Biological and biomechanical basis of long-bone diaphyseal fractures: from fracture to non-union

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ABSTRACT

Bone healing of diaphyseal fractures is a complex biological process that can often be adversely affected by patient-related and fracture-related factors and eventually end in delayed union and non-union. Surgical and non-surgical approaches have been widely applied, according to the fracture pattern and patient characteristics. For humeral diaphyseal fractures, plate fixation provided excellent results in terms of healing rate and time to union. For femoral and tibial shaft fractures, locked intramedullary nailing is considered the technique of choice. If impaired, the reparative process after intramedullary nailing can be enhanced through different surgical techniques, such as dynamization or exchange nailing. Moreover, the mechanical stability of the fracture site can be improved through augmentation plating, bone grafting or external fixation techniques, with satisfactory results.

This article aims to review the biomechanical principles of reparative osteogenesis in long bone fractures after conservative and surgical treatment. Moreover, the evidence on the current options for bone healing enhancement, and treatment and prevention of delayed union and non-union will be discussed.

KEYWORDS

Long bones, diaphyseal fractures, delayed unions, nonunions, bone healing enhancement.

Introduction

Bone healing of diaphyseal fractures is a complex mechanism, which is strictly regulated by anatomical, biological and mechanical factors. Long bone fractures often show complex fracture patterns with low bone contact, bone loss, and vascular supply disruption, which can adversely affect the healing process. Muscle and soft tissues damage, open fractures and patient-related factors increase the risk of healing impairment, which can occur up to 10% of all diaphyseal fractures [1, 2].

The present article aims to review the biological and mechanical basis of reparative osteogenesis after conservative and surgical treatment of long bone shaft fractures. Moreover, the current evidence on the effectiveness of surgical techniques to enhance bone healing will be discussed.

The biology of bone healing in long bone fractures

The long bone diaphysis has a higher cortical bone/cancellous ratio than the metaphysis and a central cavity occupied mainly by fatty marrow. The afferent vascularization of cortical bone is provided by bone marrow-derived vessels that penetrate the endosteal bone and supply at least the inner two-thirds of the entire cortex (Figure 1). The blood flow therefore has a mostly centrifugal direction. A lesser amount of vascularization is provided by periosteal vessels, with a centripetal flow direction. Periosteal arterioles can penetrate the bone only at firm fascial and muscular attachments, which are typically located at corners. The two systems have no longitudinal interconnection and when a diaphyseal fracture occurs, the vascular flow is fully interrupted [3]. Vascular supply damage is the main cause of bone healing impairment.

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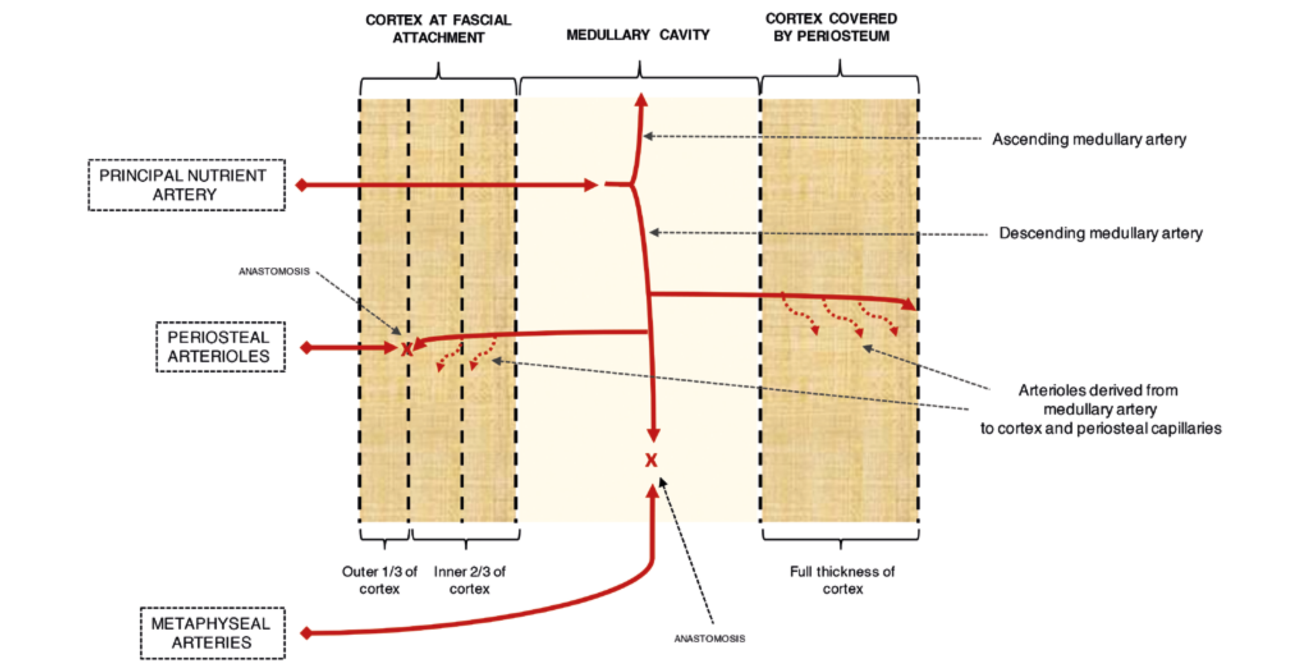
Long bone diaphyseal fractures can heal by either direct fracture healing or indirect fracture healing; the latter is a process of both intramembranous and endochondral bone formation.

Indirect fracture healing consists of endochondral ossification, mainly, and also intramembranous ossification [4]. It involves an initial acute inflammatory response, which includes the production and release of several important molecules (interleukin-6, BMP–7), and the recruitment of mesenchymal stem cells in order to generate a primary cartilaginous callus [5]. Chondrocytes proliferate and become hypertrophic, increasing the matrix deposition [6]. The bone regeneration process continues with the complete resorption of the soft callus and its replacement with a hard callus. The remodelling process converts woven bone into lamellar bone, through balanced osteoclastic resorption and osteoblastic deposition activity. The periosteal and endosteal callus are gradually reabsorbed and the diaphyseal medullary canal is restored through internal callus remodelling [7].

Figure 1 Diagram showing the afferent vascular system of the diaphysis of a mature long bone. At firm fascial attachments, the outer third of the cortex is supplied by periosteal arterioles.



The entire process can take years to complete and therefore to fully restore biomechanical properties close to those of native bone. In direct fracture healing (or contact healing), the fracture heals through intramembranous ossification. Bridging osteons restore lamellar bone through direct remodelling and the fracture heals without the formation of a periosteal callus [8]. Simultaneously, Haversian remodelling progresses through a stage in which cutter heads open tunnels that are later filled by blood vessels and osteoblastic precursors [9].

The biomechanical basis of conservative and surgical treatment

The type of healing pathway (direct or indirect) depends on the fracture pattern and the mechanical stability of the fracture site. As stated by Perren, bony bridging between the distal and proximal callus can occur only when local strain is less than the level the forming woven bone can tolerate [10].

The interfragmentary strain (IFS), defined as the ratio between the displacement and the fracture gap width, correlates with bone healing: when IFS values up to 2%, bone repair occurs by direct healing, and between 5% and 10% it occurs by indirect healing. When IFS is above 10%, the tolerance of the deformation is lower than the stress acting at the fracture site, therefore pseudarthrosis may occur [11]. As simple diaphyseal fractures require cortical continuity and rigid fixation for direct healing, it is mandatory to choose surgical techniques that provide absolute stability, such as locked intramedullary nailing, external fixation and plate internal fixation [12,13]. On the contrary, deforming forces are more tolerated in multifragmentary fractures because the overall movement is shared by several vectors. In this case, the process of indirect healing is enhanced by micro-movements and weight-bearing, so relative stability osteosynthesis techniques, such as external fixation and bridging plating, are more suitable.

Malunion, delayed union or hypertrophic non-union are all possible consequences of an excessive interfragmentary deformation that impedes bony bridging by hard callus. On the other hand, a low-strain environment caused by an over-stiff osteosynthesis could lead to delayed healing and atrophic non-union [14]. The ideal treatment should provide a temporary support which protects callus formation, and allows anatomical restoration and early mobilization. The choice of treatment type affects the stability and, therefore, the bone healing pathway (Table I).

Conservative treatment

Conservative treatment of diaphyseal long bone fractures consists of closed reduction and stabilization with an external mechanical support, such as a circular cast or a splinting device. Movement of the fragments depends on external loading, splint stiffness, and the tissue bridging the fracture [15]. Although the pressure of the surrounding tissues helps to reduce interfragmentary movement, residual motion produces a mechanical osteogenic stimulus [16].

In closed tibial shaft fractures, conservative treatment resulted in high rates of malalignment (20-67%) and delayed or non-union (0.9-17.2%) [16-18]. In a recent cohort study, union after bracing occurred in 54% of humeral shaft fractures. In another study, delayed union and non-union occurred in 27% and 13% of cases, respectively [19]. Conservative treatment of femoral shaft fracture is typically reserved for children. Although in paediatric age post-traumatic deformities are well tolerated, the literature reports limb-length discrepancy rates ranging from 0 to 25% and high rates of angularly malunion (0-19%) and rotational malunion (0-5%) [20].

Table I Bone healing pathways and treatment types in long bone shaft fractures.

TREATMENT TYPE	FRACTURE TYPE	INTERFRAGMENTARY STRAIN	HEALING PATHWAY	CALLUS TYPE
Conservative treatment	Simple Multifragmentary	++	Indirect	Periosteal Endosteal
Intramedullary nail	Simple Multifragmentary	+ ++	Direct Indirect	Cortical Periosteal Endosteal
Dynamic compression plate	Simple	-	Direct	Cortical
Locking compression plate	Multifragmentary	++	Indirect	Periosteal Endosteal
External fixator	Open Simple Multifragmentary	+ +++	Direct Indirect	Cortical Periosteal Endosteal

Intramedullary nailing

Intramedullary nailing (IMN) is the treatment of choice for closed diaphyseal fractures. IMN shares compressive, bending and torsional loads with the surrounding osseous structures [21]. The nail in the medullary canal functions as an internal splint reducing cortical bone stress and establishing a favourable mechanical stimulus for osteogenesis and mineralization of the endosteal and periosteal callus by both direct and indirect healing [22].

The mechanical properties of a nail are determined by its diameter, curvature and cross-sectional shape, as well as the characteristics of the material and the presence or absence of a slot [23]. Rotational forces are opposed by the geometric design and by the diameter of the implant. Further stabilization is achieved with proximal and distal locking screws. Depending on the positioning of transverse locking screws, the fracture can be stabilized through a more rigid (static) configuration or an elastic (dynamic) configuration.

Fracture compression is the most important factor affecting the stability of simple fractures. Direct contact of the implant with the cortical ends increases its rigidity and resistance to tensile and torsional forces. Moreover, static locking screws are often associated to obtain reduced interfragmentary movement and promote primary direct healing [24]. In unstable multifragmentary fractures, compression cannot be applied, so the number of locking screws and their size are essential factors in achieving sufficient stability. Several studies on tibial shaft fractures have shown that single distal locking fails more often than two or three distal screws [23].

IMN procedures do not directly alter the fracture site and therefore, despite the effect of endosteal necrosis, the periosteal vascular supply is preserved. The debris produced by reaming accumulates at the fracture site, acting as autologous bone graft. Although lower rates of healing impairment have been reported after reamed IMN, evidence comparing reamed with unreamed IMN for closed femoral, tibial and humeral diaphyseal fractures is still insufficient [25,26].

Nowadays, reamed IMN is the treatment of choice in unstable closed tibia fractures, due to high rates of union and low rates of malunion or rotational malalignment [17,27]. Non-union rates range from 0 to 5.5% [28].

According to a recent meta-analysis of IMN for femoral shaft fractures, non-union rates range from 2.5% after reamed IMN to 13.8% after unreamed IMN [29]. IMN for humeral shaft fractures provides unclear results and a wide range of non-union rates are reported in the literature (from 1.6 to 33%) [2,30].

Plate fixation

Plate fixation of diaphyseal long bone fractures leads to different pathways of fracture healing depending on the configuration and rigidity of the construct [11]. Conventionally, the dynamic compression plate (DCP) guarantees absolute stability due to the direct contact between the plate and the bone, which promotes direct healing and intramembranous ossification in the first few weeks after surgery [31]. Anatomical reduction of the fracture is essential, since gaps greater than 2 mm are associated with reduced healing potential [10].

Recently, however, greater emphasis on the need to respect the fracture environment has led to the development of implants designed to reduce contact of the plate with the bone surface, and therefore vascular impairment [11,32]. Different vascular-sparing systems have been developed, such as low contact DCPs (LC-DCPs), locking compression plates (LCPs), less invasive stabilization systems, and minimally invasive percutaneous osteosynthesis techniques [33].

LC-DCPs are conventionally used for compression fixation of simple diaphyseal fractures. The trapezoidal cross-section of the plate reduces the area of contact, preserving the periosteal tissue and vascular supply to the periosteal bone [31].

LCPs have combination holes that allow flexible fixation when the plate is used as an "internal fixator" that bridges the fracture gap and converts the axial load into compression forces [33]. The stability and rigidity of the "internal fixator" depends on the plate's length, the number of locked screws used and their location, in addition to the number of fracture fragments and the width of the bone gap [34]. LCPs are mainly applied in multifragmentary diaphyseal fractures that tolerate more interfragmentary strain; in this case, therefore, bone union occurs by indirect fracture healing [35].

Axial and rotational alignment is obtained by indirect fracture reduction, which preserves the soft tissues surrounding the fracture fragments and their periosteal vascular supply. Moreover, the locking plate configuration avoids direct contact between plate and bone surface, preventing the risk of hardware-related bone necrosis.

Plate fixation is the preferred treatment for closed humeral shaft fractures due to lower malalignment rates (0%) and high union rates (>80%) [36,37]. Plate fixation in diaphyseal tibia fractures provides union rates of up to 90%. Delayed union is reported in 1 to 7% of cases and malalignment is not reported as a common complication [38]. Radiological union by 20 weeks is obtained in 96.3% of cases [18]. Results for simple fractures showed shorter times to union without external callus formation after absolute stability fixation (<10 weeks) [39].

External fixation

External fixation of long bone fractures allows the alignment of bone segments and their stabilization through a combination of pins, screws, rods and rings assembled with unilateral, bilateral, circular or hybrid frames [40]. Compressive, distractive or neutralization forces are applied on the fracture site. External fixation is an adjustable stability technique; therefore, bone healing can be achieved by both indirect and direct healing.

External fixation is the preferred treatment for open fractures, emergencies and limb salvage procedures, in which it can be used as temporary or definitive approach [41]. Although the procedure is associated with a number of possible complications and with discomfort for the patient, some authors extensively used external fixation for closed shaft fracture with satisfactory results in terms of bone union and limb alignment. Scaglione *et al*. reported bone healing in 97.6% of 83 patients treated with external fixation for humeral shaft fractures [42]. In a large randomised blinded study, closed simple shaft fractures were treated successfully (union rate of 100%) with circular fixator and lag screws [43].

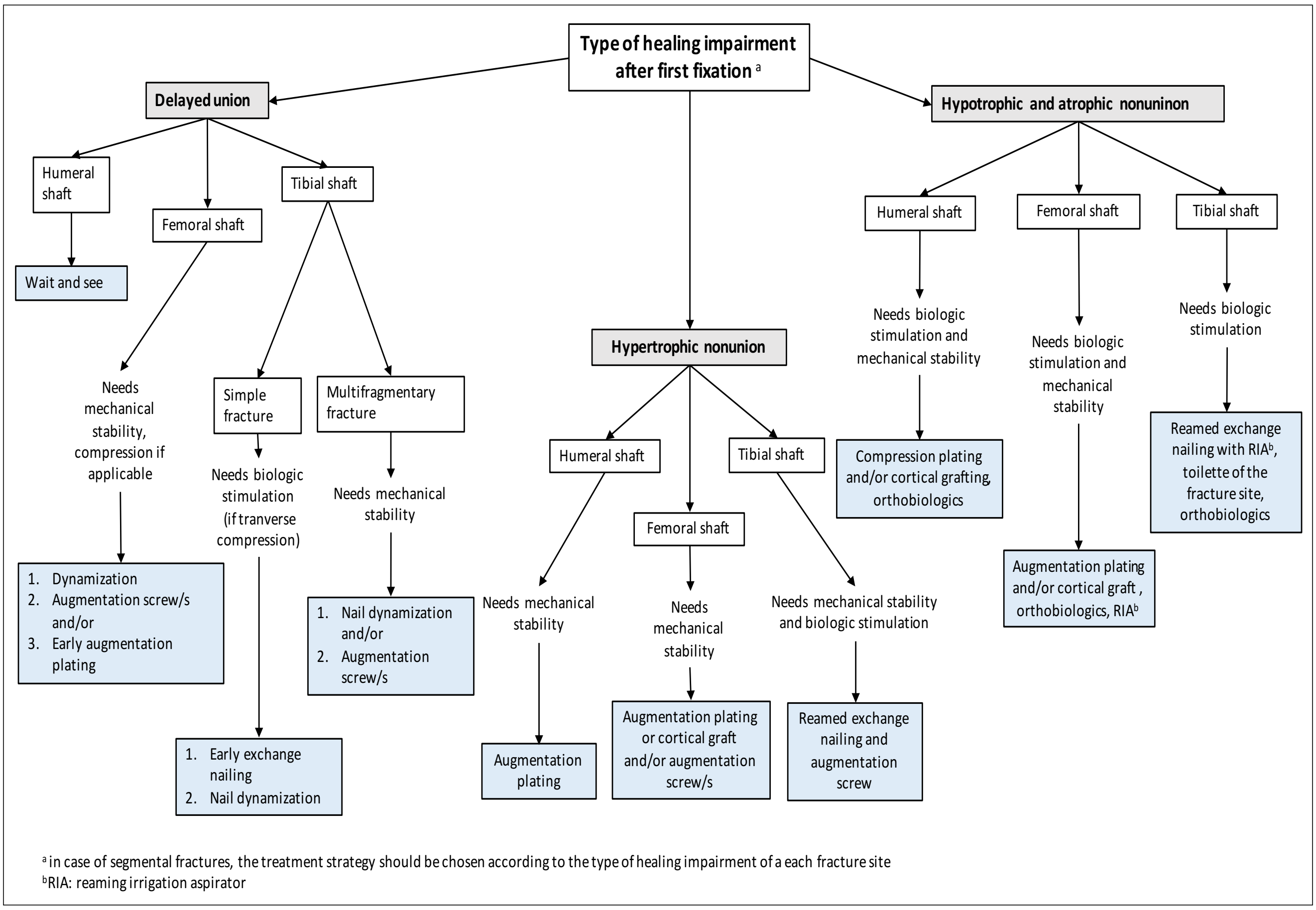
Surgical strategies for impaired bone healing.

Both mechanical and biological underlying factors can affect the normal process of bone regeneration. Different surgical approaches, such as nail dynamization, exchange nailing, augmentation plating and the use of external fixation techniques have been proposed to restore mechanical stability to the fracture site and to stimulate or augment the bone gap after impaired or insufficient healing. The proposed algorithm represents the current clinical evidence for the treatment of both delayed union and non-union of long bone fractures [44, 45] (Figure 2).

Conclusions

The successful treatment of diaphyseal fractures and the complications that can arise are a challenging problem both for the orthopaedic surgeon and for the patient. Full knowledge of the basic principles of the biology and biomechanics of bone healing is essential in order to be able to choose the treatment best suited to a specific type of fracture and patient. When traditional fixation techniques fail, modern bioengineering technologies such scaffolds, growth factors and cell therapies can, whilst preserving the local vascular supply, help to improve the outcome, resulting in a satisfactory result for the surgeon and the patient.

Figure 2 Algorithm for the treatment of diaphyseal fractures according to the type of bone healing impairment.



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