]. If closed manipulation and safe passage of a nail through the fracture site is not possible, a small incision is made to facilitate with open reduction [31]. Some authors advocate for the use of above elbow cast immobilization after fracture fixation [33,36].

Ulnar nails are inserted through the tip of the olecranon. A 2-cm longitudinal incision is made over the olecranon, and a vertical split is made in the triceps insertion to allow placement of the opening awl [30,32]. Reaming may be required based on the type of nail utilized.

Radial nails are inserted distally. The entry portal varies depending on the manufacturer's implant design, however generally 5 mm proximal to the articular surface [30,36]. Lister's tubercle serves as the primary landmark for the radius entry point. A 2-cm dorsal-radial incision is made, and the awl or reamers are used to create the entry hole [30,32]. The canal may require reaming based on the nail design. Some nails may require contouring of the nails to accommodate the radial bow (e.g. ForeSight nail). The proximal radial interlocking screws have a potential risk of posterior interosseous nerve injury during screw placement [30,39]. Therefore, interlocking should be performed no more than 3 cm distal to the radial head, from a radial direction, while holding the forearm in neutral rotation [41].

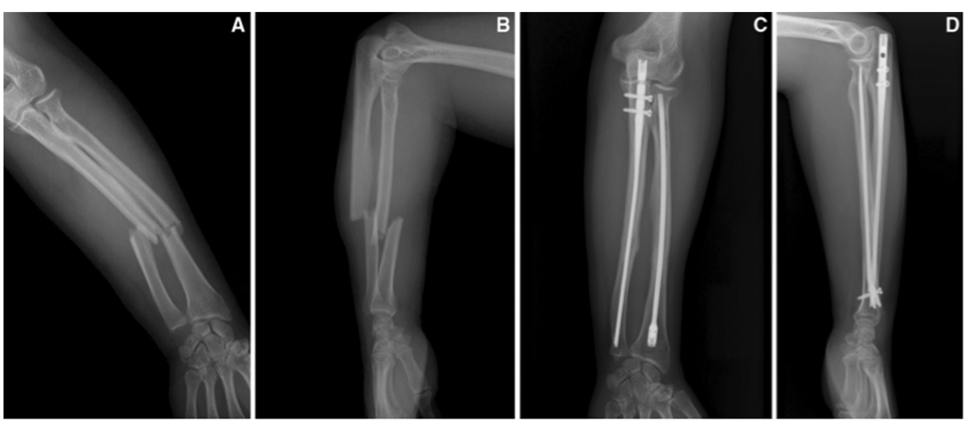


Fig. 2. A,B) Radiographs of patient with both bone forearm fracture C,D) Postoperative radiographs of intramedullary nail fixation with the Acumed Nail [33] (images used with permission).

Summary

Plate fixation of adult forearm fractures remains the gold standard. The use of interlocking intramedullary nails has been shown to be safe and effective in some small case series. However, they are inferior to plate fixation regarding biomechanical stability, re-establishment of the radial bow, and time to union. Open reduction may be required, as well as a period of immobilization post-operatively. Intramedullary nail fixation may be considered as an alternative for select diaphyseal fractures, such as those with extensive soft-tissue injury or pathologic fractures. However, the indications are limited at this time, and many advocate excluding Galeazzi, Monteggia, and severely comminuted fractures. Further research in this area is warranted, with randomized clinical trials comparing intramedullary nails to plate fixation, to help better understand their indications and outcomes.

FIBULA FRACTURES

Unstable ankle fractures with displacement, talar shift or disruption of the mortise benefit from surgical fixation. Open reduction and internal fixation (ORIF) of the fibula is the gold standard of fixation. ORIF is performed using AO principles, through the use of compression screws and a neutralisation plate to obtain anatomic fixation [42]. Potential advantages of intramedullary fixation include smaller incisions, and less soft tissue dissection. These are especially beneficial in patients with compromised skin/soft tissues, such as the elderly, and may reduce the risk of wound complications and infections [43]. Intramedullary devices may also lower the risk of hardware irritation compared to plate fixation. However, the interlocking screws may still cause local irritation, and warrant removal [44].

Types of nails

Unlocked intramedullary devices

Intramedullary fixation of the fibula has been performed in the past with use of Kirschner wires, or intramedullary screws [45,46]. Unlocked intramedullary devices such has elastic nails [47], Rush rods [48], Knowles pins [49,50], Inyo nail [51,52], and Epifisa nail [53] have been utilized for fixation of fibula fractures. While studies on unlocked intramedullary devices have shown high rates of union, complications were present, including symptomatic hardware requiring removal, nail migration and malunion [54]. Lack of rotational control with such unlocked devices is still a concern, and may have high risk of fixation failure, fibular shortening, and malunion, especially in comminuted or length unstable fractures.

Locked intramedullary nails

Advantages of locked intramedullary devices include better rotational control, improved stability and reduced risk of nail migration [54]. Several studies have reported outcomes on the use of locked intramedullary fibular nails [43,55–61]. Nails utilized include the older generation nails such as the ANK nail [57,60], XS nail [59], SST locked nail [61], and the newer generation such as the Acumed fibular nail [43,56]. The majority of these studies are retrospective, with only one prospective randomized controlled trial reported to date [43].

Bugler et al. recently presented a randomized controlled trial, comparing the Acumed fibular nail to plate fixation [43]. One hundred elderly patients (>age 65) with unstable ankle fractures were randomized to one of the two treatment groups, and followed for a total of one year. The authors reported significantly lower complications in the fibular nail group ($p = 0.002$). In the plate group, 16% of patients developed wound infections, two of which developed a wound dehiscence and required surgical debridement and hardware removal. In addition, six patients complained of hardware prominence, and one went on to a malunion. No infections or wound problems occurred in the fibular nail group, while one patient underwent reoperation for loss of reduction, one complained of a prominent locking screw, and one developed a malunion. The overall cost of treatment in the fibular nail group was less, despite the higher cost of the implant. At 1 year, fibular nail patients were significantly happier with the condition of their scar ($P = 0.02$), however functional outcomes using the Olerud Molander score showed no differences between the two groups (63 for nail vs 61 for plate groups).

A systematic review of 627 fibular fractures treated with a variety of locked intramedullary nail devices reported an overall union rate of 98% [54]. The authors noted that satisfactory functional outcomes can be expected, however, complications can be unacceptably high, which may in part be due to a learning curve. They concluded that the methodological flaws in the studies provide only poor-quality evidence for fibular nailing, and definitive conclusions cannot be made. Another recent systematic review of 375 patients reported that fibular nails may have better outcomes regarding soft tissue complications and infections, and may be advantageous in elderly patients at high risk of such complications [62]. The authors noted that there was a high risk of bias towards favourable outcomes for nails.

Technical considerations

Bulger et al. discussed their learning curve with use of the Acumed nail, and noted that the surgical technique was progressively modified to improve outcomes [56]. They reported that significant failure of fixation was noted without proximal or distal locking, such as fibular shortening and talar shift. Distal locking only, without proximal locking or blocking screws also showed similar failures. A proximal blocking screw was used in some patients to allow for maintenance of fibular length, but there was still a potential for talar shift and shortening. The authors stated that the most stable construct was anterior to posterior distal locking screws, to stabilize the distal fragment without peroneal tendon irritation; and a transverse “syndesmosis” screw to lock the nail, and prevent proximal migration, lateralization and rotation.

Summary

Modern locked intramedullary fibular nails have been shown to be the most stable, and decrease the risk of fixation failure, loss of reduction and fibular shortening. Intramedullary nail fixation of fibular fractures provides high rates of union, however, complication rates are not insignificant, and there appears to be a learning curve in the use and application of these implants. Studies demonstrate that locked intramedullary devices may help lower the risk of infections and skin and soft tissue complications, compared to plate fixation, specially in the elderly population. The cost of intramedullary fibular nails is significantly higher than plate fixation, and a concern in the face of limited health care resources. Given the limited evidence, we recommend their use be considered as an alternative for treatment of elderly patients with concerns of soft tissue complications. Further high quality research in this area is warranted to assess the newer generation of commercially available intramedullary implants.

Conflict of interests

The authors have no conflict of interests related to this manuscript.

References

[1] Judd DB, Pallis MP, Smith E, Bottoni CR. Acute operative stabilization versus nonoperative management of clavicle fractures. Am J Orthop (Belle Mead NJ) 2009;38:341–5.

[2] Lee Y-S, Lin C-C, Huang C-R, Chen C-N, Liao W-Y. Operative treatment of midclavicular fractures in 62 elderly patients: knowles pin versus plate. Orthopedics 2007;30:959–64.

[3] Mudd CD, Quigley KJ, Gross LB. Excessive complications of open intramedullary nailing of midshaft clavicle fractures with the Rockwood Clavicle Pin. Clin Orthop Relat Res 2011;469:3364–70, doi:http://dx.doi.org/10.1007/s11999-011-1867-1.

[4] Ferran NA, Hodgson P, Vannet N, Williams R, Evans RO. Locked intramedullary fixation vs plating for displaced and shortened mid-shaft clavicle fractures: a randomized clinical trial. J Shoulder Elbow Surg 2010;19:783–9, doi:http://dx.doi.org/10.1016/j.jse.2010.05.002.

[5] Smekal V, Irenberger A, Struve P, Wambacher M, Krappinger D, Kralinger FS. Elastic stable intramedullary nailing versus nonoperative treatment of displaced midshaft clavicular fractures-a randomized, controlled, clinical trial. J Orthop Trauma 2009;23:106–12, doi:http://dx.doi.org/10.1097/BOT.0b013e318190cf88.

[6] King PR, Ikram A, Lamberts RP. The treatment of clavicular shaft fractures with an innovative locked intramedullary device. J Shoulder Elbow Surg 2015;24:e1–6, doi:http://dx.doi.org/10.1016/j.jse.2014.04.018.

[7] Zehir S, Zehir R, Şahin E, Çalbıyık M. Comparison of novel intramedullary nailing with mini-invasive plating in surgical fixation of displaced midshaft clavicle fractures. Arch Orthop Trauma Surg 2015;135(3):339–44, doi:http://dx.doi.org/10.1007/s00402-014-2142-1.

[8] Kim W, McKee MD. Management of acute clavicle fractures. Orthop Clin North Am 2008;39:491–505, doi:http://dx.doi.org/10.1016/j.ocl.2008.05.006.

[9] Golish SR, Oliviero JA, Francke EI, Miller MD. A biomechanical study of plate versus intramedullary devices for midshaft clavicle fixation. J Orthop Surg Res 2008;3:28, doi:http://dx.doi.org/10.1186/1749-799X-3-28.

[10] Frigg A, Rillmann P, Perren T, Gerber M, Ryf C. Intramedullary nailing of clavicular midshaft fractures with the titanium elastic nail: problems and complications. Am J Sports Med 2009;37:352–9, doi:http://dx.doi.org/10.1177/0363546508328103.

[11] Strauss EJ, Egol KA, France MA, Koval KJ, Zuckerman JD. Complications of intramedullary Hagie pin fixation for acute midshaft clavicle fractures. J Shoulder Elbow Surg 2007;16:280–4, doi:http://dx.doi.org/10.1016/j.jse.2006.08.012.

[12] Fransen P, Bourgeois S, Rommens J. Kirschner wire migration causing spinal cord injury one year after internal fixation of a clavicle fracture. Acta Orthop Belg 2007;73:390–2.

[13] Nordback I, Markkula H. Migration of Kirschner pin from clavicle into ascending aorta. Acta Chir Scand 1985;151:177–9.

[14] Nakayama M, Gika M, Fukuda H, Yamahata T, Aoki K, Shiba S, et al. Migration of a kirschner wire from the clavicle into the intrathoracic trachea. Ann Thorac Surg 2009;88:653–4, doi:http://dx.doi.org/10.1016/j.athoracsur.2008.12.093.

[15] Chen YF, Wei HF, Zhang C, Zeng BF, Zhang CQ, Xue JF, et al. Retrospective comparison of titanium elastic nail (TEN) and reconstruction plate repair of displaced midshaft clavicular fractures. J Shoulder Elbow Surg 2012;21:495–501, doi:http://dx.doi.org/10.1016/j.jse.2011.03.007.

[16] Wijdicks FJ, Van der Meijden OA, Millett PJ, Verleisdonk EJ, Houwert RM. Systematic review of the complications of plate fixation of clavicle fractures. Arch Orthop Trauma Surg 2012;132:617–25, doi:http://dx.doi.org/10.1007/s00402-011-1456-5.

[17] van der Meijden OA, Houwert RM, Hulsmans M, Wijdicks FJ, Dijkgraaf MG, Meylaerts SA, et al. Operative treatment of dislocated midshaft clavicular fractures: plate or intramedullary nail fixation? A randomized controlled trial. J Bone Joint Surg Am 2015;97(8):613–9.

[18] Chen YF, Zeng BF, Chen YJ, Wang HM, Xue JF, Chai YM, et al. Clinical outcomes of midclavicular fractures treated with titanium elastic nails. Can J Surg 2010;53:379–84.

[19] Wijdicks FJG, Houwert RM, Millett PJ, Verleisdonk EJJM, Van Der Meijden OAJ. Systematic review of complications after intramedullary fixation for displaced midshaft clavicle fractures. Can J Surg 2013;56:58–64, doi:http://dx.doi.org/10.1503/cjs.029511.

[20] Witzel K. Intramedullary osteosynthesis in fractures of the mid-third of the clavicle in sports traumatology. Z Orthop Unfall 2007;145:639–42, doi:http://dx.doi.org/10.1055/s-2007-965616.

[21] Assobhi JEH. Reconstruction plate versus minimal invasive retrograde titanium elastic nail fixation for displaced midclavicular fractures. J Orthop Traumatol 2011;12:185–92, doi:http://dx.doi.org/10.1007/s10195-011-0158-7.

[22] Narsaria N, Singh AK, Arun GR, Seth RRS. Surgical fixation of displaced midshaft clavicle fractures: elastic intramedullary nailing versus precontoured plating. J Orthop Traumatol 2014;15:165–71, doi:http://dx.doi.org/10.1007/s10195-014-0298-7.

[23] Andrade-Silva FB, Kojima KE, Joeris A, Santos Silva J, Mattar RJ. Single, superiorly placed reconstruction plate compared with flexible intramedullary nailing for midshaft clavicular fractures: a prospective, randomized controlled trial. J Bone Joint Surg Am 2015;97:620–6, doi:http://dx.doi.org/10.2106/JBJS.N.00497.

[24] Lee YS, Huang HL, Lo TY, Hsieh YF, Huang CR. Surgical treatment of midclavicular fractures: a prospective comparison of Knowles pinning and plate fixation. Int Orthop 2008;32:541–5, doi:http://dx.doi.org/10.1007/s00264-007-0352-7.

[25] Wang X-H, Cheng L, Guo W-J, Li A-B, Cheng G-J, Lei T, et al. Plate versus intramedullary fixation care of displaced midshaft clavicular fractures. Medicine (Baltimore) 2015;94:e1792, doi:http://dx.doi.org/10.1097/md.0000000000001792.

[26] Schemitsch LA, Schemitsch EH, Kuzyk P, McKee MD. Prognostic Factors for Reoperation After Plate Fixation of the Midshaft Clavicle. J Orthop Trauma. 2015;29(12):533–7.

[27] Zlowodzki M, Zelle BA, Cole PA, Jeray K, McKee MD. Treatment of acute midshaft clavicle fractures: systematic review of 2144 fractures: on behalf of the Evidence-Based Orthopaedic Trauma Working Group. J Orthop Trauma 2005;19:504–7, doi:http://dx.doi.org/10.1097/01.bot.0000172287.44278.ef.

[28] Grassi FA, Tajana MS, D'Angelo F. Management of midclavicular fractures: comparison between nonoperative treatment and open intramedullary fixation in 80 patients. J Trauma 2001;50:1096–100, doi:http://dx.doi.org/10.1097/00005373-200106000-00019.

[29] Khan LA, Bradnock TJ, Scott C, Robinson CM. Fractures of the clavicle. J Bone Joint Surg (American Vol) 2009;91:447–60, doi:http://dx.doi.org/10.2106/JBJS.H.00034.

[30] Rehman S, Sokunbi G. Intramedullary fixation of forearm fractures. Hand Clin 2010;26:391–401, doi:http://dx.doi.org/10.1016/j.hcl.2010.04.002.

[31] Schulte LM, Meals CG, Neviaser RJ. Management of adult diaphyseal both-bone forearm fractures. J Am Acad Orthop Surg 2014;22:437–46, doi:http://dx.doi.org/10.5435/JAAOS-22-07-437.

[32] Saka G, Saglam N, Kurtulmus T, Avci CC, Akpinar F, Kovaci H, et al. New interlocking intramedullary radius and ulna nails for treating forearm diaphyseal fractures in adults: a retrospective study. Injury 2014;45:16–23, doi:http://dx.doi.org/10.1016/j.injury.2013.10.040.

[33] Lee SK, Kim KJ, Lee JW, Choy WS. Plate osteosynthesis versus intramedullary nailing for both forearm bones fractures. Eur J Orthop Surg Traumatol 2014;24:769–76, doi:http://dx.doi.org/10.1007/s00590-013-1242-x.

[34] Martin W, Field J, Kulkarni M. Intramedullary nailing of pathological forearm fractures. Injury 2002;33(6):530–2.

[35] Kose A, Aydin A, Ezirmik N, Can CE, Topal M, Tipi T. Alternative treatment of forearm double fractures: new design intramedullary nail. Arch Orthop Trauma Surg 2014;134:1387–96, doi:http://dx.doi.org/10.1007/s00402-014-2058-9.

[36] Lee YH. Interlocking contoured intramedullary nail fixation for selected diaphyseal fractures of the forearm in adults. J Bone Joint Surg 2008;90:1891, doi:http://dx.doi.org/10.2106/JBJS.G.01636.

[37] Jones D, Henley M, Schemitsch E, Tencer A. A biomechanical comparison of two methods of fixation of fractures of the forearm. J Orthop Trauma 1995; (June (9)):198–206.

[38] Hong G, Cong-Feng L, Chang-Qing Z, Hui-Peng S, Cun-Yi F, Bing-Fang Z. Internal fixation of diaphyseal fractures of the forearm by interlocking intramedullary nail: short-term results in eighteen patients. J Orthop Trauma 2005;19(6)384–436 00005131-200507000-00005 [pii].

[39] Weckbach A, Blattert T, Weiber C. Interlocking nailing of forearm fractures. Arch Orthop Trauma Surg 2006;126:309–15, doi:http://dx.doi.org/10.1007/s00402-006-0122-9.

[40] Walz M, Kolbow B, Möllenhoff G. Distale ulnafraktur als begleitverletzung des körperfernen speichenbruchs. Unfallchirurg 2006;109:1058–63, doi:http://dx.doi.org/10.1007/s00113-006-1185-3.

[41] Tabor O, Bosse M, Sims S, Kellam J. Iatrogenic posterior interosseous nerve injury: is transosseous static locked nailing of the radius feasible? J Orthop Trauma 1995;9:427–9.

[42] Ruedi T, Buckley R, Moran C. AO principles of fracture management. New York: Thieme Medical Publishers; 2007.

[43] White O, Bugler KE, Appleton P, Will E, McQueen MM, Court-Brown CM. A prospective, randomized controlled trial of a fibular nail versus standard open reduction and internal fixation for fixation of ankle fractures. Bone Joint J 2016;98 -B(9):1248–52.

[44] Bugler KE, White TO. Early routine weight bearing is safe in patients with ankle fractures. Orthopaedic Trauma Association Annual Meeting. .

[45] Ray TD, Nimityongskul P, Anderson LD. Percutaneous intramedullary fixation of lateral malleolus fractures: technique and report of early results. J Trauma 1994;36:669–75, doi:http://dx.doi.org/10.1097/00005373-199405000-00012.

[46] Bankston a B, Anderson LD, Nimityongskul P, Ab B, Ld A, Nimityongskul P. Intramedullary screw fixation of lateral malleolus fractures. Foot Ankle Int/Am Orthop Foot Ankle Soc [and] Swiss Foot Ankle Soc 1994;15:599–607, doi:http://dx.doi.org/10.1177/107110079401501105.

[47] Wang Q, Xu HG, Zhang YC, Dong LJ. Elastic nails for fibular fracture in adulttibiofibular fractures. Int J Clin Exp Med 2015;8:10086–90.

[48] Pritchett J. Rush rods versus plate osteosyntheses for unstable ankle fractures in the elderly. Orthop Rev 1993;22:691–6.

[49] Lee YS, Huang H, Le Ti-Y. Lateral fixation of AO type-B2 ankle fractures in the elderly: the Knowles pin versus the plate. Int Orthop 2007;31:817–21, doi:http://dx.doi.org/10.1007/s00264-006-0260-2.

[50] Lee YS, Chen SW. Lateral fixation of open AO type-B2 ankle fractures: the Knowles pin versus plate. Int Orthop 2009;33:1135–9, doi:http://dx.doi.org/10.1007/s00264-008-0617-9.

[51] McLennan JG, Ungersma J. Evaluation of the treatment of ankle fractures with the Inyo nail. J Orthop Trauma 1988;2:272–6, doi:http://dx.doi.org/10.1097/00005131-198802040-00002.

[52] McLennan JG, Ungersma JA. A new approach to the treatment of ankle fractures. The Inyo nail. Clin Orthop Relat Res 1986;125–36.
[53] Asloum Y, Bedin B, Roger T, Charissoux JL, Arnaud JP, Mabit C. Internal fixation of the fibula in ankle fractures. A prospective, randomized and comparative study: plating versus nailing. Orthop Traumatol Surg Res 2014;100:S255–9, doi:http://dx.doi.org/10.1016/j.otsr.2014.03.005.
[54] Jain S, Haughton BA, Brew C. Intramedullary fixation of distal fibular fractures: a systematic review of clinical and functional outcomes. J Orthop Traumatol 2014;15:245–54, doi:http://dx.doi.org/10.1007/s10195-014-0320-0.
[55] Tawari G, Kakwani R, Shankar K. Ankle fracture fixation - plate osteosynthesis versus intramedullary fibular nail. Orthop Proceedings Bone Jt J. 2012;94(B no. Supp XXXIX)):239.
[56] Bugler KE, Watson CD, Hardie aR, Appleton P, McQueen MM, Court-Brown CM, et al. The treatment of unstable fractures of the ankle using the Acumed fibular nail: development of a technique. J Bone Joint Surg – Br Vol 2012;94-B:1107–12, doi:http://dx.doi.org/10.1302/0301-620x.94b8.28620.
[57] Kara AN, Esenyel CZ, Sener BT, Merih E. A different approach to the treatment of the lateral malleolar fractures with syndesmosis injury: the ANK nail. J Foot Ankle Surg 1999;38:394–402, doi:http://dx.doi.org/10.1016/S1067-2516(99)80039-8.
[58] Ramasamy PR, Sherry P. The role of a fibular nail in the management of Weber type B ankle fractures in elderly patients with osteoporotic bone – a preliminary report. Injury 2001;32:477–85, doi:http://dx.doi.org/10.1016/s0020-1383(01)00030-4.
[59] Gehr J, Neber W, Hilsenbeck F, Friedl W. New concepts in the treatment of ankle joint fractures. The IP-XS (XSL) and IP-XXS (XXSL) nail in the treatment of ankle joint fractures. Arch Orthop Trauma Surg 2004;124:96–103, doi:http://dx.doi.org/10.1007/s00402-003-0606-9.
[60] Kabukcuoglu Y, Kucukkaya M, Eren T, Gorgec M, Kuzgun U. The ANK device: a new approach in the treatment of the fractures of the lateral malleolus associated with the rupture of the syndesmosis. Foot Ankle Int/Am Orthop Foot Ankle Soc [and] Swiss Foot Ankle Soc 2000;21:753–8.
[61] Rajeev A, Senevirathna S, Radha S, Kashayap NS. Functional outcomes after fibula locking nail for fragility fractures of the ankle. J Foot Ankle Surg 2011;50:547–50, doi:http://dx.doi.org/10.1053/j.jfas.2011.04.017.
[62] Rehman H, McMillan T, Rehman S, Clement A, Finlayson D. Intrmedullary versus extramedullary fixation of lateral malleolus fractures. Int J Surg 2015;22:54–61, doi:http://dx.doi.org/10.1016/j.ijsu.2015.07.697.

Injury, Int. J. Care Injured 48S (2017) S47–S51

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Extended applications of the reamer-irrigator-aspirator (RIA) system

Niloofar Dehghan[a,c], Emil H. Schemitsch[b,*]

[a] Li Ka Shing Institute, St. Michael's Hospital and the University of Toronto, Toronto, Canada
[b] Division of Orthopaedics, Department of Surgery, Western University, London, Canada
[c] Orthopaedic Surgeon - The CORE Institute, Banner University Medical Center, Phoenix, Arizona, USA

ARTICLE INFO

Keywords:
Reaming irrigator aspirator
Bone graft
Femoral canal
Intramedullary reaming

ABSTRACT

While the RIA system was initially designed for reaming and clearing the femoral canal contents in preparation for femoral nailing, it has since been used in various other applications in the field of orthopaedic surgery. The RIA is an ideal device for accessing large quantities of autogenous bone graft, to be used in the treatment of nonunions, segmental bone loss, or arthrodesis. The RIA has also been used for treatment of intramedullary infections and osteomyelitis, as well as intramedullary nailing of long bones with metastatic lesions, as it allows for clearing the canal of infectious/tumour burden, and lowers the risk of dissemination into the soft tissues and systemic circulation. There is also some limited evidence that the RIA may be used for clearing the femoral/tibial canal of cement debris. Despite multiple applications, the use of RIA has a risk of eccentric reaming and iatrogenic fractures. RIA is also a costly procedure, and its routine use may not be advantageous in the setting of limited health care resources.

What is RIA?

The Reamer-Irrigator-Aspirator (RIA) system (Synthes) is a simultaneous reaming and aspiration system. RIA was designed as a one-pass reamer of the femoral canal, which simultaneously irrigates and aspirates the femoral canal contents during reaming [1]. The irrigation of the canal allows for reduction of heat generated and prevents thermal necrosis [2], while the aspiration decreases the intramedullary pressure, fat embolism [1,3], and the systemic effects of reaming [4]. The one time pass also allows for a shorter surgical time [1].

The primary indication for use of the RIA system is to clear the medullary canal of bone marrow and reaming debris, for the implantation of an intramedullary nail [1]. FDA approval for this purpose was received in 2000. The use of RIA for intramedullary nailing of femoral shaft fractures may decrease the risk of fat emboli as well as systemic effects of reaming and secondary hit phenomena, which would be especially helpful for treatment of polytrauma patients [5].

The RIA system is composed of a disposable reamer head, a re-usable drive shaft, and a seal and tube assembly (Fig. 1). It is considered a one-time aggressive reamer. The smallest reamer size is 12 mm, and increases by 0.5 mm increments to maximum size of 19 mm. The reamer size should be selected by pre-operative assessment of the femoral canal size. The drive shaft is hollow, and is contained by a plastic tube, which allows for continuous irrigation at the reamer head, as well as aspiration of the reaming debris. A filter is placed between the reamer and suction canister, which allows for passage of fluid, but captures particulate matter [1] (Fig. 1). Reaming is performed by applying the advance/withdraw/pause/advance technique to maximize irrigation flow through the RIA [6]. As the collection filter fills, reaming should be stopped and the filter should be emptied before further reaming commences [1].

Complications

The RIA is considered to be an "aggressive" reamer, and the reamer head (smallest size 12 mm) may be too large to use safely in smaller individuals. The use of RIA in patients with smaller diameter canals may lead to over reaming or eccentric reaming, and cause perforation of the femoral cortex or iatrogenic fractures [1,7–12] (Fig. 2). Eccentric reaming of the proximal femur may also lead to iatrogenic femoral neck fracture, especially with use of a piriformis start point [7]. The use of RIA in patients with osteoporotic bone should also be used with caution, as inadvertent eccentric reaming of the thin cortical bone will increase the risk of fractures. Eccentric reaming may also occur in patients who lack a normally aligned medullary canal (e.g. large anterior femoral bow), or with use of pre-bent guide wires [1]. If over reaming of the

* Corresponding author at: 339 Windermere Road, Room C9-116, London, Ontario N6A 5A5, Canada.
E-mail address: emil.schemitsch@lhsc.on.ca (E.H. Schemitsch).

http://dx.doi.org/10.1016/j.injury.2017.04.025
0020-1383/

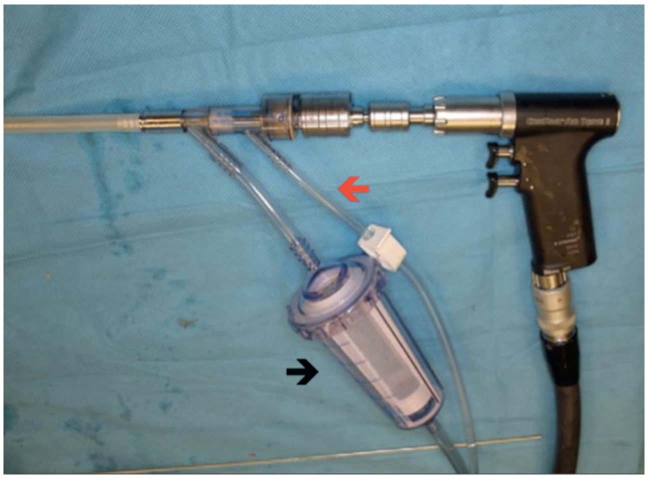


Fig. 1. RIA system with the irrigation tubing (red arrow) and filter (black arrow) (used with permission [1]).

proximal femur has taken place, prophylactic fixation should be performed [7].

Such complications may be reduced by appropriate preoperative assessment of the cortical diameter. It has been recommended to use a reamer head that is no more than 2 mm larger than the diameter of the isthmus. Appropriate start point, and central placement of the guide wire are critical. Fluoroscopy should also be used frequently during the reaming process to ensure central placement of the guide wire, and prevent eccentric reaming or violation of the knee [1,6,9]. The use of RIA in patients with a history of osteoporosis or osteopenia should be avoided, unless intramedullary stabilization is considered [9].

Other complications of the RIA system include post-operative hip or knee pain, depending on its use in an antegrade or retrograde fashion. Prolonged suction and aspiration may also lead to extensive blood loss, while blockage of the aspiration and tube assembly by debris can cause increased intramedullary pressure, and possible pulmonary embolism [11]. Dissociation of reamer head from the drive shaft has been reported in several series [5,13], as well as breakage of the drive shaft tip in the medullary canal [13].

Use of RIA for bone graft harvest

The gold standard for treatment of non-unions remains autogenous bone grafting, which contains osteoconductive, osteoinductive and osteogenic properties. Traditionally, autologous cancellous bone graft is harvested from the anterior or posterior iliac crests, which can yield about 20–40 cc of cancellous bone [7]. However, when the bony defect is large, the iliac crest may not yield a sufficient quantity of autogenous bone graft, and harvesting large quantities of bone may be associated with significant morbidity [14].

Studies have shown that RIA may be used to collect a generous volume of autologous bone graft, which contains growth factors with potency equal to or greater than autograft material from the iliac crest [1,14–16]. The reaming particles which are collected in the filter, can be utilized as ideal autograft in numerous applications in the field of orthopaedic surgery (Fig. 3) [1,17,18]. The use of RIA for harvest of autogenous bone graft was approved by the FDA in March 2005 [4].

Femoral reaming can be performed via antegrade or retrograde techniques [19], however, antegrade reaming has been reported to have a higher risk of eccentric reaming than retrograde technique [19]. A recent study reported that a mean volume of 41 ml of autogenous bone graft can be obtained from the femur, and 32.5 ml from the tibia [7]. If more bone graft is required with antegrade femoral reaming, the guide wire can be placed into the femoral condyles for a second pass.

Advantages

The advantage of using RIA for obtaining autogenous bone graft is the decreased risk of donor site morbidity, which is associated

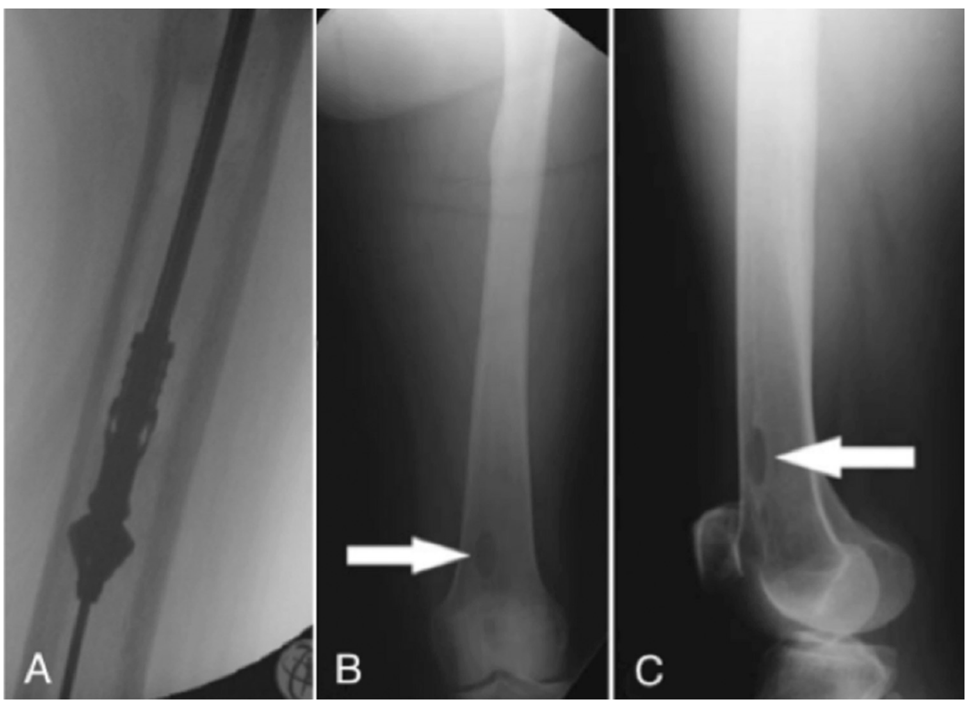


Fig. 2. RIA complications: A) Eccentric reaming [11]) B,C) Cortical perforation [7] (used with permission).

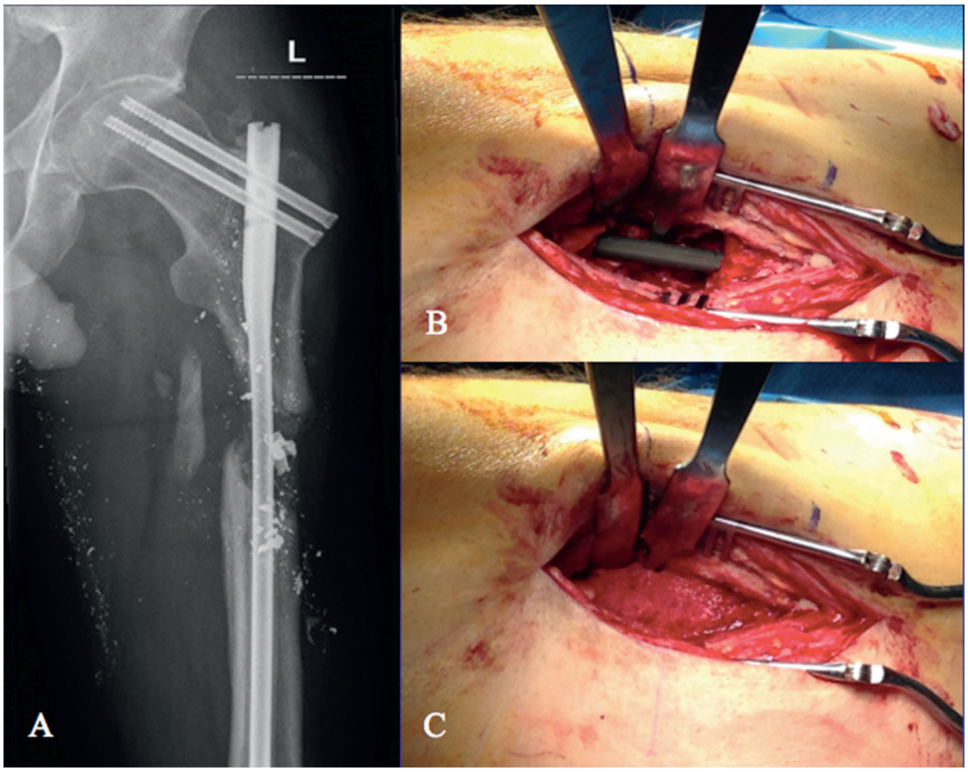


Fig. 3. Bone graft application for segmental bone defect: A) Subrochanteric femoral shaft fracture with a segmental defect from bone loss B) Intraoperative image of bone defect C) Autogenous bone graft obtained with RIA, applied to bone defect.

with autogenous bone graft harvested from the anterior or posterior iliac crests [1,7,20]. There is also a decreased risk of injury to the lateral femoral cutaneous nerve, abdominal hernia, avulsion fracture of the anterior iliac spine, or injury to the superficial clonal nerves, which are associated with ICBG harvesting [7,21].

Disadvantages

While RIA may be better tolerated by patients regarding donor site pain, it is a more costly procedure, and the risk of post-operative femoral fractures is a real concern [22]. This is especially an issue when the primary goal is harvest of autogenous bone graft, and intramedullary fixation is not performed. Many studies have reported post-operative femur fractures [22], or need for prophylactic intramedullary nail fixation of the femur due to perforation or eccentric reaming of the femoral canal [19,23,24]. Patients should be thoroughly counselled regarding the risk of fractures and other complications from the use of RIA for bone graft harvesting.

Use in the literature

Many studies have investigated the use of reaming debris obtained from RIA to treat non-unions, including segmental bone defects [5,8,11,19,22,25]. A prospective randomized controlled trial by Dawson and colleagues compared the use of RIA to autogenous ICBG for the treatment of nonunions or post traumatic bone defects [22]. Their results showed no difference between the two methods regarding rates of union, time to union, rates of infection or reoperation. However, patients in the RIA group had significantly lower donor-site pain. The authors also reported that RIA yielded a greater volume of bone graft compared with anterior ICBG (38 vs. 21 ml, $p < 0.001$), and had a shorter harvest time compared to posterior ICBG (29 vs. 41 min, $p = 0.005$). Despite the fact that RIA cost $600 USD more than ICBG, cost analysis favoured the use of RIA for larger volume harvests [22]. Other studies comparing RIA to ICBG for treatment of nonunions have also reported lower donor site pain with RIA [20].

Several small case series have described the use of RIA to obtain bone graft for arthrodesis procedures, including ankle arthrodesis [30–33], spinal fusion [26], and opening wedge high tibial osteotomy [27]. High quality studies in this area are lacking.

RIA for treatment of long bone osteomyelitis

Treatment of long bone osteomyelitis is challenging, and many patients require multiple surgical debridements to eradicate the infection. Principles of treatment include: surgical debridement and irrigation, fracture site stabilization, soft tissue coverage, and culture specific antibiotics [28]. Surgical debridement is the most important aspect in treatment of chronic osteomyelitis, and includes the removal of all internal fixation, as well as resection of sequestra, avascular bone, necrotic tissues, and sinus tracts [28,29]. When an infection develops in the presence of an intramedullary nail, there is a potential of infection extending along the entire nail and medullary canal. Therefore, following the removal of the nail, the medullary canal should be thoroughly debrided to remove the infected debris, as well as infected endosteal bone and tissue [28].

Traditionally, treatment of long bone osteomyelitis involved open debridement of the sequestrum, with debulking the bone and surround soft tissues [30]. Debridement of the medullary canal can also be performed with use of reamers, which is less invasive. RIA may be used for intramedullary canal debridement and irrigation, for management of intramedullary long bone osteomyelitis (usually following intramedullary nailing). It may also be used for treatment of intramedullary sepsis from spread of local osteomyelitis [30].

Advantages

Compared to regular reamers, RIA has a disposable reamer head, which is always sharp. It allows for simultaneous opening of the medullary canal, removal of sequestra, and promotion of vascularization. It is combined with the continuous irrigation, which prevents thermal necrosis, and helps preserve endosteal bone [30]. The aspiration minimizes the residual amount of infected fluid and tissue in the medullary canal, and decreases the propagation of infection material to the ends of the medullary canal, surrounding soft tissues, and venous system [28,30]. RIA also allows for collection of intramedullary debris, for further microbiological investigation [5].

The RIA system has been used successfully for treatment of chronic osteomyelitis in several small series [5,11,19,30]. Kanakaris et al. reported on 24 patients, 14 with femoral and 10 with tibial osteomyelitis, who underwent irrigation and debridement of the medullary canal with RIA [29]. An antibiotic impregnated cement rod was also inserted in 23 of the 24 patients, all of which had resolution of their infection. The authors recommended using a reamer head with a diameter at least 1.5 mm larger than the diameter of the medullary canal, as measured pre-operatively, or from information obtained form the initial surgical procedure.

Contraindications

RIA is not a good option for treatment of metaphyseal bone infections, as the large canal diameter will not allow for an adequate debridement. The use of RIA is contraindicated in patients with narrow medullary canals (diameter < 10 mm), and may lead to excess bone removal and iatrogenic fractures, a significant problem in the face of infection [30].

RIA for reaming of metastatic lesions

Patients with pathologic bony lesions who undergo prophylactic intramedullary nailing carry the theoretical risk of pulmonary or cerebral embolism, and tumour dissemination. Although a correlation between tumour dispersal and increased metastases has not been proven, it remains a potential concern [13]. Another concern in this patient population is the impaired pulmonary function secondary to metastatic disease, and respiratory compromise from embolic load during reaming [13].

The insertion of an implant into an intact long bone is of major concern, as it causes compression of the medullary canal and rise in the intramedullary pressure. When a fracture is present, it acts as an exhaust vent, decompressing the pressure in the medullary cavity [31]. Venting of the femur has been described to reduce intramedullary pressures during reaming, and theoretically reduce the risk of embolism [32]. While venting reduces pressurization during prophylactic reamed intramedullary nailing, some suggest that intramedullary pressures continue to exceed the estimated threshold for embolization [13]. Venting may also increase the spread of tumour to extraskeletal tissue if vented tissue is not contained [13,33].

A few small case series have reported on the use of RIA in this setting [5,13]. Research in this area is limited, and further studies are required to provide additional evidence regarding the indications and safety of RIA in this setting.

Advantages

Patients with diaphyseal femoral metastasis with pathologic or impending pathologic fractures may represent an additional indication for the use of RIA. An advantage of RIA in this setting is minimizing the intramedullary pressure during reaming an intact long bone, which lowers the risk of systemic dissemination and distal metastasis, as well as pulmonary emboli [5,13]. RIA also allows for the acquisition of multiple samples for further histological analysis, and has been shown to lower tumour burden [5,13].

Risks

It is important to note that patients with metastatic lesions have pathologic bone, and have a higher risk of eccentric reaming and cortical perforation. Care should be taken to prevent such outcomes, and intramedullary nail fixation should be performed in all such cases.

RIA for removal of residual bone cement from the medullary canal

Cement can be dislodged or retained in the medullary canal after removal of cemented arthroplasty components, or antibiotic-coated intramedullary nails. Removal of cement fragments may be performed with conventional techniques, including the use of intramedullary hooks, reverse curettes, flexible osteotomes, and stacked guide rods [34]. A cortical window can also be created to assist in cement removal.

Removal of antibiotic-coated intramedullary nails can cause debonding of the cement mantle from the nail, which can traverse the entire length of the canal, and may be too difficult to remove with conventional techniques. The use of regular reamers in this setting can be helpful, but may cause thermal bone necrosis, which is of concern. In such situations, the use of RIA may be of benefit to assist in removal of retained intramedullary cement, especially when the residual cement mantle is too distal to be reached by standard instruments.

There is limited research in this area [34]. Technical consideration are forward pressure alternated with 10–20 mm withdrawal of the reamer head, to allow aspiration of debrided cement particulate and clearing the reamer flutes. It may be necessary to disassemble the RIA system to clear cement fragments form the aspiration port. If there is difficulty advancing the reamer, the reamer head may have become dull, and should be replaced [34].

In conclusion, RIA has been found useful in different clinical situations [35–40].

It appears to be a versatile device with very few complications. Further research in this area is warranted to further identify indications and outcomes in this setting.

Conflict of interest

None.

References

[1] Giannoudis PV, Tzioupis C, Green J. Surgical techniques: how I do it? The Reamer/Irrigator/Aspirator (RIA) system. Injury 2009;40:1231–6, doi:http://dx.doi.org/10.1016/j.injury.2009.07.070.

[2] Higgins TF, Casey V, Bachus K. Cortical heat generation using an irrigating/aspirating single-pass reaming vs conventional stepwise reaming. J Orthop Trauma 2007;21:192–7, doi:http://dx.doi.org/10.1097/BOT.0b013e318038d952.

[3] Volgas DA, Burch T, Stannard JP, Ellis T, Bilotta J, Alonso JE. Fat embolus in femur fractures: a comparison of two reaming systems. Injury 2010;41:S90–3, doi:http://dx.doi.org/10.1016/S0020-1383(10)70017-6.

[4] Hartsock LA, Barfield WR, Kokko KP, Liles LL, Wind T, Green J, et al. Randomized prospective clinical trial comparing reamer irrigator aspirator (RIA) to standard reaming (SR) in both minimally injured and multiply injured patients with closed femoral shaft fractures treated with reamed intramedullary nailing (IMN). Injury 2010;41:S94–8, doi:http://dx.doi.org/10.1016/s0020-1383(10)70018-8.
[5] Kanakaris NK, Morell D, Gudipati S, Britten S, Giannoudis PV. Reaming Irrigator Aspirator system: early experience of its multipurpose use. Injury 2011;42:S28–34, doi:http://dx.doi.org/10.1016/S0020-1383(11)70009-2.
[6] Pfeifer R, Kobbe P, Knobe M, Pape H-C. Das Reamer-Irrigator-Aspirator (RIA)-system. Oper Orthop Traumatol 2011;23:446–52, doi:http://dx.doi.org/10.1007/s00064-011-0117-8.
[7] Belthur MV, Conway JD, Jindal G, Ranade A, Herzenberg JE. Bone graft harvest using a new intramedullary system. Clin Orthop Relat Res 2008;466:2973–80, doi:http://dx.doi.org/10.1007/s11999-008-0538-3.
[8] Han F, Peter L, Lau ETC, Thambiah J, Murphy D, Kagda FHY. Reamer Irrigator Aspirator bone graft harvesting: complications and outcomes in an Asian population. Injury 2015;46:2042–51, doi:http://dx.doi.org/10.1016/j.injury.2015.07.027.
[9] Lowe JA, Della Rocca GJ, Murtha Y, Liporace FA, Stover MD, Nork SE, et al. Complications associated with negative pressure reaming for harvesting autologous bone graft: a case series. J Orthop Trauma 2010;24:46–52, doi:http://dx.doi.org/10.1097/BOT.0b013e31819c0ccb.
[10] Cox G, Jones E, McGonagle D, Giannoudis PV. Reamer-irrigator-aspirator indications and clinical results: a systematic review. Int Orthop 2011;35:951–6, doi:http://dx.doi.org/10.1007/s00264-010-1189-z.
[11] Jakma TSC, Roling MA, Punt B, Reynders-Frederix P. More adverse events than expected in the outcome after use of the reamer-irrigator-aspirator. Eur J Trauma Emerg Surg 2013;40:337–41, doi:http://dx.doi.org/10.1007/s00068-013-0345-8.
[12] Giori NJ, Beaupre GS. Femoral fracture after harvesting of autologous bone graft using a reamer/irrigator/aspirator. J Orthop Trauma 2011;25:e12–4, doi:http://dx.doi.org/10.1097/BOT.0b013e3181e39bf4.
[13] Cipriano CA, Arvanitis LD, Virkus WW. Use of the reamer-irrigator-aspirator may reduce tumor dissemination during intramedullary fixation of malignancies. Orthopedics 2012;35:e48–52, doi:http://dx.doi.org/10.3928/01477447-20111122-09.
[14] McCall TA, Brokaw DS, Jelen BA, Scheid DK, Scharfenberger A V, Maar DC, et al. Treatment of large segmental bone defects with reamer-irrigator-aspirator bone graft: technique and case series. Orthop Clin North Am 2010;41:63–73, doi:http://dx.doi.org/10.1016/j.ocl.2009.08.002.
[15] Sagi HC. Qualitative and quantitative differences between bone graft obtained from the medullary canal (with a Reamer/Irrigator/Aspirator) and the iliac crest of the same patient. J Bone Jt Surg 2012;94:2128, doi:http://dx.doi.org/10.2106/JBJS.L.00159.
[16] Uppal HS, Peterson BE, Misfeldt ML, Della Rocca GJ, Volgas DA, Murtha YM, et al. The viability of cells obtained using the Reamer-Irrigator-Aspirator system and in bone graft from the iliac crest. Bone Jt J 2013;95 B:1269–74, doi:http://dx.doi.org/10.1302/0301-620X.95B9.
[17] Porter RM, Liu F, Pilapil C, Betz OB, Vrahas MS, Harris MB, et al. Osteogenic potential of reamer irrigator aspirator (RIA) aspirate collected from patients undergoing hip arthroplasty. J Orthop Res 2009;27:42–9, doi:http://dx.doi.org/10.1002/jor.20715.
[18] Wenisch S, Trinkaus K, Hild A, Hose D, Herde K, Heiss C, et al. Human reaming debris: a source of multipotent stem cells. Bone 2005;36:74–83, doi:http://dx.doi.org/10.1016/j.bone.2004.09.019.
[19] Davis RL, Taylor BC, Johnson N, Ferrel JR, Castaneda J. Retrograde versus antegrade femoral bone graft harvesting using the reamer-irrigator-aspirator. J Orthop Trauma 2015;29:370–2, doi:http://dx.doi.org/10.1097/BOT.0000000000000300.
[20] Calori GM, Colombo M, Mazza EL, Mazzola S, Malagoli E, Mineo GV. Incidence of donor site morbidity following harvesting from iliac crest or RIA graft. Injury 2014;45:S116–20, doi:http://dx.doi.org/10.1016/j.injury.2014.10.034.
[21] Ebraheim NA, Elgafy H, Xu R. Bone-graft harvesting from iliac and fibular donor sites: techniques and complications. J Am Acad Orthop Surg 2001;9:210–8.
[22] Dawson J, Kiner D, Ii WG, Swafford R, Nowotarski PJ. The Reamer –Irrigator –Aspirator as a device for harvesting bone graft compared with iliac crest bone graft: union rates and complications. J Orthop Trauma 2014;28:584–90, doi:http://dx.doi.org/10.1097/BOT.0000000000000086.
[23] Qvick LM, Ritter CA, Mutty CE, Rohrbacher BJ, Buyea CM, Anders MJ. Donor site morbidity with reamer-irrigator-aspirator (RIA) use for autogenous bone graft harvesting in a single centre 204 case series. Injury 2013;44:1263–9, doi:http://dx.doi.org/10.1016/j.injury.2013.06.008.
[24] Dimitriou R, Mataliotakis GI, Angoules AG, Kanakaris NK, Giannoudis PV. Complications following autologous bone graft harvesting from the iliac crest and using the RIA: A systematic review. Injury 2011;42:S3–15, doi:http://dx.doi.org/10.1016/j.injury.2011.06.015.
[25] Kobbe P, Tarkin IS, Pape HC. Use of the reamer irrigator aspirator system for non-infected tibial non-union after failed iliac crest grafting. Injury 2008;39:796–800, doi:http://dx.doi.org/10.1016/j.injury.2007.12.020.
[26] Nichols TA, Sagi HC, Weber TG, Guiot BH. An alternative source of autograft bone for spinal fusion: the femur: technical case report. Neurosurgery 200862:, doi:http://dx.doi.org/10.1227/01.neu.0000317390.21927.ad.
[27] Seagrave RA, Sojka J, Goodyear A, Munns SW. Utilizing reamer irrigator aspirator (RIA) autograft for opening wedge high tibial osteotomy: a new surgical technique and report of three cases. Int J Surg Case Rep 2014;5:37–42, doi:http://dx.doi.org/10.1016/j.ijscr.2013.11.004.
[28] Zalavras CG, Sirkin M. Treatment of long bone intramedullary infection using the RIA for removal of infected tissue: indications, method and clinical results. Injury 2010;41:S43–7, doi:http://dx.doi.org/10.1016/S0020-1383(10)70008-5.
[29] Kanakaris N, Gudipati S, Tosounidis T, Harwood P, Britten S. The treatment of intramedullary osteomyelitis of the femur and tibia using the Reamer-Irrigator-Aspirator system and antibiotic cement rods. Bone Jt J 2014;96 B:783–8, doi:http://dx.doi.org/10.1302/0301-620x.96b6.32244.
[30] Bellapianta J, Gerdeman A, Sharan A, Lozman J. Use of the reamer irrigator aspirator for the treatment of a 20-year recurrent osteomyelitis of a healed femur fracture. J Orthop Trauma 2007;21:343–6, doi:http://dx.doi.org/10.1097/BOT.0b013e318051532d.
[31] Dalgorf D, Borkhoff CM, Stephen DJG, Finkelstein J, Kreder HJ. Venting during prophylactic nailing for femoral metastases: current orthopedic practice. Can J Surg 2003;46:427–31.
[32] Martin R, Leighton RK, Petrie D, Ikejiani C, Smyth B. Effect of proximal and distal venting during intramedullary nailing. Clin Orthop Relat Res 2016;1996:80–9, doi:http://dx.doi.org/10.1097/00003086-199611000-00011.
[33] Roth S, Rebello M, Kreder H, Whyne C. Pressurization of the metastatic femur during prophylactic intramedullary nail fixation. J Trauma 2004;57:333–9, doi:http://dx.doi.org/10.1097/01.TA.0000082157.29723.16.
[34] Lowe JA, Vosburg C, Murtha YM, Della Rocca GJ, Crist BD. A new technique for removing intramedullary cement. J Orthop Trauma 2011;25:762–6, doi:http://dx.doi.org/10.1097/BOT.0b013e318210f218.
[35] Giannoudis PV, Gudipati S, Harwood P, Kanakaris NK. Long bone non-unions treated with the diamond concept: a case series of 64 patients. Injury 2015;46 (Suppl 8)S48–54 December.
[36] Giannoudis PV, Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury 2016;47(Suppl 6)S53–61 December.
[37] Singh R, Bleibleh S, Kanakaris NK, Giannoudis PV. Upper limb non-unions treated with BMP-7: efficacy and clinical results. Injury 2016;47(Suppl 6)S33–9, doi:http://dx.doi.org/10.1016/s0020-1383(16)30837-3 (December) PMID: 28040085 PubMed.
[38] Wu H, Shen J, Yu X, Fu J, Yu S, Sun D, et al. Two stage management of Cierny-Mader type IV chronic osteomyelitis of the long bones. Injury 2017 Feb;48 (2):511–8.
[39] Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury 2016;47(Suppl 6)S68–76 December.
[40] Aktuglu K, Günay H, Alakbarov J. Monofocal bone transport technique for bone defects greater than 5cm in tibia: our experience in a case series of 24 patients. Injury 2016;47(Suppl 6)S40–6 December.

Injury, Int. J. Care Injured 48S (2017) S52–S58

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

The role of the intramedullary implant in limb lengthening

Peter R. Calder[a,*], Maritz Laubscher[b], W. David Goodier[a]

[a] The Royal National Orthopaedic Hospital, Stanmore, Middlesex, UK
[b] Department of Orthopaedic Surgery, Groote Schuur Hospital, University of Cape Town, South Africa

ARTICLE INFO

Keywords:
Limb lengthening
Intramedullary nail
Precice lengthening nail
Distraction osteogenesis
Magnet
IM nailing
Corticotomy
Bone transport

ABSTRACT

Limb lengthening is now an accepted practice in orthopaedic surgery. The principles of distraction osteogenesis have become well established with the use of external fixators, utilizing both monolateral and ring fixators. Corticotomy technique, frame stability, lengthening rate and rhythm all contribute to the formation of bone regenerate and tissues. Complications are however common including pin-site infection, soft tissue tethering from the pins and wires resulting in pain, regenerate deformity from soft tissue forces or fracture following frame removal and patient intolerance of the frames during treatment.

Surgical techniques have changed to try and minimise these complications. The use of intramedullary nails have been used in conjunction with an external fixator or inserted after lengthening has been achieved, to reduce fixator time and prevent regenerate deformity. Implant innovation has led to the production of intramedullary lengthening nails. The initial devices used ratchet mechanisms with rotation of the bone fragments to achieve lengthening (Bliskunov, Albizzia and ISKD). More accurate control of lengthening and a reduction in pain, resulting from the manual rotation of the leg required to achieve the ratchet progression, was achieved by the use of a transcutaneous electrical conduit powered by external high frequency electrical energy (Fitbone).

The most recent implant uses an external remote controller which contains two neodymium magnets. These are placed over the nail on the skin and rotate which in turn rotates a third magnet within the intramedullary nail (Precice). This magnet rotation is converted by a motor to extend or retract the extendible rod. There are multiple nail sizes and lengths available, and early results have shown accurate control with few complications. With such promising outcomes the use of this lengthening intramedullary nail is now recommended as the implant of choice in femoral lengthening. This article is an historical account of the intramedullary device and the impact on limb lengthening.

Introduction of limb lengthening

Over the course of the 20th and early 21st century limb lengthening has become an accepted orthopaedic practice. Codivilla in 1905 published “On the means of lengthening, in the lower limbs, the muscles and tissues which are shortened through deformity” [1]. He highlighted the difficulty of lengthening a limb due to the resistance of the soft tissues and muscles. The forces required to stretch the limbs were considerable which limited the use of skin traction, to overcome this he applied the traction force directly to the skeleton with a calcaneal nail whilst the limb was held in extension and the patient under narcosis. An osteotomy was made in the femur and traction applied to acutely lengthen the limb, a plaster was then applied from pelvis to foot. After a few days a Gigli saw was used to divide the plaster at the level of the osteotomy and further traction applied, with or without narcosis. The gap in the plaster was filled in to maintain the length achieved.

The basic concept of bone osteotomy, acute lengthening and consolidation led to several different distraction devices being produced but all encountered complications due to overstretching, vascular deficiency to the fragments and insufficient fixation of the bone. It was not until after World War II that further interest in limb lengthening techniques provided the principles of today. Following initial concentration on lengthening apparatus, a focus on the biological reaction of the tissues and bone formation led to dramatic improvement in surgical outcomes.

Wagner [2,3] undertook femoral lengthening by placing 4 Shanz pins fixed to a monolateral system, an osteotomy was made with an oscillating saw and the periosteum divided. Gradual traction of approximately 1.5 mm/day was undertaken with one turn of the knob on the lengthening device. Once the desired

* Corresponding author.
E-mail address: peter.calder@rnoh.nhs.uk (P.R. Calder).

http://dx.doi.org/10.1016/j.injury.2017.04.028
0020-1383/

length had been achieved an x-ray was taken. If bone was seen between the bone ends then consolidation was expected and the frame left in situ. However in the majority of patients, especially in adults, bone continuity was absent. This unreliability of bone formation led to bone grafting and osteosynthesis using a special AO-plate being advised, if hyperaemic fibrocartilaginous tissue was present then grafting was deemed not necessary. Wasserstein [4] lengthened with a circular fixator over an unreamed flexible nail. The rate of lengthening was 1–2 mm per day and once the appropriate length was achieved the distraction gap was filled with a slotted tubular allograft.

The aim was to reduce treatment time, increase stability of fixation and ensure proper alignment. This appears to be one of the first documentation of the use of an intramedullary implant.

It was Ilizarov [5–7] in the 1950s who developed arguably the most recognised and accepted circular external skeletal fixation system attached to bone with tensioned wires. His work also highlighted the need to preserve extra-osseous and medullary blood supply with a low energy corticotomy, stable external fixation, a delay (latent period) prior to distraction and a distraction rate of 1 mm per day in frequent small steps in order to stimulate the formation of new bone and soft tissues. Once the lengthening has been achieved a stable neutral frame is maintained and the physiological use of the limb with weight bearing is undertaken to allow the bone to consolidate prior to frame removal. De Bastiani [8] used these principles with a mono-lateral frame fixed with half-pins. Their latent period was longer than Ilizarov's (14 days compared to 5–7 days) to allow callus formation before distraction was undertaken, this coined the term callotasis.

Complications during leg lengthening however still remain. Paley [9] has divided these into problems, obstacles and true complications that remain after lengthening has been completed. Soft tissue complications relate to muscle contractures, joint subluxation and dislocation and both neurologic and/or vascular injury. The regenerate bone may deviate during lengthening as a result of muscle pull, prematurely or delay in ossification and potentially deform or fracture following frame removal. Pin-site problems include local and deep infection, and soft tissue tethering with associated pain are common scenarios. Residual joint stiffness can be a persistent complication.

Modification of surgical techniques have therefore been geared towards reducing fixator time, to reduce soft tissue complications and joint stiffness but maintain good bone alignment and prevent deformity or fracture of the new bone regenerate. Intramedullary implants have been used in combination with external fixators and more recently with advanced technology as fully implantable lengthening devices to achieve these goals.

A combination of external fixation and an intramedullary nail

Paley et al. [10] first presented the concept of combining femoral lengthening with an intramedullary nail in situ in 1997. They high-light the long duration of external fixator treatment until sufficient regenerate healing and the keenness of patients to have the frame removed as soon as possible. Their comparative review confirms the advantages of lengthening over a nail (LON) with early fixator removal, protection against fracture and deformity and earlier rehabilitation with reduced joint complications. They also demonstrated statistically faster consolidation time of the regenerate even after intramedullary reaming, hypothesising that the revascularisation of the endosteal blood supply, with better stability provided by the nail and earlier functional loading results in excellent bone consolidation. The surgical technique involves accurate positioning of the fixator wires or pins to avoid contact with the nail, to reduce risk of cross contamination and intramedullary sepsis. The antegrade nail is locked proximally at time of insertion and after lengthening was achieved locked distally with concomitant ex-fix removal (Fig. 1). They confirmed that the cost of treatment and estimated blood loss was higher than the control "classical lengthening" group. They also demonstrated no significant change in mechanical axis following long lengthening segments along the anatomical axis (as directed by the nail).

The benefits of this technique must be balanced with the risk of deep infection. The rate varies from 0 to 20% in the literature [10–20], the higher percentage relates to occurrence in a small prospective randomised clinical study [20]. Deep infection developed in 3 of 28 patients which responded to nail removal and reaming. They were all stated to be heavy smokers and not compliant with pin care instructions. Song et al. [16] demonstrated a higher risk of osteomyelitis with a previous history of infection or open fracture and state that this should be taken into consideration when choosing the method of lengthening.

An alternative technique has been proposed by Rozbruch et al. [21]. In this case the limb is lengthened and then once lengthening has been completed the nail is inserted with frame removal. The frame construct is applied to enable the intramedullary nail to be inserted later without contact between the internal fixation and external fixation pins and wires. A locked reamed intramedullary nail is inserted across the regenerate bone and the frame removed. There are several advantages using this technique in comparison to LON including the ability to insert a full-length large-diameter nail which offers more stability. Without the use of concomitant internal and external devices the infection rate is theoretically lower. If a pin tract infection occurs during lengthening this may be

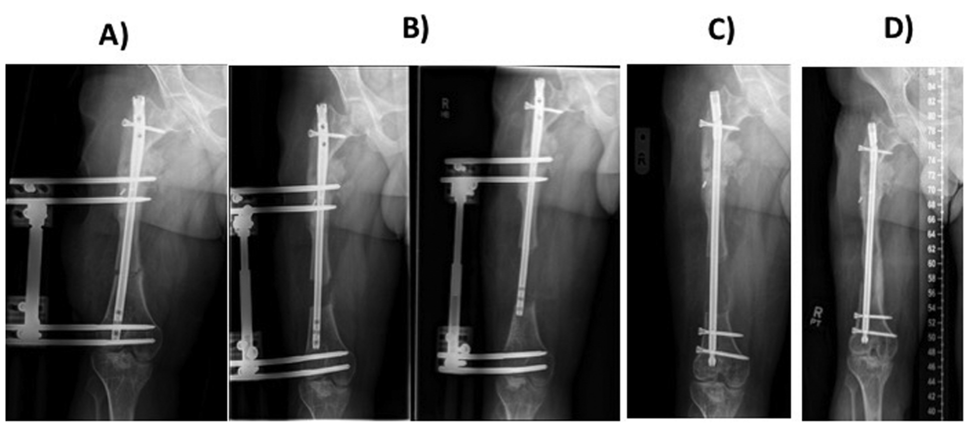


Fig. 1. Lengthening over a nail. a) Initial Construct lengthened over a humeral nail; b) Lengthening until the nail disengages with distal fragment; c) Exchange to a femoral nail with removal of external fixator; d) Bone consolidation.

addressed with antibiotics +/− removal. If there is concern over infection then the classical approach of waiting until bone consolidation can be adopted without risking intramedullary contamination. The approach also allows deformity correction using the frame prior to nail insertion, the LON requires acute correction which may compromise bone healing. Distal tibial deformity correction and lengthening could also not be performed by the LON method as the distal end of the nail would be pulled out of the distal tibial segment during treatment.

Lengthening intramedullary nails

All the above techniques still encounter the risks associated with the use of external fixators, namely pin-site infection, soft-tissue tethering due to the pins and the anti-social and functional difficulties associated with an external fixator on a limb. Innovation has led to the lengthening intramedullary nail which possesses the function of both an intramedullary nail and provide the controlled graduated distraction of the external fixator. There have been several different implants which can be broadly divided in “ratchet” and “motorised” devices.

Ratchet driven nails

- Bliskunov Nail

During the early 1980s Bliskunov, in the Ukraine developed a device which involved the nail placed within the femur connected by an articulated rod to the iliac wing [22]. The patient’s leg is rotated and the nail lengthened by a ratchet system. Once the desired length has been achieved the pelvic rod is removed and the patient encouraged to weight bear (Fig. 2a–d).

- Albizzia Nail (Medinov-AMP, Roanne, France)

The Albizzia technique was named after a flowering tree with the capacity for rapid growth. It is made of 316-L stainless steel consisting of two telescoping tubes, a threaded outer sleeve and inner rod. These are connected by double-opposed ratchet mechanism. By rotating 20° in one direction the nail is lengthened 0.07 mm, approximately 1 mm for every 15 ratchetings. Once the desired length has been achieved a retaining ring prevents further ratcheting. Fixation within the femur is with one proximal 5.5 mm locking screw and two distal locking screws (3.5 mm in the 11 mm diameter nail or 4.5 mm in the 13 and 15 mm diameter nails). Lengthening of between 60 and 100 mm may be achieved. Active dynamization occurs at the proximal locking screw, allowing shortening between the proximal and distal locking screws when the muscles contract or the patient bears weight, this is thought to enhance regenerate healing. It was subjected to animal and mechanical testing prior to clinical use [23,24].

The nail was inserted in an antegrade fashion, the intramedullary canal is initially reamed to 1 mm above the size of the nail. Flexible reamers are used initially followed by straight reamers, if there is an excessive femoral bow then a second osteotomy is required to allow passage of the straight reamer/nail and prevent perforation of the anterior cortex. The osteotomy was ideally performed using an intramedullary saw to try and preserve the periosteum. The level was below the lesser trochanter by at least 6 cm plus the desired lengthening distance proximal to the end of the nail, to ensure that the larger diameter part of the nail remained within the distal segment of the normal femur at the end of lengthening. 5 mm of lengthening was performed in surgery to open the osteotomy. Lengthening started on the 5th post-operative day, 5 ratchets performed 3 times a day (Fig. 2e). For unilateral lengthening toe-touch weight bearing is advised, for bilateral cases the use of a wheelchair is required. Once the intended length is achieved full weight bearing is allowed.

Reported results were not without complication [25–27]. Significant pain during distraction which often required further general anaesthetic and/or epidural to enable further rotation of the limb (approximately 25% of cases), in some cases pain prevented further lengthening. Other problems included failure of the nail to lengthen requiring implant exchange (7 out of 101 reported cases), non-union at the distraction site (7/101), deep infection (3/101) and in one case breakage of the nail and in another femoral fracture following nail removal. Mazeau [27] also raised the question of patient exclusion criteria following subluxation of the knee during lengthening in a case of congenital short femur with absent cruciate ligaments, despite use of a concurrent extension splint during lengthening.

- Intramedullary Skeletal Kinetic Distractor, ISKD (Orthofix, Inc, Lewisville, TX, USA)

The ISKD is a mechanically distracting intramedullary implant made of titanium alloy (Ti6Al4 V). The proximal and distal parts are internally connected with a threaded rod by two one-way clutches which are activated by rotations of 3–9°. Approximately 160 3° rotations results in 1 mm of distraction. The amount of distraction

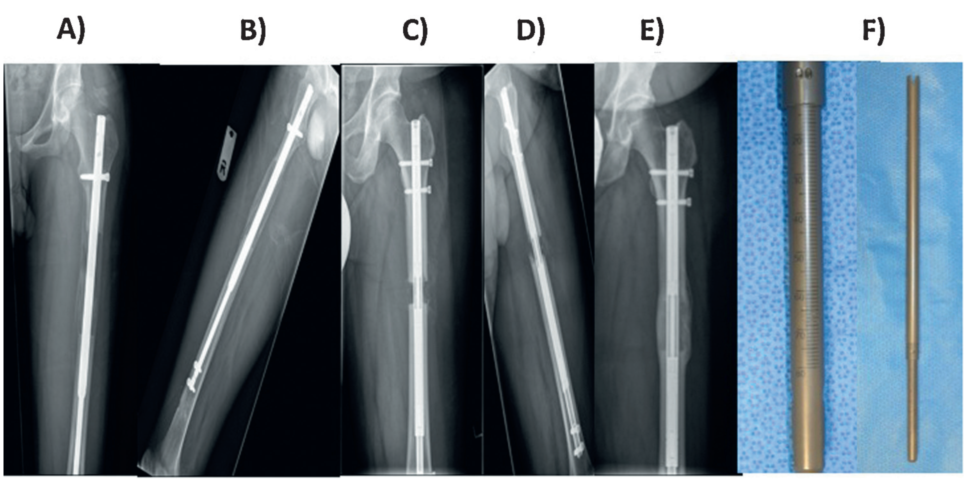


Fig. 2. Ratchet type lengthening nails. a,b) Albizzia Nail at completion of lengthening process; c,d,e) ISKD during lengthening and following consolidation; f) ISKD following removal.

can be measured using a handheld monitor which displays the polarity (North or South) of magnet positioned on the distal part of the internal threaded rod. A change of polarity is consistent with a lengthening of 0.25 mm. Like the Albizzia nail the ISKD is limited by an inability to retract after lengthening. Femoral nails have diameters of 12.5 mm and 14.5 mm, while tibial nails have diameters of 10.7 mm, 12.5 mm and 13.5 mm. The maximal distraction length of the nail is 80 mm. The results following biomechanical testing, in vivo animal testing and preliminary results in limited numbers of femoral and tibial lengthening were very favourable [28,29] (Fig. 2f–h). Patients mobilised initially non-weight bearing for the first week following insertion of the ISKD and then encouraged to walk with full-weight bearing with the aid of crutches.

The reliability of the ISKD to lengthen at a controlled rate has however been questioned by authors presenting larger series [30–32]. Uncontrolled lengthening known as a “runaway nail”, resulted in lengthening of greater than 1.5 mm per day and occurred in approximately 23% of femoral cases. There were no tibial runaway nails reported. This was thought to be related to the amount of the large diameter part of the nail within the distal femoral segment. If this was less than 80 mm then a runaway nail was more likely and it was also more likely if there had been previous intramedullary nailing [30]. Patients complained of pain and poor regenerate often resulted.

Difficulty in lengthening also occurred (24–34% of cases), requiring in some cases manipulation of the limbs under general anaesthetic. There was again a relationship to the amount of the larger diameter part of the nail within the distal segment, if this was over 125 mm then failure to lengthen was more likely. This problem was reduced by over-reaming the distal segment by 2–3 mm [30].

The outcome of ISKD lengthenings were further questioned by Mahboubian et al., who in their comparative study demonstrated that LON was associated with fewer complications than patients undergoing lengthening using the ISKD [33]. The LON group also had a better control on rate of distraction. The major complications of the ISKD group (12 nails) included 4 patients who abandoned treatment and 2 required bone grafting of poor regenerate compared to 1 patient following LON who required revision osteotomy for premature consolidation (22 LON).

Mechanical failure of the nail has also been reported, Burghardt et al. defined failure as breakage of the implant or failure of the internal mechanism to activate [34]. In a total of 242 lower-limb segment lengthening 15 ISKDs failed, a rate of 6.2%. Fracture of the device occurred in 10 and failure to lengthen occurred in 5. Two were determined to have an assembly error which prompted a recall of all nails. One jammed as a result of being forcefully implanted and no cause of failure was found for the remaining 2. The same group also re-evaluated the effect on mechanical axis following lengthening with the ISKD. They concluded that in a normally aligned limb, intramedullary lengthening along the anatomical axis of the femur results in a lateral shift of the mechanical axis by approximately 1 mm for each 1 cm of lengthening [35].

Motorized driven nails

- Fitbone (Wittenstein, Igersheim, Germany)

The Fitbone is a motorised intramedullary nail for limb lengthening and bone transport which extends through a gear-and-spindle system and enables precise controlled expansion. The prototype consisted of a 13 mm diameter straight steel nail incorporating a 10 mm motor in the proximal part. The proximal and distal ends of the nail are secured with interlocking screws. An antenna is inserted into the subcutaneous tissue and is connected to the motor by an insulated flexible wire. The antennae measures 20×4 mm and using an external transmitter placed over the antennae, high-frequency electric energy passes through the skin to the motor. The motor delivers the torque that results in axial unidirectional movement. Initial results were favourable, Baumgart et al. treated 12 patients, 11 with unilateral lengthening and the other for bone transport following tumour resection [36]. A design modification was made following a broken wire and motor failure in 2 cases. They accepted a limitation due to the large diameter of the nail restricting its use in patients with narrow intramedullary canals. The Fitbone Telescopic Active Actuator was a modification to allow variable diameters and tibial implantation. The proximal end was 12 mm in diameter compared to 10 mm in the shaft region, and an 11 mm diameter was also available. An angulated version was for tibial placement. Following insertion patients mobilise partial weight bearing during the distraction phase and then increase to full weight bearing once radiographs confirm bone consolidation, defined as corticalization on three of four sides of the regenerate.

The implant has been mostly inserted in central Europe and Australia and small case series have demonstrated overall good results [37–40]. By combining their results 39 femoral and 22 tibial lengthening’s are presented. Complications included 4 cases of implant failure to lengthen, and one broken nail following a patient fall after lengthening had been achieved. In 2 patients the desired length was not achieved but reasons why were not listed. Delayed healing of the regenerate requiring bone grafting occurred in 3 tibial and 1 femoral case. There was one superficial infection and one case of irritation in relation to the antennae, symptoms resolved on removal of the implant after lengthening had been achieved. One case developed a fixed flexion deformity of the knee following femoral lengthening, this did not resolve with physiotherapy and required hamstring lengthening.

Black et al. conducted a comparison of outcome between patients lengthened with circular external fixation and the Fitbone TAA [41]. They noted a decreased number of complications with the nail and it was their impression that patients with the nail had, on average, substantially less pain after the initial post-operative period, required less intensive physical therapy and intervention, and incurred less disruption in activities of daily living. They do admit that these observations were not quantifiable due to the retrospective review.

- Precice Nail (Ellipse Technologies, Inc, Irvine, CA, USA)

The latest intramedullary lengthening implant is the Precice nail. This is a magnet-operated telescopic internal lengthening device with an outer casing of titanium alloy (Ti-6Al–4 V) [42]. A generic rare earth magnet is connected to a gear box and screw shaft assembly within the nail (Fig. 3). An external remote controller (ERC) contains 2 rotating magnets (Fig. 4a), when placed by the patient on the skin, over the magnet within the nail, they cause this internal magnet to rotate which translates to the thinner nail element telescoping out of the thicker surrounding nail (Fig. 4b). The first generation implant (P1) was available in two diameters of 10.7 mm and 12.5 mm with 6 lengths available from 230 mm to 355 mm. The lengthening capacity was 65 mm and nail options included antegrade femoral piriformis or trochanteric entry, femoral retrograde and tibial implants. The extendable rod and magnet motor was attached to the variable length segment with a set screw (Fig. 5a, b). The nail can be both extended and retracted by altering the settings on the ERC as well as accurately setting the rate of distraction. A distance of 1 mm requires the ERC to be placed over the magnet within the nail for 7 min. The first reports appeared to show good results with accurate lengthening

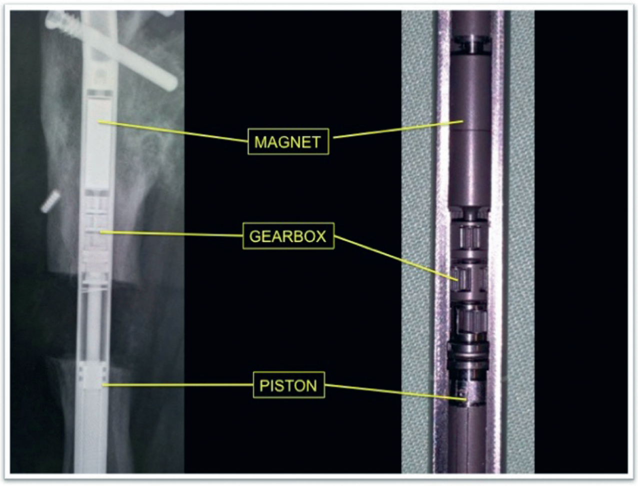


Fig. 3. Precice lengthening nail.

rates and good regenerate bone formation [43–46]. A standard protocol involving a latency period, after a pre-drilled corticotomy and graduated lengthening between 0.66 and 1 mm per day was undertaken by all the groups. The femoral canal is over-reamed 1.5–2 mm larger than the nail which is inserted long enough to have at least 3 cm of the wider part of the nail within the distracted segment after lengthening has been achieved. Patients were instructed to be non-weight bearing and physiotherapy directed at maintaining joint range of motion. Full weight bearing was allowed after regenerate consolidation has occurred in 3 of 4 cortices.

Complications encountered included implant failure; a small number of nails failed to lengthen immediately following implantation, breakage occurred at the weld following weight bearing prior to adequate regenerate formation or patient falls. Premature consolidation occurred in 9 from 120 lengthening segments reported. In the majority this was due to operator error and difficulty in positioning of the ERC was highlighted especially when application over the proximal femur is required. Alternate positioning include placing over the lateral aspect of the thigh or placing the ERC upside down and programming the distraction of the nail as retrograde instead of the antegrade position of the nail. Patient selection is important as patients with a BMI >35 may have difficulty with the ERC being too far away from the nail to function normally. The manufacturers suggest a weight cut-off of 114 kg

Fig. 4. a) ERC and controller; b) Patient using the ERC.

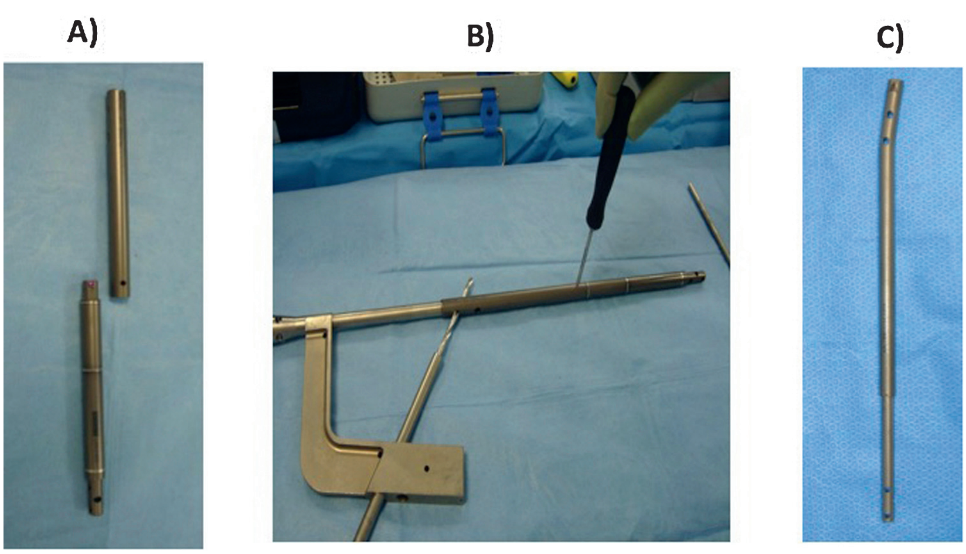


Fig. 5. a,b) Original modular nail fixed with a set screw. c) Monobloc P2 nail.

(250 lbs) and a maximum distance of 51 mm (2 in.) between the ERC and the nail. The use of a retrograde femoral nail may be indicated if the size of the proximal thigh prevents correct positioning of the ERC, distally the distance from the skin to the bone is much less. Five patients required bone grafting for poor regenerate, of these 3 were following lengthening in congenital short femur [46] and 2 following tibial lengthening [45]. 2 patients required release of the iliotibial band [43,46] and 2 patients a gastrocnemius recession following tibial lengthening [45].

During lengthening Kirane et al. observed a tendency of the varus-procurvatum malalignment at proximal femur osteotomies and valgus-procurvatum at proximal tibial osteotomies. This was greater in the tibial cases and they advised the use of blocking screws (Poller) [47] to maintain nail alignment, especially in the cases of loose fit. In their study however they demonstrated fewer complications in comparison to previous intramedullary nail systems previously discussed. Furthermore Laubscher et al. [48] have shown excellent functional outcome with fewer complications and greater patient satisfaction, with significantly less pain and better cosmetic result in comparison between the Precice nail and an external fixator used for simple femoral lengthening.

Modification of the implant has resulted in the P2 nail, which is a Monobloc implant with an additional smaller diameter of 8.5 mm (Fig. 5c). The overall starting lengths are from 195 to 365 mm and 50 mm or 80 mm lengthening targets are achievable. The P2 is at least 2 times stronger in bending fatigue strength and has 3 times stronger coupling between the gears and lead screw.

The indications of intramedullary lengthening are further explored by Shabtai ey al [49] and Laubscher at al [50]. 21 nails were prospectively followed up after insertion in patients with congenital femoral deficiency (CFD) and fibular hemimelia (FH) [49]. Prophylactic release of the iliotibial band and botulinum toxin injections to the quadriceps were performed in the CFD cases and gastrocnemius recession in the FH. Physiotherapy was for a minimum of 1 h, 5 days a week. There was one case of hip subluxation and one knee rotational subluxation treated by external fixation and soft tissue release with ligament reconstruction respectively. Bone grafting was required in 3 of 17 CFD cases and 1 of 4 FH. They concluded that the Precice offered an accurate controlled lengthening but warned against complications in this complex patient population. 3 cases of lengthening were performed in an “unstable” hip scenario, 2 cases of prior neonatal sepsis and 1 of neglected hip dislocation due to developmental dysplasia [50]. Pre-operative assessment revealed limited adduction with no pelvic dip on a single stance radiograph. A proximal valgus osteotomy performed in the traditional pelvis support osteotomy was therefore not achievable without soft tissue release of the proximal femur. Lengthening was undertaken using a retrograde Precice nail. In all cases the rate of lengthening was reduced due to thigh discomfort and hip and knee contractures. One case required soft tissue release due to a knee flexion contracture. In all cases the desired lengthening was achieved with no migration of the proximal femur (Fig. 6). The patients were able to abort their shoe raises and there was an improvement in gait pattern seen on gait analysis.

No studies have been performed on the cost-effectiveness of the Precice which remains an expensive implant. The reduction in unplanned secondary procedures required to treat external fixator complications related to pins and wires and regenerate deformity may offset the initial price of the nail.

Conclusion

The intramedullary lengthening nail is attractive in reducing the complications associated with external fixators. These include pin site irritation, infection and cosmetic scarring, malalignment of regenerate deformity and fracture following removal of the external fixator and overall an increase in patient satisfaction and ability to function in activities of daily living with the nail. The Precice nail is the latest innovation which has advantages over previous implants. There is more variation in size and lengths available including the smaller 8.5 mm diameter offering treatment to a greater population. The ability to accurately retract as well as lengthen means an ability to shorten the limb in cases of

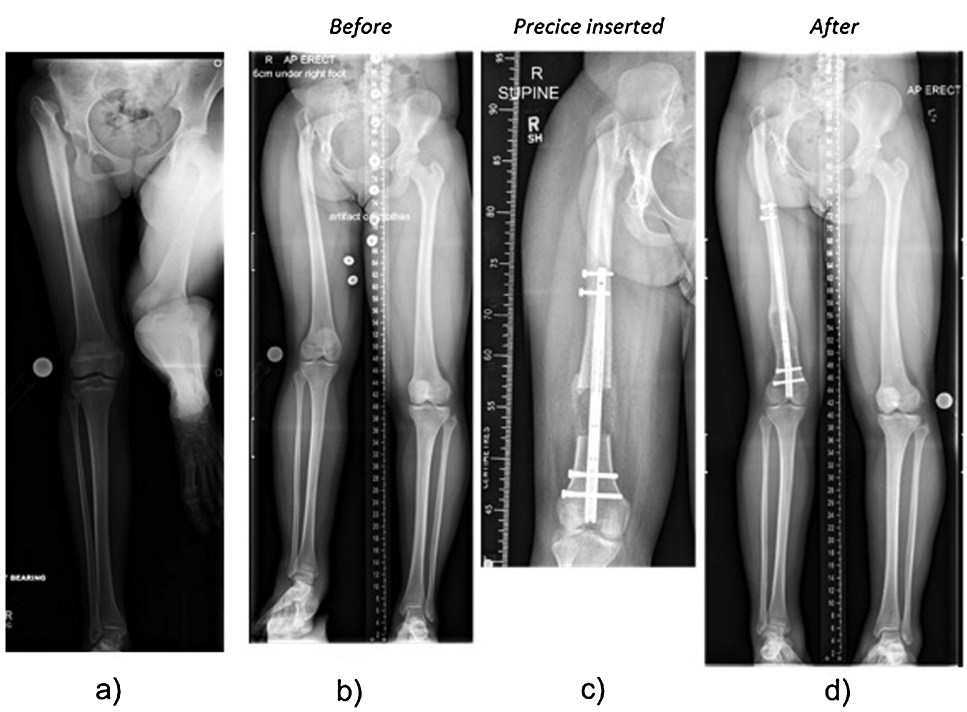


Fig. 6. a–d) Precice nail lengthening under an "unstable hip".

neuro-muscular difficulty. The latest implant is now stronger with a reduction in implant breakage although it must be stressed that patient compliance in both lengthening rate and weight-bearing status is essential for favourable outcomes.

Conflict of interest

None.

References

[1] Codivilla A. On the means of lengthening in the lower limbs, the muscles, and tissues which are shortened through deformity. Am J Orthop Surg 19052(353).
[2] Wagner H. Operative Beinverlangerung Chirurgie 1971vol. 42:. p. 260.
[3] Wagner H. Operative lengthening of the femur. Clin Orthop 1978;136:125.
[4] Wasserstein I. Twenty-five years' experience with lengthening of shortened lower extremities using cylindrical allografts. Clin Orthop 1990;250:150.
[5] Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part I the influence of stability of fixation and soft-tissue preservation. Clin Orthop 1989;238:249.
[6] Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part II the influence of the rate and frequency of distraction. Clin Orthop 1989;239:263.
[7] Ilizarov GA. Clinical application of the tension-stress effect for limb lengthening. Clin Orthop 1990;250:8.
[8] De Bastiani G, Aldegheri R, Renzi-Brivio L, Trivella G. Limb lengthening by callus distraction (callotasis). J Pediatr Orthop 1987;7(2):129.
[9] Paley D. Problems, obstacles, and complications of limb lengthening by the ilizarov technique. Clin Orthop 1990;250:81.
[10] Paley D, Herzenberg JE, Paremain G, Bhave A. Femoral lengthening over an intramedullary nail. a matched-case comparison with ilizarov femoral lengthening. J Bone Joint Surg 1997;79-A:1464.
[11] Silberg ET, Goulet JA, Greenfield ML. Femoral lengthening: conventional Ilizarov technique compared to lengthening over an intramedullary rod. Orthop Trans 1997;21:71.
[12] Simpson AH, Cole AS, Kenwright J. Leg-lengthening over an intramedullary nail. J Bone Joint Surg 1999;81-Br:1041.
[13] Kristiansen LP, Steen H. Lengthening of the tibia over an intramedullary nail, using the Ilizrov external fixator. Major complications and slow consolidations in 9 lengthenings. Acta Orthop Scan 1999;70:271.
[14] Kocaoglu M, Eralp L, Kilicoglu O, Burc H, Cakmak M. Complications encountered during lengthening over an intramedullary nail. J Bone Joint Surg 2004;68-A:2406.
[15] Watanabe K, Tsuchiya H, Sakurakichi K, Yamamoto N, Kabata T, Tomita K. Tibial lengthening over an intramedullary nail. J Orthop Sci 2005;10:480.
[16] Song HR, Oh CW, Mattoo R, Park BC, Kim SJ, Park IH, et al. Femoral lengthening over an intramedullary nail using the external fixator: risk of infection and knee problems in 22 patients with a follow-up of 2 years or more. Acta Orthop 2005;76:245.
[17] Park H, Yang K, Lee K, Joo S, Kwak Y, Kim H. Tibial lengthening over an intramedullary nail with use of an Ilizarov external fixator for idiopathic short stature. J Bone Joint Surg 2008;90-A:1970.
[18] Kim K, Lee SK, Kim KJ, Ahn J, Choy WS, Kim YI, et al. Tibial lengthening using a reamed type intramedullary nail and an Ilizarov external fixator. Int Orthop (SICOT) 2009;33:835.
[19] Sun XT, Easwar TR, Manesh S, Ryu JH, Song SH, Kim SJ, et al. Complications and outcome of tibial lengthening using the Ilizarov method with or without a supplementary IM nail. J Bone Joint Surg 2012;93-Br:782.
[20] El-Husseini TF, Ghaly NAM, Mahran MA, Al Kersh MA, Emara KM. Comparison between lengthening over nail and conventional Ilizarov lengthening: a prospective randomized clinical study. Strat Traum Limb Recon 2013;8:97.
[21] Rozbruch SR, Kleinman D, Fragomen AT, Ilizarov S. Limb lengthening and then insertion of an intramedullary nail. A case-matched comparison. Clin Orthop 2008;466:2923.
[22] Bliskunov AI. Intramedullary distraction of the femur (preliminary report). Octop Travmatol Protez 1983;10:838.
[23] Guichet JM, Grammont PM, Trouilloud P. A nail for progressive lengthening: an animal experiment with a 2 year follow-up. Chirurgie 1992;118:405.
[24] Guichet JM. Mechanical characterization of a totally intramedullary gradual elongation nail. Clin Orthop 1997;337:281.
[25] Garcia-Cimbrelo E, Curto de la Curto A, Garcia-Rey E, Cordero J. The Intramedullary elongation nail for femoral lengthening. J Bone Joint Surg 2002;84-Br:971.
[26] Guichet JM, Deromedis B, Donnan LT, Peretti G, Lascombes P. Gradual femoral lengthening with the albizzia intramedullary nail. J Bone Joint Surg 2003;85-A:838.
[27] Mazeau P, Assi C, Louahem D, L'Kaissi M, Delpont M, Cottalorda J. Complications of Albizzia femoral lengthening nail: an analysis of 36 cases. J Pediatr Orthopaedics B 2012;5:394.
[28] Cole JD, Justin D, Kasparis T, SeVlught D, Knobloch C. The intramedullary skeletal kinetic distractor (ISKD): first clinical results of a new intramedullary nail for lengthening of the femur and tibia. Injury 2001;32:129.
[29] Hankemeier S, Pape H, Gosling T, Hufner T, Richter M. Improved comfort in lower limb lengthening with the intramedullary skeletal kinetic distractor. Principles and preliminary clinical experiences. Arch Orthop Trauma Surg 2004;124:129.
[30] Simpson AH, Shalaby H, Keenan G. Femoral lengthening with the intramedullary skeletal kinetic distractor. J Bone Joint Surg 2009;91-Br:955.
[31] Kenawey M, Krettek C, Liodakis E, Hankemeier Wiebking U. Leg lengthening using intramedullary skeletal kinetic distractor: results of 57 consecutive applications. Injury 2011;42:150.
[32] Lee DH, Ryu KJ, Song HR, Han S-H. Complications of the intramedullary skeletal kinetic distractor (ISKD) in distraction osteogenesis. Clin Orthop 2014;472:3852.
[33] Mahboubian S, Seah M, Fragomen AT, Rozbruch SR. Femoral lengthening with lengthening over a nail has fewer complications than Intramedullary Skeletal Kinetic Distraction. Clin Orthop 2012;470:1221.
[34] Burghardt RD, Herzenberg JE, Specht SC, Paley D. Mechanical failure of the Intramedullary Skeletal Kinetic Distractor in limb lengthening. J Bone Joint Surg 2011;93-Br:639.
[35] Burghardt RD, Paley D, Specht SC, Herzenberg JE. The effect on mechanical axis deviation of femoral lengthening with an intramedullary telescopic nail. J Bone Joint Surg 2012;94:1241.
[36] Baumgart R, Betz A. A fully implantable motorized intramedullary nail for limb lengthening and bone transport. Clin Orthop 1997;343:135.
[37] Singh S, Lahiri A. The results of limb lengthening by callus distraction using an extending intramedullary nail (Fitbone) in non-traumatic disorders. J Bone Joint Surg 2006;88-Br:938.
[38] Krieg AH, Speth BM, Foster BK. Leg lengthening with a motorized nail in adolescents. An alternative to external fixators? Clin Orthop 2008;466:189.
[39] Dincyurek H, Kocaoglu M, Eralp IL, Bilen FE, Dikmen G. Functional results of lower extremity lengthening by motorized intramedullary nails. Acta Orthop Traumatol Turc 2012;46:42.
[40] Al-Sayyad MJ. Lower limb lengthening and deformity correction using the Fitbone motorized nail system in the adolescent patient. J Pediatr Orthopaedics B 2012;21:131.
[41] Black SR, Kwon MS, Cherkashin AM, Samchukov ML, Birch JG, Jo C-H. Lengthening in congenital femoral deficiency. A comparison of circular external fixation and a motorized intramedullary nail. J Bone Joint Surg 2015;97:1432.
[42] Paley D. Precice intramedullary limb lengthening system. Expert Rev Med Devices 2015;12(3):231.
[43] Calder PR, McGrath A, Chasseaud M, Timms A, Goodier WD. The precice intramedullary limb lengthening system. Bone Joint J 2013;95-B(Suppl. 23):11.
[44] Schiedel FM, Vogt B, Tretow HL, Schuhknecht B, Gosheger Horter MJ, et al. How precise is the PRECICE compared to the ISKD in intra-medullary limb lengthening? Acta Orthop 2014;85:293.
[45] Kirane YM, Fragomen AT, Rozbruch SR. Precision of the PRECICE internal bone lengthening nail. Clin Orthop 2014;472:3869.
[46] Paley D, Harris M, Debiparshad K, Prince D. Limb lengthening by implantable lengthening devices. Tech Orthop 2014;29:72.
[47] Krettek C, Miclau T, Schandelmaier P, Stephan C, Mohlmann U, Tscherne H. The mechanical effect of blocking screws (Poller screws) in stabilizing tibia fractures with short proximal or distal fragments after insertion of small-diameter intramedullary nails. J Orthop Trauma 1999;13:550.
[48] Laubscher M, Mitchell C, Timms A, Goodier D, Calder P. Outcome of femoral lengthening: a comparison of the Precice Intramedullary Lengthening nail and the LRS external fixator lengthening system. Bone Joint J 2015;97-B(Suppl. 5):1.
[49] Shabtai L, Specht SC, Standard SC, Herzenberg JE. Internal lengthening device for congenital femoral deficiency and fibular hemimelia. Clin Orthop 2014;472:3860.
[50] Laubscher M, Mitchell C, Timms A, Goodier D, Calder P. Femoral lengthening with an unstable hip: a case series. Bone Joint J 2015;97-B(Suppl. 5):4.

Injury, Int. J. Care Injured 48S (2017) S59–S63

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Complications of intramedullary nailing—Evolution of treatment

Dirk Wähnert*, Dominic Gehweiler

Department of Trauma, Hand and Reconstructive Surgery, University Hospital Münster, Münster, Germany

ARTICLE INFO

Keywords:
Angular stable
Intramedullary nailing
Biomechanics
Nail locking
Augmentation

ABSTRACT

Intramedullary nailing of diaphyseal long bone fractures is a standard procedure in today's trauma and orthopedic surgery due to the numerous advantages (e.g. minimal invasive, limited soft tissue damage, load stability). In the last decade indications have been extended to the metaphyseal region. This was associated with problems and complications due to the reduced bone-implant interface. The changed anatomical conditions lead to decreased implant anchorage. Newly developed locking solutions overcome most of these problems. First, the number and also the orientation of the locking screws were adapted to allow a multiplanar locking. This results in increased implant anchorage in the soft metaphyseal bone, thus construct stability significantly improved. Additional options like angular stable locking have been introduced and furthermore enhanced construct stability especially in poor bone stock. As a perspective locking screw augmentation shows promising results in first biomechanical testing.

Introduction

Today, intramedullary nailing is standard of care for most long bone diaphyseal fractures [1–4]. This technique has a lot of advantages making it superior compared to open reduction and internal fixation using plates and screws. The soft tissue damage is reduced significantly when using indirect reduction and intramedullary nailing, additionally, the periosteum and the fracture hematoma is preserved. Thus, complications like wound infection and non-union are decreased compared to open reduction and internal fixation procedures. The majority of patients treated with an intramedullary nail are allowed to fully weight bear immediately after surgery. These characteristics make intramedullary nailing of diaphyseal long bone fractures a minimal invasive and safe treatment option [2,5,6].

In the last years indications of intramedullary nailing have been extended to include even more metaphyseal fractures [7,8]. This was linked to some problems and complications due to the decreased biomechanical stability [1,8]. Especially the difference in size between the nail diameter and the metaphyseal diameter results in a small nail-cortex contact. Additionally, the diminished cortical bone support of the metaphyseal region limits construct stability [9]. Fractures of the distal third of tibia treated with intramedullary nailing frequently result in varus, valgus or torsional deformities and non-unions [10–14]. To improve construct stability of intramedullary metaphyseal long bone fractures implants have been adapted. Especially the modifications of locking options improved implant anchorage. Multiplanar locking, compression screws and angular stability are a few options to increase construct stability and decrease complication rates. This article will present biomechanical background of these modern locking solutions.

Locking solutions

Various modifications and new developments of locking options have been introduced to reduce the complications and make the benefits of intramedullary nailing applicable even in metaphyseal long bone fractures.

First of all the number and the sites of the locking holes were adapted to address the needs of very proximal or distal fractures. Traditional tibia nails offer two to three proximal locking holes (Fig. 1A,B) in contrast the modern nails offer up to five proximal locking options (Fig. 1C). This is the same for distal locking, the traditional nails offer two to three, the modern four locking holes (Fig. 1), but not only the number of holes makes the difference. The modern nails also have different locking bolt orientation, thus a multiplanar locking can be performed to increase construct stability (Fig. 1C). In their biomechanical study Wolinsky et al. investigated the influence of proximal locking on axial and

* Corresponding author at: University Hospital Muenster, Department of Trauma, Hand and Reconstructive Surgery, Albert-Schweitzer-Campus 1, Building W1, 48149 Muenster, Germany.

E-mail address: dirk.waehnert@ukmuenster.de (D. Wähnert).

http://dx.doi.org/10.1016/j.injury.2017.04.032
0020-1383/

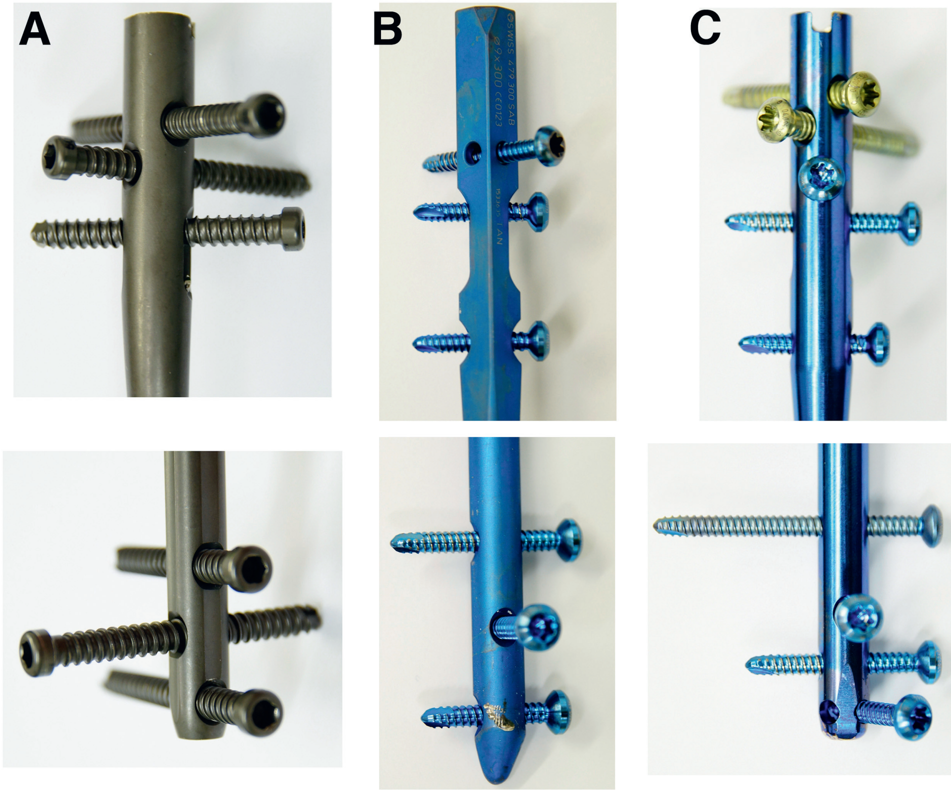


Fig. 1. Different tibia nails showing traditional nails A and B with limited locking options and a modern tibia nail C. (A) Stryker (Schönkirchen, Germany) T2 tibia nail with three proximal locking options (upper row) and three distal locking options (lower row). (B) Synthes (Solothurn, Switzerland) UTN tibia nail with three locking options proximal (upper row) and distal (lower row). (C) Synthes (Solothurn, Switzerland) Expert tibia Nail with five locking options proximal (upper row) and four locking options distal (lower row).

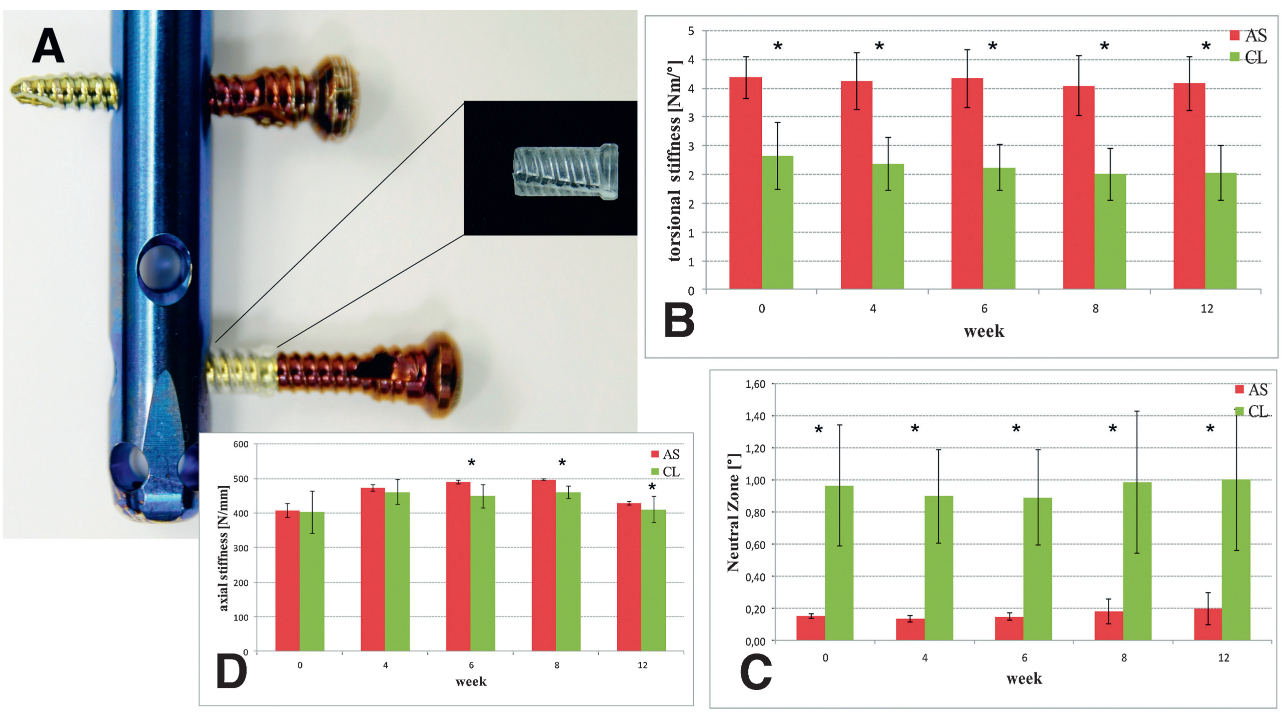


Fig. 2. (A) Angular stable locking System (ASLS, Synthes, Solothurn, Switzerland). Special screws with three different diameters a preassembled with a biodegradable polylactide sleeve. During screw locking the sleeve is expanded and thus blocks the locking screw in the nail hole. (B) Results of torsional stiffness at the different time points. (C) Results of torsional neutral zone at the different time points. (D) Results of axial stiffness at the different time points. Significant differences ($p < 0.05$) marked with *.

torsional stiffness in a proximal tibia fracture model. They compared four different locking procedures and found that adding a transverse locking screw significantly increased axial stiffness by 28% and torsional stiffness up to 28% compared to proximal two screw locking [15]. These results were confirmed by the work of Freeman at al. [16].

Another innovation introduced to enhance metaphyseal nail anchorage was the angular stable locking. Angular stability was introduced for plate and screw osteosynthesis to provide a higher bone implant stability even in osteoporotic bone. Biomechanical and clinical studies showed the advantages of angular stable plating compared to conventional screw and plate fixation [17–20]. This concept has been adapted to intramedullary nails to address the problems of reduced implant anchorage especially in the metaphyseal region. Therefore, different angular stable locking options for intramedullary nails were introduced. One option to achieve an angular stable locking is the implementation of a thread or a kind of sealing ring into the nail's locking hole. Another possibility to achieve angular stable locking represents the angular stable locking system (ASLS, Synthes, Solothuern, Switzerland). Whereby a sleeve is applied over a special locking screw (Fig. 2A). During locking procedure the sleeve expands (due to different screw diameters) and thus angular stable locked screws are created.

This technique was investigated in several biomechanical studies. Gueorguiev et al. compared the interfragmentary movement of angular stable versus conventional locked tibia nails in an unstable distal tibia fracture model. Therefore, they used eight pairs of fresh-frozen human tibiae with either two conventional or two angular stable medio-lateral distal locking screws in an expert tibia nail (ETN, Synthes, Solothurn, Switzerland). Under cyclic testing they found significant reduction of the neutral zone in medio-lateral direction. Additionally, the fracture gap angulation was significantly reduced in the angular stable locked group. In this study angular stable locking had no significant influence on the number of cycles until failure, but the angular stability reduced the influence of the bone mineral density within the first 20,000 cycles [21].

Within another study Gueorguiev et al. investigated the potential of angular stable locking in unstable distal tibia fractures. Therefore, ten pairs of fresh-frozen human tibiae were randomly assigned to either conventional locking (three conventional locking screws proximally and three distally) or angular stable locking (two conventional and one angular stable screw proximally and two angular stable screws distally). Cyclic testing was performed using combined axial and torsional loading until failure. In this investigation the angular stable group showed significant higher torsional stiffness and a significant reduced neutral zone as well as significant less torsional deformation. Therefore, Gueorguiev et al. concluded that angular stable locking has the potential to maintain fixation stability while reducing the number of locking screws [22].

Our group investigated the angular stable locking system (ASLS, Synthes, Solothurn, Switzerland) working with a special screw and biodegradable polylactide sleeve. Therefore we used eight pairs of porcine tibiae in combination with the Expert Tibia Nail (ETN, Synthes, Solothurn, Switzerland) and a three screw distal locking (either angular-stable or conventional). Measurements of axial stiffness and range of motion ($\pm$50 N) as well as torsional stiffness, range of motion and neutral zone ($\pm$5 Nm) were done after instrumentation and after four, six, eight and twelve weeks using a servo hydraulic testing machine (Instron 8874, Instron, High Wycombe, Bucks, United Kingdom). Meanwhile the specimens were stored in phosphate-buffered saline at a temperature of 37 °C and a pH-value of 7,4. The initial measurements after instrumentation showed a significant (70%) higher torsional stiffness for the angular stable locked group (Fig. 2B). Additionally, the range of motion and the neutral zone were significantly reduced in the

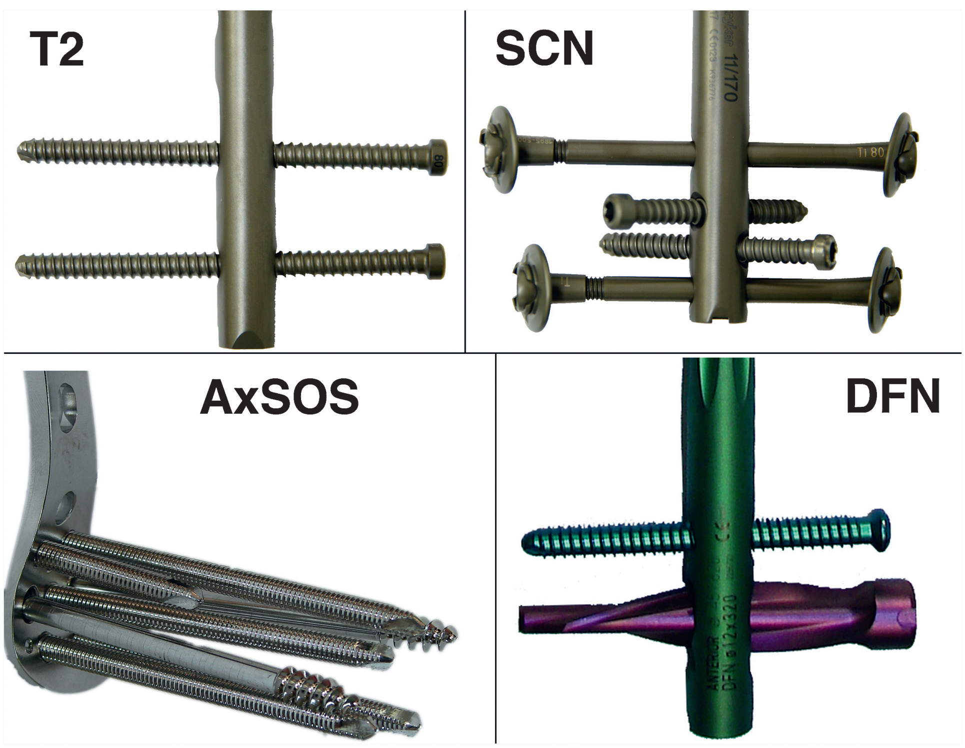


Fig. 3. Implants compared in the study: T2 nail (Stryker, Schönkirchen, Germany) with two distal locking bolts (upper row left), SCN (Stryker, Schönkirchen, Germany) with four distal locking bolts (two with medial nuts, upper row right), DFN (Synthes, Solothurn, Switzerland) with distal screw and spiral blade locking (lower row right) and the AxSOS angular stable plate (Stryker, Schönkirchen, Germany) with five angular stable locking screws and two cancellous screws (lower row left).

angular stable locked group. The neutral zone could be reduced by factor eight (Fig. 2C). In axial loading angular stability also significantly increased stiffness (10%) and reduced range of motion (12%) (Fig. 2D) [23]. Looking at the different time points (up to twelve weeks), the angular-stable group showed significantly higher torsional stiffness at all time points (at least 60%) compared to the conventionally locked group (Fig. 2B). Looking at the neutral zone we found at least five times higher values in the conventional locked group (Fig. 2C). Under axial loading the stiffness was found to be maximum 10% higher in the angular stable group compared to the conventionally locked group (Fig. 2D). We found no significant change of the torsional mechanical properties over the twelve weeks within both groups. Regarding axial stiffness and axial range of motion we found significant differences in the angular stable group over the twelve weeks [24].

These two studies show that the angular stable locking system for intramedullary nails using a special screw and biodegradable sleeve provides higher initial and long-term stability. Especially under torsional loading the differences determined in the biomechanical studies may have clinical relevance due to the known negative effect of torsional and shear stresses on fracture healing. The differences found for axial stability may not be clinically relevant due to their small magnitude, so that necessary axial micro-motions should only be affected minimally. From a mechanical point of view this system has the potential to increase the nail-screw anchorage in metaphyseal fractures, and thus can reduce complications like secondary loss of reduction and mal- or non-union.

The adaption of intramedullary nail locking mechanisms was not limited to tibia nails, also femoral nails have been modified to address metaphyseal fractures. Our group investigated three different intramedullary nails and an angular stable plate construct in an osteoporotic distal femur intraarticular fracture model (Fig. 3) [25]. Therefore, a custom made osteoporotic bone model of the distal femur was used with five specimens per group. An AO 33 C2 fracture model was fixed with either the T2 femoral nail (T2, Stryker, Schönkirchen, Germany, Fig. 3) with two lateral-to-medial distal locking bolts, the T2 supracondylar nail (SCN, Stryker, Schönkirchen, Germany, Fig. 3) with two oblique distal locking screws and two lateral-to-medial condylar bolts with additional medial nuts, the distal femoral nail (DFN, Synthes, Solothurn, Switzerland, Fig. 3) with distal spiral blade and screw locking or the AxSOS angular stable locking plate (Stryker, Schönkirchen, Germany, Fig. 3) with five angular stable and two cancellous screws for distal locking. In a second step the SCN and the DFN have been compared using eight pairs of fresh-frozen human femora. Biomechanical testing was performed on a servo hydraulic testing machine (Instron 8874, Instron, High Wycombe, Bucks, United Kingdom). Specimens were loaded under internal and external rotation up to 10 Nm. Afterwards cyclic axial loading was applied until failure. Our investigation showed significantly higher torsional stiffness, lower range of motion and neutral zone for the angular stable plate construct compared to the other constructs (Fig. 4). The SCN achieved nearly comparable results regarding torsional stiffness, range of motion and neutral zone. Furthermore, the SCN had the highest torsional strength. Axial stiffness was also the highest for the SCN. The lowest values were achieved with the angular stable plate. The ranking of the constructs for axial cycles to failure was the SCN, with the highest number of cycles, followed by the AxSOS, the DFN and the T2 with the lowest number of cycles until failure (Fig. 4). These findings from the osteoporotic artificial model were comparable with the findings in the human cadaveric bone (for SCN and DFN). Failure modes under cyclic axial load were also comparable in both, the artificial and human bone model [25].

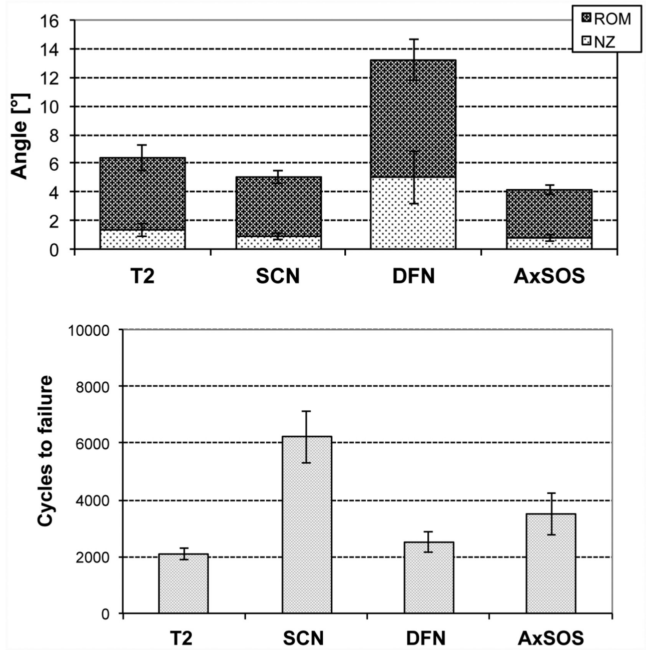


Fig. 4. Results of torsional testing showing the range of motion and neutral zone for the tested implants (upper row) and the number of cycles to failure (lower row).

This study shows the relevance of distal locking in intramedullary nailing. The type of locking can significantly affect the stabilization of the bone-implant-construct. In our study, the SCN with a four screw distal locking showed comparable torsional stability to the angular stable AxSOS plate and superior axial stability compared to all other tested implants. These characteristics make the SCN a preferable implant for the stabilization of complex distal femoral fractures, especially in osteoporotic bone.

Looking beyond the modifications of locking screws and mechanisms a new add on, the cement augmentation, has been described. Cement augmentation is already in clinical use for the treatment of osteoporotic proximal humerus fractures using cannulated and perforated screws in combination with the PHILOS plate (Synthes, Solothurn, Switzerland). The first implant with the option of augmentation was the proximal femoral nail (PFNA, Synthes, Solothurn, Switzerland) with a perforated helical blade. Klos et al. developed and investigated a technique for augmentation of locking screws in hindfoot nail arthrodesis [26]. Many patients considered for pantalar arthrodesis have poor bone stock due to immobilization or osteoporosis. Thus, a sufficient anchorage of the locking screws is hard to achieve. Klos et al. investigated the potential of augmenting the calcaneal screws in a hindfoot arthrodesis nail. Therefore, they used eight pairs of fresh frozen human lower knee specimens. They were instrumented with hindfoot arthrodesis nails (HAN, Synthes, Solothurn, Switzerland) with special cannulated and perforated screws; one of each pair was augmented using bone cement. Biomechanical testing showed a significantly higher stiffness and lower range of motion for plantar-/dorsiflexion in the augmented group. The neutral zone was significantly smaller for the augmented specimens under varus/valgus, plantar-/dorsiflexion and internal/external rotation. The number of cycles to failure was also significantly higher for the augmented specimens. Only two of the augmented screws broke. This study shows that locking screw augmentation significantly increases mechanical stability and thus should be considered as salvage procedure [26].

Conclusion

Intramedullary nailing of diaphyseal long bone fractures is a standard procedure in today's trauma and orthopedic surgery. In the last decade indications have been extended to the metaphyseal region. This was associated with problems and complications due to the different anatomical requirements regarding bone-implant interface. Newly developed locking solutions overcome most of these problems. First, the number and also the orientation of the locking screws allow a multiplanar locking to increase implant anchorage in the soft metaphyseal bone. Additional options like angular stable locking have been introduced to enhance construct stability. As a perspective locking screw augmentation shows promising results in first biomechanical testing.

Conflict of interest

None.

References

[1] Bedi A, Le TT, Karunakar MA. Surgical treatment of nonarticular distal tibia fractures. J Am Acad Orthop Surg 2006;14:406–16.
[2] Im GI, Tae SK. Distal metaphyseal fractures of tibia: a prospective randomized trial of closed reduction and intramedullary nail versus open reduction and plate and screws fixation. J Trauma 2005;59:1219–23 discussion 23.
[3] Mohammed A, Saravanan R, Zammit J, King R. Intramedullary tibial nailing in distal third tibial fractures: distal locking screws and fracture non-union. Int Orthop 2008;32:547–9.
[4] Tyllianakis M, Megas P, Giannikas D, Lambiris E. Interlocking intramedullary nailing in distal tibial fractures. Orthopedics 2000;23:805–8.
[5] Janssen KW, Biert J, van Kampen A. Treatment of distal tibial fractures: plate versus nail: a retrospective outcome analysis of matched pairs of patients. Int Orthop 2007;31:709–14.
[6] Vallier HA, Le TT, Bedi A. Radiographic and clinical comparisons of distal tibia shaft fractures (4 to 11 cm proximal to the plafond): plating versus intramedullary nailing. J Orthop Trauma 2008;22:307–11.
[7] Duda GN, Mandruzzato F, Heller M, Schutz M, Claes L, Haas NP. Mechanical borderline indications in the treatment of unreamed tibial nailing. Unfallchirurg 2003;106:683–9.
[8] Kuhn S, Hansen M, Rommens PM. Extending the indications of intramedullary nailing with the Expert Tibial Nail. Acta Chir Orthop Traumatol Cech 2008;75:77–87.
[9] Papadakis SA, Segkos D, Katsiva V, Panagiota P, Balanika A, Stavrianos V, et al. Intramedullary bone formation after intramedullary nailing. J Orthop Trauma 2009;23:288–93.
[10] Bhandari M, Guyatt GH, Swiontkowski MF, Schemitsch EH. Treatment of open fractures of the shaft of the tibia. J Bone Joint Surg Br 2001;83:62–8.
[11] Bilat C, Leutenegger A, Ruedi T. Osteosynthesis of 245 tibial shaft fractures: early and late complications. Injury 1994;25:349–58.
[12] Court-Brown CM, McBirnie J. The epidemiology of tibial fractures. J Bone Joint Surg Br 1995;77:417–21.
[13] Drosos G, Karnezis IA, Bishay M, Miles AW. Initial rotational stability of distal tibial fractures nailed without proximal locking: the importance of fracture type and degree of cortical contact. Injury 2001;32:137–43.
[14] Kahn KM, Beals RK. Malrotation after locked intramedullary tibial nailing: three case reports and review of the literature. J Trauma 2002;53:549–52.
[15] Wolinsky PR, Dennis D, Crist BD, Curtiss S, Hazelwood SJ. The biomechanics of varied proximal locking screw configurations in a synthetic model of proximal third tibial fracture fixation. J Orthop Trauma 2011;25:175–9.
[16] Freeman AL, Craig MR, Schmidt AH. Biomechanical comparison of tibial nail stability in a proximal third fracture: do screw quantity and locked, interlocking screws make a difference. J Orthop Trauma 2011;25:333–9.
[17] Gautier E, Sommer C. Guidelines for the clinical application of the LCP. Injury 2003;34(Suppl. 2):B63–76.
[18] Kim T, Ayturk UM, Haskell A, Miclau T, Puttlitz CM. Fixation of osteoporotic distal fibula fractures: a biomechanical comparison of locking versus conventional plates. J Foot Ankle Surg 2007;46:2–6.
[19] Miller DL, Goswami T. A review of locking compression plate biomechanics and their advantages as internal fixators in fracture healing. Clin Biomech (Bristol, Avon) 2007;22:1049–62.
[20] Seide K, Triebe J, Faschingbauer M, Schulz AP, Puschel K, Mehrtens G, et al. Locked vs unlocked plate osteosynthesis of the proximal humerus – a biomechanical study. Clin Biomech (Bristol, Avon) 2007;22:176–82.
[21] Gueorguiev B, Wahnert D, Albrecht D, Ockert B, Windolf M, Schwieger K. Effect on dynamic mechanical stability and interfragmentary movement of angle-Stable locking of intramedullary nails in unstable distal tibia fractures: a biomechanical study. J Trauma 2011;70(2):358–65, doi:http://dx.doi.org/10.1097/TA.0b013e3181dbaaaf.
[22] Gueorguiev B, Ockert B, Schwieger K, Wahnert D, Lawson-Smith M, Windolf M, et al. Angular stability potentially permits fewer locking screws compared with conventional locking in intramedullary nailed distal tibia fractures: a biomechanical study. J Orthop Trauma 2011;25:340–6.
[23] Wahnert D, Stolarczyk Y, Hoffmeier KL, Raschke MJ, Hofmann GO, Muckley T. The primary stability of angle-stable versus conventional locked intramedullary nails. Int Orthop 2012;36:1059–64.
[24] Wahnert D, Stolarczyk Y, Hoffmeier KL, Raschke MJ, Hofmann GO, Muckley T. Long-term stability of angle-stable versus conventional locked intramedullary nails in distal tibia fractures. BMC Musculoskelet Disord 2013;14:66.
[25] Wahnert D, Hoffmeier KL, von Oldenburg G, Frober R, Hofmann GO, Muckley T. Internal fixation of type-C distal femoral fractures in osteoporotic bone. J Bone Joint Surg Am 2010;92:1442–52.
[26] Klos K, Wahnert D, Gueorguiev B, Schwieger K, Hofmann GO, Windolf M, et al. Development of a technique for cement augmentation of nailed tibiotalocalcaneal arthrodesis constructs. Clin Biomech (Bristol, Avon) 2010;25:576–81.

Injury, Int. J. Care Injured 48S (2017) S64–S68

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Technical considerations to avoid delayed and non-union

Tristan E. McMillan, Alan J. Johnstone*

Trauma and Orthopaedic Department, Aberdeen Royal Infirmary, Foresterhill, Aberdeen, UK

ARTICLE INFO

Keywords:
Intramedullary nailing
Non-union
Reduction
Malalignment
Entry point

ABSTRACT

For many years intramedullary nails have been a well accepted and successful method of diaphyseal fracture fixation. However, delayed and non unions with this technique do still occur and are associated with significant patient morbidity. The reason for this can be multi-factorial. We discuss a number of technical considerations to maximise fracture reduction, fracture stability and fracture vascularity in order to achieve bony union.

Introduction

The delayed or non union of fractures is typically the result of a number of influencing factors. Most commonly these include infection, metabolic or endocrine abnormalities, impaired vascularity, and inadequate biomechanical stability at the fracture site. Certain factors are patient specific and somewhat out of the control of the operating surgeon, however, others can be addressed through a careful and focused surgical approach. This article is aimed on the intra-operative technical considerations of intramedullary nail (IMN) fixation, their influence, and provide insight and alternatives to achieving an optimal surgical result. Specifically, we will focus on fracture reduction, improving fracture stability where IMN fixation used in isolation provides inadequate stability and fracture vascularity.

Fracture reduction

A fractures capacity to unite decreases with increasing distance between the fracture surfaces. Large fracture gaps between bony fragments have been shown to directly affect healing [1]. Furthermore, research by Bhandari et al. showed the presence of a post-reduction fracture gap to be a major risk factor for reoperation ($p < 0.0001$) [2]. Placement of an IMN alone does not result in adequate, anatomical fracture reduction. A common pitfall in intramedullary (IM) fixation is proceeding with fixation prior to achieving anatomical alignment and regardless of advances in implants and implant design, surgical technique remains of paramount importance.

Ideally, fracture reduction is achieved indirectly, thereby not disturbing the fracture haematoma. This is largely achieved through the application of longitudinal traction together with rotational adjustment, and is most commonly performed on the traction table for fractures of the femur although free hand methods are popular of IM nailing of the tibia, and humerus. Within our unit, we prefer to perform intramedullary fixation of the tibia, with the leg free, flexed over a radiolucent bolster and the application of manual traction as and when it is required. This permits complete control of the limb intra-operatively and ease of imaging, however this technique relies heavily on the skill of the surgeon and his assistant to achieve and maintain reduction. In both setups, direct external pressure can be applied to assist neutralisation of the fracture deforming forces. In some circumstances, this alone is insufficient to achieve the desired reduction. In such cases, percutaneous bone reduction clamps, supplementary Poller (blocking) screws or temporary blocking wires or a percutaneous pin (joystick) can be utilised. Despite these percutaneous techniques, on occasions the fracture site needs to be opened for direct reduction and held temporarily with clamps or plates clamped over the fracture site during the insertion of the IMN. Once reduced, some surgeons prefer to hold certain femoral fracture configurations by using cerclage wire fixation and or the addition of a plate applied over the fracture using unicortical screws so as to avoid impeding IMN insertion.

The approach and entry for tibial nails can be challenging due to the influence of the patellar tendon and patella. Conventionally, a parapatellar approach using either medial or lateral approaches, or a midline *trans*-tendinous approach, with the knee in approximately 90°of flexion is performed. With proximal fractures, the pull of the extensor mechanism on the tibial tuberosity resulting in

* Corresponding author at: Consultant Trauma & Orthopaedic Surgeon, MBChB, FRCSE Orth, Aberdeen Royal Infirmary, Foresterhill, Aberdeen, AB25 2ZN, UK.
E-mail address: a.johnstone@nhs.net (A.J. Johnstone).

http://dx.doi.org/10.1016/j.injury.2017.04.019

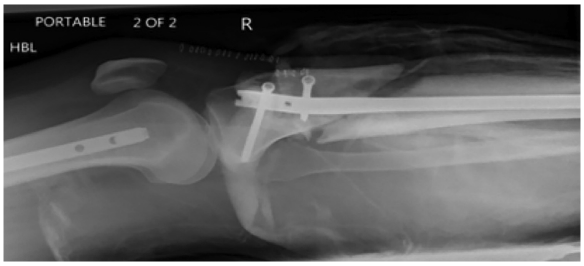


Fig. 1. Radiograph of a proximal tibial fracture, fixed with an IMN through an infra-patellar approach, with a residual apex anterior flexion deformity.

an apex anterior flexion and anterior translation deformity is exaggerated with flexion of the knee. This is demonstrated in Fig. 1.

However, within the last decade, interest has been growing in the use of a semi-extended supra-patellar approach, particularly for fractures involving the proximal tibia [3]. To date, our centre's experience, as part of a multicentre randomised control trial, has been extremely positive and to date is the only RCT comparing infrapatellar with suprapatellar nail insertion. Preliminary results have found this approach to achieve a statistically more accurate nail entry point and a statistically significant improvement in IMN position within the tibia resulting in an improvement in fracture alignment, when compared to the standard medial parapatellar approach where the knee in flexed during IMN insertion [4]. Furthermore, the semi-extended suprapatellar approach leads to significant improvements in the incidence and severity of anterior knee pain and anterior knee discomfort when kneeling compared with the infrapatellar approach.

Achieving the desired entry point on the tibia is crucial, as and incorrect entry point can lead to loss of reduction at the fracture site post nail insertion as well as iatrogenic valgus malalignment due to the less than optimal alignment of the nail within the tibia. To obtain ideal nail placement it is essential that the surgical approach permits optimal placement of the guide-wire and subsequent centralised reaming of the canal prior to nail insertion. Good quality fluoroscopic images to confirm entry position on two planes is also essential. To some degree the exact tibial entry point varies depending upon the nail design and in particular the size of the Herzog bend in the proximal part of the nail. This said, in most modern tibial nails, the Herzog bend has been reduced considerably compared with earlier designs and therefore has little bearing upon final nail alignment although it must be emphasised that nail designs that have sizeable Herzog bends are not suitable for insertion using a supra-patellar, semi-extended approach. When an infra-patellar entry point is being used, the entry is most commonly used medial parapatellar approach commonly results in over medialisation of the starting point resulting in a valgus deformity of the tibia especially with proximal or segmental fractures. Although by using a lateral parapatellar approach malalignment is less likely, it is still well recognized that varus malalignment can occur at the fracture site. Finally, a more distal starting point on the tibia can cause procurvatum.

For fractures involving the proximal femur, and especially subtrochanteric fractures where the psoas muscle creates a strong flexion deforming force upon the proximal fragment, the most common mistake is to inert a nail when the fracture is inadequately reduced. In addition, an excessively lateral entry point precipitates a varus deformity at the fracture lateral cortex gapping and limited bone contact (Fig. 2) and subsequent delayed or non union with the potential for implant failure.

Fracture stability

Instability at the fracture site is the primary mechanical cause for aseptic delayed or non union, and results from excessive fracture motion that impairs fracture healing. IMN fixation provides load sharing characteristics and confers relative stability at the fracture site. However, the degree of stability is influenced significantly by the chosen intramedullary nail, its rigidity and the proximal and distal locking screw options available. This is directly influenced by materials used, nail diameter, wall thickness and the dimensions of the cross screws.

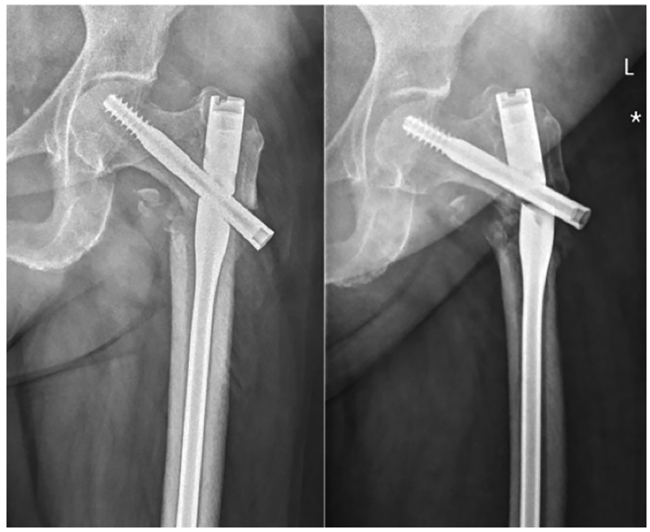


Fig. 2. Radiographs displaying varus deformity, lateral cortical gapping and subsequent fixation failure as a result of lateral nail entry in a subtrochanteric femoral fracture.

Intramedullary reaming is frequently used to increase the area of cortical contact and to allow for insertion of a larger diameter nail. This increase in diameter confers greater nail bending stiffness, with stiffness proportional to the radius to the power of 4. The other benefit of reaming is that the bone contact within the isthmus is increased that in turn reduces the working length of the nail both proximal and distal to the isthmus with an associated increase in stability. This said, surgeons should always remain conscious of the detrimental effects of reaming and the risk of osteocutaneus necrosis with over-reaming [5]. Additionally, proceeding with reaming prior to achieving optimal reduction, causes eccentric reaming and is likely to lead to further deterioration in the reduction when the nail is inserted.

In the evolution of intramedullary devices, the addition of locking screws, that limit rotational and axial movement, also improve fracture stability. Although surgeons and industry commonly focus upon the properties of the IMN, one cannot over emphasise the importance of the cross screws that essentially connect the IMN to the bone. In particular, the mechanical properties of the cross screws heavily influence the overall structural stability of the IMN combined with the bone. Biomechanical research has shown that cross screw length, core diameter and alloy from which the screws are manufactured greatly affects overall fracture stability. Shorter, thicker cross screws made form a more resilient alloy such as stainless steel add to the overall stability of the construct. Although additional screws do add to overall fracture stability, one should appreciate that long screws places at the extremes of bones, where the cortices are thinnest and therefore provide limited screw purchase, do not add significantly to the stability of the overall construct [6]. This increase in screw length is associated with increased deflection with loading, and a subsequent decrease in stability combined with a tendency to pull out from the cortical bone [7]. (Fig. 3). For this reason, in situations where increased fracture stability is required, the locking options that are closest to the midpoint of the

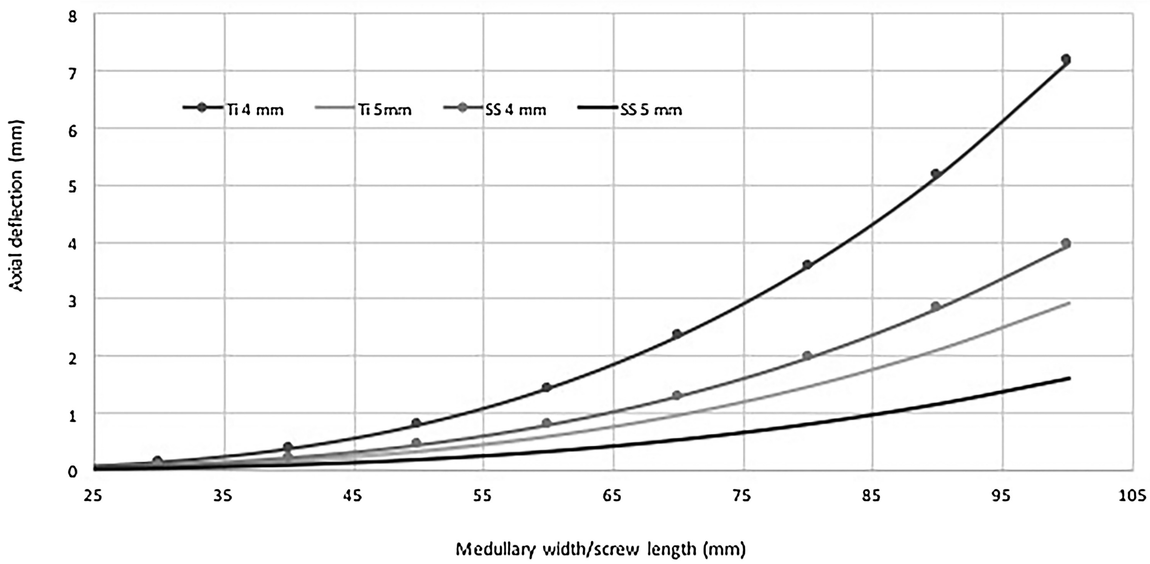


Fig. 3. Graph showing the change in axial deflection experienced with increasing stainless steel and titanium screw length.

nail should be used whenever possible. Additional fracture stability can be achieved by using IMNs that permit cross screws to be inserted at oblique angles to each other. In effect this configuration prevents slippage of the nail along the length of the cross screw. A similar effect can be achieved by using inserts that are housed within the cross screw holes within the nail. These permit the cross screws to truly engage with the nail adding to overall construct stability.

Due to the widening of the medullary cavity at the metaphysis of long bones, there is clearly no contact between the nail and the cortices making fractures within these regions are particularly difficult stabilise with intramedullary fixation. In addition to standard locking screws, blocking screws, placed adjacent to the nail to prevent unwanted medio-lateral or antero-posterior movement of the nail within the metaphyseal regions [8]. IM nail fixation can also be augmented using plates that depending upon the manner in which they are used, add additional stability to the IMN construct.

Additional screws (Poller screws) and plates can also be used prior to preparing the canal of the bone before nail insertion. In these circumstances Poller screws are used as buttresses to prevent the intramedullary guide wire, reamer, and subsequently nail from becoming mal-aligned within the metaphyseal regions of long bones. Plates are used in a different way by optimising fracture alignment prior to preparation of the intramedullary canal and also to permit traction to be applied to the bone with the plate in situ. In effect the plate has recreated one of the cortices and permits easier alignment of the fracture prior to insertion of the IMN. Despite the use of Poller screws and blocking screws, it is still not always possible to fully optimise fracture alignment and stability prior to and after IMN insertion (Fig. 4).

The cautious use of supplementary plate fixation in combination with intramedullary nailing is an invaluable technique in the surgeon's armamentarium. It is reserved for the more complex fracture patterns and should be case selective, as it comes with the disadvantage of disrupting the soft tissues, fracture haematoma and periosteum. Plates can also be used to salvage poor fixations using IM nails in an attempt to improve fracture alignment, and overall bone biomechanics. Depending upon the desired effect, plates can be used to correct malalignment by using them as a buttress (Fig. 5), reduce the tendency for a corrected deformity to reform by applying the plate in tension (Fig. 6), and to apply compression around a nail to promoted fracture union (Fig. 7).

Fig. 4. A complex, comminuted proximal tibial fracture fixed with an IMN and utilisation of Poller screws to improve alignment and stability.

Fig. 5. Radiograph showing the use of a supplementary plate, used as a buttress to correct mal-alignment.

Fracture vascularity

Inadequate blood supply is a major cause of impaired fracture healing, leading to delayed and non union. Patent vasculature to the fracture site is therefore of significant importance [9,10]. Long bones also all depend upon the surrounding musculature to supply

Fig. 6. A revision of a subtrochanteric non-union with IMN fixation and a lateral plate in tension.

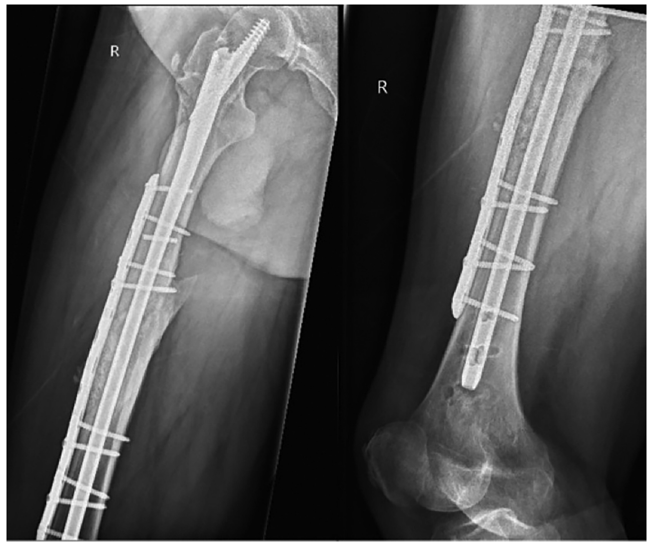


Fig. 7. A femoral diaphyseal non union treated with exchange nailing and addition of a supplementary plate to apply further compression.

a proportion of their blood supply and subsequent delivery of nutrients. Since the femur is encapsulated in muscle it is usually well vascularized. By comparison, the tibia, with its sizeable subcutaneous border, has a poorer blood supply and injury to the anterior and deep posterior muscle compartments will result in a reduced blood supply to the tibia. It is well recognized that the lower leg is prone to the development of Acute Compartment Syndrome (ACS) with the incidence of this syndrome being somewhere in the region of 10% according to the literature although some researchers believe the figure to be much higher. Not surprisingly, patients who develop ACS are prone to develop delayed and non unions. Although the ACS/delayed and non union association is well proven, the possibility that localized muscle ischaemia around the fracture site is also a distinct possibility leading to delayed and non union. One factor that could easily influence the degree of local muscle ischaemia is the technique used to undertake IMN insertion. In particular, slight fracture gapping following nail insertion is very common resulting at times in quite large gaps that are obvious, but also small gaps that are less obvious unless looked for. The analogy of a 'Chinese finger trap' phenomenon is useful in that one can appreciate that any degree of fracture distraction will result in tensioning of the immediate surrounding musculature and increase in pressure in the associated muscle compartment that will in turn reduce local muscle vascularity. Usually these gaps can be eliminated or significantly reduced if back-slapping of the nail is undertaken after the distal cross screws have been inserted. As part of a larger study investigating ACS after tibial fractures, Elliott and Johnstone presented their findings of intra-operative monitoring of intra-compartmental pressure for patients undergoing IM nailing. Significant peak pressures occurred with every stage of the procedure but perhaps of even more significance was a period of elevated pressure that persisted from the time that the nail had been inserted until the procedure was over. For the purpose of their study, all tibial nails were inserted using traction apparatus as was the norm in their unit at that time, and releasing traction at the end of the procedure reduced intracompartmental pressure to within an acceptable range for the majority of patients. However, of all of the patients who had fracture distraction to any degree, including those with small gaps, 62% had unacceptably high IC pressures (diagnostic of ACS) that only resolved after back-slapping of the fractures. Overall, a mean drop in IC pressure of 15 mmHg was achieved for all patients with any degree of fracture distraction ($p < 0.005$) [11]. Although it is wrong to directly relate these pressure findings to the presence of localised fracture ischaemia, the findings of this study are thought provoking and raise the possibility that attention to detail really matters. The findings of this study are also interesting given the findings of Bhandari et al., whereby they showed that the presence of a post-reduction fracture gap to be a major risk factor for reoperation.

Conclusion

Delayed unions and non unions of fractures continue to be of great interest [12–15] to both clinicians and scientists since they are associated with significant patient morbidity. Whilst intramedullary nails provide an excellent form of fracture fixation, good surgical technique is essential to ensure a positive outcome. This is particularly pertinent in the more complex fracture patterns and those affecting the proximal and distal regions of long bones. A patient specific approach, focusing on fracture reduction to restore alignment, attainment of adequate fracture stability whilst minimising insult to the fractures vascularity, should decrease the incidence of progression to delayed and non unions [2].

Conflict of interest

None.

References

[1] Augat P, Margevicius K, Simon J, Wolf S, Suger G, Claes L. Local tissue properties in bone healing: influence of size and stability of the osteotomy gap. J Orthop Res 1998;16:475–81.
[2] Bhandari M, Tornetta P, Sprague S, Najibi A, Petrisor B, Griffith L, et al. Predictors of reoperation following operative management of fractures of the tibial shaft. J Orthop Trauma 2003;17(5):353–61.
[3] Tornetta P, Collins E. Semiextended position for intramedullary nailing of the proximal tibia. Clin Orthop Relat Res 1996;328:185–9.
[4] Johnstone AJ, Munro C, Caba P, Escriba I, Forward D, Graf M. The suprapatellar variant of the semi-extended surgical approach improves intramedullary nail position compared with the conventional medial parapatellar surgical approach. Presented at OTA Meeting. Unpublished work.
[5] Leunig M, Hertel R. Thermal necrosis after tibial reaming for intramedullary nail fixation. J Bone Joint Surg (Br) 1996;78-B:584–7.
[6] Karuppiah S, Johnstone AJ. Distal locking in femoral intramedullary nailing system: is one cross screw sufficient. J Biomed Sci Eng 2012;5:593–6.
[7] Karuppiah SV, Johnstone AJ, Shepherd DET. How cross screw lengths influence the stiffness of intramedullary nail systems. J Biomed Sci Eng 2010;2:612–6.
[8] Krettek C, Stephan C, Schandelmaier M, Richter H, Pape C, Miclau T. The use of Poller screws as blocking screws in stabilising tibial fractures treated with small diameter intramedullary nails. JBJS (Br) 1999;81(6):963–8.
[9] Lu C, Miclau T, Hu D, Marcucio Ralph S. Ischemia leads to delayed union during fracture healing: a mouse model. J Orthop Res 2007;25:51–61.
[10] Dickson KF, Katzman S, Paiement G. The importance of the blood supply in the healing of tibial fractures. Contemp Orthop 1995;30:489–93.
[11] Elliott KGB, Johnstone AJ. Fracture distraction following intramedullary nail insertion: another significant risk factor for acute compartment syndrome. Bone Joint J 2004;86(Suppl. 3):375.
[12] Stavrou PZ, Ciriello V, Theocharakis S, Gudipati S, Tosounidis TH, Kanakaris NK, et al. Prevalence and risk factors for re-interventions following reamed intramedullary tibia nailing. Injury 2016;47(December (Suppl. 7)):S49–52.
[13] Metcalfe CW, Harrison WD, Nayagam S, Narayan B. Negligence claims following non-union and malunion of long bone fractures: an analysis of 15 years of data. Injury 2016;47(October (10)):2312–4.
[14] Fischer C, Doll J, Tanner M, Bruckner T, Zimmermann G, Helbig L, et al. Quantification of TGF-ß1, PDGF and IGF-1 cytokine expression after fracture treatment vs. non-union therapy via masquelet. Injury 2016;47(February (2)):342–9.
[15] Santolini E, West R, Giannoudis PV. Risk factors for long bone fracture non-union: a stratification approach based on the level of the existing scientific evidence. Injury 2015;46(December (Suppl. 8)):S8–S19.

Injury, Int. J. Care Injured 48S (2017) S69–S75

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Fracture healing: A review of clinical, imaging and laboratory diagnostic options

Brian P. Cunningham[a], Sloane Brazina[b], Saam Morshed[b], Theodore Miclau III[b,*]

[a] Regions Hospital, Saint Paul, MN, USA
[b] Orthopaedic Trauma Institute San Francisco, CA, USA

ARTICLE INFO

ABSTRACT

A fundamental issue in clinical orthopaedics is the determination of when a fracture is united. However, there are no established "gold standards," nor standardized methods for assessing union, which has resulted in significant disagreement among orthopaedic surgeons in both clinical practice and research. A great deal of investigative work has been directed to addressing this problem, with a number of exciting new techniques described. This review provides a brief summary of the burden of nonunion fractures and addresses some of the challenges related to the assessment of fracture healing. The tools currently available to determine union are discussed, including various imaging modalities, biomechanical testing methods, and laboratory and clinical assessments. The evaluation of fracture healing in the setting of both patient care and clinical research is integral to the orthopaedic practice. Weighted integration of several available metrics must be considered to create a composite outcome measure of patient prognosis.

Introduction

There are an estimated six million fractures occurring annually in the United States, with 5–10% of these fractures proceeding to nonunion [1]. While no standardized definition of nonunion exists among orthopaedic surgeons, the Food and Drug Administration (FDA) defines nonunion as a fracture that persists for a minimum of nine months without signs of healing for at least three months [2]. The risk of developing nonunion varies significantly across cases and is attributable to a variety of factors. A history of smoking, for example, is one variable that has been demonstrated to increase risk of nonunion in long bone fractures by 12% [3]. Injury type, particularly open fractures, and anatomical location, such as the scaphoid bone, can also predispose a patient to nonunion [4–8]. Infection can present as a delay or failure of fracture repair, and the clinician should always consider this in their differential diagnosis.

Treating patients with nonunions requires a dramatic utilization of resources, which are significantly greater than those fractures that have uncomplicated healing [9–12]. A recent study demonstrates the enormous cost discrepancy between treating tibial shaft nonunions. The median total care cost for nonunions was reported as $25,556, more than double the $11,686 required to treat a standard tibia fracture [9].

Determining fracture union is a routine part of clinical care and plays a significant role in downstream decision-making, such as advancing a patient's weight-bearing status, proceeding to hardware removal and surgical intervention in fractures determined to have delayed healing or nonunions. Considerable disagreement among orthopaedic surgeons exists regarding radiographic and clinical criteria to define fracture union, in addition to the temporal component required for diagnosis of delayed or failed union [13]. This variability also exists in clinical research with a systematic review demonstrating eleven different criteria utilized to define union [14]. Similarly, clinical trials indicate a lack of objective tools to radiographically or clinically assess fracture healing, making union as a nebulous primary outcome [15].

The determination of fracture union is a critical decision in clinical orthopaedics; however there is no standard method to evaluate clinical fracture healing. This review provides an overview of some of the challenges in assessing fracture healing, examines the modalities currently available to diagnose nonunion, and discusses preferred methods for evaluation and decision making.

Challenges

Healing is a multifactorial process affected by a host of biological factors, injury characteristics and the mechanical

* Corresponding author at: University of California, San Francisco (UCSF) & Zuckerberg San Francisco General Hospital (ZSFGH), Orthopaedic Trauma Institute, 2550 23rd St Bldg. 9, 2nd Floor, San Francisco, California, USA,
E-mail address: Theodore.Miclau@ucsf.edu (T. Miclau).

http://dx.doi.org/10.1016/j.injury.2017.04.020
0020-1383/

environment. This complex system can be simplified into several stages of healing, beginning with hematoma formation, followed by inflammatory response, cell proliferation and differentiation, and finally ossification with subsequent remodeling of the new bone [16]. The interaction of these biological systems is poorly understood; however, the fundamental progression of fracture healing has been elucidated in a classic work by Mckibbin [17] and further described by Einhorn [18] and many others. There are numerous variables that affect the healing process and many ways in which this progression can be altered, resulting in delayed healing or, in extreme cases, nonunion.

Various patient-related factors have been reported to alter fracture healing. Female patients of advanced age have demonstrated comparatively poor healing outcomes and a potential increase in nonunion rate. Research suggests that deceased estrogen levels and generally diminished biologic activity may be responsible for the observed trends [19]. Metabolic and endocrine abnormalities are well established etiologies of nonunions. A recent study of patients with unexplained nonunions found that 83% of participants exhibited previously undiagnosed metabolic or endocrine abnormalities after being evaluated by an endocrinologist [20]. A history of smoking, diabetes and NSAID use have also been documented to delay the healing process and increase the risk of nonunion among patients [21–24].

Certain characteristics of fractures can also influence the progression of healing. Disruption of the soft tissue envelope through either an open fracture [25] or open reduction during intramedullary nailing [24] has been shown to increase the risk of nonunion. The degree of fracture comminution has also been shown to increase the risk of nonunion in open fractures, likely due to substantial damage of the periosteum and soft tissue at the fracture site [26,27]. The presence of a fracture gap has also been indicated to increase the nonunion risk [28], however, this variable must be taken in context with the fracture type (simple versus comminuted) and fixation strategy (compression or nail, bridge or external fixator).

The mechanical environment surrounding the fracture can also affect the healing process. This is highly dependent on the fracture characteristics and the fixation technique utilized. Perren's theory of interfragmentary strain postulates that reparative tissue will develop at a fractures site in accordance to the strain tolerance of the tissue and the local strain environment between fracture fragments [98]. According to this theory, simple fracture line that is not compressed and neutralized will have a higher likelihood for nonunion relative to a fracture site exposed to a high strain environment. Some technical factors can also affect union, for example, reamed femoral nailing reports a higher union rate than unreamed femoral nailing [29].

The various patient factors, biological and mechanical components combine to influence the rate of fracture healing. Some fractures are notoriously slow to heal, while certain patient populations, such as children, heal remarkably quickly. These challenges make predicting fracture union extremely difficult and further necessitate reliable quantitative assessments of healing.

Evaluation modalities

The tools currently available to assess fracture healing can be broadly divided into four categories: (1) Imaging studies, (2) mechanical assessment, (3) serologic markers and (4) clinical examination. We will briefly discuss each of these categories as well as their current use in research and clinical practice.

Imaging studies

Radiography. Radiographic assessment remains the mainstay of fracture healing evaluation. Clinicians' familiarity with radiography, combined with the technology's widespread availability, low cost, and limited radiation exposure make this imaging modality highly appealing [13]. Unfortunately, radiographs have not been shown to be reliable or accurate when used to define union or determine the stage of healing [30–32]. In a recent study, radiographs of tibia shaft fractures treated with intramedullary nails were reviewed at the three-month follow up visit by three independent reviewers. Results showed a diagnostic accuracy of only 62% − 74%, with a sensitivity of 62% and a specificity of 77% [33]. Two radiographic scoring systems, the Radiographic Union Score for Hip (RUSH) and the Radiographic Union Score for Tibia (RUST), have been shown to increase agreement among surgeons and radiologists in assessing fracture repair [34–37]. After illustrating the limitations of older radiographic scoring systems, researchers showed that the assessment of the number of cortices bridged by callus had higher reliability in determining healing through use of these new scoring systems [38].

The RUSH score requires clinicians to first evaluate if the fracture is completely healed after initial review of the patient's radiographs. Then, the reviewer completes the RUSH checklist to assess the extent of cortical bridging, cortical visibility of fracture line, trabecular consolidation and disappearance of trabecular fracture line (Appendix A, Table 1). Bone cortices are evaluated across two different axes: anteroposterior and mediolateral. Responses are scored and added, with the overall RUSH score ranging from 10 (no healing) to 30 (complete union) [35,37]. Researchers demonstrated that the RUSH checklist was most effective at increasing agreement between radiologists and orthopaedic surgeons when used within zero to three months post-surgery, compared to six or more months post-surgery (Appendix A, Table 2). This finding was observed for both femoral neck and interochanteric fractures, with interobserver agreement reported extremely high (ICC $\geq$ 0.85) [35].

The RUST score is based on callus formation and the visibility of fracture lines at four cortices observed on anteroposterior and lateral radiographs. A minimum score of four indicates no healing and a maximum score of twelve is awarded to a healed fracture (Appendix A, Table 3). The overall interobserver agreement has been reported as high for RUST score (ICC $\geq$ 0.8).

The RUST score was recently modified (mRUST) to determine union in distal femur fractures. The mRUST scoring system further subdivides cortical assessment to consider the presence of bridging callus, whereby a score of "1" = no callus, "2" = callus present, "3" = bridging callus and "4" = remodeled bone with no visible fracture line [39]. Similar to RUST, mRUST is used to evaluate four cortices present on anteroposterior and lateral radiographs, with the total score per fracture ranging from four to sixteen. Results showed moderate interobserver agreement with slightly improved agreement in fractures treated with intramedullary nails (Appendix A, Table 4. ICC = 0.53; nails: 0.58 versus plates: 0.51). Fracture healing was also determined by the percentage of radiograph reviewers who declared union across various total RUST and mRUST scores (Appendix A, Table 5).

Since the RUST score was introduced into clinical practice, several studies have been conducted to evaluate the reliability and efficacy of the RUST score to predict nonunion. In their 2014 study, Ali et al. support the continued use of the RUST score as a reliable method of assessing nonunion fractures and improving consensus among medical care providers [40]. Radiography images of sixty-five patients with simple diaphyseal tibia fractures were independently assessed by an orthopaedic surgeon and radiologist using RUST score methodology. The patients' identity and fracture duration were withheld from the evaluating physicians. Intraclass correlation coefficients with 95% confidence intervals revealed statistically significant agreement between orthopaedic surgeon and radiologist. This finding, in addition to the demonstrated reproducibility of results, encourages the recommendation of the RUST score as a decisive evaluation of patient progress along the healing continuum, with the potential to predict a fracture that will fail to heal. While both scores show promise, the lack of a gold standard inhibits the validation of the tools to predict union. It is likely that larger clinical studies will compare RUST and RUSH scores against other available outcome measures in an effort to validate their use in isolation.

Computed tomography. Computed tomography (CT) is superior to plain radiography in assessment of union and visualization of fracture lines [41]. Although computed tomography sensitivity for detecting nonunion has been reported to approach 100%, the specificity is only 62% [42]. The discrepancies between using radiography and CT scans to detect union are accentuated in fractures that are treated with absolute stability where primary bone healing predominates and limited callus is produced. The presence of beam-hardening artifacts from internal fixation presents a limitation of CT. Modern software can be used to reduce image degradation from these artifacts, but the resolution remains affected when the region of interest is adjacent to metal implants. Despite evidence of improved diagnostic accuracy, the high cost and radiation dose of CT scans limits their widespread use in the assessment of fracture healing.

A new technology called virtual stress testing (VST) improves image resolution by using CT-based finite element analysis. Use of this technology was recently expanded from the application of predicting the risk of fracture to evaluation of fracture repair. In a pilot VST study, complex tibia fractures were treated with ring fixators to identify patients at high risk for refracture, malunion or surgical revision if the hardware was removed. The study retrospectively analyzed sixty-six patients who had undergone CT imaging two to four weeks prior to removal of their ring fixators. Researchers were able to successfully predict nine of the eleven complications through the use of VST [43]. More prospective studies with larger sample sizes are required to validate this technology and expand its use.

Ultrasonography. Although ultrasound is unable to penetrate cortical bone, evidence suggests that it is capable of detecting callus formation before radiographic changes are visible [44,45]. A pilot study demonstrated that ultrasound was able to correctly predict union in a shorter period of time than radiography [46], with a 97% positive predictive value and 100% sensitivity [47]. Ultrasound was also shown to substantially reduce the overall time needed to determine healing compared to traditional radiography: 6.5 weeks versus 19 weeks, respectively. While ultrasound has the benefits of being low cost, noninvasive and requires no radiation exposure, its use is highly operator dependent. As ultrasound technology advances, many of these limitations will likely be addressed and further prospective validation will be studied.

18F PET-MRI. By combining the superior soft tissue imaging of MRI and the semi-quantitative metabolic radiotracer uptake rates of PET, 18F PET-MRI imaging shows promise as a technique to evaluate fracture healing. A 2015 study published by Crönlein et al. illustrates the superiority of PET-MR in detecting early-stage stress reactions in the lower extremity, relative to traditional radiography, computed tomography, and MRI alone [48]. Evaluation of delayed healing using cellular metabolism-based imaging may be a more direct measure of biological activity and improve the time to diagnosis. While PET-MR predominantly exists in the research sphere due to cost, preliminary studies suggest this imaging modality may be the frontier of high-resolution orthopaedic imaging.

Mechanical property testing

Understanding the stability and modulating the stiffness of a composite bone-implant construct is common practice in orthopaedic surgery. Mechanical testing quantifies fracture properties directly rather than using imaging as a proxy. Bone stiffness increases as a fracture progresses from early phases of callus formation to union [49,50]. This concept serves as the foundation for biomechanical testing and vibrational methodologies. The primary limitation to the clinical use of mechanical testing techniques is the interference of internal fixation on measurements of stiffness.

Measurements of stiffness. Biomechanical testing methods can be divided into direct and indirect measurements of stiffness. With a direct measurement, the displacement angle across a fracture is measured through radiographs or analysis of four-point bending in the setting of an applied load [51,52]. Indirect testing measures the strain through an external fixation device using strain gauges [50]. Direct measurements assume the degree of deflections during bending are inversely proportional to the stability of the fracture. For accurate analysis, this method can only be utilized in a setting without internal hardware or a cast. A reliable threshold for union of non-operative tibial fractures was established as 7 Nm per degree at twenty weeks post-injury [53]. Tibial shaft fractures treated with external fixation were studied using the indirect technique. A threshold of 15 Nm per degree was a better predictor of refracture than radiographic evaluation ($P = 0.02$) and decreased the time to weight-bearing ($P = 0.02$) [50,54].

Vibrational testing. Vibrational testing is a noninvasive, painless assessment that utilizes either resonant frequency or computerized sonometry to evaluate mechanical properties of fractures. Resonant frequency analysis (RFA) is based on the principle that a direct correlation exists between the natural frequency of a beam and its stiffness. This notion can be applied to orthopaedic analysis where long bones act as beams [55]. Early work proposed that an estimation of the Young's modulus of bone in vivo could be used to assess bone quality [56]. Subsequently, the healing process has been demonstrated to change the resonant frequency of the bone [55–58]. Further work shows that resonant frequency correlated well with bending rigidity of the tibia, time-to-fracture healing [57], and torsional stiffness [59]. Despite its promise as a quantitative tool for fracture healing assessment, RFA does not have the ability to differentiate fracture healing versus the inherent stability provided by intramedullary nail fixation [55].

Quantitative UltrasonometryQuantitative ultrasonometry. The efficiency of quantitative ultrasonometry as a measurement of bone healing has been studied using ultrasound propagation velocity (USPV) across fractures throughout various stages of healing [60]. In a 1994 study, two sound transducers were positioned on each end of tibial fractures treated with external fixators. Computational analysis of vibration reaction and sound propagation identified signs of delayed union prior to radiographic diagnosis [61]. The development of a more precise system has produced similar results in vitro and was reported to be accurate in predicting a simulated fracture gap using ultrasound propagation velocity [62]. Investigators have demonstrated effectiveness in numerous synthetic models including "phantoms," which use a simplified model of clinical fractures, omitting variables such as soft tissue damage. Overlaying soft tissue presents a challenge for imaging of subcutaneous bones in in vivo studies utilizing computerized sonography. Compared with other biomechanical methods used to monitor fracture healing, quantitative ultrasound technologies are low-cost, safe with some systems portable and potentially wearable [63]. Unfortunately, there is a lack of large-scale reports detailing the diagnostic accuracy and reliability of this modality in the orthopaedic space. This presents a major barrier to the use of quantitative ultrasound in clinical and research practice.

Serologic markers

The ability to detect nonunions prior to radiographic evidence would lower medical costs and result in better patient outcomes. Serologic biomarkers are gaining popularity as possible early predictors of fracture healing [64–67]. Serum concentrations of a number of biological markers in normal and delayed fracture healing have been identified. Levels of tartrate-resistant acid phosphatase 5b (TRACP 5b) and C-terminal cross-linking telopeptide of type I collagen (CTX) are reportedly significantly lower in patients who developed nonunions [68]. These molecules are an indication of osteoclast activity in the fracture environment.

Transforming growth factor-beta 1 (TGF-β1) is another serologic marker that has been widely studied over the past decade and is a critical regulator of fracture healing [69–73]. TGF-β1 has been detected in the fracture callus of both human and animal models [64,74], and its systemic and local administration enhances bone remodeling in animal models [71–75]. Systemic changes of TGF-β1 levels in patients with long bone fractures have been inconsistent with evidence that serum levels may decline more precipitously in patients with delayed healing [76], while other studies have not found a significant difference in the TGF-β1 concentrations between delayed and normal fracture healing cohorts [77].

Collagen III amino-terminal propeptide (PIIINP) is a cleavage product formed during collagen synthesis [65]. Research suggests that serum levels become elevated during the early stages of fracture repair [78] and subsequently normalize before radiographic and clinical assessment present evidence of healing. Further studies have demonstrated this phenomenon in isolated tibial shaft fractures with serum PIIINP levels significantly higher in patients who demonstrated delayed healing at ten weeks [79].

Osteoblast-derived serum markers have also been useful indicators of bone remodeling and have potential to predict nonunion. Numerous targets have been evaluated, including bone-specific alkaline phosphatase (ALP), procollagen type-I N-terminal propeptide (PINP), procollagen type-I C-terminal propeptide (PICP) and osteocalcin [80,81]. Ajai et al. investigated the differences in serum ALP levels across ninety-five healed and nonunion fracture cases [82]. Elevated ALP levels six months post-fracture were observed in delayed healing and nonunion patients, compared to more moderate serum levels among successfully healed patients. ALP levels were found to correlate with RUST scores for all patients studied, making ALP serum levels a relatively reliable predictor of problematic healing. Ajai et al. cite three weeks post-fracture as the earliest time point at which ALP serum levels become an accurate predictor of nonunion.

In their 2012 study, Sarahrudi et al. show a correlation between elevated sclerostin serum levels, a wnt signaling antagonist, and successful healing of long bone fractures [83]. Although their findings were not statistically significant ($P = 0.06$), decreased sclerostin levels were evident in patients with impaired fracture healing after reoperation for nonunion. Future studies with larger patient cohorts are necessary to further investigate the feasibility of using sclerostin serum levels as a predictive measure of nonunion fractures.

Unfortunately the use of biomarkers as diagnostic tools remains problematic. The secretion of cytokines and biologic markers such as TGF-β1 [84], macrophage colony stimulating factor (M-CSF) and vascular endothelial growth factors (VEGF) [85] represents a highly complicated regulatory system which is influenced by a number of patient factors and conditions. A recent systematic review on the clinical use of serologic biomarkers as diagnostic tools reported that no strong recommendations for their adoption could be made at this time [86].

Clinical assessment of healing

Despite the advances in imaging, biomechanics and serology, physical exam remains the primary method of determining fracture union in clinical practice. The lack of full weight-bearing serves as a critical diagnostic tool in the orthopaedic clinic [87]. A 2008 systematic review examined 59 previously published studies that used clinical criteria to assess union. It was found that an absence of pain, tenderness at the fracture site upon weight-bearing or palpation, and the ability to weight-bear were the most commonly used criteria to evaluate fracture healing [15]. Interestingly, evaluating the clinician's ability to judge stiffness and weight-bearing through physical exam has not been reliable, as a poor correlation between experience and diagnostic accuracy exists [88,89]. The increased use of patient reported outcomes (PRO) in assessing fracture healing suggests a shift towards patient-centric orthopaedic care [15].

Patient-reported outcome assessments currently in use either measure general physical and psychological health [90,91], or are disease-specific [92,93]. Eighty patients were recently studied using a generic quality of life PRO to evaluate changes in baseline score after treatment of long bone nonunion fractures. All patients with healed nonunions demonstrated improved scores and decreased pain levels. This finding was observed to a greater degree in patients who achieved union by final follow up. These results suggest that it maybe possible to track fracture healing via PROs and future studies are needed to investigate the potential of using PROs for diagnosis of nonunion. Computer-assisted testing that has implemented item response theory has streamlined the process of gathering patient reported outcomes, as demonstrated by the National Institutes of Health PROMIS Initiative [94]. Similar, more efficient instruments are currently being validated in a number of different orthopaedic clinical settings, including trauma [95].

Conclusion

Fracture healing involves a complex interplay of biological pathways and mechanical forces [96–101]. The healing process occurs on a continuum that varies dramatically based on fracture location and type, choice of treatment, and other host and injury related factors. Dichotomizing this complicated healing phenomenon is a clear oversimplification, resulting in the loss of valuable information. The lack of a standardized definition of nonunion impairs our ability to compare findings across studies. Recent developments of the RUSH and RUST score aim to improve reliability among surgeons. Serologic markers also show promise in accurately predicting the rate and quality of fracture healing; however, these results must be considered within the larger context of the clinical examination.

The future of fracture healing assessment should focus on further validation of the currently available tools and the development of patient reported outcome instruments. The quality of these tools should be determined by evaluating their measurement properties, including reliability, validity and reproducibility [102]. Defining a gold standard that integrates clinical, radiographic, biological and biomechanical factors of healing has proven to be a difficult task; committees to determine clinical healing may help increase agreement with these factors [103]. However, these methods may fail to completely measure the impact of treatment on overall health-related quality of life. Measurement of patient-reported outcomes of healing can compliment information gleaned from imaging modalities and physical examination, as well as demonstrate ways in which a clinical intervention can impact overall health.

Conflict of interest

The authors do not have any conflicts related to this study and no grant funding was used during the duration of the investigation.

Appendix A.

Table 1a Radiographic Union Score for Hip (RUSH).

Section 1: General Impression
Using your overall general impression, has the fracture healed?
☐ Healed ☐ Not Healed
Section 2: RUSH
1) Cortical Index – Bridging

Cortex	No Cortical Bridging Score = 1	Some Cortical Bridging Score = 2	Complete Cortical Bridging Score = 3	Total Score (Range: 4 to 12)
Anterior Cortex	☐	☐	☐	
Posterior Cortex	☐	☐	☐	
Medial Cortex	☐	☐	☐	
Lateral Cortex	☐	☐	☐	
Overall Score				

2) Cortical Index – Disappearance of the Fracture Line

Cortex	Fracture Line Fully Visible Score = 1	Some Evidence of Fracture Line Score = 2	No Evidence of Fracture Line Score = 3	Total Score (Range: 4 to 12)
Anterior Cortex	☐	☐	☐	
Posterior Cortex	☐	☐	☐	
Medial Cortex	☐	☐	☐	
Lateral Cortex	☐	☐	☐	
Overall Score				

Adapted from Chiavaras, M. et al. [37]

Table 1b Radiographic Union Score for Hip (RUSH).

Section 2: RUSH, Continued
3) Trabecular Index – Consolidation

	No Consolidation Score = 1	Some Consolidation Score = 2	Complete Consolidation Score = 3	Total Score (Range: 1 to 3)
Amount of Consolidation	☐	☐	☐	

4) Trabecular Index – Disappearance of Fracture the Line

	Fracture Line Fully Visible Score = 1	Some Evidence of Fracture Line Score = 2	No Evidence of Fracture Line Score = 3	Total Score (Range: 1 to 3)
Fracture Line	☐	☐	☐	

OVERALL RUSH SCORE (Range: 10–30):
Quality of the Callus
1) What is the quality of the callus formation?
☐ None ☐ Minimal Callus ☐ Moderate Callus ☐ Exuberant Callus
None is defined as no callus formation being present. Minimum callus is defined as slightly evident bridging across fracture ends. Moderate callus is defined as clearly evident bridging callus across the fracture site. Exuberant callus is defined as protuberant bridging across the fracture site
Quality of the Image
1) Is quality of the image acceptable?
☐ Yes ☐ No
2) Did the quality of the image imhibit your assessment?
☐ Yes ☐ No
3) Did the placement/position of the hardware inhibit yout assessment by obscuring fracture visibility?
☐ Yes ☐ No
Adapted from Chiavaras, M. et al. [37]

Table 2 ICC Values: RUSH at 0–3 and 6+ Months.

	ICC Value	
Fracture Type	0–3 months	6+ months
Femoral Neck	0.709	0.466
Intertrochanteric	0.816	0.536

Adapted from Bhandari, M. et al. [35]

Table 3 Overview of the RUST Score.

Score per Cortex	Callus	Fracture Line
1	Absent	Visible
2	Present	Visible
3	Present	Invisible

Adapted from Kooistra, B. et al. [34]

Table 4 ICC Values: RUST versus mRUST.

	RUST		Modified RUST (mRUST)	
	ICC	95% CI	ICC	95% CI
All				
Sum	0.63	0.57–0.68	0.68	0.63–0.73
Medial	0.51	0.45–0.57	0.60	0.54–0.66
Lateral	0.47	0.41–0.53	0.52	0.46–0.59
Anterior	0.60	0.53–0.66	0.64	0.58–0.70
Posterior	0.44	0.38–0.51	0.54	0.48–0.61
Nail				
Sum	0.67	0.59–0.76	0.74	0.68–0.81
Medial	0.55	0.46–0.65	0.64	0.55–0.73
Lateral	0.62	0.53–0.71	0.70	0.62–0.78
Anterior	0.56	0.47–0.66	0.63	0.54–0.72
Posterior	0.52	0.43–0.62	0.61	0.52–0.70

(*Continued*)

	RUST		Modified RUST (mRUST)	
	ICC	95% CI	ICC	95% CI
Plate				
Sum	0.53	0.55–0.62	0.59	0.51–0.67
Medial	0.49	0.41–0.57	0.57	0.50–0.65
Lateral	0.26	0.19–0.34	0.28	0.21–0.36
Anterior	0.49	0.42–0.58	0.52	0.45–0.61
Posterior	0.39	0.31–0.48	0.50	0.42–0.58

CI = Confidence interval.
Adapted from Litrenta J. et al., 2015 [39].

Table 5 RUST versus mRUST: Percentage of Reviewers Assigning Union.

	RUST			**Modified RUST (mRUST)**		
Score	8	9	10	9	11	13
% United	42	76	94	16	62	91

Fig. *adapted* from Litrenta J. et al., 2015 [39].

References

[1] Einhorn TA. Enhancement of fracture-healing. J Bone Joint Surg Am 1995;77 (no. 6):940–56.
[2] United States Food and Drug Administration (USFDA), Office of Device Evaluation, Guidance Document for Industry and CDRH Staff for the Preparation of Investigational Device Exemptions and Premarket Approval Application for Bone Growth Stimulator Devices, 1988.
[3] Scolaro JA, Schenker ML, Yannascoli S, Baldwin K, Mehta S, Ahn J. Cigarette smoking increases complications following fracture. J Bone Joint Surg Am 2014;96(April (8)):674–81.
[4] Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. J Orthop Trauma 2005;19(3):151–7.
[5] Tzioupis C, Giannoudis PV. Prevalence of long-bone non-unions. Injury 2007;38(2):S3–9.
[6] Osman N, Touam C, Masmejean E, Asfazadourian H, Alnot JY. Results of non-operative and operative treatment of humeral shaft fractures. A series of 104 cases. Annales de Chirurgie de la Main et du Membre Supérieur 1998;17 (3):195–206.
[7] Wolinsky PR, McCarty E, Shyr Y, Johnson K. Reamed intramedullary nailing of the femur: 551 cases. J Trauma 1999;46(3):392–9.
[8] Winquist RA, Hansen Jr. ST, Clawson DK. Closed intramedullary nailing of femoral fractures. A report of five hundred and twenty cases. J Bone Joint Surg 1984;66(4):529–39.
[9] Antonova E, Le TK, Burge R, Mershon J. Tibia shaft fractures: costly burden of nonunions. BMC Musculoskeletal Disord 201314: article 42.
[10] Dahabreh Z, Calori GM, Kanakaris NK, Nikolaou VS, Giannoudis PV. A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7. Int Orthop 2009;33(5):1407–14.
[11] Beaver R, Brinker MR, Barrack RL. An analysis of the actual cost of tibial nonunions. J Louisiana State Med Soc 1997;149(6):200–6.
[12] Kanakaris NK, Giannoudis PV. The health economics of the treatment of long-bone non-unions. Injury 2007;38(2):S77–84.
[13] Bhandari M, Guyatt GH, Swiontkowski MF, Tornetta III P, Srpague S, Schemitsch EH. A lack of consensus in the assessment of fracture healing among orthopaedic surgeons. J Orthop Trauma 2002;16(8):562–6.
[14] Corrales LA, Morshed S, Bhandari M, Miclau T. Variability in the assessment of fracture-healing in orthopaedic trauma studies. J Bone Joint Surg Am. 2008;90(September (9)):1862–8.
[15] Morshed S, Corrales L, Genant H, Miclau III T. Outcome assessment in clinical trials of fracture-healing. J Bone Joint Surg Am 2008;90(1):62–7.
[16] Harwood PJ, Newman JB, Michael ALR. An update on fracture healing and non-union. Orthop Trauma 2010;24(1):9–23.
[17] McKibbin B. The biology of fracture healing in long bones. J Bone Joint Surg B 1978;60(2):150–62.
[18] Marsell R, Einhorn TA. The biology of fracture healing. Injury 2011;42(6):551–5.
[19] Calori GM, Albisetti W, Agus A, Iori S, Tagliabue L. Risk factors contributing to fracture non-unions. Injury 2007;38(2):S11–8.
[20] Brinker MR, O'Connor DP, Monla YT, Earthman TP. Metabolic and endocrine abnormalities in patients with nonunions. J Orthop Trauma 2007;21(8): 557–70.
[21] McKee MD, DiPasquale DJ, Wild LM, Stephen DJ, Kreder HJ, Schemitsch EH. The effect of smoking on clinical outcome and complication rates following Ilizarov reconstruction. J Orthop Trauma. 2003;17(10):663–7.
[22] Schmitz MA, Finnegan M, Natarajan R, Champine J. Effect of smoking on tibial shaft fracture healing. Clin Orthop Relat Res. 1999;365:184–200.
[23] Giannoudis PV, MacDonald DA, Matthews SJ, Smith RM, Furlong AJ, De Boer P. Nonunion of the femoral diaphysis: the influence of reaming and non-steroidal anti-inflammatory drugs. J Bone Joint Surg Br. 2000;82(5):655–8.
[24] Malik MH, Harwood P, Diggle P, Khan SA. Factors affecting rates of infection and nonunion in intramedullary nailing. J Bone Joint Surg Br. 2004;86 (4):556–60.
[25] Arslan H, Subaşý M, Kesemenli C, Ersuz H. Occurrence and treatment of nonunion in long bone fractures in children. Arch Orthop Trauma Surg. 2002;122(9–10):494–8.
[26] Noumi T, Yokoyama K, Ohtsuka H, Nakamura K, Itoman M. Intramedullary nailing for open fractures of the femoral shaft: evaluation of contributing factors on deep infection and nonunion using multivariate analysis. Injury 2005;36(9):1085–93.
[27] Triffin P, Greg PJ. Depression of bone blood flow after brunt trauma. Acta Orthop Scand 1994;65(2):195–8.
[28] Pihlajamäki HK, Salminen ST, Böstman OM. The treatment of nonunions following intramedullary nailing of femoral shaft fractures. J Orthop Trauma 2002;16(6):394–402.
[29] Duan X, Li T, Mohammed AQ, Xiang Z. Reamed intramedullary nailing versus unreamed intramedullary nailing for shaft fracture of femur: a systematic literature review. Arch Orthop Trauma Surg 2011;131(October (10)):1445–52.
[30] Hammer RRR, Hammerby S, Lindholm B. Accuracy of radiologic assessment of tibial shaft fracture union in humans. Clin Orthop 1985;199:233–8.
[31] De Bruine D, Bramer JAM, et al. The reliability of plain radiography in experimental fracture healing. Skeletal Radiol 2001;30(3):151–6.
[32] Davis BJ, Roberts PJ, Moorcroft CI, Brown MF, Thomas PBM, Wade RH. Reliability of radiographs in defining union of internally fixed fractures. Injury 2004;35(6):557–61.
[33] Yang JS, Otero J, McAndrew CM, Ricci WM, Gardner MJ. Can tibial nonunion be predicted at 3 months after intramedullary nailing? J Orthop Trauma 2013;27(11):599–603.
[34] Kooistra BW, Dijkman BG, Busse JW, Sprague S, Schemitsch EH, Bhandari M. The radiographic union scale in tibial fractures: reliability and validity. J Orthop Trauma 2010;24(1):S81–6.
[35] Bhandari M, Chiavaras MM, Parasu N, et al. Radiographic union score for hip substantially improves agreement between surgeons and radiologists. BMC Musculoskelet Disord 201314: article 70.
[36] Whelan DB, Bhandari M, Stephen D, et al. Development of the radiographic union score for tibial fractures for the assessment of tibial fracture healing after intramedullary fixation. J Trauma 2010;68(3):629–32.
[37] Chiavaras MM, Bains S, Choudur H, et al. The Radiographic Union Score for Hip (RUSH): the use of a checklist to evaluate hip fracture healing improves agreement between radiologists and orthopedic surgeons. Skeletal Radiol 2013;42(8):1079–88.
[38] Whelan DB, Bhandari M, McKee MD, et al. Interobserver and intraobserver variation in the assessment of the healing of tibial fractures after intramedullary fixation. J Bone Joint Surg B 2002;84(1):15–8.
[39] Litrenta J, Tornetta III P, Mehta S, Jones C, O'Toole RV, Bhandari M, et al. Determination of radiographic healing: an assessment of consistency using RUST and modified RUST in metadiaphyseal fractures. J Orthop Trauma 2015;29(11):516–20.
[40] Ali, et al. Reliability of the RUST score for the assessment of union in simple diaphysial tibial fractures. Int J Biomed Res 2014;05(05):333–5.
[41] Braunstein EM, Goldstein SA, Ku J, Smith P, Matthews LS. Computed tomography and plain radiography in experimental fracture healing. Skeletal Radiol 1986;15(1):27–31.
[42] Bhattacharyya T, Bouchard KA, Phadke A, Meigs JB, Kassarjian A, Salamipour H. The accuracy of computed tomography for the diagnosis of tibial nonunion. J Bone Joint Surg—Ser A 2006;88(4):692–7.
[43] Petfield JL, Kluk M, Shin E, et al. Virtual stress testing of regenerating bone in Tibia fractures. Proceedings of the 23rd Annual Scientific Meeting of Limb Lengthening and Reconstruction Society. .
[44] Craig JG, Jacobson JA, Moed BR. Ultrasound of fracture and bone healing. Radiol Clin North Am 1999;37(4):737–51.
[45] Moed BR, Kim EC, van Holsbeeck M, et al. Ultrasound for the early diagnosis of tibial fracture healing after static interlocked nailing without reaming: histologic correlation using a canine model. J Orthop Trauma 1998;12 (3):200–5.
[46] Moed BR, Watson JT, Goldschmidt P, van Holsbeeck M. Ultrasound for the early diagnosis of fracture healing after interlocking nailing of the tibia without reaming. Clin Orthop Relat Res 1995;310:137–44.
[47] Moed BR, Subramanian S, van Holsbeeck M, et al. Ultrasound for the early diagnosis of tibial fracture healing after static interlocked nailing without reaming: clinical results. J Orthop Trauma 1998;12(3):206–13.
[48] Crönlein, et al. Visualization of stress fractures of the foot using PET-MRI: a feasibility study. Eur J Med Res 2015;20:99.
[49] Chehade MJ, Pohl AP, Pearcy MJ, Nawana N. Clinical implications of stiffness and strength changes in fracture healing. J Bone Joint Surg Am 1997;79(1): 9–12.

[50] Richardson JB, Cunningham JL, Goodship AE, O'Connor BT, Kenwright J. Measuring stiffness can define healing of tibial fractures. J Bone Joint Surg B 1994;76(3):389–94.
[51] Edholm P, Hammer R, Hammerby S, Lindholm B. The stability of union in tibial shaft fractures: its measurement by a non-invasive method. Arch Orthop Trauma Surg 1984;102(4):242–7.
[52] Edholm P, Hammer R, Hammerby S, Lindholm B. Comparison of radiographic images: a new method for analysis of very small movements. Acta Radiol—Diagn 1983;24(3):267–72.
[53] Marsh D. Concepts of fracture union, delayed union, and nonunion. Clin Orthop 1998;355(supplement):S22–30.
[54] Richardson JB, Kenwright J, Cunningham JL. Fracture stiffness measurement in the assessment and management of tibial fractures. Clin Biomech 1992;7(2):75–9.
[55] Tower SS, Beals RK, Duwelius PJ. Resonant frequency analysis of the tibia as a measure of fracture healing. J Orthop Trauma 1993;7(6):552–7.
[56] Jurist JM. In vivo determination of the elastic response of bone. I. Method of ulnar resonant frequency determination. Phys Med Biol 1970;15(3):417–26.
[57] Benirschke SK, Mirels H, Jones D, Tencer AF. The use of resonant frequency measurements for the noninvasive assessment of mechanical stiffness of the healing tibia. J Orthop Trauma 1993;7(1):64–71.
[58] Alizad A, Walch M, Greenleaf JF, Fatemi M. Vibrational characteristics of bone fracture and fracture repair: application to excised rat femur. J Biomech Eng 2006;128(3):300–8.
[59] Lowet G, Dayuan X, van der Perre G. Study of the vibrational behaviour of a healing tibia using finite element modelling. J Biomech 1996;29(8):1003–10.
[60] Siegel M, Anast GT, Fields T. The determination of fracture healing by measurement of sound velocity across the fracture site, Surgery. Gynecol Obstetr 1958;107(3):327–32.
[61] Fellinger M, Leitgeb N, Szyszkowitz R, et al. Early detection of delayed union in lower leg fractures using a computerised analysis of mechanical vibration reactions of bone for assessing the state of fracture healing. Arch Orthop Trauma Surg 1994;113(2):93–6.
[62] Njeh CF, Kearton JR, Hans D, Boivin CM. The use of quantitative ultrasound to monitor fracture healing: a feasibility study using phantoms. Med Eng Phys 1999;20(10):781–6.
[63] Protopappas VC, Vavva MG, Fotiadis DI, Malizos KN. Ultrasonic monitoring of bone fracture healing. Ultrasonics Ferroelectr Freq Control 2008;55(June (6)):1243–55.
[64] Bostrom MP. Expression of bone morphogenetic proteins in fracture healing. Clin Orthop 1998;355(supplement):S116–23.
[65] Cox G, Einhorn TA, Tzioupis C, Giannoudis PV. Bone-turnover markers in fracture healing. Bone Joint J 2010;92(3):329–34.
[66] Einhorn TA. The cell and molecular biology of fracture healing. Clin Orthop 1999;355(supplement):S7–S21.
[67] Hoesel LM, Wehr U, Rambeck WA, Schnettler R, Heiss C. Biochemical bone markers are useful to monitor fracture repair. Clin Orthop 2005;440:226–32.
[68] Moghaddam A, Müller U, Roth HJ, Wentzensen A, Grützner PA, Zimmermann G. TRACP 5b and CTX as osteological markers of delayed fracture healing. Injury 2011;42(8):758–64.
[69] Joyce ME, Jingushi S, Bolander ME. Transforming growth factor-β in the regulation of fracture repair. Orthop Clin North Am 1990;21(1):199–209.
[70] Barnes GL, Kostenuik PJ, Gerstenfeld LC, Einhorn TA. Growth factor regulation of fracture repair. J Bone Miner Res 1999;14(11):1805–15.
[71] Lind M, Schumacker B, Soballe K, Keller J, Melsen F, Bunger C. Transforming growth factor-β enhances fracture healing in rabbit tibiae. Acta Orthop Scand 1993;64(5):553–6.
[72] Wildemann B, Schmidmaier G, Ordel S, Stange R, Haas NP, Raschke M. Cell proliferation and differentiation during fracture healing are influenced by locally applied IGF-I and TGF-beta1: comparison of two proliferation markers, PCNA and BrdU. J Biomed Mater Res B: Appl Biomater 2003;65(1):150–6.
[73] Joyce ME, Roberts AB, Sporn MB, Bolander ME. Transforming growth factor-beta and the initiation of chondrogenesis and osteogenesis in the rat femur. J Cell Biol 1990;110(6):2195–207.
[74] Si Y, Jin L, Yang GL Tipoe, White FH. Expression of BMP-2 and TGF-β1 mRNA during healing of the rabbit mandible. Eur J Oral Sci 1997;105(4):325–30.
[75] Schmidmaier G, Wildemann B, Heeger J, et al. Improvement of fracture healing by systemic administration of growth hormone and local application of insulin-like growth factor-1 and transforming growth factor-β1. Bone 2002;31(1):165–72.
[76] Zimmermann G, Henle P, Küsswetter M, et al. TGF-ü1 as a marker of delayed fracture healing. Bone 2005;36(5):779–85.
[77] Sarahrudi K, Thomas A, Mousavi M, et al. Elevated transforming growth factor-beta 1 (TGF-β1) levels in human fracture healing. Injury 2011;42(8):833–7.
[78] Stoffel K, Engler H, Kuster M, Riesen W. Changes in biochemical markers after lower limb fractures. Clin Chem 2007;53(1):131–4.
[79] Kurdy NMG. Serology of abnormal fracture healing: the role of PIIINP, PICP, and BsALP. J Orthop Trauma 2000;14(1):48–53.
[80] Hankenson, et al. Biological perspectives of delayed fracture healing. Injury 2014;45(02):S8–S15.
[81] Sousa, et al. Bone turnover markers for early detection of fracture healing disturbances: a review of the scientific literature. Ann Braz Acad Sci 2015;87(2):1049–61.
[82] Ajai, et al. Evaluation of serum alkaline phosphatase as a biomarker of healing process progression of simple diaphyseal fractures in adult patients. Int Res J Biol Sci 2013;2(February (2)):40–3.
[83] Sarahrudi K, et al. Strongly enhanced levels of sclerostin during human fracture healing. J Orthop Res 2012;(October):1549–55.
[84] Kaiser G, Thomas A, Kottstorfer J, Kecht M, Sarahrudi K. Is the expression of transforming growth factor-Beta1 after fracture of long bones solely influenced by the healing process? Int Orthop 2012;36(10):2173–9.
[85] Köttstorfer J, Kaiser G, Thomas A, et al. The influence of non-osteogenic factors on the expression of M-CSF and VEGF during fracture healing. Injury 2013;44(7):930–4.
[86] Pountos I, Georgouli T, Pneumaticos S, Giannoudis PV. Fracture non-union: can biomarkers predict outcome? Injury 2013;44(12):1725–32.
[87] (a) Bhandari M, Chiavaras M, Ayeni O, et al. Assessment of radiographic fracture healing in patients with operatively treated femoral neck fractures. J Orthop Trauma 2013;27(9):e213–9;
(b) Govender S, Csimma C, Genant HK, et al. Recombinant human bone morphogenetic protein-2 for treatment of open tibial fractures a prospective, controlled, randomized study of four hundred and fifty patients. J Bone Joint Surg A 2002;84(12):2123–34.
[88] Webb J, Herling G, Gardner T, Kenwright J, Simpson AHRW. Manual assessment of fracture stiffness. Injury 1996;27(5):319–20.
[89] Hammer R, Norrbom H. Evaluation of fracture stability: a mechanical simulator for assessment of clinical judgement. Acta Orthop Scand 1984;55(3):330–3.
[90] Theis JC. Clinical priority criteria in orthopaedics: a validation study using the SF36 quality of life questionnaire. Health Serv Manage Res 2004;17(1):59–61.
[91] McHorney CA, Ware Jr. JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31(3):247–63.
[92] Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand). The Upper Extremity Collaborative Group (UECG). Am J Ind Med 1996;29(6):602–8.
[93] Bellamy N. WOMAC: a 20-year experiential review of a patient-centered self-reported health status questionnaire. J Rheumatol 2002;29(12):2473–6.
[94] Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol 2010;30(November (11)):1179–94.
[95] Hung M, Clegg DO, Greene T, Saltzman CL. Evaluation of the PROMIS physical function item bank in orthopaedic patients. J Orthop Res 2011;29(June (6)):947–53.
[96] Squyer ER, Dikos GD, Kaehr DM, Maar DC, Crichlow RJ. Early prediction of tibial and femoral fracture healing: are we reliable? Injury 2016;47(December (12)):2805–8.
[97] Lange M, Brandt D, Mittlmeier T, Gradl G. Proximal humeral fractures: non-operative treatment versus intramedullary nailing in 2-, 3- and 4-part fractures. Injury 2016;477(December):S14–9.
[98] Kim SM, Oh SM, Cho CH, Lim SJ, Moon YW, Choi SH, et al. Fate of subchondral fatigue fractures of femoral head in young adults differs from general outcome of fracture healing. Injury 2016;47(December (12)):2789–94.
[99] Giannoudis PV, Gudipati S, Harwood P, Kanakaris NK. Long bone non-unions treated with the diamond concept: a case series of 64 patients. Injury 2015;46(Suppl 8):S48–54.
[100] Dallari D, Rani N, Sabbioni G, Mazzotta A, Cenacchi A, Savarino L. Radiological assessment of the PRF/BMSC efficacy in the treatment of aseptic nonunions: a retrospective study on 90 subjects. Injury 2016;47(November (11)):2544–50.
[101] Giannoudis PV, Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury 2016;47(Suppl. 6):S53–61.
[102] Scholtes A, Terwee CB, Poolman RW. What makes a measurement instrument valid and reliable? Injury 2011;42(3):236–40.
[103] Vannabouathong C, Sprague S, Bhandari M. Guidelines for fracture healing assessments in clinical trials. Part I: definitions and endpoint committees. Injury 2011;42(3):314–6.

Injury, Int. J. Care Injured 48S (2017) S76–S81

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Treatment of aseptic non-union after intramedullary nailing without removal of the nail

Christos Garnavos

Orthopaedic Department of "Evangelismos" General Hospital, 45 Ipsilantou St, Athens 10676, Greece

ARTICLE INFO

Keywords:
Non-union
Delayed union
Intramedullary nailing
Long bone fracture
Without nail removal
Nail retention
Ultrasound/electrical stimulation
Nail dynamisation
Biological stimulation
Augmentation plating

ABSTRACT

Failure of bone healing after intramedullary nailing of a diaphyseal long bone fracture is a severe complication that requires an effective management to ensure the best chances for successful bone-union and termination of a long period of incapacity and morbidity for the sufferers. Traditional procedures require removal of the existing nail and re-fixation with wider nail, plate or external fixation constructs. The concept that bone union can be obtained with the existing nail in situ is gaining popularity as its removal adds trauma and potential complications and prolongs the operating time. This article reviews all techniques that have been proposed for the management of aseptic diaphyseal long bone non-unions that stimulate bone healing without removing the existing nail.

Introduction

Uncomplicated diaphyseal fractures of the femur and tibia are universally treated with closed, locked intramedullary nailing that offers high healing rates and fewer complications if compared with other treatment methods [1,2]. Intramedullary nailing is less popular for the management of diaphyseal humeral fractures. However, whenever surgery is indicated, for a humeral shaft fracture the technique is gaining popularity among the orthopaedic surgeons over the last decades [3,4].

Aseptic non-union is a severe complication that can occur after the management of a long bone fracture with intramedullary nailing. It ranges from 0% to 12.5% in the femur and tibia while it happens more frequently in the humerus (10–15%) [2,5–9].

Several techniques have been described for the management of non-union that occurs after intramedullary nailing. Most frequently, the existing nail is removed and the non-united site is either re-reamed and re-nailed or fixed with plate or external fixation devices [10–14].

Despite the logical thinking that in the event of non-union the implant that has been initially used should be removed and replaced, the idea to retain the intramedullary nail and seek for adjuncts that will re-activate the healing process and avoid the, sometimes cumbersome, removal of the nail, appears equally attractive. As it is generally accepted that most diaphyseal long bone aseptic non-unions occur either due to insufficient biological environment (atrophic non-union) or due to instability (hypertrophic non-union), it has been proposed that these non-unions could be treated either with the provision of suitable biological stimulus or by adding stability or both without removing the existing nail and thus reducing surgical trauma, operating time and complications. With common denominator the maintenance of the initially implanted intramedullary nail, proposed techniques include the use of electrostimulation or pulsed low-intensity ultrasound, dynamisation of the nail, use of external fixation over the existing nail, infusion of biological stimulus in the non-union site, and augmentation plating [15–23]. The aim of this article is to review the treatment methods that have been proposed for the management of diaphyseal long bone non-unions that occur after intramedullary nailing and do not require removal of the nail.

Ultrasound stimulation

On 1983 Duarte published the first report about the use of Low Intensity Pulsed Ultrasound System (LIPUS) for stimulating bone osteogenesis in animals [24]. Since then there have been several studies investigating the usefulness of ultrasound stimulation in the management of aseptic delayed unions and non-unions in humans with variable success. In a review published on 2008, Romano et al. reported that the stimulation of delayed-unions or non-unions through LIPUS had a healing rate from 70 to 93% in different non-randomised studies [25]. The authors mentioned that the advantages of ultrasound stimulation include the avoidance of additional complex operations for the treatment of non-unions, efficacy, safety, ease of use and favorable cost/benefit

E-mail address: cgarn@otenet.gr (C. Garnavos).

http://dx.doi.org/10.1016/j.injury.2017.04.022
0020-1383/

ratio. However, it was recognised that the use of ultrasound stimulation for the treatment of delayed-unions and non-unions has a long healing time, there was lack of randomised controlled studies and the correct indications for the effective application of the method were not broad. The final guidance of the National Institute of Clinical Excellence (NICE) in the United Kingdom regarding the use of EXOGEN ultrasound bone healing system for the management of non-unions or delayed healing of fractures concluded that although there is some radiological evidence that supports the use of the system in fractures with delayed healing, there were substantial uncertainties about the effectiveness of the system between 3 and 9 months after fracture. These uncertainties result in a range of cost consequences, some cost saving and others that are more costly than current management [26]. In a more recent review by Ebrahim et al. it was concluded that the evidence regarding the usefulness of ultrasound stimulation in delayed union and non-union is extremely weak, inconclusive and insufficient to support its use and the authors proposed that large trials with safeguards against bias are required to clarify the role of ultrasound stimulation in non-union populations [27]. The lack of substantive recent studies investigating the usefulness of ultrasound stimulation for the management of aseptic delayed-unions and non-unions generates skepticism about the effectiveness of the method, bearing in mind the increasing popularity of alternative approaches which offer more predictable results.

Electrostimulation

Electrostimulation does not require removal of the implant that has been used for the fixation of a fracture and has been tried in the management of aseptic non-unions of long bone fractures since the late seventies [28]. Following initial reports, significant research has been carried out about the efficacy of electromagnetic stimulation to promote bone healing in delayed unions and non-unions. Recently, Mollon et al. and Griffin et al. reviewed the relevant published data in order to investigate the evidence regarding the effectiveness of electromagnetic stimulation in the management of non-unions of long bone fractures [29,30]. Both reviews concluded that although the available evidence suggests that electromagnetic field stimulation may offer some benefit in the treatment of aseptic delayed union and non-union of long bone fractures, it is inconclusive and insufficient to inform current practice and proposed further well-conducted randomised controlled trials.

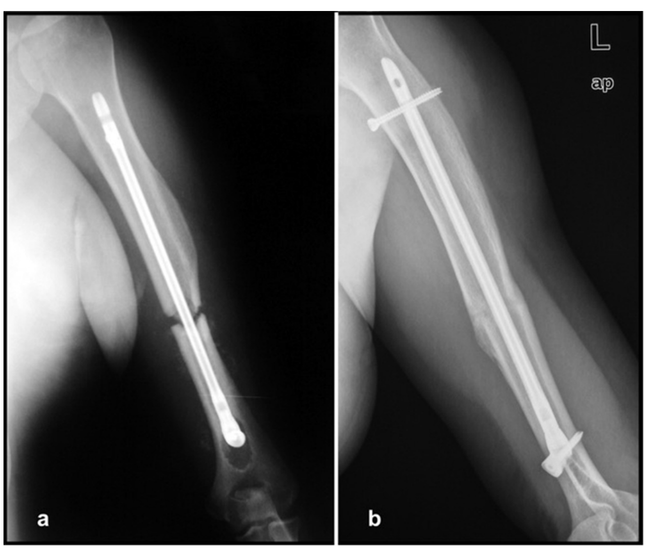


Fig. 1. a. A diaphyseal humeral fracture treated initially with retrograde intramedullary nailing 4 months after fixation (delayed-union stage), just before the percutaneous infusion of concentrated bone marrow. b. Complete bone healing one year later.

Dynamisation of the nail

Dynamisation of the nail is the procedure where the surgeon converts the mode of stabilisation of an intramedullary nail from static to dynamic by removing the proximal or distal statically locked screws. In this way, axial forces generated by weight bearing, compress the ununited fracture site and promote bone union [31,32]. Although the technique is minimally invasive and popular between orthopaedic surgeons, there are limited data that support its use. Regarding the management of aseptic femoral non-unions, Wu reported 10 cases of persisting non-union after dynamising 24 nails in ununited femoral fractures while Pihlajamäki et al. experienced four cases of persisting non-union after dynamising seventeen nails in un-united femoral fractures [5,33]. Furthermore, both studies stressed that dynamisation of the nail predisposed to marked shortening of the bone with the highly comminuted or oblique fractures being in higher risk of developing this complication and suggested that dynamization should be preserved for patients without segmental bony defects.

Recently, Litrenta et al. studied 88 patients who underwent dynamisation of the nail for the treatment of aseptic tibial non-union, comparing their results with 91 patients who also suffered an ununited tibial fracture and underwent exchange nailing [34]. They reported 83% and 90% respectively union rates for the two groups and concluded that non-unions of fractures with no cortical contact or with a “gap” or comminution should not be considered

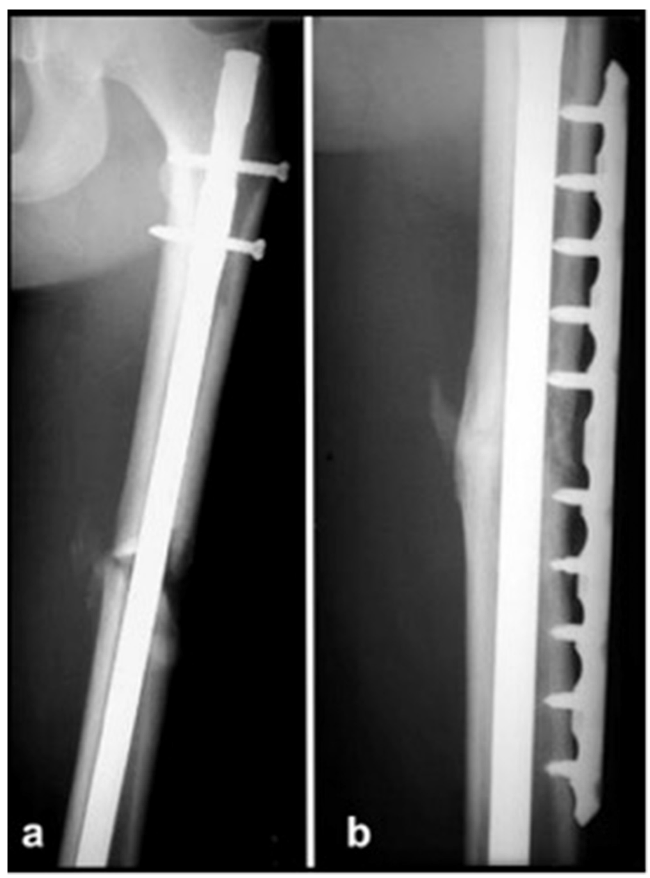


Fig. 2. a. Non-united diaphyseal femoral fracture, 8 months after fixation with static intramedullary nailing. b. Augmentation plating and sound union 10 months later. (Case provided by Prof. P. Megas, University of Patras, Greece).

good candidates for dynamisation. Yang et al. suggested that experienced orthopaedic trauma surgeons could predict the increased probability of a fracture not to unite at about 3 months from injury, using as parameters the mechanism of injury and consecutive x-rays [35]. Such prediction could permit early decision regarding the dynamisation of a femoral or tibial nail at the delayed-union stage and prohibit the development of non-union on the grounds of a non-comminuted or complex fracture. Based on personal experience and limited bibliographic data, it could be proposed that dynamisation of a nail has limited role in the management of established diaphyseal femoral and tibial non-unions. Likewise, dynamisation should not be used in non-united humeral shaft fractures, as the humerus is a non-weight bearing bone and dynamisation cannot be applied effectively in a long bone of the upper limb.

External fixation over the existing nail

In 2002 Menon et al. presented their positive experience with the use of Ilizarov external Fixation for the treatment of non-united diaphyseal fractures of the femur tibia and humerus while leaving the intramedullary nail in situ [14]. Up to now, there have been few reports about this technique [20,22,36]. All involved small number of selected “difficult” cases, with common characteristic the high success rate in achieving bone union. Other advantages include the minimal invasiveness and lack of necessity for bone grafting. However, it is unanimously recognised that applying an external fixation construct with the intramedullary nail in situ is a demanding procedure. Nevertheless, the retention of the nail maintains and secures alignment (especially if lengthening is also performed for the management of bone defects) and increases mechanical stability, which allows weight bearing throughout the course of treatment. It also allows the use of simpler frame constructs with less number of wires and pins, and earlier removal of the external fixator. Drawbacks of the technique include frequent poor patient compliance, risk for pin related complications and joint stiffness.

Biological stimulation

The value of the biological stimulation for the treatment of aseptic non-unions of fractures has been recognised since many years, especially after the classic works of Phemister and Urist [37,38]. However, in the past, infusion of biological stimulus (mainly in the form of autologous bone graft) has been constantly used in conjunction with additional interventions, such as internal or external fixation of the non-union site or revision of pre-existing implants. On 2007 Bhargava et al. reported the succesful treatment of 2 femoral shaft non-unions with percoutaneous injection of bone marrow without removing the pre-existing nail [39]. Shortly afterwards, Giannoudis et al. reported the successful treatment of one humeral and three tibial diaphyseal non-unions, without removing the pre-existing nail, by infusing autologous bone graft mixed with BMP-7 in the non-united site [40].

Concentrated bone marrow aspirate that can be obtained and administered percoutaneously, seems to be an attractive alternative to more invasive techniques used for the management of atrophic diaphyseal non-union that has been previously treated with intramedullary nailing. Fig. 1 Unfortunately, in some studies, where biological stimulus is used for the treatment of non-unions, there is limited information regarding important parameters that could be useful for assessing the efficacy of the method in specific sub-groups of patients who have suffered the non-union. Desai et al., treated 49 patients with femoral, tibial and humeral non-union by injecting bone marrow aspirate concentrates mixed with demineralized bone matrix (DBM) and/or recombinant human

Table 1
Articles reporting treatment of aseptic long bone non-unions with Augmentation Plating

Article	Bone	Pts	Treatment Details	Union Rate (%)	Time to Union (months)
Ueng et al. [49]	F	17	AP and ABG in 7 cases	100	7.0
Gerber et al. [50]	H	6	Augmentation wave-plating and ABG	100	4.0
Choi & Kim, [51]	F	15	AP with ABG	100	7.2
Nadkarni et al. [17]	F (7) T (2) H (2)	11	AP and ABG	100	6.2
Birjandinejad et al. [18]	F(25) T(13)	38	AP and ABG when > 1 cm of bony defect existed between segments or < 50% of bony contact	94.7 (F 25) (T 11)	4.78
Chen et al. [52]	F	50	Debridement, decortication, AP and ABG	100	6.0
Gao et al. [53]	F	13	Debridement, AP and ABG	100	7.5
Hakeos et al. [54]	F	7	Nail dynamisation, compression via the plate or tensioning device, re-lock the nail, AP with ABG,	100	5.0
Said et al. [55]	F	14	AP with compression and ABG in 9 cases	100	4.3
Lin et al. [56]	F	22	Decortication, AP with ABG	100	5.5
Ye & Zheng. [57]	F (4) T (2)	6	AP with ABG	100	4.5
Khanfour & Zakzouk. [58]	F	11	AP with ABG	100	7.5
Ateschrang et al. [59]	T	28	Nail dynamisation and AP without ABG	96.4 (27/28)	5.0
Park & Yang. [60]	F	39	Decortication, AP with ABG	97 (38/39)	6.1
Jhunjhunwala & Dhawale. [61]	F	40	Nail dynamisation and AP. ABG in atrophic nonunions ons	97.5 (39/40)	4.0
Chiang et al. [62]	F	30	Nail dynamisation and AP. ABG in 17 cases, BMPs in 19 cases (both in 14 cases)	96.6 (29/30)	4.3
Gessmann et al. [63]	H	37	Debridement, decortication, AP, nail dynamisation in 3 cases, ABG in 34 cases	97 (36/37)	6.0

Abbreviations: Pts = patients, F = Femur, T = Tibia, H = Humerus, AP = Augmentation, Plating, ABG = Autologous Bone Graft, BMPs = Bone Morphogenetic Proteins.

bone morphogenetic protein-2 (BMP-2) and they reported an overall 79.6% healing rate [41]. Although all patients had undergone previous surgical fixation of their fractures, there is no information about either the method of fixation or the maintenance/revision of the fixation at the time of grafting. However, one of the two illustrated examples that demonstrate the efficacy of the technique refers to the management of a diaphyseal tibial non-united fracture, without removal of the existing nail. Likewise, Sugaya et al. treated successfully 6 out of 7 patients with femoral and tibial non-unions, who had previously undergone intramedullary nailing, with percoutaneous bone marrow grafting, depicting that the nail was not removed or exchanged [42]. While the maintenance/removal of the initially inserted nail is not defined, Guimaraes et al., treated successfully eight out of sixteen atrophic femoral diaphyseal non-unions with percutaneous concentrated autologous bone marrow grafting [43]. The authors focus on the aspiration technique and the concentration process as being of paramount importance to increase the incidence of a successful outcome. They concluded that the efficacy of percutaneous autologous concentrated bone marrow grafting technique seems to be predominantly related to the number of osteoprogenitors available in the aspirate. Another parameter that may play important role in the efficacy of the biological stimulation technique is the timing of the grafting procedure. Le Nail et al., performed percoutaneous grafting with autologous concentrated bone marrow aspirate in 39 previously open fractures, that were delaying to unite or were not united, 8 of which had been initially treated with intramedullary nailing [44]. While the authors reported that they did not proceed to any additional surgical procedure at the time of grafting, depicting that the existing intramedullary nails were not removed, the result was successful in 23 cases (53.5%). Unfortunately, there is no information about the success of the procedure specifically in the patients who had undergone intramedullary nailing. However, the authors focused in the effect of timing from injury to the final outcome and they concluded that bone marrow autologous concentrate procedure has better results if performed at a later timing (more than 110 days) from the accident. Contradictory were the conclusions of Gross et al., who treated a cohort of 45 cases with autologous bone marrow injection for atrophic diaphyseal non-union [45]. While the initial operative procedures are not clearly defined, it is mentioned that one patient underwent dynamisation of a pre-existing nail at the timing of grafting and thus it can be depicted that there was at least one case of intramedullary nailing that was left in situ. The authors found a negative co-relation between the time elapsed before the grafting procedure and the healing rate of the non-union and thus recommended an earlier intervention. Furthermore, they investigated the effect of the quality of the grafting material and found that the number of CFU-F (Colony Forming Unit Fibroblastic) affected the healing time more than the healing rate.

The treatment of atrophic diaphyseal non-unions with the use of biological stimulus seems gaining popularity. Most authors agree that autologous bone graft or concentrated bone marrow aspirate should be used and that the intervention should be done early (if possible at the “delayed-union” stage) [41–48]. The anticipation that a good outcome can be obtained without removing a pre-existing implant, such as a nail, offers an attractive alternative, as the intervention is kept minimal with little or no compromise on the stability of the fixation. However, other interventions and parameters should be investigated, such as the necessity for nail dynamisation or the size of the fracture gap that can be “grafted” with substantial chances for success. Furthermore, the response to the treatment of each specific long bone or of the fracture location within the same long bone in relation to various important conditions (e.g. closed or open fractures) remains to be defined.

Augmentation plating

On 1997 Ueng et al. recognised that non-union that occurs in cases of diaphyseal femoral fractures treated with intramedullary nailing may be due to residual instability [49]. The authors applied an “augmentative” plate in 17 non-united femoral fractures that were primarily treated with intramedullary nailing, without removing the nail, aiming to increase the stability of fracture fixation. The authors reported that all non-unions healed at a mean time of 7 months without complications and concluded that a plate together with the retained intramedullary nail provides strong mechanical environment and optimal healing rate, allowing full weight bearing and vigorous rehabilitation immediately after the operation.

This approach uses the load-sharing capacity of the nail with good axial and bending strength, while the plate provides additional rotational control, as it is believed that rotational instability is the main cause for the non-unions of the diaphyseal long bone fractures. Fig. 2 Since the initial description, many surgeons adopted the technique and there have been several

Table 2
Studies comparing Augmentation Plating with other techniques for the treatment of aseptic long bone non-unions.

Article	Bone	Comparison Study Details	Union	Result / Comments
Park et al. [64]	F	- 7pts treated with EN - 11pts treated with AP and autologous bone graft	EN 2/7 AP 11/11	AP with autogenous bone grafting may be better option for nonisthmal femoral non-unions, especially when a bone defect exists
Ateschrang et al. [65]	T	- 25pts treated with EN - 23pts treated with nail dynamisation and AP	EN 24/25 AP 22/23	Both safe and straightforward surgical procedures with equivalent high success rates of union. AP has shorter operating time and less time for union but requires an additional incision and sometimes necessitate removal of the plate
Jiang et al. [66]	F	- 15pts treated with nail removal and Plating [EP] - 12pts treated with nail dynamisation and AP	EP 15/15 AP 12/12	AP is better than EP in terms of union time, operation time, bleeding and return to activities.
Ru et al. [67]	F	- 87pts treated with EN - 93pts treated with AP and autologous bone graft	EN 75/87 AP 93/93	AP obtains a higher bone union rate and shorter time to union than EN

Abbreviations: Pts = patients, F = Femur, T = Tibia, AP = Augmentation Plating, EN = Exchange Nailing, EP = Exchange Plating.

reports, with common denominator the high efficacy of the technique in the management of diaphyseal aseptic non-unions of the femur, tibia and humerus (Table 1).

To verify the usefulness of the technique for the management of long bone diaphyseal aseptic non-unions, comparison studies have been recently conducted. Three compared augmentation plating with exchange nailing and one compared augmentation plating with plating after removal of the nail (exchange plating) (Table 2)

All four studies concluded that augmentation plating provides the best results, regarding the non-union healing, the operating time and the faster return to previous activities. However, Ateschrang et al. stress that the technique has drawbacks such as the additional incision and the patients' complains that often necessitate the removal of the plate [50].

Conclusions

Based on the best available evidence, it can be concluded that the value of Ultrasound and/or Electromagnetic stimulation, as sole therapeutic tools, is declining and should be considered as subsidiary methods for the management of aseptic long bone non-unions that occur after intramedullary nailing. Dynamisation of the nail can be a good treatment option, if performed early (preferably at the "delayed union" stage), with significant advantage the minimal invasiveness of the technique. External fixation over the existing nail can provide good healing rates, however the technique is demanding and cumbersome for the patients and should be reserved for difficult or persisting cases with deformity that could be corrected with the use of external fixation constructs. Infusion of biological stimulus (usually concentrated bone marrow) within the non-union site, with the nail in situ, has shown to be a good alternative. The method is minimally invasive, as both the aspiration and the infusion of the biological stimulus can be done percutanously. However, there is evidence that the effectiveness of the technique is better if performed at an earlier rather that at a later stage. Additionally, it could be proposed that if an open approach is required for the application of a bulky graft material, the addition of an augmentation plate should be considered.

As it has been generally accepted that the long bone diaphyseal non-union after intramedullary nailing occurs usually due to instability, it can be anticipated that should be treated with provision of additional stability, which is easier to achieve with the addition of a plate (augmentation plating). The method can be used in conjunction with dynamisation of the existing nail, prior to the application of the plate and/or application of bone graft or other biological stimuli at the non-union site and thus enhance the healing rates. Bearing in mind the best available evidence, it can be concluded that, in the presence of an intramedullary nail, augmentation plating provides the best healing rates and should be highly considered for the management of long bone aseptic non-union that happens after intramedullary nailing.

References

[1] Ricci WM, Gallagher B, Haidukewych GJ. Intramedullary nailing of femoral shaft fractures: current concepts. J Am Acad Orthop Surg 2009;17(May (5)):296–305.
[2] Lambiris E, Tyllianakis M, Megas P, Panagiotopoulos E. Intramedullary nailing: experience in 427 patients. Bull Hosp Jt Dis 1996;55(1):25–7.
[3] Garnavos C. Diaphyseal humeral fractures and intramedullary nailing: can we improve outcomes? Indian J Orthop 2011;45(May (3)):208–15.
[4] Rommens PM, Kuechle R, Bord T, Lewens T, Engelmann R, Blum J. Humeral nailing revisited. Injury 2008;39(December (12)):1319–28.
[5] Pihlajamaki HK, Salminen ST, Bostman OM. The treatment of nonunions following intramedullary nailing of femoral shaft fractures. J Orthop Trauma 2002;16(July (6)):394–402.
[6] Wu CC. Exchange nailing for aseptic nonunion of femoral shaft: a retrospective cohort study for effect of reaming size. J Trauma 2007;63(October (4)):859–65.
[7] Brinker MR, O'Connor DP. Exchange nailing of ununited fractures. J Bone Joint Surg Am 2007;89(January (1)):177–88.
[8] Liu GD, Zhang QG, Ou S, Zhou LS, Fei J, Chen HW, et al. Meta-analysis of the outcomes of intramedullary nailing and plate fixation of humeral shaft fractures. Int J Surg 2013;11(9):864–8.
[9] Garnavos C, Lasanianos N, Kanakaris NK, Arnaoutoglou C, Papathanasopoulou V, Xenakis T. A new modular nail for the diaphyseal fractures of the humerus. Injury 2009;40(June (6)):604–10.
[10] Zelle BA, Gruen GS, Klatt B, Haemmerle MJ, Rosenblum WJ, Prayson MJ. Exchange reamed nailing for aseptic nonunion of the tibia. J Trauma 2004;57 (November (5)):1053–9.
[11] Court-Brown CM, Keating JF, Christie J, McQueen MM. Exchange intramedullary nailing. Its use in aseptic tibial nonunion. J Bone Joint Surg Br 1995;77(May (3)):407–11.
[12] Babhulkar S, Pande K. Nonunion of the diaphysis of long bones. Clin Orthop Relat Res Feb 2005;431:50–6.
[13] Rodriguez-Merchan EC, Gomez-Castresana F. Internal fixation of nonunions. Clin Orthop Relat Res 2004;(February (419)):13–20.
[14] Menon DK, Dougall TW, Pool RD, Simonis RB. Augmentative Ilizarov external fixation after failure of diaphyseal union with intramedullary nailing. J Orthop Trauma 2002;16(August (7)):491–7.
[15] Brighton CT, Black J, Friedenberg ZB, Esterhai JL, Day LJ, Connolly JF. A multicenter study of the treatment of non-union with constant direct current. J Bone Joint Surg Am 1981;63(January (1)):2–13.
[16] Frankel VH, Mizuho K. Management of non-union with pulsed low-intensity ultrasound therapy?international results. Surg Technol Int 2002;(September (10)):195–200.
[17] Nadkarni B, Srivastav S, Mittal V, Agarwal S. Use of locking compression plates for long bone nonunions without removing existing intramedullary nail: review of literature and our experience. J Trauma 2008;65(August (2)):482–6.
[18] Birjandinejad A, Ebrahimzadeh MH, Ahmadzadeh-Chabock H. Augmentation plate fixation for the treatment of femoral and tibial nonunion after intramedullary nailing. Orthopedics 2009;32(June (6)):409.
[19] Ueng SW, Liu HT, Wang IC. Augmentation plate fixation for the management of tibial nonunion after intramedullary nailing. J Trauma 2002;53(September (3)):588–92.
[20] Brinker MR, O'Connor DP. Ilizarov compression over a nail for aseptic femoral nonunions that have failed exchange nailing: a report of five cases. J Orthop Trauma 2003;17(November–December (10)):668–76.
[21] Taylor KF, McHale KA. Ilizarov external fixation salvage of failed intramedullary fixation of tibia with nail retention. Am J Orthop (Belle Mead NJ) 2004;33(September (9)):461–7.
[22] Patel VR, Menon DK, Pool RD, Simonis RB. Nonunion of the humerus after failure of surgical treatment: management using the Ilizarov circular fixator. J Bone Joint Surg Br 2000;82(September (7)):977–83.
[23] Garnavos C, Mouzopoulos G, Morakis E. Fixed intramedullary nailing and percutaneous autologous concentrated bone-marrow grafting can promote bone healing in humeral-shaft fractures with delayed union. Injury 2010;41 (June (6)):563–7.
[24] Duarte LR. The stimulation of bone growth by ultrasound. Arch Orthop Trauma Surg 1983;101(3):153–9.
[25] Romano CL, Romano D, Logoluso N. Low-intensity pulsed ultrasound for the treatment of bone delayed union or nonunion: a review. Ultrasound Med Biol 2009;35(April (4)):529–36.
[26] Higgins A, Glover M, Yang Y, Bayliss S, Meads C, Lord J. EXOGEN ultrasound bone healing system for long bone fractures with non-union or delayed healing: a NICE medical technology guidance. Appl Health Econ Health Policy 2014;12(October (5)):477–84.
[27] Ebrahim S, Mollon B, Bance S, Busse JW, Bhandari M. Low-intensity pulsed ultrasonography versus electrical stimulation for fracture healing: a systematic review and network meta-analysis. Can J Surg 2014;57(June (3)): E105–18.
[28] Bassett CA, Mitchell SN, Norton L, Pilla A. Repair of non-unions by pulsing electromagnetic fields. Acta Orthop Belg 1978;44(September–October (5)):706–24.
[29] Mollon B, da Silva V, Busse JW, Einhorn TA, Bhandari M. Electrical stimulation for long-bone fracture-healing: a meta-analysis of randomized controlled trials. J Bone Joint Surg Am 2008;90(November (11)):2322–30.
[30] Griffin XL, Costa ML, Parsons N, Smith N. Electromagnetic field stimulation for treating delayed union or non-union of long bone fractures in adults. Cochrane Database Syst Rev 20114: CD008471.
[31] Wu CC, Shih CH. A small effect of weight bearing in promoting fracture healing. Arch Orthop Trauma Surg 1992;112(1):28–32.
[32] Yokota H, Tanaka SM. Osteogenic potentials with joint-loading modality. J Bone Miner Metab 2005;23(4):302–8.
[33] Wu CC. The effect of dynamization on slowing the healing of femur shaft fractures after interlocking nailing. J Trauma 1997;43(August (2)):263–7.
[34] Litrenta J, Tornetta 3rd P, Vallier H, Firoozabadi R, Leighton R, Egol K, et al. Dynamizations and exchanges: success rates and indications. J Orthop Trauma 2015;29(December (12)):569–73.
[35] Yang JS, Otero J, McAndrew CM, Ricci WM, Gardner MJ. Can tibial nonunion be predicted at 3 months after intramedullary nailing? J Orthop Trauma 2013;27 (November (11)):599–603.
[36] Azzam W, El-Sayed M. Ilizarov distraction osteogenesis over the preexisting nail for treatment of nonunited femurs with significant shortening. Eur J Orthop Surg Traumatol 2016(January (25)).

[37] Phemister DB. Treatment of ununited fractures by onlay bone grafts without screw or tie fixation and without breaking down of the fibrous union. J Bone Joint Surg Am 1947;29(October (4)):946–60.
[38] Urist MR. Bone: formation by autoinduction. Science 1965;150(November (3698)):893–9.
[39] Bhargava R, Sankhla S, Gupta A, Changani R, Gagal K. Percutaneous autologus bone marrow injection in the treatment of delayed or nonunion. Indian J Orthop 2007;41(January (1)):67–71.
[40] Giannoudis PV, Kanakaris NK, Dimitriou R, Gill I, Kolimarala V, Montgomery RJ. The synergistic effect of autograft and BMP-7 in the treatment of atrophic nonunions. Clin Orthop Relat Res 2009;467(December (12)):3239–48.
[41] Desai P, Hasan SM, Zambrana L, Hegde V, Saleh A, Cohn MR, et al. Bone mesenchymal stem cells with growth factors successfully treat nonunions and delayed unions. HSS J 2015;11(July (2)):104–11.
[42] Sugaya H, Mishima H, Aoto K, Li M, Shimizu Y, Yoshioka T, et al. Percutaneous autologous concentrated bone marrow grafting in the treatment for nonunion. Eur J Orthop Surg Traumatol 2014;24(July (5)):671–8.
[43] Guimaraes JA, Duarte ME, Fernandes MB, Vianna VF, Rocha TH, Bonfim DC, et al. The effect of autologous concentrated bone-marrow grafting on the healing of femoral shaft non-unions after locked intramedullary nailing. Injury 2014;(November (45))S7–S13 Suppl 5.
[44] Le Nail LR, Stanovici J, Fournier J, Splingard M, Domenech J, Rosset P. Percutaneous grafting with bone marrow autologous concentrate for open tibia fractures: analysis of forty three cases and literature review. Int Orthop 2014;38(September (9)):1845–53.
[45] Gross JB, Diligent J, Bensoussan D, Galois L, Stoltz JF, Mainard D. Percutaneous autologous bone marrow injection for treatment of delayed and non-union of long bone: a retrospective study of 45 cases. Biomed Mater Eng 2015;25(Suppl. 1):187–97.
[46] Flierl MA, Smith WR, Mauffrey C, Irgit K, Williams AE, Ross E, et al. Outcomes and complication rates of different bone grafting modalities in long bone fracture nonunions: a retrospective cohort study in 182 patients. J Orthop Surg Res 2013;8:33.
[47] Sen MK, Miclau T. Autologous iliac crest bone graft: should it still be the gold standard for treating nonunions? Injury 2007;(March (38))S75–80 Suppl 1.
[48] Garnavos C, Mouzopoulos G, Morakis E. Fixed intramedullary nailing and percutaneous autologous concentrated bone-marrow grafting can promote bone healing in humeral-shaft fractures with delayed union. Injury 2010;41 (June (6)):563–7.
[49] Ueng SW, Chao EK, Lee SS, Shih CH. Augmentative plate fixation for the management of femoral nonunion after intramedullary nailing. J Trauma 1997;43(October (4)):640–4.
[50] Ateschrang A, Karavalakis G, Gonser C, Liener U, Freude T, Stockle U, et al. Exchange reamed nailing compared to augmentation compression plating leaving the inserted nail in situ in the treatment of aseptic tibial non-union: a two-centre study. Wien Klin Wochenschr 2013;125(May (9–10)):244–53.
[51] Choi YS, Kim KS. Plate augmentation leaving the nail in situ and bone grafting for non-union of femoral shaft fractures. Int Orthop 2005;29:287–90.
[52] Chen CM, Su YP, Hung SH, et al. Dynamic compression plate and cancellous bone graft for aseptic non-union after intramedullary nailing of femoral fracture. Orthopedics 2010;33:393.
[53] Gao KD, Huang JH, Tao J, et al. Management of femoral diaphyseal non-union after nailing with augmentative locked plating and bone graft. Orthop Surg 2011;3:83–7.
[54] Hakeos WM, Richards JE, Obremskey WT. Plate fixation of femoral non-unions over an intramedullary nail with autogenous bone grafting. J Orthop Trauma 2011;25:84–9.
[55] Said GZ, Said HG, el-Sharkawi MM. Failed intramedullary nailing of femur: open reduction and plate augmentation with the nail in situ. Int Orthop 2011;35:1089–92.
[56] Lin CJ, Chiang CC, Wu PK, et al. Effectiveness of plate augmentation for femoral shaft non-union after nailing. J Chin Med Assoc 2012;75:396–401.
[57] Ye J, Zheng Q. Augmentative locking compression plate fixation for the management of long bone non-union after intramedullary nailing. Arch Orthop Trauma Surg 2012;132:937–40.
[58] Khanfour AA, Zakzouk SA. Distal femur non-union after interlocked intramedullary nailing. Successful augmentation with wave plate and strut graft. Acta Orthop Belg 2012;78:492–9.
[59] Ateschrang A, Albrecht D, Stockle U, et al. High success rate for augmentation compression plating leaving the nail in situ for aseptic diaphyseal tibial non-unions. J Orthop Trauma 2013;27:145–9.
[60] Park J, Yang KH. Indications and outcomes of augmentation plating with decortication and autogenous bone grafting for femoral shaft non-unions. Injury 2013;44:1820–5.
[61] Jhunjhunwala HR, Dhawale AA. Is augmentation plating an effective treatment for non-union of femoral shaft fractures with nail in situ? Eur J Trauma Emerg Surg 2015.
[62] Chiang JC, Johnson JE, Tarkin IS, et al. Plate augmentation for femoral non-union: more than just a salvage tool? Arch Orthop Trauma Surg 2016;136:149–56.
[63] Gessmann J, Konigshausen M, Coulibaly MO, et al. Anterior augmentation plating of aseptic humeral shaft non-unions after intramedullary nailing. Arch Orthop Trauma Surg 2016.
[64] Park J, Kim SG, Yoon HK, Yang KH. The treatment of nonisthmal femoral shaft non-unions with im nail exchange versus augmentation plating. J Orthop Trauma 2010;24:89–94.
[65] Ateschrang A, Karavalakis G, Gonser C, et al. Exchange reamed nailing compared to augmentation compression plating leaving the inserted nail in situ in the treatment of aseptic tibial non-union: a two-centre study. Wien Klin Wochenschr 2013;125:244–53.
[66] Jiang L, Pan Z, Zheng Q. Augmentation plating in hypertrophic non-union after nail fixation of femoral shaft fracture compared with exchange plating. Chin Med J (Engl) 2014;127:2900–5.
[67] Ru JY, Niu YF, Cong Y, et al. Exchanging reamed nailing versus augmentative compression plating with autogenous bone grafting for aseptic femoral shaft non-union: a retrospective cohort study. Acta Orthop Traumatol Turc 2015;49:668–75.

Injury, Int. J. Care Injured 48S (2017) S82–S90

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Current treatment of infected non-union after intramedullary nailing

A. Hamish Simpson*, Jerry S.T. Tsang

Department of Trauma and Orthopaedics, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, UK

ARTICLE INFO

ABSTRACT

Non-union is a devastating consequence of a fracture. Non-unions cause substantial patient morbidity with patients suffering from loss of function of the affected extremity, increased pain, and a substantial decrease in the quality of life. The management is often associated with repeated, unsuccessful operations resulting in prolonged hospital stays, which has social and economic consequences to both the patient and the healthcare system. The rates of non-union following intramedullary (IM) nailing vary according to anatomical location. There is currently no consensus regarding the treatment of infected non-unions following IM nailing, but the most common procedures reported are; exchange IM nail with antibiotic suppression or excision of the non-union, (stabilisation with external fixation or less commonly plate or IM nail) and then reconstruction of the bone defect with distraction osteogenesis or the Masquelet technique. This article explores the general principles of treatment, fixation modalities and proposes a treatment strategy for the management of infected non-unions following intramedullary nailing.

Introduction

Non-union is a devastating consequence of a fracture. Non-unions cause substantial patient morbidity [1] with patients suffering from loss of function of the affected extremity, increased pain, and a substantial decrease in the quality of life [2]. The management is often associated with repeated, unsuccessful operations resulting in prolonged hospital stays, which has social and economic consequences to both the patient and the healthcare system. Non-unions are expensive to manage, with estimates of treatment costs ranging from £7000 to £79,000 ($10,000–$114,000) per case [3–6]. Approximately 200 long bone non-union cases per annum occur per million population [7], indicating an estimated total of 150,000 in Europe each year. The rates of non-union following intramedullary (IM) nailing vary according to anatomical location [8]. The rates of tibia non-union following IM nailing vary from 0 to 4% [9] for closed fractures and increase to 36% for Gustilo and Anderson grade IIIB [10] injuries [9]. Reported rates of secondary surgery to achieve union in femoral diaphyseal fractures range from 0 to 14%, with an average of 2.4%. Even following nailing of open femoral fractures, the rates of non-union are low ranging from 0 to 4.8% [9]. The non-union rate in the humerus following IM nail fixation has been found to range from 0 to 50% [11–22]. Infection has been found to be a cause in ~30% of femoral and tibial diaphyseal non-unions following IM nailing [23,24]. The rate of infected non-unions has been found to be lower in the humerus at ~4% [13,25]. There is currently no consensus regarding the treatment of infected non-unions following IM nailing [26], but the most common procedures reported are; exchange IM nail with antibiotic suppression or excision of the non-union, (stabilisation with external fixation or less commonly plate or IM nail) and then reconstruction of the bone defect with distraction osteogenesis or the Masquelet technique.

General treatment concepts

Infected non-unions have 2 interrelated orthopaedic problems; (a) deep bone infection and (b) a failure of fracture healing. Various strategies exist, which treat:

(a) the fracture then the infection definitively, (e.g. exchange IM nailing)
(b) the infection definitively then the fracture, (e.g. excision of the non-union and secondary bone transport or Masquelet technique)
(c) both at the same time, (e.g. acute shortening)

* Corresponding author at: Department of Trauma and Orthopaedics, University of Edinburgh, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh, EH16 4SA, UK.
E-mail address: Hamish.Simpson@ed.ac.uk (A. H. Simpson).

http://dx.doi.org/10.1016/j.injury.2017.04.026
0020-1383/

(d) neither specifically (e.g. amputation)

In order to decide which strategy is best for a given patient with an intramedullary nailed fracture, that has a failure of healing associated with infection, it is important to determine whether the infection can be suppressed and the fracture healing recommenced with adjunctive treatments until union has occurred. If this is possible then a treatment programme with a shorter rehabilitation time can be offered to the patient. If this is not possible, then it will be necessary to excise the non-union.

For all 4 of the strategies above, deep tissue sampling [27] and the delivery of systemic and/or local antibiotic therapy guided by culture results is routine.

The guiding principles for the management of infected non-unions regardless of previous fixation method includes:

(i) Surgical debridement with excision/removal of necrotic and foreign material
(ii) Dead space management.
(iii) Bone stabilisation
(iv) Wound closure (direct or with soft tissue reconstruction)
(v) Reconstitution of skeletal integrity

Current controversy lies in the choice of fixation modality to achieve bone stability [26], optimal delivery of local antibiotics [28,29] and the methods required to reconstitute bone loss [30]

General considerations when formulating a treatment strategy for infected non-unions following intramedullary fixation

Host factors

The age of the patient, the presence of chronic disease (e.g. diabetes mellitus), use of medications, alcohol consumption and tobacco usage may alter the potential to eradicate the infection and for the bone defects to heal [31]. Modifiable host risk factors for non-union should be addressed in the pre-operative period [32–34].

Antibiotic therapy

Systemic antibiotic treatment may be inadequate or ineffective in patients with poorly vascularised infected tissues and osteonecrosis, which is often present in cases of osteomyelitis [28]. Moreover, the bacteria have the ability to produce a protective hydrated matrix of polysaccharide and protein, forming a slimy layer known as a biofilm. A biofilm can be further defined as an 'assemblage of microbial cells that is irreversibly associated with a surface and enclosed in a matrix of primarily polysaccharide material [35]. Internal fixation or inadequate debridement provides a nidus for bacterial adherence and biofilm formation. Bacterial biofilms play a role in the majority of recalcitrant healthcare-associated infections such as periprosthetic joint infections and chronic osteomyelitis [36]. Formation of biofilms leads to a reduction in antimicrobial susceptibility in many bacterial species, such as *Staphylococcus*. One mechanism is the failure of antimicrobial agents to penetrate the full depth of the biofilm due to the presence of an exopolysaccharide matrix. Secondly, the growth rate of bacterial cells within a biofilm is substantially reduced in comparison with planktonic cells as cells growing in biofilms are commonly nutrient depleted [37]. Reduced growth rates lead to reduced susceptibility to antimicrobials designed to target fast growing and reproductive planktonic bacterial cells. The reduced metabolic activity of bacterial cells embedded within biofilms mimic this nutrient depleted state correlating with reduced antimicrobial susceptibility. Finally, it has been hypothesised that cells present in a biofilm may induce a specific “biofilm phenotype”. This ‘biofilm phenotype’ has been likened to a spore-like state entered into by some of the bacteria resulting in reduced susceptibility to antibiotics and disinfectants. Reduced antimicrobial susceptibility to ß-lactams, quinolones and glycopeptides has been observed in biofilms formed by *S. aureus* [38]. Minimum inhibitory concentrations (MIC) required to treat sessile bacteria within biofilms have been shown to be up 800 greater than that required in the treatment of planktonic cells [39–41]. Systemic antibiotics cannot reach such high concentrations at the bone-biofilm interface site and as such can be ineffective. Certain bacteria such as mycobacteria are a particular problem in immunocompromised patients and need special antibiotic regimens [42]. A further postulated cause of recalcitrant infection is the presence of bacteria within host cells, such as osteoblasts [43]. The intracellular location of the bacteria protects them from the host immune system and from antibiotics, except for a few such as rifampicin [44].

Thus, the local delivery of antibiotics appears to be a key component of the success of the overall management of infected non-unions [29,45,46].

Bio-absorbable antibiotic delivery systems

Biodegradable carriers are seen as theoretically advantageous, because of the potential reduction in the risk of persistent or secondary infections and the need for removal of the implant. Examples include allograft bone [47], collagen fleeces [48], polyesters, polyanhidrides, amylose starch, alginates, chitosans, composite carriers [28,49] and calcium-based carriers [50,51]. They have been shown to have better drug elution profiles than PMMA [28], although methods of enhancing the release of antibiotic have been reported [52,53]. Newer composite systems also offer osteoinductive and osteoconductive properties [54]. However with a paucity of in vivo evidence their clinical effectiveness is difficult to evaluate.

Debridement of dead bone

Following intramedullary reaming and nail insertion the inner 1/3 to 2/3rds of the cortex loses perfusion because the endosteal circulation is destroyed and bone marrow blocks the intercortical canals [55–57]. There is then a reactive increase in periosteal blood flow in order to maintain circulation in the cortical bed [58,59], converting the usual centrifugal flow of arterial blood to a centripetal dominant system. However, there is likely to be a cylinder of dead bone of varying thickness surrounding the intramedullary nail, which needs to be removed. This is achieved by sequential reaming from original nail size in 0.5 mm diameter increments, until there is no fibrous membrane and no sclerotic white reaming debris. On the final reamer there should only be bony fragments with a healthy appearance. This will be approximately 1–2 mm greater than the largest reamer used previously. More recently the Reamer Irrigator Aspirator (RIA) system has been used to perform this intramedullary debridement [60].

As the remaining cortex is entirely dependent on the periosteum for its survival it is crucial to preserve the periosteal blood flow. In canine and lapine tibia studies [61], after 4–6 weeks the endosteal blood vessels were shown to have reformed, however in these early stages after intramedullary reaming it is vital to avoid any stripping of the remaining periosteum, such as might occur during plating or injudicious simultaneous open debridement.

Reconstitution of bone

It is important to consider the bone loss following debridement by its anatomical location in the bone and the extent of the defect in terms of the length of bone involved and whether the defect comprises partial or segmental circumferential loss. Segmental defects of greater than 2 cm are unlikely to heal spontaneously following skeletal stabilisation alone. Those involving less than 50% of the circumference can heal spontaneously but often require additional treatment to restore normal volume and strength[62]. For larger defects bone grafting with or without induced membranes or bone transport are the main techniques. In deciding which technique to employ it is important to consider the size of the defect, associated treatment time, complications, requirement for further surgery and patient impact [30].

Alternative fixation modalities (Table 1)

Plating

Plating is technically difficult in situations with infection and subsequent bone loss. In the presence of overt infection the plate acts as a nidus for biofilm formation. Extensive exposure may be required if there is a segmental defect to bridge resulting in significant periosteal stripping. The presence of segmental defects will compromise the stability of plate fixation. Plating is biomechanically unfavourable in the presence of a defect due to cantilever loading. New designs of plates, such as locking compression plates and minimally invasive systems overcome the soft tissue and biomechanical issues. Lengthening of the bone is much more difficult when a plate has been used for fixation. A plate spanning a segmental defect will prevent use of distraction osteogenesis or segmental bone transport. Therefore, plates are seldom the treatment of choice in infected diaphyseal fractures of the lower limb, but they continue to be useful for covertly infected non-unions of lower limb metaphyses [26] and humeral [25] fractures.

Plating with or without bone grafting is the mainstay of definitive fixation for metaphyseal non-unions in the humerus and femur. However, exchange nailing can be used in the femur and tibia if there is sufficient metaphysis to engage a locking nail.

External fixation

External fixation is a versatile method of treating non-unions, particularly in the presence of infection and bone loss and may be deployed in almost any location. Circular frames such as the Ilizarov are useful with extensive defects following debridement, particularly if distraction osteogenesis is being planned, or if there is an additional deformity requiring correction. The use of fine wires limits the surface area for bacterial adherence and biofilm formation. Shortening of the bone can be used to facilitate closure of soft tissue defects [63], with the frame being subsequently used to restore length. External fixators can be used in the lower limb in conjunction with intramedullary nailing for bone transport. Frames have the advantage that they can be used in any location including periarticular defects with short juxta-articular segments. They can also be used to lengthen and transport bone, and correct deformity. As with other methods, external fixation has specific drawbacks. It may not be possible to remove the frame for many months and pin-track infections may require urgent medical or surgical treatment [64]. This is particularly the case in the femur and humerus. Fine-wire fixators applied too close to joints, particularly the knee, can result in septic arthritis [65]. Compliance with frames when they are in place for long periods can be a problem[62]. It has been suggested that use of circular frame should be reserved for infected non-unions in the proximal and distal metaphysis of the tibia [66], large bone defects in the tibia diaphysis (>6 cm) [66], and the distal humerus [67]

Ilizarov treatment has been found to be associated with union rates close to 100% in the management of infected diaphyseal non-unions of the tibia [68–70]. Studies of Ilizarov frames using monfocal and bifocal techniques to treat infected non-unions with and without bone defects of the tibia report union rates between 85 and 100% [66,71–73], however between 30 and 90% of tibial cases require secondary surgery. Union results are similar in the femur, ranging between 95 and 100% [74–79]. However they are associated with a 55–100% rate of pin-track infection [75–77], up to 70% malunion [76] and up to 30% requirement for bone grafting

Table 1
Skeletal fixation with for infected nonunions following intramedullary nailing: the advantages and disadvantages.

Advantages	Disadvantages
Exchange nailing	
Stable fixation	Not applicable for all metaphyseal fractures
Can bridge long defects	High complication rate when used in the humerus
Can be inserted with minimal soft tissue and periosteal disruption	Not suitable alone for defects > 6 cm
Low rates of malunion	Nidus for biofilm formation
Shortening and lengthening can be accomplished relatively easily	
Can be used in conjunction with external fixation to lengthen bone	
Allow easy access to soft tissues for bone grafting/flap cover	
Plates	
Versatile method of treating upper/lower limb metaphyseal fractures	Poor results in tibial and femoral diaphyseal fractures
Good treatment for humeral diaphyseal nonunions	Standard plating technique requires extensive dissection
Minimally invasive plate designs now available	Plate failure may occur in situations where prolonged union times are expected
	Does not easily allow shortening and lengthening
	Cannot easily be used in conjunction with external fixation
	Not suitable alone for defects > 6 cm
	Nidus for biofilm formation
External fixation	
Can be used on upper/lower limb for metaphyseal/diaphyseal fractures Frame	Cumbersome, poor patient acceptance
Can be used to shorten or lengthen bone	Frame may have to left on for prolonged periods
Bone transport possible	Pin-track infection
Can be used to compress the fracture site to stimulate healing	Risk of septic arthritis when used close to a joint, especially the knee
Correction of angular or rotational deformity possible	Not ideal on the femur or humerus
Long defects (>6 cm) can be treated	
Smaller nidus for biofilm formation	

[75]. There are no studies in the literature reporting its use in infected humerus non-unions following IM nailing. Brinker et al. reported a series of six patients with infected distal non-union following plating, with all six going on to unite free of infection.

Treatment strategies

Exchange nailing

Ability to suppress the infection to union

For exchange nailing to be successful, it is necessary to eradicate or suppress the infection until union has occurred. To achieve this (as with single stage revision arthroplasty [80,81]) it is important to have identified the organism and for it to be sensitive to an antibiotic that can be delivered locally and/or for it to be sensitive to an oral agent that does not inhibit fracture repair [82–87] and that the patient can tolerate.

To assess whether patients have the ability to progress to union, we evaluated whether there was periosteal callus on any of the cortices, bearing in mind that the amount of periosteal callus and it location will be substantially influenced not only by the nature of the initial injury but also by the way in which the fracture was previously treated [62].

We examined a consecutive cohort of 20 femora and 35 tibiae undergoing exchange nailing for diaphyseal aseptic ($n = 38$) and septic ($n = 17$) non-union at a single centre from 2003 to 2010. Of this cohort 49 non-unions had complete radiographic records (19 femora and 30 tibiae) allowing evaluation of the periosteal callus [88]. If the periosteal callus was absent from the fracture site on all 4 cortices (Fig. 1), there was a relative risk ratio (RRR) 5.00 ($p = 0.006$) of exchange nail failure in septic non-unions. Receiver operator characteristic curve analysis (Fig. 2) of number of cortices with periosteal reaction for predicting exchange nail failure in both septic and aseptic cases found an area under the curve of 0.79 (95% confidence interval 0.675–0.904, $p < 0.0001$). A summary of the curve cut-off co-ordinates for the infected cases is shown in Table 2. If there were no cortices with periosteal callus at the fracture site this had a positive predictive value 75% and negative predictive value 100% i.e. if none of the cortices had callus within 5 mm, of the fracture site, there was a 75% chance the patient would need 3 or more exchange nails to obtain union. Conversely if periosteal callus was present on at least one cortex within 5 mm of the fracture site there was a 100% chance the fracture would unite following 1 or 2 exchange nail procedures.

The technique

Exchange nailing for the treatment of an infected long bone non-unions involves removal of the current intramedullary nail, reaming of the medullary canal, and placement of an intramedullary nail that is larger in diameter than the removed nail [89,90] following debridement and irrigation. It provides stable fixation, allows bridging of long defects, and can be inserted with minimal soft tissue and periosteal disruption [62]. The soft tissues can be readily accessed for further wound debridement and soft-tissue cover, and joints can be mobilised readily.

It has been established that reaming of the medullary canal increases periosteal blood flow and stimulates periosteal new-bone formation [55], which in turn aids in healing of the non-union. However in order for the above process to occur the bone and periosteum adjacent to the fracture site must be biologically active. It is therefore crucial to preserve the periosteal blood supply when managing infected non-unions following IM nailing [59].

Exchange nailing associated with bone loss/debridement has some limitations. There may not be adequate bone proximally or distally to allow stable fixation with a nail [26]. In the humerus, the medullary canal becomes narrow and flat at the lower end, which

Fig. 1. (a), (b), and (c). Plain radiographs of diaphyseal nonunions demonstrating the varying location of periosteal reaction relative to the fracture site.

may limit the possibility of achieving satisfactory stability with a nail in the presence of bone loss [13,62].

Court-Brown et al. [89] described a protocol for the treatment of infected tibia diaphyseal non-unions. This protocol has been

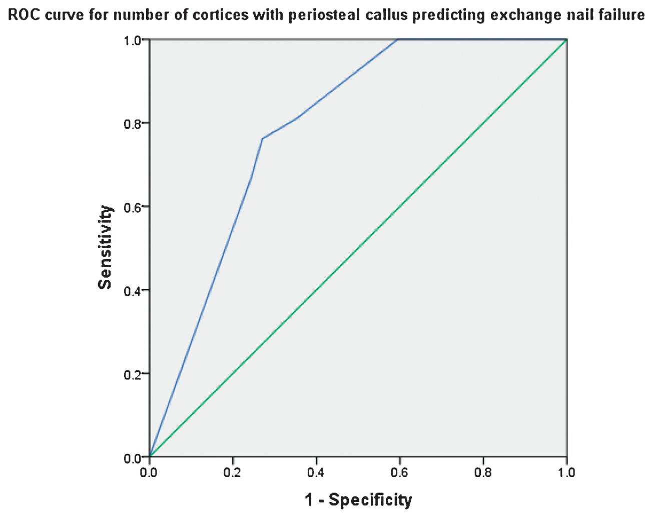


Fig. 2. Receiver operator characteristic curve for number of cortices with periosteal callus at fracture site predicting exchange nail failure.

reported to achieve eradication of the infection with bone union in 12/13 cases (92.3%). More recent series have reported union and eradication of infection in 27/31 (87.1%) tibiae but 19/31 required more than one exchange nail procedure to achieve union [24]. Similar results have been found with this protocol in the femur [23,91,92]. Tsang et al. found that 9/11 (82%) infected femoral non-unions went on to unite but with 6/11 (55%) requiring more than one exchange nail procedure in order to achieve union. Some smaller series have found that the presence of infection was not associated with failure if organism-specific antibiotics were started from the time of exchange nailing [91,92].

Custom made antibiotic-coated cement rods and cement-coated nails

Antibiotic-coated cement rods were first used in the 1990s with recent studies reporting promising results in the treatment of chronic osteomyelitis and infected nonunions [93]. Numerous techniques for the intraoperative fabrication of antibiotic rods have been described including the use of a mould [94,95], manual rolling of the cement [96], or the use of a chest drain tubing as a mould [97–103]. They can be inserted with minimal soft tissue and periosteal disruption. When used in combination with systemic antibiotics and as part of a staged treatment strategy, eradication and union rates in excess of 95% and 90%, respectively have been reported. However due to PMMA being non-biodegradable it can act as a nidus for glycocalyx-producing bacteria despite the presence of local antibiotics. The resulting biofilm can lead to persistence of the infection or development of secondary infections [28]. Technical difficulties described include removal of the custom-made device from the medullary canal [104], cement-nail debonding [94], fracture of the rod within the medullary canal [98] and removing the chest drain tubing from the cured cement nail [103].

Antibiotic impregnated IM nails

Antibiotic-coated IM nails were initially developed to prevent bacterial colonisation and subsequent biofilm formation during primary fixation of open fractures. Examples include the Expert Tibial Nail (ETN) PROtect^{TM} (DepuySynthes, Johnson/Johnson company, Inc New Jersey, USA). The ETN PROtect^{TM} implant is a titanium alloy (titanium – 6% aluminium – 7% niobium) cannulated nail used for intramedullary fixation of tibia fractures. The fully resorbable antibiotic coating consists of an amorphous poly(D,L-lactide) (PDLLA) matrix containing gentamicin sulphate [105]. After implantation, the gentamicin sulphate is delivered to the surrounding tissue in a burst release profile starting at the moment of implantation. Drug kinetic studies have shown that the PROtect implant releases over 40% of its antibiotic within 1 h, 70% within 24 h and 80% within 48 h after implantation [106]. It offers high concentrations of antibiotics locally in addition to the other benefits of exchange nailing.

Two stage excision of the non-union

Two-stage revision arthroplasty is the gold standard for the treatment of periprosthetic infections with removal of the prosthesis followed by placement of an antibiotic impregnated spacer and parenteral antibiotic therapy with delayed reimplantation of prostheses once the infection has been eradicated [107–109]. It has been suggested infected non-unions should be treated in a similar manner using a planned series of surgical procedures [26,45].

The infected intramedullary nail is removed, the canal is reamed as indicated above and dead bone at the non-union excised. The dead space is obliterated with vascular tissue or antibiotic impregnated material and the bone is stabilised (see Table 1). External fixation is frequently used in these situations. However, following removal of the infected primary IM nail implantation of an antibiotic-impregnated nail or antibiotic-loaded polymethylmethacrylate cement spacer has been reported to provide temporary internal splinting and elute high concentrations of an antimicrobial drug locally in the medullary canal [98,100,110]. With the final treatment stage being removal of the antibiotic-impregnated nail or spacer and definitive internal fixation [26,100].

The defect can then be filled using techniques such as bone transport or the Masquelet technique.

Bone transport

The use of a frame to carry out bone transport to bridge a defect is an alternative to shortening for longer defects. Circular frames are now more popular for the tibia than uniaxial devices since they confer greater stability and there is more flexibility in the configuration of the frame. There is also more scope for correcting rotational or angular malalignment which may occur during the course of treatment [62]. Union rates reported after Ilizarov treatment are close to 100% [68–70]. However, Ilizarov treatment

Table 2
Receiver operating characteristics curve cut-off co-ordinates for number of cortices with periosteal callus at fracture site predicting requirement for more than two exchange nailing procedures in infected nonunions.

Number of cortices	Sensitivity	Specificity	Positive predictive value	Negative predictive value	p-value
0	100%	90.9%	75%	100%	0.02
≤1	100%	81.8%	60%	100%	0.02
≤2	100%	72.7%	50%	100%	0.02
≤3	100%	45.5%	33.3%	100%	0.02
≤4	100%	0%	21.4%	0%	0.02

requires a second procedure to remove the frame and several years to regain function after frame removal [2].

Modified Masquelet technique

A further option for defects of 6 cm or more following radical debridement is the modified Masquelet technique [111,112]. During the first stage of the Masquelet technique a polymethylmethacrylate (PMMA) cement spacer is implanted at the site of the bone defect and the limb is stabilised with an external fixator. The cement spacer had two roles in the original description. The first one was mechanical as it prevented fibrous tissue invasion of the recipient site. The second role was biological as the PMMA induced the surrounding membrane that was able to revascularise the bone graft and prevent its resorption. A third role was as a medium for the local delivery of high concentrations of antibiotics at the infected non-union site [111].

Following placement of a PMMA spacer the soft tissue envelope is repaired (if necessary with vascularised flap). At the second stage, approximately 6–8 weeks later, the cement spacer is carefully removed ensuring that the formed “induced membrane” is minimally disturbed; and the defect is filled with morcellised cancellous autologous bone graft (with additional bone graft substitute if the graft is insufficient, not exceeding a 1:3 ratio). The bone is usually stabilised with a plate, but other means of fixation can be used [113]. The induced membrane has been shown to be highly vascularised, osteoinductive [114], and even osteogenic [115]. Defects up to 25 cm have been reported to have fully consolidated with the Masquelet technique within 12 months [113].

One stage excision of the non-union

The infected intramedullary nail is removed, the canal is reamed as indicated above and dead bone at the non-union excised back to two healthy matching bone ends. The limb is then acutely shortened and these bone ends opposed. The limb is then stabilised, most commonly with external fixation but other modalities have been used (Table 1). This technique has the advantage of (i) obliterating the dead space between the bone ends and (ii) reducing the size of the soft-tissue defect and potentially avoiding the need for a free flap [63] by using a reverse Z plasty instead. The technique is limited by the amount of acute shortening that can be tolerated. This is dependent on the state of the soft tissues and the site of the defect; indurated chronically infected tissues and arteriosclerotic vessels tolerate shortening less well, whereas young supple tissues may allow 10 cms of acute shortening. In certain locations close to joints, the vessels are less mobile, for instance at the ‘trifurcation’ of the popliteal artery and in these cases far less acute shortening is tolerated. As a rule of thumb 5 cms of shortening is possible, but in all cases it is important to monitor the pulses before and after acute shortening.

A corticotomy is then created through a healthy area of bone away from the zone of injury. The bone can then be lengthened at the same time as obtaining bony union.

This procedure should be considered if the associated soft-tissue defect is shorter than that of the bone. In the upper limb, shortening of 2–4 cm may be tolerated without significant functional impairment, obviating the need for subsequent lengthening.

The lengthening can be performed at a later time and intramedullary nails have been developed with lengthening capacity [116,117], which should be considered if the infection has been eradicated. Alternatively, lengthening can be accomplished over a nail after union by creating an osteotomy through healthy bone and applying a uniaxial fixator [118–121]. There are reports of the subsequent lengthening being performed acutely followed by plating or nailing [122,123] but the length regained by

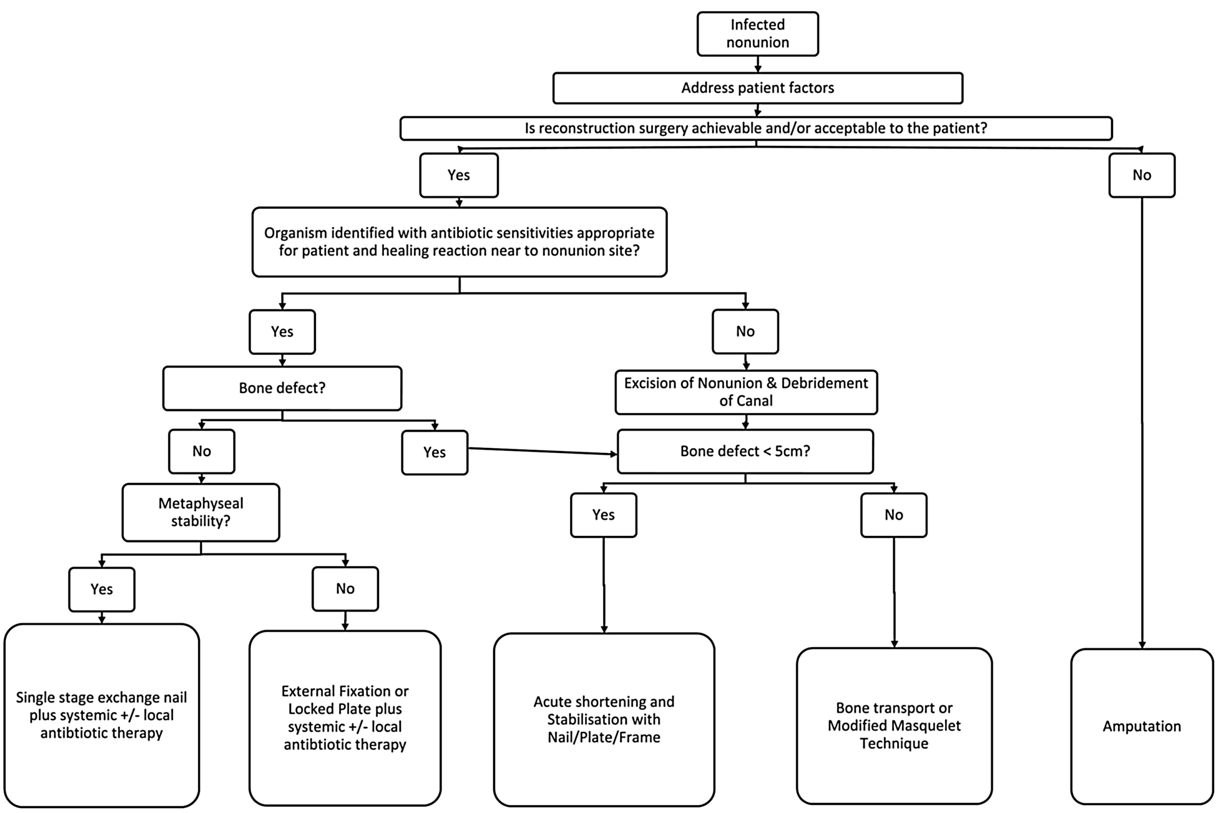


Fig. 3. Infected nonunions are treated using this algorithm. Infected delayed unions show progression of healing and are best treated with suppression of infection ± exchange nailing.

this method is limited, with an average of 4 cm, and despite supplementary bone graft being used, non-union and delayed union are significant risks.

Overall, bone shortening and subsequent lengthening is associated with a lower complication rate than bone transport techniques [124–127].

Amputation

Although amputation is seldom regarded as a palatable option by either patient or surgeon, it may be a wise choice in some situations. Some patients may be poor candidates to undergo a prolonged reconstructive procedure involving limb lengthening or bone transport for social or medical reasons. Various other general factors need to be taken into account [128]. Elderly patients or patients with other risk factors such as smoking, alcohol abuse, steroid treatment, diabetes and occlusive arterial disease, may be better advised to accept amputation rather than risk a prolonged attempt at limb reconstruction with multiple surgical interventions and a high rate of complication. The available evidence suggests that in patients with severe limb injury the functional outcome and the chance of returning to work is no different with amputation or limb salvage [128].

Conclusion

Treatment of long bone non-unions remain challenging with a great burden to the health care systems [129–134]. The majority of infected non-unions following IM nailing can be treated with exchange nailing. However, patients should be warned of the likelihood of needing several exchange nailing procedures to achieve union. The median time to union of staged exchange nail procedures is similar to time required to obtain union if an Ilizarov procedure had been carried out instead of the exchange nailing procedures [24]. However, exchange nailing is less likely to be successful in patients who have non-unions (1) without any periosteal reaction at the fracture site, (2) without a known readily treatable bacteria and (3) with a bone defect. Patients with non-unions with these features should be treated with excision of the non-union and acute shortening or a staged protocol with adjuvant local antibiotic therapy and subsequent reconstruction with an induced membrane technique or an Ilizarov distraction osteogenesis procedure (Fig. 3).

Conflict of interest

None.

References

[1] Egol KA, Gruson K, Spitzer AB, Walsh M, Tejwani NC. Do successful surgical results after operative treatment of long-bone nonunions correlate with outcomes? Clin Orthop Relat Res 2009;467:2979–85.
[2] Barker KL, Lamb SE, Simpson AHRW. Functional recovery in patients with nonunion treated with the Ilizarov technique. J Bone Joint Surg Br 2004;86:81–5.
[3] Kanakaris NK, Calori GM, Verdonk R, Burssens P, De Biase P, Capanna R, et al. Application of BMP-7 to tibial non-unions: a 3-year multicenter experience. Inj J Care Injury 2008;39:S83–90.
[4] Patil S, Montgomery R. Management of complex tibial and femoral nonunion using the Ilizarov technique, and its cost implications. J Bone Joint Surg-Br 2006;88B:928–32.
[5] Dahabreh Z, Calori GM, Kanakaris NK, Nikolaou VS, Giannoudis PV. A cost analysis of treatment of tibial fracture nonunion by bone grafting or bone morphogenetic protein-7. Int Orthop 2009;33:1407–14.
[6] Dahabreh Z, Dimitriou R, Giannoudis PV. Health economics: a cost analysis of treatment of persistent fracture non-unions using bone morphogenetic protein-7. Inj J Care Injury 2007;38:371–7.
[7] Mills LA, Simpson AHRW. The relative incidence of fracture non-union in the Scottish population (5.17 million): a 5-year epidemiological study. BMJ Open 2013;3.
[8] Mills L, Tsang S, Hooper G, Keenan G, Simpson A. The multifactorial aetiology of fracture non-union and the importance of searching for latent infection. Bone Joint Res 2016;2016:In–press.
[9] Court-Brown C, McQueen M, Tornetta III P. Trauma. Orthopaedic surgery essentials. 1st ed. Philadelphia: Lippincott Williams and Wilkins; 2006.
[10] Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984;24:742–6.
[11] Lin J, Hou SM, Hang YS, Chao EY. Treatment of humeral shaft fractures by retrograde locked nailing. Clin Orthop Relat Res 1997;14:147–55.
[12] Lin J, Hou SM. Antegrade locked nailing for humeral shaft fractures. Clin Orthop Relat Res 1999;20:201–10.
[13] Robinson CM, Bell KM, Court-Brown CM, McQueen MM. Locked nailing of humeral shaft fractures: experience in Edinburgh over a two-year period. J Bone Joint Surg Br 1992;74:558–62.
[14] Bain GI, Sandow MJ, Howie DW. Treatment of humeral shaft fractures with the Seidel intramedullary nail. Aust N Z J Surg 1996;66:156–8.
[15] Ma J, Xing D, Ma X, Gao F, Wei Q, Jia H, et al. Intramedullary nail versus dynamic compression plate fixation in treating humeral shaft fractures: grading the evidence through a meta-analysis. PLoS One 2013;8:e82075.
[16] Flinkkilä T, Hyvönen P, Lakovaara M, Linden T, Ristiniemi J, Hämäläinen M. Intramedullary nailing of humeral shaft fractures: a retrospective study of 126 cases. Acta Orthop Scand 1999;70:133–6.
[17] Flinkkilä T, Ristiniemi J, Hämäläinen M. Nonunion after intramedullary nailing of humeral shaft fractures. J Trauma 2001;50:540–4.
[18] Ingman AM, Waters DA. Locked intramedullary nailing of humeral shaft fractures Implant design, surgical technique, and clinical results. J Bone Joint Surg Br 1994;76:23–9.
[19] Moojen DJF, Zwiers JH, Scholtes VAB, Verheyen CCPM, Poolman RW. Similar success rates for single and multiple debridement surgery for acute hip arthroplasty infection. Acta Orthop 2014;85:383–8.
[20] Mulier T, Seligson D, Sioen W, van den Bergh J, Reynaert P. Operative treatment of humeral shaft fractures. Acta Orthop Belg 1997;63:170–7.
[21] Rommens PM, Verbruggen J, Broos PL. Retrograde locked nailing of humeral shaft fractures. A review of 39 patients. J Bone Joint Surg Br 1995;77:84–9.
[22] Kurup H, Hossain M, Andrew JG. Dynamic compression plating versus locked intramedullary nailing for humeral shaft fractures in adults. Cochrane Database Syst Rev 2011;CD005959.
[23] Tsang S, Mills L, Baren J, Frantzias J, Keating J, Simpson A. Exchange nailing for femoral diaphyseal fracture non-unions: risk factors for failure. Injury 2015;46:2404–9.
[24] Tsang S, Mills LA, Baren J, Frantzias J, Keating JF, AHRW Simpson. Exchange nailing for nonunion of diaphyseal fractures of the tibia. Our results and an analysis of the risk factors for failure. Bone Joint J 2016;98 B:534–41.
[25] McKee MD, Miranda MA, Riemer BL, Blasier RB, Redmond BJ, Sims SH, et al. Management of humeral nonunion after the failure of locking intramedullary nails. J Orthop Trauma 1996;10:492–9.
[26] Brinker MR, O'Connor DP. Exchange nailing of ununited fractures. J Bone Joint Surg-Am 2007;89A:177–88.
[27] Atkins BL, Athanasou N, Deeks JJ, Crook DW, Simpson H, Peto TE, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. The OSIRIS Collaborative Study Group. J Clin Microbiol 1998;36:2932–9.
[28] El-Husseiny M, Patel S, MacFarlane RJ, Haddad FS. Biodegradable antibiotic delivery systems. J Bone Joint Surg Br 2011;93:151–7.
[29] Lalidou F, Kolios G, Tavridou A, Drosos GI. Bone grafts as carriers for local antibiotic delivery for the treatment and prevention of bone infections. Surg Technol Int 2014;25:239–45.
[30] Giannoudis PV. Treatment of bone defects: bone transport or the induced membrane technique? Injury 2016;47:291–2.
[31] Gaston MS, Simpson AHRW. Inhibition of fracture healing. J Bone Joint Surg-Br 2007;89B:1553–60.
[32] Swanson EA, Garrard EC, O'Connor DP, Brinker MR. Results of a systematic approach to exchange nailing for the treatment of aseptic tibial nonunions. J Orthop Trauma 2015;29:28–35.
[33] Swanson EA, Garrard EC, Bernstein DT, O'Connor DP, Brinker MR. The results of a systematic approach to exchange nailing for the treatment of aseptic femoral nonunions. J Orthop Trauma 2014;29:21–7.
[34] Calori GM, Phillips M, Jeetle S, Tagliabue L, Giannoudis PV. Classification of non-union: need for a new scoring system? Inj J Care Injury 2008;39:S59–63.
[35] Donlan RM. Biofilms Microbial life on surfaces. Emerg Infect Dis 2002;8:881–90.
[36] O'Gara JP, Humphreys H. Staphylococcus epidermidis biofilms: importance and implications. J Med Microbiol 2001;50:582–7.
[37] Mah TFC, O'Toole GA. Mechanisms of biofilm resistance to antimicrobial agents. Trends Microbiol 2001;9:34–9.
[38] Chuard C, Vaudaux PE, Proctor RA, Lew DP. Decreased susceptibility to antibiotic killing of a stable small colony variant of Staphylococcus aureus in fluid phase and on fibronectin-coated surfaces. J Antimicrob Chemother 1997;39:603–8.
[39] Gristina AG, Costerton JW. Bacterial adherence to biomaterials and tissue: the significance of its role in clinical sepsis. J Bone Joint Surg Am 1985;67:264–73.

[40] Costerton JW, Lewandowski Z, Caldwell DE, Korber DR, Lappin-Scott HM. Microbial biofilms. Annu Rev Microbiol 1995;49:711–45.
[41] Stewart PS, Costerton JW. Antibiotic resistance of bacteria in biofilms. Lancet 2001;358:135–8.
[42] Mahale YJ, Aga N. Implant-associated mycobacterium tuberculosis infection following surgical management of fractures: a retrospective observational study. Bone Joint J 2015;97-B:1279–83.
[43] Ellington JK, Elhofy A, Bost KL, Hudson MC. Involvement of mitogen-activated protein kinase pathways in Staphylococcus aureus invasion of normal osteoblasts. Infect Immunity 2001;69:5235–42.
[44] Mohamed W, Sommer U, Sethi S, Domann E, Thormann U, Schütz I, et al. Intracellular proliferation of S. aureus in osteoblasts and effects of rifampicin and gentamicin on S. aureus intracellular proliferation and survival. Eur Cell Mater 2014;28:258–68.
[45] Kanakaris NK, Tosounidis TH, Giannoudis PV. Surgical management of infected non-unions: an update. Injury 2015;46(Suppl. 5):S25–32.
[46] Struijs PAA, Poolman RW, Bhandari M. Infected nonunion of the long bones. J Orthop Trauma 2007;21:507–11.
[47] Edmondson MC, Day R, Wood D. Vancomycin iontophoresis of allograft bone. Bone Joint Res 2014;3:101–7.
[48] Leung AHC, Hawthorn BR, Simpson AHRW. The effectiveness of local antibiotics in treating chronic osteomyelitis in a cohort of 50 patients with an average of 4 years follow-up. Open Orthop J 2015;9:372–8.
[49] Rand BCC, Penn-Barwell JG, Wenke JC. Combined local and systemic antibiotic delivery improves eradication of wound contamination: an animal experimental model of contaminated fracture. Bone Joint J 2015;97-B:1423–7 d.
[50] Fleiter N, Walter G, Bösebeck H, Vogt S, Büchner H, Hirschberger W, et al. Clinical use and safety of a novel gentamicin-releasing resorbable bone graft substitute in the treatment of osteomyelitis/osteitis. Bone Joint Res 2014;3:223–9.
[51] Romanò CL, Logoluso N, Meani E, Romanò D, De Vecchi E, Vassena C, et al. A comparative study of the use of bioactive glass S53P4 and antibiotic-loaded calcium-based bone substitutes in the treatment of chronic osteomyelitis: a retrospective comparative study. Bone Joint J 2014;96-B:845–50.
[52] Wendling A, Mar D, Wischmeier N, Anderson D, McIff T. Combination of modified mixing technique and low frequency ultrasound to control the elution profile of vancomycin-loaded acrylic bone cement. Bone Joint Res 2016;5:26–32.
[53] Chang YH, Tai CL, Hsu HY, Hsieh PH, Lee MS, Ueng SWN. Liquid antibiotics in bone cement: an effective way to improve the efficiency of antibiotic release in antibiotic loaded bone cement. Bone Joint Res 2014;3:246–51.
[54] Chai F, Hornez J-C, Blanchemain N, Neut C, Descamps M, Hildebrand HF. Antibacterial activation of hydroxyapatite (HA) with controlled porosity by different antibiotics. Biomol Eng 2007;24:510–4.
[55] Danckwardt-Lillieström G. Reaming of the medullary cavity and its effect on diaphyseal bone. A fluorochromic, microangiographic and histologic study on the rabbit tibia and dog femur. Acta Orthop Scand Suppl 1969;128:1–153.
[56] Klein MP, Rahn BA, Frigg R, Kessler S, Perren SM. Reaming versus non-reaming in medullary nailing: interference with cortical circulation of the canine tibia. Arch Orthop Trauma Surg 1990;109:314–6.
[57] Grundnes O, Reikerås O. Acute effects of intramedullary reaming on bone blood flow in rats. Acta Orthop Scand 1993;64:203–6.
[58] Reichert IL, McCarthy ID, Hughes SP. The acute vascular response to intramedullary reaming: microsphere estimation of blood flow in the intact ovine tibia. J Bone Joint Surg Br 1995;77:490–3.
[59] Whiteside LA, Ogata K, Lesker P, Reynolds FC. The acute effects of periosteal stripping and medullary reaming on regional bone blood flow. Clin Orthop Relat Res 1978;131:266–72.
[60] Kanakaris N, Gudipati S, Tosounidis T, Harwood P, Britten S, Giannoudis PV. The treatment of intramedullary osteomyelitis of the femur and tibia using the Reamer-Irrigator-Aspirator system and antibiotic cement rods. Bone Joint J 2014;96-B:783–8.
[61] Rhinelander FW. Tibial blood supply in relation to fracture healing. Clin Orthop Relat Res 1974;105:34–81.
[62] Keating JF, Simpson AH, Robinson CM. The management of fractures with bone loss. J Bone Jt Surg – Br 2005;87-B:142–50.
[63] Simpson AH, Andrews C, Giele H. Skin closure after acute shortening. J Bone Joint Surg Br 2001;83:668–71.
[64] Jauregui JJ, Bor N, Thakral R, Standard SC, Paley D, Herzenberg JE. Life- and limb-threatening infections following the use of an external fixator. Bone Joint J 2015;97-B:1296–300.
[65] Hutson JJ, Zych GA. Infections in periarticular fractures of the lower extremity treated with tensioned wire hybrid fixators. J Orthop Trauma 1998;12:214–8.
[66] Ring D, Jupiter JB, Gan BS, Israeli R, Yaremchuk MJ. Infected nonunion of the tibia. Clin Orthop Relat Res 1999;369:302–11.
[67] Brinker MR, O'Connor DP, Crouch CC, Mehlhoff TL, Bennett JB. Ilizarov treatment of infected nonunions of the distal humerus after failure of internal fixation: an outcomes study. J Orthop Trauma 2007;21:178–84.
[68] Shahid M, Hussain A, Bridgeman P, Bose D. Clinical outcomes of the Ilizarov method after an infected tibial non union. Arch Trauma Res 2013;2:71–5.
[69] Venkatesh Gupta S, Govindappa CV, Rakesh Reddy M. Treatment of infective non-union of diaphyseal fractures with Ilizarov external fixation. Open Access Orthop 2014;2:1–6.
[70] Megas P, Saridis A, Kouzelis A, Kallivokas A, Mylonas S, Tyllianakis M. The treatment of infected nonunion of the tibia following intramedullary nailing by the Ilizarov method. Inj J Care Inj 2010;41:294–9.
[71] Madhusudhan TR, Ramesh B, Manjunath K, Shah HM, Sundaresh DC, Krishnappa N. Outcomes of Ilizarov ring fixation in recalcitrant infected tibial non-unions – a prospective study. J Trauma Manag Outcomes 2008;2:6.
[72] García-Cimbrelo E, Martí-González JC. Circular external fixation in tibial nonunions. Clin Orthop Relat Res 2004;419:65–70.
[73] Bose D, Kugan R, Stubbs D, McNally M. Management of infected nonunion of the long bones by a multidisciplinary team. Bone Joint J 2015;97-B:814–7.
[74] Yin P, Ji Q, Li T, Li J, Li Z, Liu J, et al. A systematic review and meta-analysis of Ilizarov methods in the treatment of infected nonunion of tibia and femur. PLoS One 2015;10:e0141973.
[75] Blum ALL, BongioVanni JC, Morgan SJ, Flierl MA, dos Reis FB. Complications associated with distraction osteogenesis for infected nonunion of the femoral shaft in the presence of a bone defect: a retrospective series. J Bone Joint Surg Br 2010;92:565–70.
[76] Krishnan A, Pamecha C, Patwa JJ. Modified Ilizarov technique for infected nonunion of the femur: the principle of distraction-compression osteogenesis. J Orthop Surg (Hong Kong) 2006;14:265–72.
[77] Saridis A, Panagiotopoulos E, Tyllianakis M, Matzaroglou C, Vandoros N, Lambiris E. The use of the Ilizarov method as a salvage procedure in infected nonunion of the distal femur with bone loss. J Bone Joint Surg Br 2006;88:232–7.
[78] Arora R. Usefulness of Ilizarov's procedure in infected non-union of tibia and femur. JK Sci J Med Educ Res 2003;5:22–5.
[79] Maini L, Chadha M, Vishwanath J, Kapoor S, Mehtani A, Dhaon BK. The Ilizarov method in infected nonunion of fractures. Injury 2000;31:509–17.
[80] Gehrke T, Zahar A, Kendoff D. One-stage exchange: it all began here. Bone Joint J 2013;95-B:77–83.
[81] Buchholz HW, Elson RA, Engelbrecht E, Lodenkämper H, Röttger J, Siegel A. Management of deep infection of total hip replacement. J Bone Joint Surg Br 1981;63-B:342–53.
[82] Pountos I, Georgouli T, Blokhuis TJ, Pape HC, Giannoudis PV. Pharmacological agents and impairment of fracture healing: what is the evidence? Injury 2008;39:384–94.
[83] Pountos I, Georgouli T, Bird H, Kontakis G, Giannoudis PV. The effect of antibiotics on bone healing: current evidence. Expert Opin Drug Saf 2011;10:935–45.
[84] Isefuku S, Joyner CJ, Simpson AH. Toxic effect of rifampicin on human osteoblast-like cells. J Orthop Res 2001;19:950–4.
[85] Isefuku S, Joyner CJ, Simpson AHRW. Gentamicin may have an adverse effect on osteogenesis. J Orthop Trauma 2003;17:212–6.
[86] Miclau T, Edin ML, Lester GE, Lindsey RW, Dahners LE. Effect of ciprofloxacin on the proliferation of osteoblast-like MG-63 human osteosarcoma cells in vitro. J Orthop Res 1998;16:509–12.
[87] Edin ML, Miclau T, Lester GE, Lindsey RW, Dahners LE. Effect of cefazolin and vancomycin on osteoblasts in vitro. Clin Orthop Relat Res 1996;333:245–51.
[88] Tsang S, Mills LA, Baren J, Frantzias J, Keating JF, Simpson AHRW. Absence of periosteal reaction is predictive of exchange nail failure for diaphyseal fracture non-union. Unpubl Work 2016.
[89] Court-Brown CM, Keating JF, McQueen MM. Infection after intramedullary nailing of the tibia: incidence and protocol for management. J Bone Joint Surg-Br 1992;74:770–4.
[90] Courtbrown CM, Keating JF, Christie J, McQueen MM, Court-Brown CM. Exchange intramedullary nailing: its use in aseptic tibial nonunion. J Bone Joint Surg-Br 1995;77B:407–11.
[91] Hak DJ, Lee SS, Goulet JA. Success of exchange reamed intramedullary nailing for femoral shaft nonunion or delayed union. J Orthop Trauma 2000;14:178–82.
[92] Klemm KW. Treatment of infected pseudarthrosis of the femur and tibia with an interlocking nail. Clin Orthop Relat Res 1986;212:174–81.
[93] Conway J, Mansour J, Kotze K, Specht S, Shabtai L. Antibiotic cement-coated rods: an effective treatment for infected long bones and prosthetic joint nonunions. Bone Joint J 2014;96-B:1349–54.
[94] Thonse R, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. J Orthop Trauma 2007;21:258–68.
[95] Thonse R, Conway JD. Antibiotic cement-coated nails for the treatment of infected nonunions and segmental bone defects. J Bone Joint Surg-Am 2008;90A:163–74.
[96] Shyam AK, Sancheti PK, Patel SK, Rocha S, Pradhan C, Patil A. Use of antibiotic cement-impregnated intramedullary nail in treatment of infected non-union of long bones. Indian J Orthop 2009;43:396–402.
[97] Wasko MK, Borens O. Antibiotic cement nail for the treatment of posttraumatic intramedullary infections of the tibia: midterm results in 10 cases. Injury 2013;44:1057–60.
[98] Paley D, Herzenberg JE. Intramedullary infections treated with antibiotic cement rods: preliminary results in nine cases. J Orthop Trauma 2002;16:723–9.
[99] Bhadra AK, Roberts CS. Indications for antibiotic cement nails. J Orthop Trauma 2009;23:S26–30.
[100] Madanagopal SG, Seligson D, Roberts CS. The antibiotic cement nail for infection after tibial nailing. Orthopedics 2004;27:709–12.

[101] Qiang Z, Jun PZ, Jie XJ, Hang L, Bing LJ, Cai LF. Use of antibiotic cement rod to treat intramedullary infection after nailing: preliminary study in 19 patients. Arch Orthop Trauma Surg 2007;127:945–51.
[102] Riel RU, Gladden PB. A simple method for fashioning an antibiotic cement-coated interlocking intramedullary nail. Am J Orthop (Belle Mead NJ) 2010;39:18–21.
[103] Kim JW, Cuellar DO, Hao J, Seligson D, Mauffrey C. Custom-made antibiotic cement nails: a comparative study of different fabrication techniques. Injury 2014;45:1179–84.
[104] Lee H-J, Kim G-U, Kang SY, Lee J-S, Jung H-J. An improved technique for removing intramedullary antibiotic beads in osteomyelitis of the tibial shaft. Surg Infect (Larchmt) 2014;15:838–42.
[105] Schmidmaier G, Wildemann B, Stemberger A, Haas NP, Raschke M. Biodegradable poly(D,L-lactide) coating of implants for continuous release of growth factors. J Biomed Mater Res 2001;58:449–55.
[106] Metsemakers WJ, Reul M, Nijs S. The use of gentamicin-coated nails in complex open tibia fracture and revision cases: a retrospective analysis of a single centre case series and review of the literature. Injury 2015;46:2433–7.
[107] Haddad FS, Muirhead-Allwood SK, Manktelow AR, Bacarese-Hamilton I. Two-stage uncemented revision hip arthroplasty for infection. J Bone Joint Surg Br 2000;82:689–94.
[108] Ibrahim MS, Raja S, Khan MA, Haddad FS. A multidisciplinary team approach to two-stage revision for the infected hip replacement: a minimum five-year follow-up study. Bone Joint J 2014;96-B:1312–8.
[109] George DA, Gant V, Haddad FS. The management of periprosthetic infections in the future: a review of new forms of treatment. Bone Joint J 2015;97-B:1162–9.
[110] Ohtsuka H, Yokoyama K, Higashi K, Tsutsumi A, Fukushima N, Noumi T, et al. Use of antibiotic-impregnated bone cement nail to treat septic nonunion after open tibial fracture. J Trauma-Injury Infect Crit Care 2002;52:364–6.
[111] Giannoudis PV, Faour O, Goff T, Kanakaris N, Dimitriou R. Masquelet technique for the treatment of bone defects: tips-tricks and future directions. Injury 2011;42:591–8.
[112] Wang X, Luo F, Huang K, Xie Z. Induced membrane technique for the treatment of bone defects due to post-traumatic osteomyelitis. Bone Joint Res 2016;5:101–5.
[113] Masquelet AC, Fitoussi F, Begue T, Muller GP. Reconstruction of the long bones by the induced membrane and spongy autograft. Ann Chir Plast Esthétique 2000;45:346–53.
[114] Pelissier PH, Masquelet AC, Bareille R, Pelissier SM, Amedee J. Induced membranes secrete growth factors including vascular and osteoinductive factors and could stimulate bone regeneration. J Orthop Res 2004;22:73–9.
[115] Gruber HE, Ode G, Hoelscher G, Ingram J, Bethea S, Bosse MJ. Osteogenic, stem cell and molecular characterisation of the human induced membrane from extremity bone defects. Bone Joint Res 2016;5:106–15.
[116] Simpson AHWR, Shalaby H, Keenan G. Femoral lengthening with the intramedullary skeletal kinetic distractor. J Bone Joint Surg Br 2009;91:955–61.
[117] Aston WJS, Calder PR, Baker D, Hartley J, Hill RA. Lengthening of the congenital short femur using the Ilizarov technique: a single-surgeon series. J Bone Joint Surg Br 2009;91:962–7.
[118] Raschke MJ, Mann JW, Oedekoven G, Claudi BF. Segmental transport after unreamed intramedullary nailing: preliminary report of a Monorail system. Clin Orthop Relat Res 1992;282:233–40.
[119] Paley D, Herzenberg JE, Paremain G, Bhave A. Femoral lengthening over an intramedullary nail: a matched-case comparison with Ilizarov femoral lengthening. J Bone Joint Surg Am 1997;79:1464–80.
[120] Li G, Berven S, Athanasou NA, Simpson AH. Bone transport over an intramedullary nail: a case report with histologic examination of the regenerated segment. Injury 1999;30:525–34.
[121] Simpson AH, Cole AS, Kenwright J. Leg lengthening over an intramedullary nail. J Bone Joint Surg Br 1999;81:1041–5.
[122] Murray DW, Kambouroglou G, Kenwright J. One-stage lengthening for femoral shortening with associated deformity. J Bone Joint Surg Br 1993;75:566–71.
[123] Johnson EE. Acute lengthening of shortened lower extremities after malunion or non-union of a fracture. J Bone Joint Surg Am 1994;76:379–89.
[124] Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part II. The influence of the rate and frequency of distraction. Clin Orthop Relat Res 1989;239:263–85.
[125] Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part I. The influence of stability of fixation and soft-tissue preservation. Clin Orthop Relat Res 1989;238:249–81.
[126] Dagher F, Roukoz S. Compound tibial fractures with bone loss treated by the Ilizarov technique. J Bone Joint Surg Br 1991;73:316–21.
[127] Saleh M, Rees A. Bifocal surgery for deformity and bone loss after lower-limb fractures: comparison of bone-transport and compression-distraction methods. J Bone Joint Surg Br 1995;77:429–34.
[128] Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. N Engl J Med 2002;347:1924–31.
[129] Giannoudis PV, Gudipati S, Harwood P, Kanakaris NK. Long bone non-unions treated with the diamond concept: a case series of 64 patients. Injury 2015;46(December (Suppl. 8)):S48–54.
[130] Giannoudis PV, Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury. 2016;47(December (Suppl. 6)):S53–61.
[131] Singh R, Bleibleh S, Kanakaris NK, Giannoudis PV. Upper limb non-unions treated with BMP-7: efficacy and clinical results. Injury 2016;47(December (Suppl. 6))S33–9, doi:http://dx.doi.org/10.1016/s0020-1383(16)30837-3 PubMed PMID: 28040085.
[132] Wu H, Shen J, Yu X, Fu J, Yu S, Sun D, et al. Two stage management of Cierny-Mader type IV chronic osteomyelitis of the long bones. Injury 2017;48 (February (2)):511–8.
[133] Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury 2016;47(December (Suppl. 6)):S68–76.
[134] Aktuglu K, Günay H, Alakbarov J. Monofocal bone transport technique for bone defects greater than 5 cm in tibia: our experience in a case series of 24 patients. Injury 2016;47(December (Suppl. 6)):S40–6.

Injury, Int. J. Care Injured 48S (2017) S91–S93

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Management of traumatic bone defects: Metaphyseal versus diaphyseal defects

Taco J. Blokhuis

Department of Surgery, Maastricht University Medical Center +, Postbus 5800, 6202 AZ Maastricht, The Netherlands

ARTICLE INFO

Keywords:
Bone defect
Bone substitute
Induced membrane technique
RIA

ABSTRACT

Although bone defects after trauma appear in different locations and forms, many clinicians have adopted a single strategy to deal with any defect. In this overview, a distinction is made between metaphyseal, or cancellous defects, and diaphyseal, or cortical defects. The treatment goals and background of these two types of defects are discussed in order to describe the difference in strategy and hence the difference in treatment method.

Introduction

Bone defects appear in many shapes and sizes. However, tailor-made approaches are seldom chosen. Many clinicians are familiar with a strategy to deal with bone defects, but have adopted one strategy that fits all. Enormous developments have taken place over the past decades in bone substitutes, but also in knowledge on bone biology. Therefore, the standpoint that a single technique or material should be sufficient to cover all different bone defects, is outdated. In this overview, a distinction between two types of bone defects is made; metaphyseal and diaphyseal bone defects. These two types of defects behave differently, as their biological and mechanical environment [1] is unequal. Moreover, the treatment goals in these two types is not the same. Where mechanical support for a joint surface and restoring bone stock are the main goals in the metaphyseal defects, restoring cortical continuity is the objective on diaphyseal defects. For these reasons, metaphyseal and diaphyseal bone defects require a differentiated approach.

Metaphyseal defects

Impression fractures around a joint are the usual cause for traumatic metaphyseal defects. Osteotomies, i.e. the high tibial osteotomy in degenerative gonarthrosis, is another common cause for metaphyseal defects, but these are beyond the scope of this overview. The treatment goals in these defects are 1) temporary mechanical support of the affected articular surface, 2) healing or filling of the defect itself, and 3) restoration of bone stock to accommodate prosthesis placement in a later stage. The necessity of achieving these three goals depends on the patient and the location and extent of the defect. An elderly patient with an extensive proximal tibia fracture differs, obviously, from a young patient with a joint depression fracture of the calcaneus. Still, healing of the defect should be achieved, in order to reach one or more of the mentioned goals.

The biological environment of metaphyseal defects is generally good. With the exception of specific sites such as the femoral head [2], vascular supply to cancellous bone is generous, and bone turnover is higher than in cortical bone [3]. For these reasons it is often assumed that a defect due to a fracture will heal by itself. A fracture hematoma should form and the cascade of bone healing would be initiated, resulting in filling of the defect. Unfortunately, increasing pre-clinical evidence shows that this is not the case [4,5]; cancellous defects that are not filled with a bone substitute will only generate limited amounts of newly formed bone, leaving the majority of the defect open. In a recent clinical study using high resolution CT imaging on wrist fractures [6] it was shown for the first time in patients that healing of metaphyseal defects is not fast and straightforward. In wrist fractures with major cancellous bone loss, those that required reduction upon initial treatment, imaging at 12 weeks still showed significant changes in bone density. Moreover, volumetric bone mineral density for the trabecular bone in all fractures decreased significantly to 2 years. Although the clinical outcome in these elderly patients is good, these data support the idea that healing of a metaphyseal or cancellous defect is a long and slow process, and that it could benefit from support.

Numerous studies have investigated the effect of bone substitutes in metaphyseal bone defects. Prospective studies have shown beneficial effect of bone substitutes in specific indications, specifically in tibia plateau fractures [7], calcaneus fractures [8,9] and distal radius fractures [10]. Although the quality of the

E-mail address: Taco.Blokhuis@mumc.nl (T.J. Blokhuis).

http://dx.doi.org/10.1016/j.injury.2017.04.021
0020-1383/

evidence in these indications would benefit from larger clinical trials [11], the clinical evidence supports the hypothesis that a filled defect will heal faster than a defect left open, irrespective of the chosen method of fixation. Ideally, a bone substitute material should provide initial support to the articular surface that is affected by the fracture. However, it should also resorb over time at a rate similar to the surrounding metaphyseal bone, and provide osteoconduction for ingrowing new bone. The available materials used as bone substitutes range from bioglass [12,13] and synthetic polymers to calcium phosphates [10,14]. The immense range of commercial products available illustrates that many properties of these materials can be altered according to the (theoretical) needs of the clinician. However, choosing a specific bone substitute material should be based on the considerations mentioned before. Treating metaphyseal defects require a resorbable bone substitute with substantial initial compression strength, allowing ingrowth of cancellous bone at a high rate while preventing secondary subsidence of the reduced joint fracture.

Diaphyseal defects

In contrast to metaphyseal defects, diaphyseal or cortical defects are rarely caused by low energy trauma or simple compression. High energy trauma resulting in comminuted fractures or initial bone loss is often combined with severe soft tissue injury and additional injuries in other areas in the same patient. Another important cause for diaphyseal defects is resection of bone, i.e. after an infected non-union. The treatment goals are different from metaphyseal defects as well. Treatment is aimed at restoring continuity of the affected extremity, including the cortical bone. This goal can be achieved by bone transport or by stimulating bone growth in the defect [15]. This latter method is the subject of this overview. Taking the less favorable biology compared to metaphyseal bone into account, the healing of diaphyseal defects can be much more challenging and requires more effort than simply filling the defect. It is in this field that the components of the so-called Diamond Concept should act together: vascularity, cells, scaffolds, osteoinductive signals, and a proper mechanical environment [16] are all prerequisites to achieve healing. These components are discussed in more detail below.

Local vascularity requires adequate soft tissue coverage [17] and cessation of smoking. It can also be improved by the induced membrane technique in selected cases [18]. Using this technique, which has been implemented widely over the last decade or so, a neo-periosteum is formed around the defect. This neo-periosteum stimulates osteogenesis by temporary expression of factors such as VEGF, IL-6, Col-1, and increased alkaline phosphatase activity [19]. The technique yields excellent results in clinical series [15,18,20]. Most of the success of this technique is due to its relative simplicity and the radical improvement of the local biological environment. The cells and scaffolds as components of the Diamond Concept can be provided by the patient himself. It is evident that cells are necessary in sufficient numbers to initiate healing [21] and that osteoconduction is an essential part of bone regeneration. However, autograft obtained from the iliac crest is associated with significant drawbacks, such as limited volume and complications. The use of a reamer-irrigator-aspirator (RIA) -device overcomes these problems, although its use is invasive and therefore not without risk [22]. There are, however, more important arguments than graft volume or complication rate to choose RIA over iliac crest bone grafting. From a biological perspective, RIA graft material is superior compared to iliac crest bone, containing more growth factors and expressing more genes associated with vascular and skeletal tissues [23,24]. Moreover, the osteogenic capacity of the RIA material is higher than that of iliac crest bone graft [25,26]. When needed, the RIA material can be combined with a bone substitute. Reasons to do so can be limited volume of the graft or improvement of handling of the graft material, which can be rather liquid after harvesting. The added bone substitute should provide some scaffolding, have binding properties for the proteins from the RIA material, and participate in the remodeling of the graft material. By doing so, it can be used as an instrument in monitoring the healing process; it should gradually disappear on the radiographs and be replaced by newly formed bone. Finally, the mechanical environment is a factor well-known to most orthopaedic trauma surgeons. Creating the correct amount of stability, either using plates or intramedullary nails, is part of the daily routine. However, loading of a defect is often overlooked. As mechanical loading has beneficial effects on bone healing [27] it is an important part of treatment of the patient, and providing sufficient stability to allow weight bearing early after treatment of a diaphyseal bone defect should be achieved.

In conclusion, treatment of posttraumatic bone defects requires a differentiated approach and continues to be a clinical challenge for both the surgeon and the patient [28–33]. The local environment of the defect should determine the treatment. The difference between a metaphyseal and a diaphyseal defect, as illustrated in this overview, should be a first step in choosing the appropriate treatment method.

Conflict of interest

None.

References

[1] Kelly NH, Schimenti JC, Ross FP, van der Meulen MC. Transcriptional profiling of cortical versus cancellous bone from mechanically-loaded murine tibiae reveals differential gene expression. Bone 2016(February).
[2] Kumar MN, Belehalli P, Ramachandra P. PET/CT study of temporal variations in blood flow to the femoral head following low-energy fracture of the femoral neck. Orthopedics 2014;37(6):e563–70.
[3] Wong KK, Piert M. Dynamic bone imaging with 99mTc-labeled diphosphonates and 18F-NaF: mechanisms and applications. J Nucl Med 2013;54(4):590–9.
[4] Malhotra A, Pelletier MH, Yu Y, Christou C, Walsh WR. A sheep model for cancellous bone healing. Front Surg 2014;1:37.
[5] Voor MJ, Yoder EM, Burden Jr. RL. Xenograft bone inclusion improves incorporation of hydroxyapatite cement into cancellous defects. J Orthop Trauma 2011;25(8):483–7.
[6] de Jong JJ, Heyer FL, Arts JJ, Poeze M, Keszei AP, Willems PC, et al. Fracture repair in the distal radius in post-menopausal women: a follow-up two years post-fracture using HRpQCT. J Bone Miner Res 2015;31(5):1114–22.
[7] Russell TA, Leighton RK. Comparison of autogenous bone graft and endothermic calcium phosphate cement for defect augmentation in tibial plateau fractures. A multicenter, prospective, randomized study. J Bone Joint Surg Am 2008;90(10):2057–61.
[8] Schildhauer TA, Bauer TW, Josten C, Muhr G. Open reduction and augmentation of internal fixation with an injectable skeletal cement for the treatment of complex calcaneal fractures. J Orthop Trauma 2000;14(5):309–17.
[9] Wee AT, Wong YS. Percutaneous reduction and injection of Norian bone cement for the treatment of displaced intra-articular calcaneal fractures. Foot Ankle Spec 2009;2(2):98–106.
[10] Larsson S, Bauer TW. Use of injectable calcium phosphate cement for fracture fixation: a review. Clin Orthop Relat Res 2002;2(395):3–32.
[11] McNamara IR, Smith TO, Shepherd KL, Clark AB, Nielsen DM, Donell S, et al. Surgical fixation methods for tibial plateau fractures. Cochrane Database Syst Rev 2015;9:CD009679.
[12] Day RM. Bioactive glass stimulates the secretion of angiogenic growth factors and angiogenesis in vitro. Tissue Eng 2005;11(5–6):768–77.
[13] Keshaw H, Forbes A, Day RM. Release of angiogenic growth factors from cells encapsulated in alginate beads with bioactive glass. Biomaterials 2005;26 (19):4171–9.
[14] Blokhuis TJ, Termaat MF, den Boer FC, Patka P, Bakker FC, Haarman HJ. Properties of calcium phosphate ceramics in relation to their in vivo behavior. J Trauma 2000;48(1):179–86.
[15] Giannoudis PV. Treatment of bone defects: bone transport or the induced membrane technique? Injury 2016;47(2):291–2.
[16] Giannoudis PV, Einhorn TA, Schmidmaier G, Marsh D. The diamond concept—open questions. Injury 2008;39(Suppl. 2):S5–8.

[17] Gopal S, Majumder S, Batchelor AG, Knight SL, De BP, Smith RM. Fix and flap: the radical orthopaedic and plastic treatment of severe open fractures of the tibia. J Bone Joint Surg Br 2000;82(7):959–66.
[18] Auregan JC, Begue T. Induced membrane for treatment of critical sized bone defect: a review of experimental and clinical experiences. Int Orthop 2014;38 (9):1971–8.
[19] Aho OM, Lehenkari P, Ristiniemi J, Lehtonen S, Risteli J, Leskela HV. The mechanism of action of induced membranes in bone repair. J Bone Joint Surg Am 2013 3;95(7):597–604.
[20] El-Alfy BS, Ali AM. Management of segmental skeletal defects by the induced membrane technique. Indian J Orthop 2015;49(6):643–8.
[21] Hernigou P, Poignard A, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nonunions. Influence of the number and concentration of progenitor cells. J Bone Joint Surg Am 2005;87(7):1430–7.
[22] Qvick LM, Ritter CA, Mutty CE, Rohrbacher BJ, Buyea CM, Anders MJ. Donor site morbidity with reamer-irrigator-aspirator (RIA) use for autogenous bone graft harvesting in a single centre 204 case series. Injury 2013;44(10):1263–9.
[23] Sagi HC, Young ML, Gerstenfeld L, Einhorn TA, Tornetta P. Qualitative and quantitative differences between bone graft obtained from the medullary canal (with a Reamer/Irrigator/Aspirator) and the iliac crest of the same patient. J Bone Joint Surg Am 2012;94(23):2128–35.
[24] Schmidmaier G, Herrmann S, Green J, Weber T, Scharfenberger A, Haas NP, et al. Quantitative assessment of growth factors in reaming aspirate, iliac crest, and platelet preparation. Bone 2006;39(5):1156–63.
[25] Kuehlfluck P, Moghaddam A, Helbig L, Child C, Wildemann B, Schmidmaier G. RIA fractions contain mesenchymal stroma cells with high osteogenic potency. Injury 2015;46(Suppl. 8):S23–32.
[26] van der Bel R, Blokhuis TJ. Increased osteogenic capacity of Reamer/Irrigator/Aspirator derived mesenchymal stem cells. Injury 2014;45(12):2060–4.
[27] Bailon-Plaza A, van der Meulen MC. Beneficial effects of moderate, early loading and adverse effects of delayed or excessive loading on bone healing. J Biomech 2003;36(8):1069–77.
[28] Giannoudis PV, Gudipati S, Harwood P, Kanakaris NK. Long bone non-unions treated with the diamond concept: a case series of 64 patients. Injury 2015;46 (December (Suppl. 8)):S48–54.
[29] Giannoudis PV, Harwood PJ, Tosounidis T, Kanakaris NK. Restoration of long bone defects treated with the induced membrane technique: protocol and outcomes. Injury 2016;47(December (Suppl. 6)):S53–61.
[30] Singh R, Bleibleh S, Kanakaris NK, Giannoudis PV. Upper limb non-unions treated with BMP-7: efficacy and clinical results. Injury 2016;47(December (Suppl. 6)):S33–9.
[31] Wu H, Shen J, Yu X, Fu J, Yu S, Sun D, Xie Z. Two stage management of Cierny-Mader type IV chronic osteomyelitis of the long bones. Injury 2017;48 (February (2)):511–8.
[32] Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury 2016;47(December (Suppl. 6)):S68–76.
[33] Aktuglu K, Günay H, Alakbarov J. Monofocal bone transport technique for bone defects greater than 5 cm in tibia: our experience in a case series of 24 patients. Injury 2016;47(December (Suppl. 6)):S40–6.