

Surgical approach to bone healing in osteoporosis

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Summary

Osteoporotic fractures represent one of the most common cause of disability and one of the major voice in the health economic budget in many countries of the world. Fragility fractures are especially meta-epiphyseal fractures, in skeletal sites with particular biomechanic characteristic (hip, vertebrae), complex and with more fragments, with slow healing process (mineralization and remodeling) and co-morbidity. The healing of a fracture in osteoporotic bone passes through the normal stages and concludes with union of the fracture although the healing process is prolonged. Fractures in the elderly osteoporotic patients represent a challenge to the orthopaedic surgeons. Osteoporosis does not only increase the risk of fracture but also represents a problem in osteofixation of fractures in fracture treatment. The major technical problem that surgeons face, is the difficulty to obtain a stable fixation of an implant due to osteoporotic bone. The load transmitted at the bone-implant interface can often exceed the reduced strain tolerance of osteoporotic bone.

In the treatment of osteoporotic fractures it is important to consider different aspects: general conditions of elderly patient and comorbidity, the reduced muscular and bone mass and the increased bone fragility, structural modifications as medullary expansion.

The aim of surgical treatment is to obtain a stable fixation that reduces pain and permits an early mobilization.

KEY WORDS: osteoporosis, bone healing, fractures fixation.

Introduction

Osteoporosis represents the most common skeletal disease, affecting approximately 200 million people all over the world (1). Prevalence of osteoporosis increases dramatically with aging; in women, for example, it goes from a 5% prevalence at 50 year old to 50% at 85 years old (2). National osteoporosis foundation (NOF) counts that in the United States, in 2002, approximately 7,8 million women over 50 year old suffered by osteoporosis and 21,8 million by osteopenia; it is estimated that in 2020 ap-

proximately 41 million women will be osteoporotic or osteopenic (3).

Osteoporosis is a relevant disease in its clinical and epidemiological aspects because of the consequent fractures. Osteoporotic fractures represent, in facts, one of the most common cause of disability and one of the major voice in the health economic budget in many countries of the world. The most common fracture sites in the elderly osteoporotic patients are: hip (subcapital femur fractures, intertrochanteric fractures, subtrochanteric fractures), ankle, proximal humerus, wrist, vertebrae.

It is estimated that 1 women out of 2 and 1 men out of 4 over 50 year old, will develop a fracture in their lifetime; a previous fracture increases the risk of a new fracture from 2 to 5 times. However, only a small number of patients undergo an osteoporotic evaluation and treatment (4). The 55% of people over 50 year old have an increased fracture risk because of low level of bone mass (5).

It is estimated that the incidence of fracture will increases 2 to 4 times in the next decades because of the aging of population. In Europe from 12% to 17% of the population over 65 in 2002, from 20% to 25% in 2025 (6). Furthermore, independent from skeletal site, a fracture increase from 50% to 100% the probability of a new fracture in another site (7, 8).

Fragility fractures are especially meta-epiphyseal fractures, in skeletal sites with particular biomechanic characteristic (hip, vertebrae), complex and with more fragments, with slow healing process (mineralization and remodeling) and co-morbidity (9).

Bone fragility in osteoporosis depends on the modifications of mechanical and structural properties of bone:

- reduction of mineral content (provides strenght and stiffness) and proteic content (limits the damage consequent to an impact and influences bone mechanical properties);
- reduction of the ability to oppose to deformations (rigidity), to absorb energy (resistance), to adapt to repetitive loads (fatigue resistance), to inhibit the progression of a lesion (resistance to fracture);
- increase of anisotropy (major number of trabeculae with an orientation on the principal load axis) and therefore increase of fracture risk for abnormal loads (falls);
- increase of microdamages (manifestation related to repetitive micro-stress on bony tissue, age-related).

With aging it's possible to observe an increase of microdamages that perhaps the physiological mechanism of repair are not able to contrast. The healing of a fracture in osteoporotic bone passes through the normal stages and concludes with union of the fracture although the healing process is prolonged (10).

The biological activity of the osteoblast, as for other mesenchymal cells, is influenced negatively by aging.

Doll et al., in 2003, demonstrated that osteoblasts in elderly people present alterations in cytology and cytoskeletal structure, a reduced synthesis of alkaline phosphatase, osteocalcin and collagen, a reduced expression of RUNX 2, typical proliferation and differentiation pre-osteoblastic factor. Everything is related to a reduction of osteo-progenital cells, of the number and activity of osteoblasts, and to a reduction of physiological stimuli as mechanical stress (11).

The formation of bone callus is also influenced. Many experi-

mental studies, in fact, have demonstrated that in elderly patients a decreased number of osteoblasts is present, and they result even less active (12). Fractures in the elderly osteoporotic patients represent a challenge to the orthopaedic surgeons, that have an unique opportunity because fragility fractures are the first sign in a patients suffering by osteoporosis; often they are the first and sometimes the only doctors seen by patients with fragility fractures; they may have a central role in optimizing the treatment, not only of the fracture but of the osteoporotic process too.

Osteoporosis does not only increase the risk of fracture but also represents a problem in osteofixation of fractures in fracture treatment (13).

The major technical problem that surgeons face is the difficulty in obtaining a stable fixation of an implant due to osteoporotic bone. The load transmitted at the bone-implant interface can often exceed the reduced strain tolerance of osteoporotic bone (14).

In the treatment of osteoporotic fractures it is important to consider different aspects:

- general conditions of elderly patient and comorbidity;
- the reduced muscular and bone mass and the increased bone fragility;
- structural modifications as medullary expansion.

The aim of surgical treatment is to obtain a stable fixation that reduces pain and permits an early mobilization.

Discussion

Biological aspects

Biological processes which enhance the healing potential of osteoporotic fractures should be considered useful as surgery (14). Bone grafts (autograft and allograft) are the ideal devices because they contain osteogenic bone cells, marrow cells, and an osteoconductive collagen matrix (15). A variety of biological devices are available or under development, with different composition, mechanism of action, and clinical results (16, 17). Bone graft substitutes try to mimic the components of an autogenous bone graft by reproducing the property of bone matrix (biological and structural) (18).

Ceramics such as calcium phosphates and sulfates – strong in compression but weak in tension and shear, with osteoconductive and osteointegrative properties – are hydroxyapatite and tricalcium phosphate (19, 20).

Various growth factors are expressed during fracture healing (TGF-beta, insulin-like growth factor, PDGF) and various cell types and growth receptors are present within fracture callus, depending on the stage of healing, leading to a “window of opportunity” for directed use of specific growth factors. Bone morphogenetic proteins (BMPs, rhBMP-7, rhBMP-2) are the most potent osteoinductive agents. Appropriate dosages, optimum time, modes of delivery, duration of treatment, and precise clinical indications for use have to be studied further. It will also be important to determine their applicability to elderly patients with osteoporotic fractures, to justify the cost of the treatment (19). Osteoinductive demineralized bone matrix results from bone demineralization and is attributed to matrix-associated bone morphogenetic proteins (21). It is available in different formulations: freeze-dried powder, granules, strips, gel, paste, and putty alone or in combination with allograft bone chips or calcium sulfate granules (19). Platelet-rich plasma (PRP) is a novel osteoinductive therapeutic approach that is increasingly used in treatment of such complications of bone healing processes (22, 23); it contains many growth factors (PDGF, TGF- β , VEGF, IGF, EGF and antimicrobial proteins) that can help in bone heal-

ing in combination with graft (19). Orthopaedic tissue engineering combines the use of three-dimensional scaffold materials, cells, and release of growth factors to enhance bone formation (24). A highly porous artificial extracellular matrix or scaffold is essential to the attachment, proliferation and differentiation of bone cells (osteoblasts, osteoclasts and osteocytes) and the formation of bone tissue (25). Coating implants with different devices, such as hydroxyapatite coated pins and screw, could be useful to enhance bone healing (25, 26). Implant surfaces could also be used to deliver growth factors (BMP-2, BMP-7), transforming growth factor (TGF- β) or fibroblast growth factor (FGF) locally to guide bone ingrowth.

Surgical and technical aspects

Fracture healing is a complex biological process with a temporal and spatial sequence that may be influenced by biological (age, gender, disease) and mechanical (reduction, osteosynthesis) factors (28). Osteoporotic patients is characterized by poor bone quality, loss of bone mass and microarchitectural deterioration of bone tissue (13, 29). The fractures in these patients present the surgeon with difficult treatment decision and surgical fixation (30). When fragility fractures occur, urgent treatment is needed (31). The attention is on improving pharmacological therapy in order to preserve bone mass and thus decrease fracture risk (28), but the major problem facing the surgeon is the difficulty in obtaining secure fixation of an implant to osteoporotic bone, when surgery is necessary, which is reflected in a dramatic increase in the rate of failure of implant fixation (13, 14, 29). There is less cortical and cancellous bone, so that the pull-out strength of implants is reduced (14). Pullout is a possibility, especially if low density bone is encountered (32). Some changes in surgical technique are required, including the use of relative stability techniques (14, 33). Current studies mainly focus on preventing osteoporotic fractures. In recent years, the literature has provided evidence of non-physiological fracture healing in osteoporotic bone, with important implications (28). The fractures in osteoporotic patient have specific findings about the site, anatomo-pathology, therapeutic approach, almost always surgical, and the prognosis. Fractures of the osteoporotic proximal femur, together with vertebral fractures, very common in osteoporotic patients, are a significant source of mortality and morbidity (34, 35). They compromise the functional activity of the patient and worsen the co-morbidities, including the osteoporosis itself. The therapeutic approach to osteoporotic fractures requires prompt mobilization with full loading of the affected limb as soon as possible, and treatment of chronic disease including the osteoporosis (35). The specific demands involved in the treatment of osteoporotic fractures calls for specific solutions (36). The main treatment goal should be preservation of function even at the expense of restoration of exact anatomy (36). In general, researchers and developers have worked on three different approaches: adapted anchoring implants, improved load distribution, and augmentation techniques (33). The load can often exceed the strain tolerance of osteoporotic bone. This may result in microfracture, resorption of the bone, failure of fixation (14) and increased rate of complications (non-union, malunion, re-operation). Various treatment methods and innovations have been attempted in order to improve the past poor results (37). The surgical techniques and devices, which are able to restore as well as possible the local anatomy with a reduced strain at the bone implant interface, are auspicious in osteoporotic bone fractures (14, 38). Cornell CN et al. found that surgeons are learning to modify the classic techniques of internal fixation to adapt them to the elderly population; screws should be placed into the best quality of bone available; when using plate fixation, stable bone contact at the frac-

ture site is the most important factor in reducing strain in the plate (39). Augmentation techniques may improve anchorage in osteoporotic bone, using bone autograft or allograft, bone cement or bone substitute. Fracture treatment of patients with osteoporosis really needs an interdisciplinary approach (33). It is difficult to reproduce in clinical studies the influence of osteoporosis on implant fixation, due to the lack of accurate osteoporosis assessment, absence of complication definitions and heterogeneous inclusion criteria in these studies (40).

Common fractures seen in geriatric population

Fractures of the proximal humerus

Fractures of the proximal humerus, very common in geriatric population, remain a difficult problem. They are often complex with associated damage to the muscles of the rotator cuff leading to poor shoulder function. Over the last decades several techniques have been applied for treatment. Widely accepted is the initiation of a conservative treatment regimen for undisplaced fractures, however the standard treatment for displaced fractures, especially three and four part fractures, is still the focus of scientific debate (41). In elderly patients, osteopenic bone, often in combination with a thin and or ruptured rotator cuff, predisposes to unpredictable clinical results. Closed reduction and percutaneous pinning, tension band wiring, intramedullary nailing, plate fixation, and hemiarthroplasty have demonstrated mixed results. Osteoporosis makes internal fixation problematic and frequently contributes to failed fixation and poor clinical results (42). Traditional open reduction may lead to more accurate reduction but the extensive tissue dissection doubles the risk of avascular necrosis and fracture disease (43). Malunion, non-union and avascular necrosis have been reported in patients treated by open reduction and internal fixation. The operative treatment of displaced fractures is therefore a technical challenge. A minimally invasive technique that lead to biological and biomechanical advantages is intramedullary nailing, giving stability to the fracture during healing without the risk of mechanical failure of the device. Fixation with intramedullary nail theoretically offers better fixation, but results have shown an increased risk of shoulder pain and decreased range of motion (43). If there is an unstable or comminuted lateral metaphyseal fracture failure of fixation or fracture displacement may occur (44). Several new locked plate devices have been developed because research suggests plates with attached (locked) screws may provide improved fracture stability and healing (45). Locking the screw to the plate mechanically recreates a point of cortical bone contact (46), which may be useful in the poor cancellous bone of the proximal humerus. Locking plates also have a preconfigured shape and screw direction, which may reduce hardware complications. Early clinical results using the locking proximal humerus plates have been promising, although no comparisons with other techniques have been published (47). Percutaneous reduction and fixation of such fractures would therefore seem to be desirable since this is a minimally invasive technique with minimal fixation, maximizes anatomical restoration, maintain cuff integrity, minimal or no scar, and easy implant removal (48).

Fracture of the distal radius

Wrist fractures are most likely to occur in women over 65 years old, but are increasing also in white women between 45 and 60 years of age (49). Osteoporosis renders simple fractures unstable and makes distal bone fixation a challenge. While most frac-

tures of the distal radius can be treated by conservative means, unstable distal radius fractures require surgical fixation. For these fractures various methods of surgical treatment have been reported. Open reduction and internal fixation with plates is a valid treatment of displaced extra- and intraarticular fractures. Conventional buttress plating provides poor distal screw purchase and often requires bone grafting. Dorsal plate fixation is associated with soft tissue problems, impingement of the plate on the extensor tendons which may result in poor function. The difficulty obtaining reliable fixation in osteoporotic bone presents a challenge to the surgeon that has been partially addressed by newer implants with screws that directly engage the plate, creating fixed angle bolts that have better fixation in osteoporotic bone (50). The introduction of fixed-angle internal fixation implants for the treatment of distal radius fractures provides a solution to the challenge of distal fragment fixation; these implants do not require screw purchase into the distal fragment and therefore are less likely to loosen and toggle (51, 52). They function as nails, giving support by interference fit or acting as an internal buttress. Subchondral support pegs do not induce interfragmentary compression but firmly maintain bony alignment and rely on the substantial healing capability of the distal radius. These implants can be thought of as metaphyseal prosthesis transferring the articular loads from the subchondral bone across the fractured metaphysis to the intact diaphyseal bone. Specific advantages of volar fixed-angle plating include stable fixed-angle support that permits early active wrist rehabilitation, direct fracture reduction, and fewer soft-tissue and tendon problems. Biomechanical data indicate that, when loaded to failure, volar fixed-angle plates have significant strength advantages over dorsal plating. Volar fixed-angle plating is advantageous in elderly osteopenic patients and for high-energy comminuted fractures and malunions requiring osteotomy (53).

Spine fractures

Osteoporotic vertebral compression fractures have previously been treated non-operatively, given the tremendous morbidity associated with open fixation in elderly patients who often have multiple comorbidities (54). Recent advances in surgical technique, including vertebroplasty and kyphoplasty (55, 56), have replaced non-operative treatment, with significant results in term of morbidity and recovery of functional activity of the patients. Percutaneous vertebral augmentation offers a minimally invasive approach for the treatment of vertebral compression fractures. Both methods allow for the introduction of bone cement into the fracture site (56). Kyphoplasty and vertebroplasty are safe and effective, and have a useful role in the treatment of painful osteoporotic vertebral compression fractures that do not respond to conventional treatments; both are minimally invasive procedures for the stabilization of osteoporotic vertebral fractures leading to a statistically significant reduction in pain (57). Kyphoplasty offers the additional advantage of realigning the spinal column and regaining height of the fractured vertebra (58), which may help decrease the pulmonary, gastrointestinal, and early morbidity consequences related to these fractures (30). Both procedures are technically demanding (59-61). The restoration of vertebral height and reduction of kyphosis may have an influence on the long term clinical outcome (57). However, their value remains to be confirmed by prospective randomized trials (14, 59).

Fractures of the proximal femur

In 1990 an estimated 1.3 million fractures of the hip occurred worldwide (62), a figure which is expected to double by 2025

and to increase to 4.5 million by 2050. The average age of these patients is about 80 years and 75% are female. Approximately half of these fractures will be intracapsular.

Although internal fixation with lag screw or dynamic hip screw is recommended for most non-displaced fractures of the femoral neck, the optimal treatment for displaced fractures of the femoral neck is controversial. Options for operative treatment of displaced include: reduction and internal fixation; unipolar hemiarthroplasty; bipolar hemiarthroplasty; and total hip arthroplasty (63).

Comorbidities of the patients and current socioeconomic changes in healthcare led to reconsideration of closed reduction and internal fixation of femoral neck fractures as an alternative treatment modality. With correct decision-making, proper reduction, and proper consideration of the biomechanical principle of three-point fixation, minimally invasive screw fixation of femoral neck fractures is a safe and inexpensive procedure even in elderly patients (64). The treatment of extracapsular fractures is less controversial and require internal fixation. Many internal fixation devices have been recommended for the treatment of pertrochanteric fractures, including extramedullary and intramedullary implants. The sliding hip screw is a tried and tested device for fixation of these fractures with excellent results reported (65). An intramedullary implant inserted in a minimally invasive manner is better tolerated in the elderly (66). The dynamic hip screw (DHS) seems to have a biomechanical disadvantage when compared with intramedullary devices because the load bearing in the proximal femur is predominantly shared by the calcar. Intramedullary devices have a shorter lever arm and have reduced tensile strain on the implant reducing the risk of implant failure (67). On the other hand the intramedullary nail has a significantly increased risk of fracture at the tip of nail. Studies comparing the gamma nail and sliding hip screw have found higher incidence of complications and re-operation rates with the gamma nail and no difference in long term functional outcomes (68). The intramedullary nails are better implants for unstable reverse oblique fractures while the sliding hip screw better for stable inter-trochanteric fractures (69). External fixation for pertrochanteric fractures has been mainly used in elderly high-risk patients (70). It should be considered as an alternative for elderly and frail patients, those with multiple injuries, those with unstable, complex fractures which may not be adequately treated by internal fixation (71).

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