Fracture Care in the Elderly

15

Jay M. Zampini and Christopher M. Bono

Introduction

As life expectancy around the globe continues to increase [1], the prevalence of osteoporosis is expected to increase along with fractures. Osteoporosis insidiously converts bone, the primary organ of support and mobility, from rigid beams to veritable "empty eggshells" that can fail under physiologic conditions of daily living. Fractures do not occur simply as a result of poor bone quality but of the interaction between the strength of the bone and its ability to withstand the forces that are exerted on the bone. These forces are a function of muscular strength, balance, dexterity, cognitive function, and falls. These issues, coupled with severe medical comorbidity, can increase the risk of surgical intervention [2, 3]. Postoperative morbidity and mortality can also be increased, however, by delaying treatment [4–6]. The concept that elderly and osteoporotic patients have unique care requirements has been given considerable attention in recent years and has led to the development of distinct areas of study and treatment in orthopaedics, traumatology, and spinal surgery [7–9]. Additionally, several mechanical, biologic, and technical advances have made the treatment of osteoporosis related injuries safer and more successful and will be discussed in detail. The purpose of this chapter is to review the impact of osteoporosis on the manner in which fractures occur, are stabilized, and heal with attention to fractures that occur commonly and are likely to be encountered in clinical practice.

J.M. Zampini, MD • C.M. Bono, MD (✉)
Division of Spine Surgery,
Department of Orthopaedic Surgery,
Harvard Medical School,
Brigham and Women's Hospital,
75 Francis Street, Boston,
MA 02115, USA
e-mail: jzampini@partners.org; bonocm@me.com

Mechanism of Bone Injury

Fractures occur when an applied force, the product of mass and acceleration, exceeds the capacity of the bone to absorb and transmit that force. Fractures can be described by a number of important attributes. These include the number of fragments, or comminution, the degree of separation of fragments, or displacement, angulation in the cardinal anatomic planes, and involvement of an articular surface. Bone fractures differently in patients with osteoporosis than in patients with adequate bone density. Whereas bone with adequate mineral density typically fractures following high-energy events such as a fall from a height or motor vehicle collision (a force applied by a massive object or at high acceleration), fractures in osteoporotic bone can occur following low-energy trauma

G. Duque, D.P. Kiel (eds.), *Osteoporosis in Older Persons: Advances in Pathophysiology and Therapeutic Approaches*, DOI 10.1007/978-3-319-25976-5_15

such as a fall from the standing position or even from participating in activities of daily living and exercise (a physiologic mass at low acceleration). The clinical manifestation of this difference is the observation of less comminuted, more displaced fractures in young healthy bone compared to more comminuted, less displaced fractures in osteoporotic bone. A specific example of this is the proximal weight-bearing region (plateau) of the proximal tibia. In patients with adequate bone mineral density, a large portion of a tibial plateau will split off following a forceful impact with the femoral condyles. In the osteoporotic patient, the femoral condyle will crush the subchondral cancellous bone of the tibial plateau, leading to depression of the articular surface into the void created by the crumbled bone (Fig. 15.1).

The mechanism of injury for spinal fractures similarly varies with bone mineral density. Young vertebral bodies can sustain tremendous axial compressive loads because of the trabecular support beams with numerous cross-connections. A vertebral body of adequate bone mineral density can be compared to an unopened beverage can. Provided one had excellent balance, one could support his or her weight on the can without damaging it. A substantial force applied to the can could burst it, in much the same way that a substantial force applied to a normal vertebra causes the vertebra to burst and fragments to displace widely. If the can were emptied of beverage, the same maneuver would cause the can to collapse and be crushed. In the osteoporotic spine, the vertebral body is “emptied” of trabecular support and cross connections, rendering it capable of being crushed under physiologic forces or minor trauma. The morphology of an osteoporotic fracture typically shows central depression the endplates of lumbar vertebrae and wedge shaped deformity of thoracic vertebrae (Fig. 15.2). Further information regarding specific fracture patterns and the differences between normal and osteoporotic bone will be discussed below.

A final morphologic difference between fractures in osteoporotic bone and bone of adequate mineral density has been reported to result from prolonged treatment of osteoporosis with the bisphosphonate class of antiresorptive agents. Initially, reports of subtrochanteric fractures of the femur, usually associated with high-energy trauma, were sporadically reported to have occurred following a low-energy event [10–13]. Analyses of these reports ultimately revealed a relative risk of such atypical fractures that increased with longer duration of bisphosphonate use, with the American Society of Bone and Mineral Research reporting an incidence of 78 fractures per 100,000 patients after 8 years of medication usage compared to 2 fractures per

Fig. 15.1 A tibial plateau fracture in patients with osteoporosis results in depression of the articular surface and compaction of the underlying cancellous bone (*arrow*)

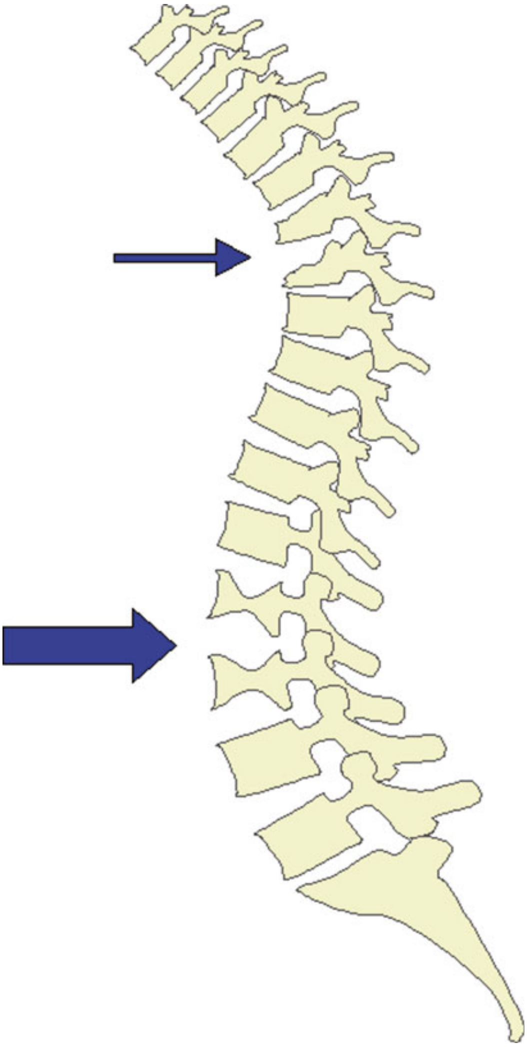

Fig. 15.2 Wedge fractures are more common in the thoracic spine (*small arrow*), while central depression fractures are more frequent in the lumbar spine (*large arrow*). These patterns are likely the result of the mechanical alignment of the spine in these regions

100,000 patients using bisphosphonates for 2 years [11]. An atypical femur fracture is associated with a prodrome of pain before the fracture. The radiographic appearance of a fracture line emanates from the lateral cortex and progresses medially; there is thickening or "beaking" of the bone at the fracture site (Fig. 15.3). Additionally, atypical fractures of the pelvis [14] and ulna [15] have been reported.

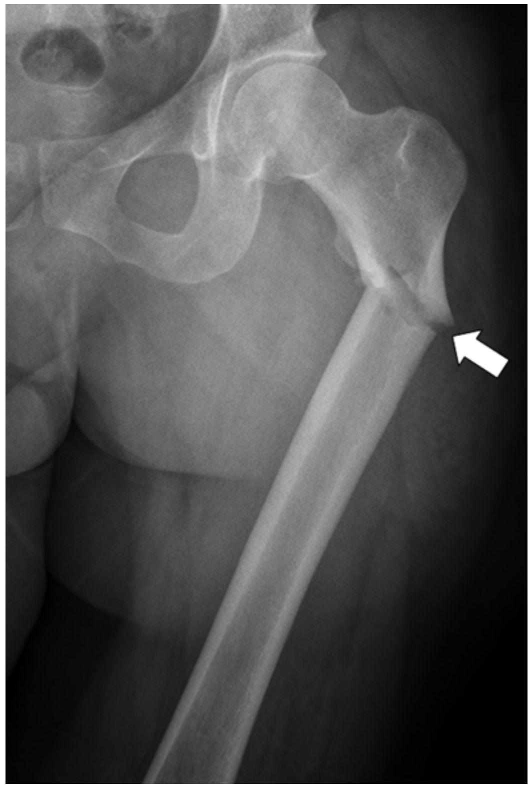

Fig. 15.3 An atypical femur fracture is identified by thickening, or "beaking," of the bone at the fracture site (*arrow*)

Fixation Challenges in Osteoporotic Bone

The clinical importance of the prior discussion of fracture morphology and mechanism, aside from assisting in communication between healthcare providers, is to determine the optimal method of definitive fracture treatment. A general goal of fracture care is to restore and maintain anatomic alignment during fracture healing. Manipulation of bone fragments at the time of surgery is often required to reduce fracture displacement and angulation. Once anatomic alignment has been achieved, it is typically held in place with metallic implants such as screws, plates, and rods. This inherently mechanical process is akin to anchoring an object into a household wall. A screw placed into a wooden stud would achieve excellent purchase, or hold, capable of supporting a heavy object without fail (Fig. 15.4a). A screw placed only into plaster with no other support, however, would lose purchase as the head is advanced to the wall and the threads turned, crumbling the brittle plaster and allowing the screw to be pulled from the wall with minimal effort (Fig. 15.4b). Screw fixation in osteoporotic bone can result in that same disconcerting feel that nothing is holding, and, without taking proper measures, can lead to early failure of fracture stabilization [16, 17].

To overcome these challenges, several solutions have been engineered to provide better fixation in suboptimal situations. Since the primary device of fracture fixation is the screw, much attention has been given to improve this common and ancient simple machine. In some circumstances, screws with a larger ratio of external thread diameter to internal shaft diameter can be used to apply the force of fixation over a larger bone surface area. Devices have also been designed to gain fixation by placing multiple screws into the bone, each of which would individually have insufficient purchase. The multiplicity of points of fixation, often coupled with the ability to lock the screws rigidly to the plate, provides better stabilization of fractures in weakened bone [18]. Another example of screw

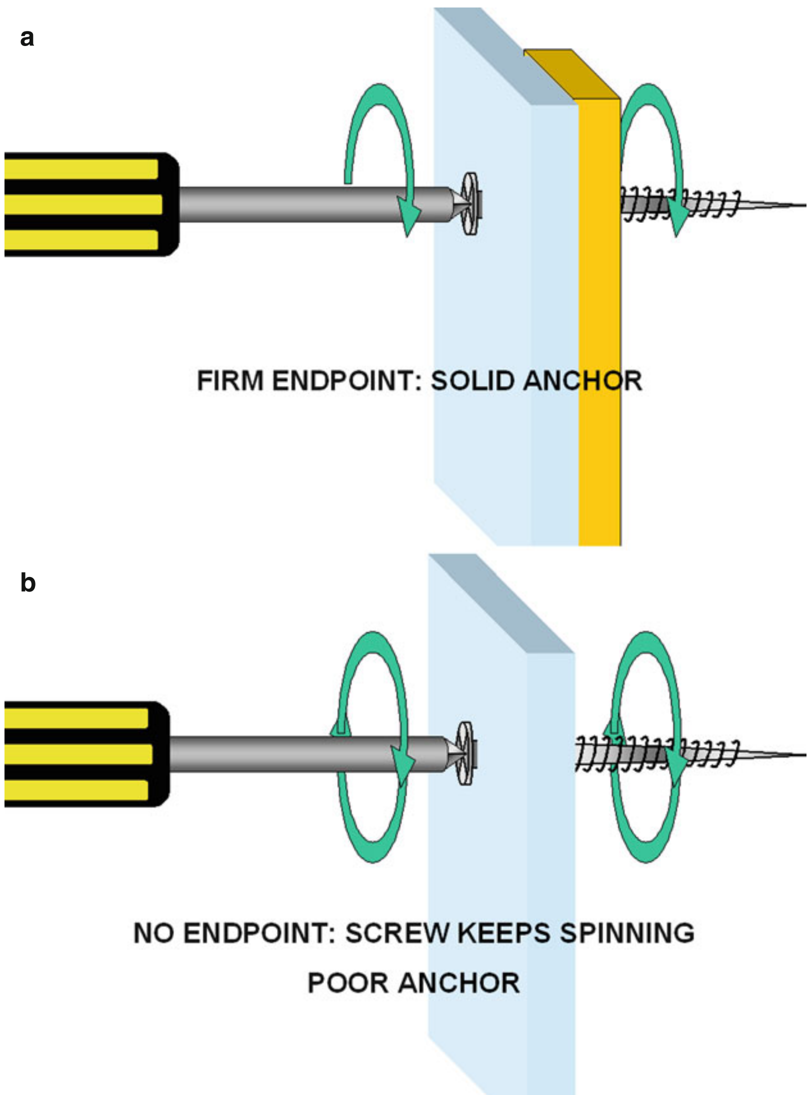

Fig. 15.4 In normal bone, a screw achieves excellent purchase with a firm endpoint. Using the described analogy of inserting a screw in to a plaster wall, this would be analogous to "catching" the beam (**a**). In contrast, inserting screws into osteoporotic bone yields no endpoint, analogous to "missing" the beam (**b**). The screw can be turned indefinitely with no endpoint as it spins in place

engineering is the design of some screws with a threaded cap that can be applied to the tip of the screw and allow the device to function more like a nut and bolt, gaining strength by pressing firmly against the stronger cortical bone surface instead of relying on thread purchase in weakened trabecular bone. Finally, additional screw purchase can be gained by augmenting the bone with polymethylmethacrylate (PMMA) bone cement. PMMA begins as viscous fluid that can be injected into bone to interdigitate into the spaces between bone trabeculae. The fluid polymerizes into a hard solid (the nonmedical variety of this substance is acrylic). Screw purchase is gained by dispersing the force of fixation over the much larger surface area gained by the interdigitation of cement and bone [19]. This concept is applied in vertebroplasty and kyphoplasty, methods of vertebral augmentation for osteoporotic compression fractures, and will be discussed in further detail below.

Changing the location of the fixation device can also aid in its ability to stabilize a fracture. Intramedullary nails, though not initially developed for osteoporotic bone, are inserted into the medullary cavity of long bones, such as the femur, tibia, and humerus. In contrast to plates, intramedullary devices are located closer to the weightbearing axis of the bone (Fig. 15.5). This allows the fracture ends of the bone to bear more of the load than would be allowed by a plate. Sliding hip screws rely on a similar principle in that they allow the broad cancellous surfaces of an intertrochanteric fracture to sustain the majority of the load. The primary function of the implant, therefore, is to keep the fragments aligned but not to bear load.

Finally, there are methods of treating fractures that do not rely on screw-based implants or fracture reduction. For example, most surgeons consider an arthroplasty (that is, joint replacement) to be the treatment of choice for elderly patients

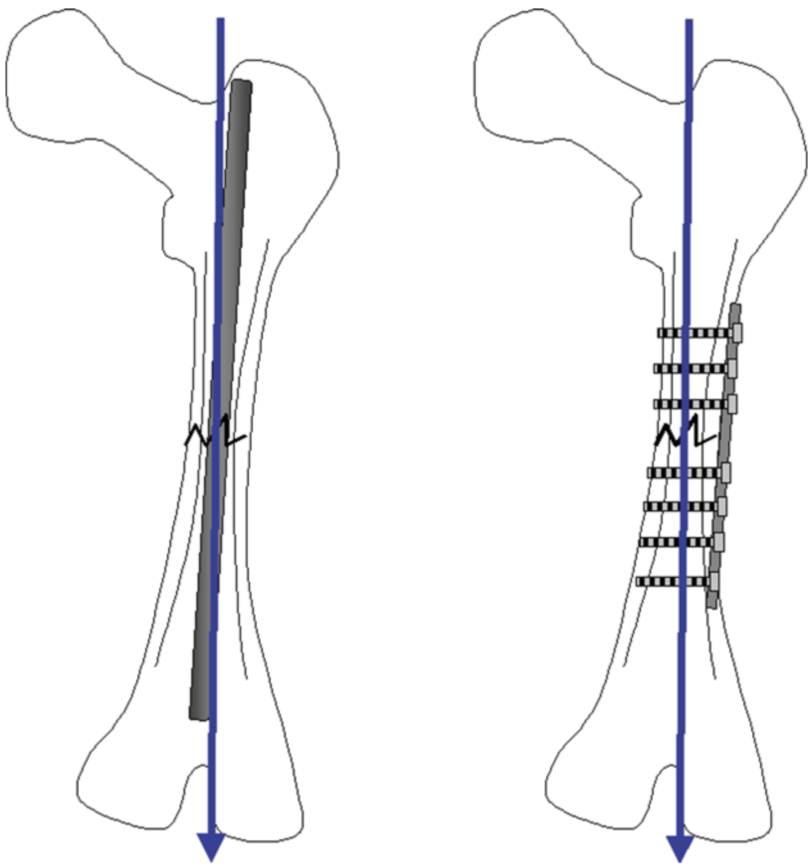

Fig. 15.5 An An intramedullary nail is better aligned with the weight-bearing axis of a bone (*left*), which may have advantages in osteoporotic patients. Plates and screws lie farther away from the weight-bearing axis (*right*)

with femoral neck fractures of the hip [20] and certain fractures of the proximal humerus [21]. Such a treatment circumvents the need to reduce and stabilize a fracture and provide an optimal environment for fracture healing, as it involves removal and replacement of the fractured segment of bone. Furthermore, the prosthesis is usually secured to the bone with PMMA cement, which is preferred over so-called press-fit fixation, in the setting of osteoporotic bone. Such a fixation method does not directly rely on bone density as much as screw, plate, or rod fixation.

Timing of Fracture Treatment in the Elderly

The optimal time for surgical treatment of fractures in older patients has been a matter of continuous debate, although the issues have, in many ways, stayed the same [22]. Factors that influence the decision include the anatomic structure injured, the effect of the fracture on mobilization and ambulation, and the overall medical condition of the patient.

In general, and despite the opinion occasionally rendered through social media [23], the goals of fracture fixation are to provide the patient with optimal ability to mobilize from recumbency, ambulate, and participate in activities of daily living. This is best understood through clinical examples. Hip fracture is perhaps the paradigm of injury that impairs these three functions. Nonoperative management leaves patients recumbent, placing them at high risk for pressure ulcers, thromboembolic events, and pulmonary decompensation. Furthermore, nonoperative treatment has been shown to result in a higher mortality rate [24]. Early surgical treatment would, therefore, minimize the time during which a patient would be completely incapacitated and unable to mobilize from bed [4–6]. This factor must be counterbalanced with a careful consideration of the patient's medical history, current medical condition, and ability to improve the current medical condition. These assessments will typically result in surgery that can be optimally performed within two [4] to four days [25] of injury. The current recommendation is to perform surgery for hip fractures as early as medically allowable and ideally within 48 h of injury [26]. Ongoing studies to evaluate the feasibility of accelerated surgical care within a mean of approximately 6 h following diagnosis [27], underscore the observation that patients are often in optimal condition at the time of presentation to the hospital and tend to decline during the hospitalization.

Vertebral fractures represent another commonly encountered group of injuries that can have detrimental effect on quality of life, pulmonary function, and the ability to perform activities of daily living. While hip fractures have immediately negative effects, vertebral compression fractures are more insidious but result in a six- to ninefold increase in 1 year mortality similar to that of hip fractures [28]. The traditional treatment of vertebral compression fractures (VCF) has included oral analgesic medications, advising the avoidance of painful activities, and counseling the patient that the fracture will heal in time and that pain will soon subside [29]. Nearly two-thirds of patients with symptomatic VCF actually will experience enough pain relief within 6 weeks to return to pre-fracture level of activities and thereby avoid the risks of prolonged inactivity. In contradistinction, persistently painful fractures can lead to physical deconditioning, emotional and psychological distress, and dependence on pain medications. The development of percutaneous vertebral augmentation, also known as vertebroplasty and kyphoplasty, has introduced an alternative for these patients where none previously existed [30–33]. Whereas most studies report that the procedure effectively reduces pain and quickly, a more important effect attesting to the ability of the procedures to restore function, similar to that of hip fracture surgery, has been a reported reduction in mortality risk for patients treated with vertebral augmentation than with nonsurgical treatment [34, 35]. This is, of course, not without surgical risk, a thorough discussion of which is included below. The challenge with VCFs is determining which patients would benefit from nonsurgical care and which would benefit from early performance of vertebral augmentation. No consensus has been reached regarding the optimal timing of vertebral augmentation as there has for hip fracture fixation. Patients confined to a bed or chair with severe pain appear to have the most to lose by waiting, similar to a hip fracture patient, and would therefore benefit from an early decision to perform vertebral augmentation. For patients able to mobilize but who complain of pain severe enough to limit other activities, a trial of nonoperative care for 4–6 weeks may be ample time to determine if pain relief will be adequate or if vertebral augmentation would be of benefit.

Bone Healing Challenges in Osteoporotic Bone

The rate and quality of bone healing is compromised in patients with osteoporosis compared to patients without osteoporosis. Animal studies have demonstrated this effect with femur fractures and fracture callus in standardized models of osteoporotic bone [36, 37]. Clinical studies have similarly shown delayed healing and poor rates of spinal fusion in elderly, osteoporotic patients [38]. The biologic basis for this has been reported to result from the reduced number and proliferative capacity of bone marrow mesenchymal stem cells (MSCs) that occurs with advanced age [39]. These findings highlight the importance of maintaining an optimal healing environment at the surgical site through meticulous surgical technique as well as biologic, pharmacologic, and electrophysiologic alteration of the healing site.

Surgical Solutions

The disadvantaged state of osteoporotic bone healing can be made worse through improper surgical technique. A fracture limits the endosteal blood supply to the bone by the disruption the internal architecture and vasculature of the bone. Modern techniques of fracture surgery emphasize the importance of maintaining blood supply to the fracture site through meticulous handling of the periosteum and surrounding muscular envelope. This leads to less devitalization of the bone's remaining blood supply and optimizes healing of the fracture and surgical site. A concrete application of this theory can be seen in the use of intramedullary fixation and percutaneously applied fixation plates. Both techniques involve external manipulation of the fracture, insertion of the device distant from the fracture site, and avoidance of direct access of the fracture site. Screws are also inserted percutaneously to the plate for fixation of the fracture (Fig. 15.6). In a similar method, instrumentation has been developed for the percutaneous insertion of pedicle screws and rods for instrumented stabilization of spinal fusion, thus avoiding the damage to the vasculature that occurs with open exposure of the spine for fusion.

Biologic Solutions

Healing and growth of any bone requires three elemental factors: source of cells capable of producing bone (ostengenecity), a stimulatory factor to induce the bone-producing cells to form bone (osteoinductivity), and a scaffold of material sufficient to guide the production of bone (osteoconductivity). Biologic optimization of bone healing can target any or all of these factors. In relation to the above discussion regarding the reduced number and function of MSCs in osteoporosis and advanced age, several products have been developed to either increase the concentration of a patient's native stem cells or to transplant allogeneic stem cells at the time of surgery. A patient's own MSCs can be harvested from bone marrow by aspiration of the iliac crest using a Jamshidi needle. Commercially available products such as BMAC (Harvest Technologies, Inc, Munich, Germany) process the bone marrow using sterile centrifugation and isolation of the buffy coat to achieve a reported eightfold increase in the concentration of MSCs [40, 41]. Similarly, osteogenic cell density can be increased at a fracture or spinal fusion site using commercially available allogeneic MSC products such as Cellentra VCBM (Biomet, Warsaw, IN), Trinity

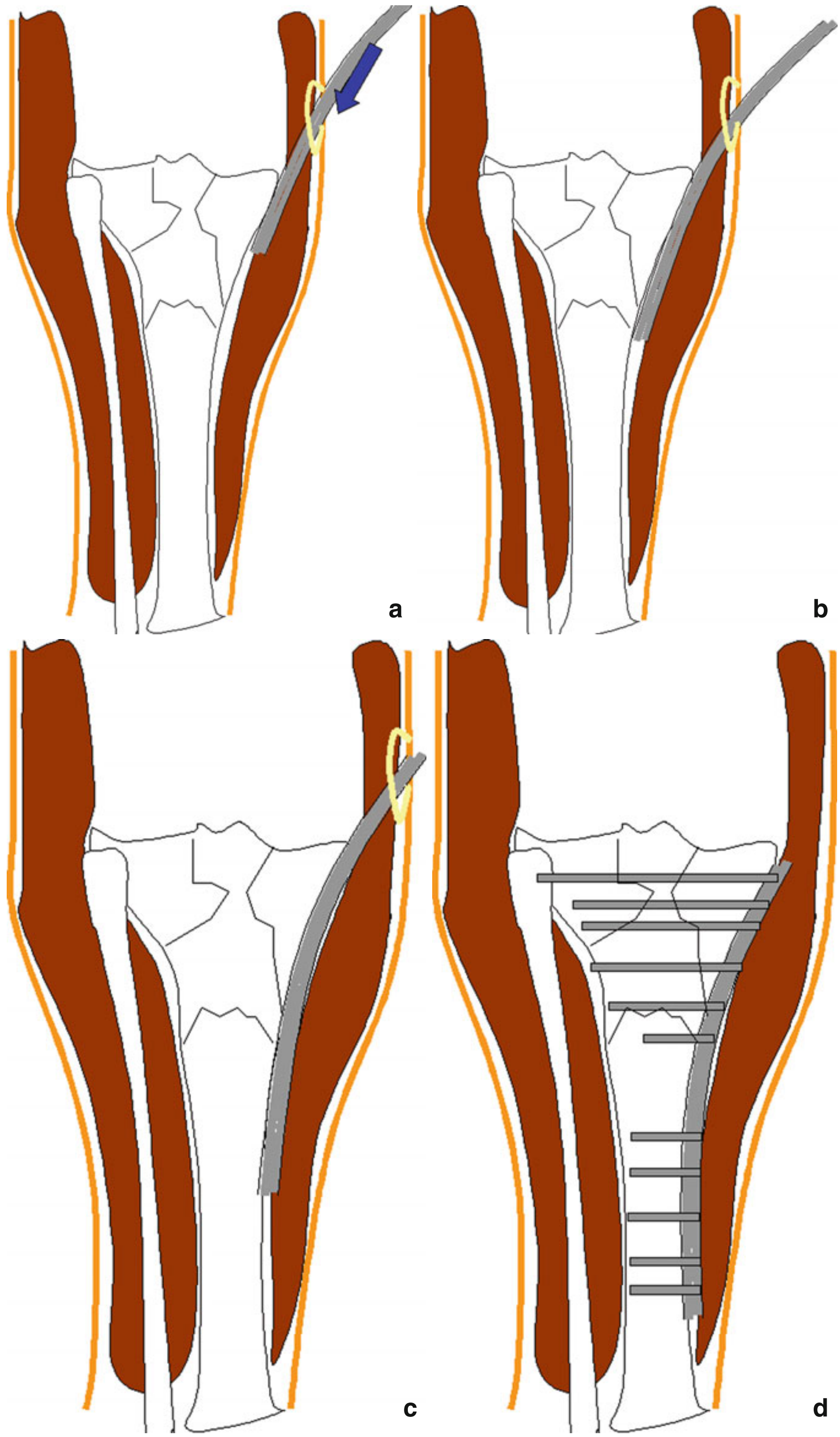

Fig. 15.6 If Suclosed reduction can be achieved, less invasive methods of plate fixation can be used in osteoporotic and elderly patients. In contrast to formal open fixation, these methods utilize smaller incision (*arrow*) in the skin through which a plate is introduced under the muscle (**a**). The plate is then slid along the periosteal surface (**b**) until it is in an acceptable position (**c**). The plate is then held in place with screws (**d**) that are inserted in a percutaneous manner using specialized alignment guides

Evolution (Orthofix, Lewisville, TX), and Osteocel (Nuvasive, San Diego, CA). These products provide the osteogenicity necessary for fracture and spinal fusion healing and have been shown to produce none of the immune reactions typical of other unmatched, potentially incompatible allogeneic tissue transplant [42, 43].

Osteogenic cells can be induced to form bone through the stimulatory effects of the so-called bone morphogenic proteins (BMPs), a group of compounds of the transforming growth factor-beta superfamily. Through recombinant DNA technology, BMP-2 is commercially available for implantation to augment fracture and spinal fusion healing and is marketed under the trade name Infuse (Medtronic, Memphis, TN). Another product, BMP-7, was previously marketed as OP-1 (Olympus Biotech, Center Valley, PA) but the production has ceased and the product is no longer available. BMPs have demonstrated positive effects on fracture healing in animal models as well as in human studies of open fractures and nonunions of the tibia [44, 45]. In the spine, BMP-2 has been studied extensively and has been reported to result in successful fusion in nearly all patients undergoing anterior lumbar fusion [46] and in 60–85 % of the more commonly performed posterolateral fusion [47–52]. While none of these studies were performed to determine explicitly the effect of BMP on healing of osteoporotic bone, data have been reported showing a positive effect on fracture healing [53, 54] and spinal fusion [55, 56] in experimental models of osteoporosis. While the use of recombinant human BMP sounds like a potential cure for all of the challenges encountered in bone healing in osteoporosis, recent attention has been turned to methodologic biases that were not initially reported in many of the human trials of BMP [57]. These flaws, caused in large part by faulty trial design, peer review, and financial conflict of interest, led to underreporting of the risk of complications of the use of BMP including bone resorbtion and implant displacement, urogenital events, infection, radiculitis, ectopic bone formation, and malignancy. Subsequent review of trial data revealed a risk of complications 10–50 times higher than that which was originally reported. Currently, the potential benefit of using BMP-2 must be weighed against the potential risk of complications for any individual patient.

Pharmacologic Solutions

Recent animal data have suggested that some pharamacological agents used to treat osteoporosis may also have a positive effect on fracture healing. The best example of this is parathyroid hormone (PTH). Under normal physiologic conditions, PTH functions to increase circulating calcium by inducing reabsorbtion of bone. In daily, pulsatile, supraphysiologic doses, the opposite effect has been observed, leading to a net increase in bone mineral density [58]. Through recombinant DNA technology, a truncated form of PTH is produced and marketed as teraparatide (Forteo, Eli Lilly and co., Indianapolis, IN). A systematic review of several case reports [59] and two randomized controlled trials [60, 61] have repeatedly shown that recombinant PTH in pulsatile doses can accelerate healing of fractures in patients with osteoporosis, particularly fractures of the wrist and pelvis. Additionally, recombinant PTH also appears to accelerate bone healing in spinal fusion in rat [62, 63] and rabbit models of osteoporosis [64]. These results should be approached with caution as studies in human patients have not yet shown the same effect. Also, the increase in bone density of the fusion mass and acceleration of fusion may not be accompanied by a commensurate increase in functional strength of the bone [65]. Further study is required before recombinant PTH should be applied widely to patients undergoing spinal fusion.

Bisphosphonates are antiresorptive medications that have been proposed for use to augment spinal fusion in osteoporotic patients. Early reports of bisphosphonate use in spinal fusion demonstrated clear detrimental effects [66, 67]. More recent reports have been mixed with some showing weaker bone strength following bisphosphonate use [68], some showing no difference in treatment and control groups

[69–71], and some suggesting improved healing [72]. At this time, the lack of consensus and wide variability between reported effects suggest that more information should be gathered before prescribing or continuing the use of bisphosphonates for osteoporotic patients undergoing spinal fusion. Bisphosphonate use in fracture healing, on the other hand, has not been shown to have a detrimental effect [73]. A recent meta-analysis of randomized controlled trials of bisphosphonate use following osteoporotic fractures reports that no detrimental effect exists but does not necessarily suggest that a beneficial effect exists either. At the very least, it does appear that there is no delay in healing imparted by the impairment of osteoclast function induced by the bisphosphonates.

Electrophysiologic Solutions

Bone has been observed to develop electrical potentials at areas of mechanical compression and tension [74]. This finding, coupled with the observation that bone shows a greater propensity to form new bone under compression (Wolff's law), has led to the development of electromagnetic devices designed to stimulate the production of bone in addition to what would be produced under physiologic conditions. These devices have been applied to fracture and spinal fusion healing. There is conflicting evidence, however, concerning the efficacy of electrical stimulation on spinal fusion or fracture healing. A recent systematic review found no consistent evidence to support or refute the use of electrical stimulation devices to enhance spinal fusion [75]. The use of bone growth stimulators appears to be more encouraging in extremity fractures, particularly of the tibial shaft [76, 77]. Perhaps this is a result of the targeted bone being located in a more subcutaneous location and therefore closer to the device compared to spinal fusion. Notwithstanding these observations, there are no data concerning the efficacy of electrical stimulation to enhance spinal fusion or fracture healing in elderly or osteoporotic patients.

Specific Injuries and Treatment in the Osteoporotic and Elderly Patient

Hip Fractures

As discussed above, hip fracture is perhaps the paradigmatic fracture in the osteoporotic patient and, although some of the surgical details have evolved, the general approach to treatment has not changed much in the past few decades. Hip fractures can be classified according to anatomic region and can be generally grouped into those fractures that occur within the joint capsule (Fig. 15.7) and those that occur outside the capsule (Fig. 15.8). The former category is comprised of the subcapital and femoral neck fractures and the latter the intertrochanteric fractures. The joint capsule is the most important distinction because it is the location of the blood vessels that supply the femoral neck and head. Compression or disruption of these vessels will compromise perfusion and potentially lead to impaired fracture healing and osteonecrosis of the femoral head. Minimally displaced or impacted fractures do not typically compromise the capsular vasculature and can be found to heal reliably with internal fixation through a minimally invasive procedure. This is best achieved using multiple parallel screws placed across the fracture site into the femoral neck and head (Fig. 15.9). The fracture fragments are compressed together by screws designed to allow thread purchase in the head fragment only and not across the fracture itself. This increases stability of the fragments and promotes healing through bone compression. The screws are placed through a small incision or stab incisions that incur little blood loss and minimal disruption of the soft tissue surrounding the fracture.

Treatment of displaced fractures is somewhat more controversial. Because fracture displacement can compress or disrupt the blood supply to the femoral head and neck, a decision must be made either to reduce the fracture to the anatomic position and perform internal fixation or to abandon the hope of fracture healing and perform prosthetic replacement of the proximal femur or

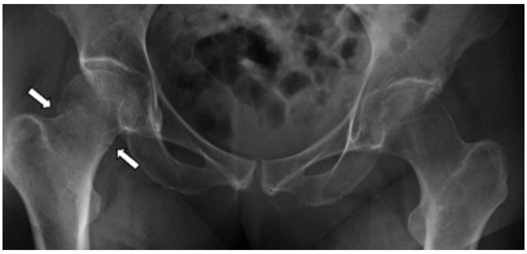

Fig. 15.7 Femoral neck fractures (*arrows*) occur within the hip capsule. Displaced femoral neck fractures can disrupt the capsule along with the blood supply to the femoral head

Fig. 15.8 Intertrochanteric fractures occur outside the hip capsule and do not typically disrupt the blood supply to the proximal femur. As a result, reduction and internal fixation routinely leads to adequate fracture healing

hip. The advantage of reduction and internal fixation is that it can be performed in a minimally invasive fashion as described above. This benefit must be weighed against the potential that the fracture may still not heal; widely displaced fractures are often found at the time of surgery to have

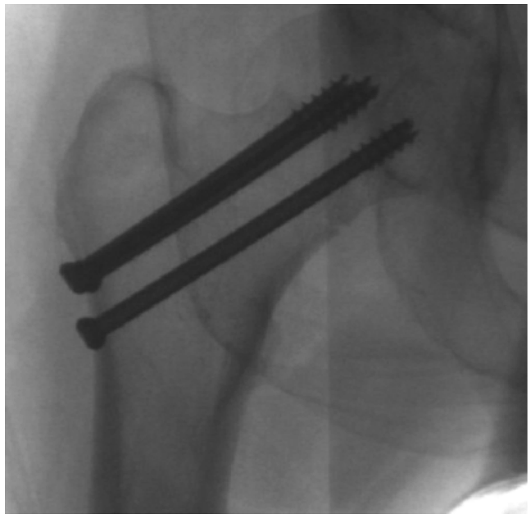

Fig. 15.9 Non-displaced or anatomically reduced femoral neck fractures can be stabilized with three lag screws and have a reasonable likelihood of healing

disrupted the vasculature as opposed to have simply compressed it. A fracture nonunion or hip osteonecrosis can lead to pain, ambulatory compromise, and further operations. Prosthetic replacement (Fig. 15.10) can eliminate these concerns and may result in a lower reoperation rate and better long-term hip function [20, 78, 79]. Although partial prosthetic replacement of the hip (hemiarthroplasty) has been performed successfully for decades, recent attention has been given to total hip replacement for hip fracture. With global life expectancy increasing, a patient treated at 65 years of age with a hemiarthroplasty may live with the prosthesis for an additional 20 years. During this period, the patient would be subjected to the possibility of degeneration of the acetabulum and pain resulting from the articulation with the prosthesis. Total hip arthroplasty replaces both the acetabulum and proximal femur and eliminates this possibility. The reported long term success with total hip arthroplasty for femoral neck fracture [20, 79] has led to a change in the treatment of femoral neck fractures with more surgeons favoring total hip arthroplasty at this time than in the past [80]. At this time, a preponderance of evidence suggests that healthy, high-functioning patients would be best served with a total hip arthroplasty; a patient with limited pre-injury

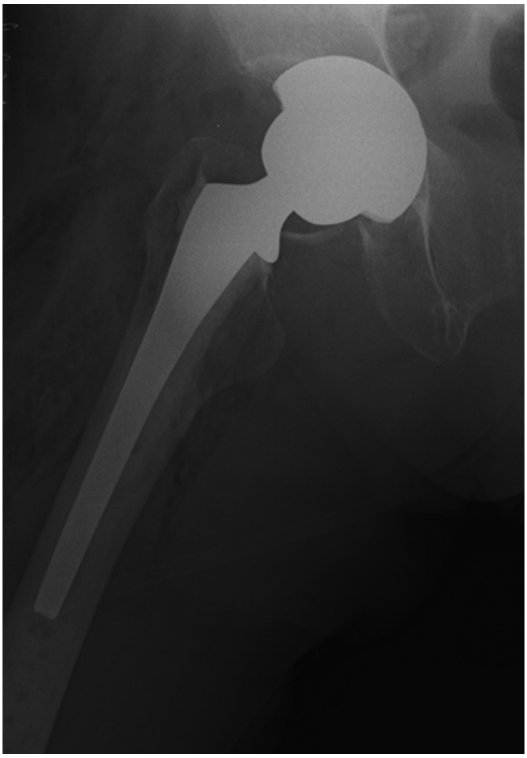

Fig. 15.10 Displaced femoral neck fractures have a poor likelihood of healing and are better treated with arthroplasty

mobility would benefit from hemiarthroplasty; a nonambulatory patient or patient with severe cognitive dysfunction would be best treated with reduction and internal fixation [78, 79].

Intertrochanteric fractures occur within the broad, cancellous, extracapsular region between the greater and lesser trochanters (Fig. 15.8). Displacement does not compromise the blood supply to the fracture site and these fractures therefore have a high rate of healing. Treatment of intertrochanteric fractures is less controversial than femoral neck fractures. Most surgeons agree that early internal fixation is optimal to prevent proximal femoral shortening, angulation, and deformity, and to more rapidly restore pre-injury ambulatory function than with nonoperative treatment. Perhaps the only source of debate is whether to use a sliding hip screw or an intramedullary nail. A sliding hip screw provides and maintains compression across the fracture site during fracture healing. The procedure has been used for decades and was once the primary method of intertrochanteric fracture fixation. The disadvantage of the technique is that splitting of the vastus lateralis is often required and is associated with high intraoperative blood loss. As a "minimally invasive" alternative, intramedullary devices were introduced for intertrochanteric fixation. The procedure, while more technically challenging, offered the potential advantages of less perceived blood loss as well as mechanically optimal positioning of the implant relative to the weight-bearing axis. Early reports of intramedullary nail fixation reported equivalent outcomes and complication rates with a lower rate of allogeneic blood transfusion [81]. More recent reports have that surgical complications, risk of blood loss, and systemic effects of surgery are equivalent [82, 83]. A preponderance of evidence appears to support the use of either device for fixation of intertrochanteric fractures, possibly with intramedullary nails serving more comminuted, unstable fractures better and with a lower risk of revision surgery.

Thoracic and Lumbar Fractures

The most common vertebral injury in patients with osteoporosis is the compression fracture (Fig. 15.2). These injuries can occur during normal physiologic functions such as coughing, sneezing, and turning in bed or with low-energy events such as grocery transport or vehicular encounter with the unpredictable roadway topography that characteristically follows a New England winter. Pain can be acute or insidious in onset and can have an impact that varies from mild nuisance to complete debilitation with significantly diminished quality and duration of life [28]. The long-term effects of vertebral compression fractures can be chronic pain, deformity (kyphosis), pulmonary compromise, and early gastrointestinal satiety [84, 85].

Traditional treatment of vertebral compression fractures focused on mitigation of symptoms and would often be met with a protracted course of pain management and activity modification, possibly with prolonged bed rest. Vertebral augmentation is a family of techniques first developed in the 1980s as vertebroplasty for percutaneous stabilization of vertebral fractures [31]. The procedure is performed by inserting a large bore needle percutaneously and with radiographic guidance down the axis of the pedicle into the fractured vertebral body. PMMA is then injected as a viscous fluid through the needle into the vertebral body and is allowed to cure into a solid. By interdigitating into the trabeculae and fracture lines, the fracture, and thereby the pain generator, is stabilized. First-generation vertebroplasty techniques were found to result in PMMA extrusion from the vertebral body into the venous system and spinal canal in 20–70 % of cases [30, 33], a complication which can produce devastating consequences including pulmonary embolus, respiratory distress, and injury to the spinal cord and nerve roots. This complication led to the development of kyphoplasty, a modified form of vertebral augmentation during which an inflatable balloon tamp is inserted through the needle first and inflated to create a cavity into which the PMMA can be injected [33]. The balloon tamp provides for safer and more reproducible injection of the cement with less risk of extrusion and may allow for at least partial restoration the height of the vertebral body lost as a result of the compression fracture (Fig. 15.11). In practice, vertebral height restoration appears to be influenced more by the acuity of the fracture and fracture mobility more than the balloon; simply placing a patient prone on an operating table that fosters lordosis – or stated in another way, hyperextends the spine – will increase the vertebral height in a relatively acute fracture but not in a chronic, partially healed fracture. The creation of a cavity for injection of the PMMA is, however, a real advantage over early-generation vertebroplasty. Using a balloon tamp to create a cavity into which PMMA can be injected has been reported to reduce the occurrence of cement extrusion to approximately 9 % [33].

Vertebral augmentation is indicated for treatment of persistent pain from unhealed osteoporotic compression fractures. Since many VCFs

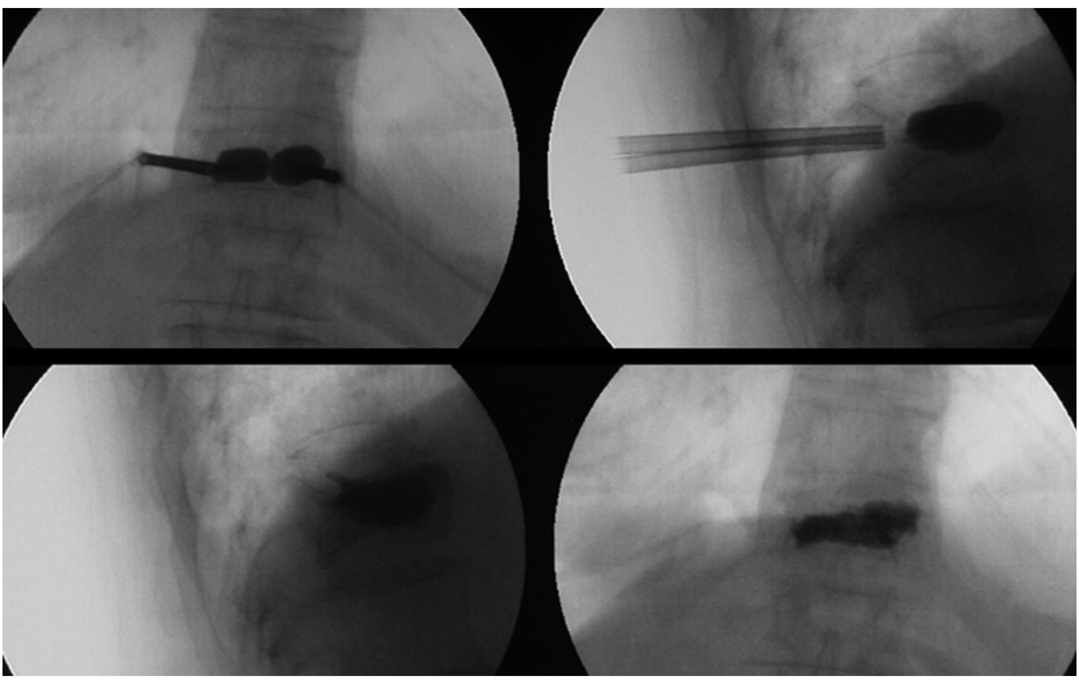

Fig. 15.11 A vertebral compression fracture can be treated with kyphoplasty. A balloon tamp is inserted and inflated to create a void and reduce fracture displacement (*top row*). The balloon is then deflated and removed and bone cement is injected to fill the void and stabilize the fracture

will be healed and discovered incidentally at the time of initial radiographic imaging, it is imperative to confirm that a newly discovered VCF is indeed acute or shows radiographic findings of abnormal bone activity consistent with painful conditions. This information is most often obtained by the magnetic resonance imaging (MRI) demonstration of increased signal on the STIR sequence or decreased signal on the T1 sequence, both of which are consistent with bone edema. Abnormal radiotracer uptake on a bone scan can provide similar information in patients unable to undergo MRI. In the authors' experience, fractures as old as 1–2 years can still have dramatic pain relief, provided that appropriate imaging findings confirm that the fracture has not healed and that edema is still present. Active spinal infection and uncorrectable coagulopathy are relative contraindications to vertebral augmentation. A burst fracture is also a contraindication to vertebral augmentation. These fractures are identified by the presence of fragments of the vertebral body displaced into the spinal canal (Fig. 15.12). In contrast to the simple compression fracture which, by definition, has an intact posterior wall of the vertebral body, displaced fracture fragments can compress and injure the spinal cord and cauda equina and can be displaced further by cement injection during vertebral augmentation [86, 87].

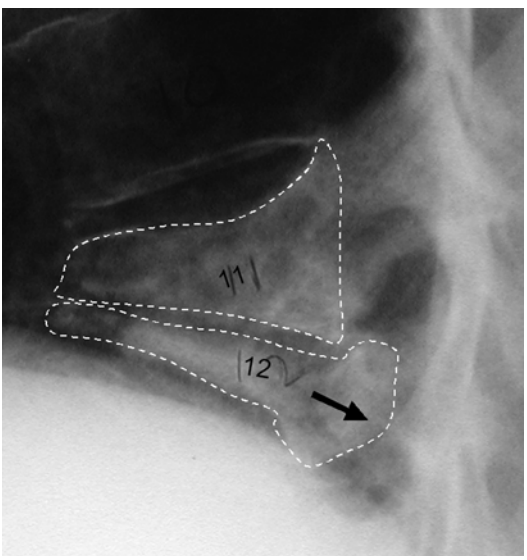

Fig. 15.12 A senile burst fracture (*bottom*, T12) can be distinguished from a simple compression fracture (*top*, T11) by the presence of posteriorly displaced vertebral body fragments that can impinge upon the spinal cord or cauda equina

Early reports of vertebral augmentation documented outcomes that rank among the most successful of any spine procedure. Rates of pain relief have been reported to reach 90–100 % with significant functional improvement as well [30, 88, 89]. These studies reported rapid relief of pain in patients treated with vertebral augmentation. After 6–12 months, patients treated with or without vertebral augmentation reported similar functional outcomes. These early reports, although describing nonrandomized patient cohorts, appear to corroborate the natural history of pain relief following VCF and suggest that vertebral augmentation can provide earlier achievement of optimal pain relief in the right patients.

Two randomized, sham-procedure controlled trials were reported in 2009 [90, 91] which have questioned the efficacy of vertebroplasty and led to considerable debate [92, 93]. Both trials reported equivalent pain relief in patients undergoing the actual vertebroplasty procedure as did patients undergoing a well designed sham procedure. These studies have provided the best evidence to date regarding vertebral augmentation and have changed the willingness of some primary care providers to refer VCF patients for evaluation for vertebroplasty [94]. The study authors have identified several limitations of the studies including patient enrollment that did not meet power requirements by the a priori analysis, skewed patient crossover from sham to vertebroplasty, possible treatment of fractures older than what has observed to show the best result with vertebral augmentation. Additional limitations of the study have been identified as well including the bias introduced by unwillingness of patients in the most severe pain to consent to randomization and a possibility that some of the treated fractures did not have adequate pretreatment imaging to confirm acuteness. Similar studies have not been performed to evaluate kyphoplasty as of yet. In total, it appears that suboptimal data have driven many of the decisions to perform vertebral augmentation and that even the most optimal information so far may be suboptimal. Further high-quality evidence is required to present the final answer to this hotly debated question. The authors currently recommend vertebral augmentation only to patients presenting with severe functional impairment.

One final challenge in the treatment of osteoporotic VCF is the occurrence of subsequent fractures following initial fracture treatment. It has been suggested that vertebral augmentation can increase stresses at adjacent osteoporotic vertebrae and thereby increase the risk of adjacent fractures. While subsequent fractures undeniably occur in patients following vertebral augmentation, it is unclear if these fractures are sequellae of the procedure or of the natural history of severe osteoporosis. At this time, reports are mixed but appear to document that additional fractures will occur in 11–30 % of patients with symptomatic VCF regardless of the treatment of the index fracture [30, 95, 96]. When treating a patient with a VCF, it is imperative that systemic anti-osteoporosis therapy be administered to reduce the likelihood of another VCF, which may be overlooked by both the referring and consulting physicians.

Odontoid Fractures

The odontoid process, or dens, is the unique cranial projection from the vertebral body of C2 that serves as an axis around which the ring of C1 rotates. The odontoid process is held securely between the anterior arch of C1 and transverse ligament. It is found to be a point of stress concentration that is susceptible to unique fracture patterns because it is a narrow junction of bone between two relatively rigid spinal segments (namely, the occiput-C1 complex, and the subaxial spine, the mobility of which is typically diminished as a result of disc degeneration).

This arrangement predisposes the odontoid to a fracture pattern that occurs commonly in elderly osteoporotic individuals, whose ambulatory balance and ability to brace for a fall may be compromised. The usual mechanism is fall forward in which the patient's forehead strikes the ground or an item of furniture. The impact produces an extension moment that displaces the head, C1, and fragment of the odontoid process posteriorly (Fig. 15.13). Because the ratio of spinal canal

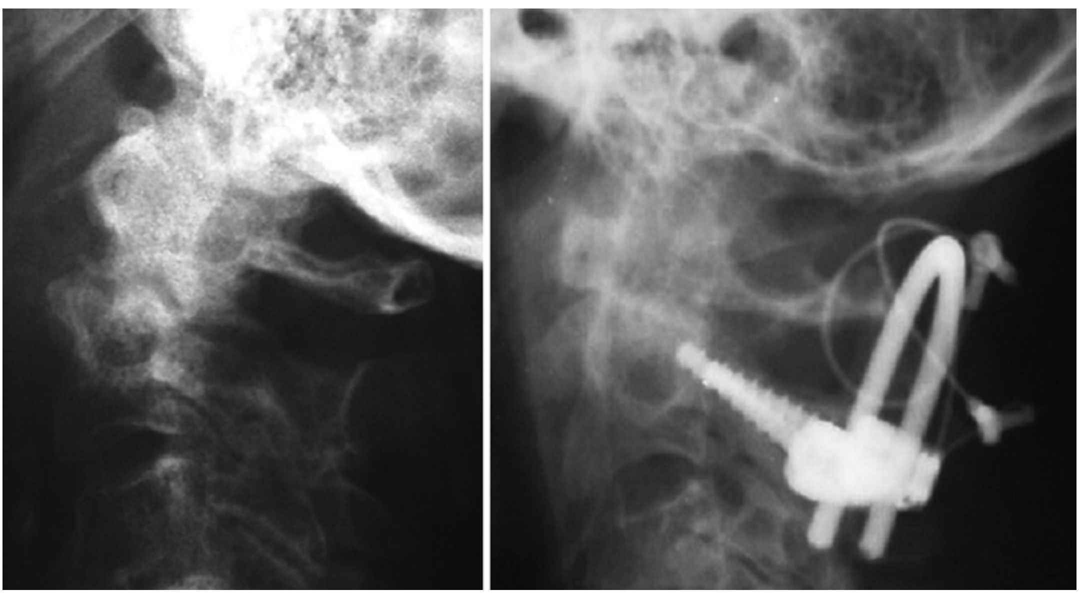

Fig. 15.13 Odontoid fractures are common in the elderly (*left*), often presenting with posterior displacement thats result from falling forward and striking the forehead or face. In some cases, stabilization is recommended, which can involve a posterior C1-C2 fusion with instrumentation (*right*)

diameter to spinal cord diameter is approximately three to one at this spinal level, even large amounts of displacement can be tolerated without neural compression. Thus, neurologic deficits infrequently result from odontoid fractures. There are wide differences among spine care providers in the approach to treatment of odontoid fractures in older and osteoporotic patients with consensus regarding the optimal method of treatment lacking [97]. Proponents of nonsurgical care would apply a hard or soft cervical orthosis collar for spinal immobilization until the fracture heals. Surgical treatment involves stabilization of the fracture either with transfixation of the fracture with screws placed from an anterior approach or fusion of C1-C2 from a posterior approach. Surgical treatment recently has been reported to have no more a deleterious impact on a patient mortality than nonsurgical treatment and may even prolong survival in certain age groups [98, 99]. Additionally, nonoperative treatment has been found to result in a higher rate of fracture nonunion (up to 22 %) [100]. Fracture nonunion does not appear to have a negative impact on patient outcome but does often lead to delayed surgery. Although further, high quality study of this fracture are required [97], current evidence appears to favor surgical treatment for odontoid fractures in younger (less than 75 years old), highly functional geriatric patients with fracture displacement or neurological deficit.

Distal Radius Fractures

As a result of the impairment of ambulatory function and reaction time that occur with increasing age, a fall on to an outstretched hand is a common occurrence that can lead to a distal radius fracture. The metaphyseal bone of the distal radius, like that of the vertebral body and hip, is affected more than the cortical or subchondral bone and fails upon loading. Along the osteoporosis time line, fractures of the distal radius occur earlier than hip fractures. They should be interpreted as an indicator of significant bone loss and a warning sign that a hip fracture may be imminent, particularly within the first month following the event [101]. Compared with the general population, patients who have sustained an osteoporotic distal radius fracture are at twice the risk for a subsequent hip fracture [102], and should thus be considered for systemic anti-osteoporosis therapy.

Treatment of distal radius fractures includes cast immobilization or surgical stabilization. Selection of the optimal treatment should be guided by the fracture pattern and the patient's functional demands. Nondisplaced fractures should be treated in a well-molded cast for approximately 6 weeks. Longer periods of immobilization can lead to worsened osteopenia and wrist stiffness. Treatment of displaced fractures is somewhat more controversial. A fall on to an outstretched hand typically produces a dorsally angulated fracture. Malunion with a small degree of dorsal angulation can be well tolerated. Greater amounts of angulation, however, can lead to improper function of the hand and wrist that would compromise patient independence and ability and should be reduced through fracture manipulation. Reduction into anatomic alignment can sometimes be maintained with a cast but will often fall back into malalignment as the comminuted fragments undergo remodeling during early fracture healing. These fractures are therefore typically treated with surgical stabilization. Fixation can be achieved by transfixing the fracture with percutaneously placed pins, an external fixator, or an internal fixation plate and screws. External fixation devices represent a method of fixation that avoids direct exposure of the fracture site, potentially limiting devitalization of the bone as discussed above. The technique has been shown to maintain an anatomic alignment superior to cast immobilization [103]. Regardless, even in cases of malunion, functional outcome has been shown to be acceptable [104]. A major objection to external fixation is the requirement that the devices span the carpus and immobilize the wrist during fracture healing. Internal fixation plates mitigate this risk by limiting fixation to the distal radius and allowing free motion of all wrist and hand joints. Low profile plates have been designed to be supported by the dense cortical and subchondral bone with screws that lock directly to the plate, thereby acting as a fixed-angle device and avoiding the fixation challenges of the osteoporotic metaphysis [105]. Recently, advanced percutaneous pinning techniques have been developed to take advantage of the benefits of both the external fixation device (i.e. limited fracture manipulation and devitalization) and internal fixation (facilitating rapid restoration of joint mobility) [106].

A final method of stabilizing osteoporotic fractures of the distal radius involves mechanical augmentation of the metaphyseal bone with injectable cements in a manner similar to vertebral augmentation. Calcium phosphate cements marketed under the trade names Norian SRS and ChronOS Inject (DePuy-Synthes, Raynham, MA) have been reported to improve patient reported outcome and histological evidence of bone formation [107, 108]. The fracture stabilization provided by the injectable bone cement allows for earlier mobilization of the wrist compared with cast treatment alone. In summary, several surgical developments have allowed for successful fixation of severe distal radius fractures in the osteoporotic patient. These advances, however, must be considered as tools to assist fracture care only. Distal radius fractures in osteoporotic patients do not fare as well functionally as patients with normal bone mineral density and should be considered high risk for a complication of treatment [109].

Tibial Plateau Fractures

Proximal tibial fractures occur in the bone supporting the knee. Fractures that involve the articular surface of the proximal tibia are referred to as tibial plateau fractures. In osteoporotic patients, as discussed above, the fractures commonly present with depression of the articular surface into the trabecular bone of the proximal tibial metaphysis. This produces an incongruent articular surface which can lead to painful arthritis. Occult tibial plateau fractures have been recognized as a cause of chronic knee pain in the elderly [110, 111].

A primary goal of surgical treatment of tibial plateau fractures is restoration of the joint surface. When large fracture fragments are present, direct, open reduction and internal fixation is often the optimal method of treatment (Fig. 15.14). If only a portion of the joint surface is depressed with the cortical rim of the proximal tibia remaining intact, the fracture reduction can be performed using less invasive methods. Through a small incision, a window can be made in the cortex of the proximal tibia and a bone tamp inserted to push fracture fragments back into the normal anatomic position. Recently, techniques have been developed utilizing the balloon tamps initially designed for vertebral kyphoplasty [112]. The balloon tamp is inserted percutaneously and inflated under radiographic guidance to reduce the fracture fragments to the anatomic position. In osteoporotic bone, compression and reduction of the fracture fragments using any method can lead to large voids in the proximal tibia that must be filled to support the anatomic alignment. These gaps can be filled either with bone graft in a technique known as impaction or compaction grafting [113] or with PMMA bone cement. Bone grafting offers the advantage of being fully incorporated into the patient's bone but with the caveat that the reabsorption that occurs during remodeling can lead to recurrence of fracture displacement. Bone cement, on the other hand, will assume the exact shape of the void and interdigitate into the bony trabeculae. The nonresorbability can protect against recurrent fracture displacement but can lead to a tissue reaction with osteolysis at the border of the PMMA. The risks and benefits of both techniques, therefore, must be weighed with each individual patient during surgical planning.

Following fracture reduction, internal fixation is typically performed to support and maintain the anatomic alignment of fracture fragments. Percutaneously placed screws are often adequate for stabilization of tibial plateau fractures. Screw fixation in osteoporotic bone can be augmented using PMMA bone cement injected to fill fracture voids or independently for the augmentation of screw fixation as described above. The PMMA is injected as a fluid and then a screw is inserted, allowing the PMMA to cure and harden around the screws. This increases the strength of the

Fig. 15.14 Tibial plateau fractures are often stabilized with a plate and screws

screw fixation by providing a broader area of implant-bone interface. The interface can also be enhanced by utilizing a plate designed to accommodate multiple screws that thread into, or "lock," into the plate. The stability and strength are gained not simply from screw purchase into bone but from the fixation to the plate. Promising results using this device in osteoporotic bone have been reported [114]. Despite these techniques, fracture fixation in the elderly and osteoporotic still presents a challenge. Perhaps the greatest word of caution has been a report that internal fixation of tibial plateau fractures in the elderly is associated with a tenfold increase in fixation failure when compared to fracture fixation in younger, nonosteoporotic bone [115].

Conclusions

The treatment of fractures in elderly, osteoporotic patients presents formidable challenges as a result of the interplay between impaired bone healing, impaired bone fixation, and impaired general medical health. Over the past few decades, several advances have been made to improve internal fixation devices, bone and healing augmentation methods, and multidisciplinary care teams to improve the outcome of fracture treatment in the elderly. As the population ages, we must continue to strive for more effective methods of fracture prevention and care.

References

1. World Health Organization Global Health Observatory (GHO): Life Expectancy. http://www.who.int/gho/mortality_burden_disease/life_tables/situation_trends_text/en/. Accessed 20 Nov 2014.
2. Battacharyya T, Iorio R, Healy WL. Rate of and risk factors for acute inpatient mortality after orthopaedic surgery. J Bone Joint Surg Am. 2002;84:562–72.
3. Streubel PN, Ricci WM, Wong A, Gardner MJ. Mortality after distal femur fracture in elderly patients. Clin Orthop Relat Res. 2011;479:1188–96.
4. Zuckerman JD, Skovron ML, Koval KJ, et al. Postoperative complications and mortality associated with operative delay in older patients who have a fracture of the hip. J Bone Joint Surg Am. 1995;77-A:1551–6.
5. Hamlet WP, Lieberman JR, Freedman EL, et al. Influence of health status and the timing of surgery on mortality in hip fracture. Am J Orthop. 1997;26:621–7.
6. McGuire KJ, Bernstein J, Polsky D, Silber JH. The 2004 Marshall Urist Award: Delays until surgery after hip fracture increases mortality. Clin Orthop Relat Res. 2004;428:294–301.
7. Moore L, Turgeon AF, Sirois M-J, Lavoie A. Trauma centre outcome performance: a comparison of young adults and geriatric patients in an inclusive trauma system. Injury. 2012;43(9):1580–5.
8. Bielza Galindo R, Ortiz Espada A, Arias Munana E, et al. Opening of an acute orthogeriatric unit in a general hospital. Rev Esp Geriatr Gerontol. 2013;48(1):26–9.

9. Pape HC, Friess T, Liener U, et al. Development of geriatric trauma centers – an effort by the German Society for Trauma and Orthopaedics. Injury. 2014;45(10):1513–5.
10. Desai PA, Vyas PA, Lane JM. Atypical femoral fractures: a review of the literature. Curr Osteoporos Rep. 2013;11(3):179–87.
11. Shane E, Burr D, Abrahamsen B, 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(1):1–23.
12. Shane E, Burr D, Ebeling PR, 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(11):2267–94.
13. Schilcher J, Koeppen V, Aspenberg P, Michaelsson K. Risk of atypical femoral fracture during and after bisphosphonate use. N Engl J Med. 2014;371(10): 974–6.
14. Patel V, Graves L, Lukert B. Pelvic fractures associated with long-term bisphosphonate therapy – case report. J Musculoskelet Neuronal Interact. 2013;13(2):251–4.
15. Tan SH, Saseendar S, Tan BH, et al. Ulnar fractures with bisphosphonate therapy: a systematic review of published case reports. Osteoporos Int. 2015;26: 421–9.
16. Goh JC, Shah KM, Bose K. Biomechanical study on femoral neck fracture fixation in relation to bone mineral density. Clin Biomech. 1995;10:304–8.
17. Spangler L, Cummings P, Tencer AF, et al. Biomechanical factors and failure of transcervical hip fracture repair. Injury. 2001;32:223–8.
18. Davis AT, Israel H, Cannada LK, Bledsoe JG. A biomechanical comparison of one-third tubular plates versus periarticular plates for fixation of osteoporotic distal fibula fractures. J Orthop Trauma. 2013;27(9):e201–7.
19. Wahnert D, Lange JH, Schulze M, et al. A laboratory investigation to assess the influence of cement augmentation of screw and plate fixation in a simulation of distal femoral fracture in osteoporotic and non-osteoporotic bone. Bone Joint J. 2013;95-B(10): 1406–9.
20. Keating JF, Grant A, Masson M, et al. Randomized comparison of reduction and fixation, bipolar hemiarthroplasty, and total hip arthroplasty. Treatment of displaced intracapsular hip fractures in healthy older patients. J Bone Joint Surg Am. 2006;88: 249–60.
21. Maier D, Jaeger M, Izadpanah K, et al. Proximal humeral fracture treatment in adults. J Bone Joint Surg Am. 2014;96(3):251–61.
22. [No authors listed]. Hip fractures in the elderly. Lancet. 1967;2(7505):34.
23. Orthopedia vs. anesthesia (orthopaedics, anaesthetics, conversation). YouTube. 2010. https://www.youtube.com/watch?v=3rTsvb2ef5k. Accessed 24 Nov 2014.
24. Hoerer D, Volpin G, Stein H. Results of early and delayed surgical fixation of hip fractures in the elderly: a comparative retrospective study. Bull Hosp Jt Dis. 1993;53:29–33.
25. Moran CG, Wenn RT, Sikand M, et al. Early mortality after hip fracture: is delay before surgery important? J Bone Joint Surg Am. 2005;87:483–9.
26. Koval KJ, Cooley MR. Clinical pathway after hip fracture. Disabil Rehabil. 2005;27:1053–60.
27. Hip Fracture Accelerated Surgical Treatment and Care Track (Hip ATTACK) Investigators. Accelerated care versus standard care among patients with hip fracture: the HIP ATTACK pilot trial. CMAJ. 2014;186(1):E52–60.
28. Cauley JA, Thompson DE, Ensrud KC, et al. Risk of mortality following clinical fractures. Osteoporos Int. 2001;11:556–61.
29. Rao RD, Singrakhia MD. Painful osteoporotic vertebral fracture. J Bone Joint Surg Am. 2003;85:2010–22.
30. Alvarez L, Alcaraz M, Perez-Hiqueras A, et al. Percutaneous vertebroplasty: functional improvement in patients with osteoporotic compression fractures. Spine. 2006;31:1113–8.
31. Deramond H, Depriester C, Galibert P, et al. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results. Radiol Clin North Am. 1998;36:533–46.
32. Barr JD, Barr MS, Lemley TJ, et al. Percutaneous vertebroplasty for pain relief and spinal stabilization. Spine. 2000;25:923–8.
33. Lieberman IH, Dudeny S, Reinhart MK, Bell G. Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures. Spine. 2001;26:1631–7.
34. Zampini JM, White AP, McGuire KJ. Comparsison of 5766 vertebral compression fractures treated with or without kyphoplasty. Clin Orthop Relat Res. 2010;468:1773–80.
35. Edidin AA, Ong KL, Lau E, Kurtz SM. Mortality risk for operated and nonoperated vertebarl fracture patients in the medicare population. J Bone Miner Res. 2011;26(7):1617–26.
36. Namkung-Matthai H, Appleyard R, Jansen J, et al. Osteoporosis influences the early period of fracture healing in a rat osteoporotic model. Bone. 2001;28: 80–6.
37. Meyer RA, Tsahakis PJ, Martin DE, et al. Age and ovariectomy impair both the normalization of mechanical properties and the accretion of mineral by the fracture callus in rats. J Orthop Res. 2001;19:428–35.
38. Simmons E, Kuhele J, Lee J, et al. Evaluation of metabolic bone disease as a risk factor for lumbar fusion. Spine J. 2002;2:99S.
39. Kucera T, Soukup T, Krs O, Urban K, Sponer P. Bone healing capacity in patients undergoing total hip arthroplasty. Acta Chir Orthop Traumatol Czech. 2012;79(1):52–8.
40. Jager M, Jelinek EM, Wess KM, et al. Bone marrow concentrate: a novel strategy for bone defect treatment. Curr Stem Cell Res Ther. 2009;4(1): 34–43.

41. Petri M, Namazian A, Wilke F, et al. Repair of segmental lone-bone defects by stem cell concentrate augmented scaffolds: a clinical and positron emission tomography-computed tomography analysis. Int Orthop. 2013;37:2231–7.
42. LeBlanc K, Tammik C, Rosendahl K, et al. HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells. Exp Hematol. 2003;31(10):890–6.
43. Gomez-Barrena E, Rosset P, Muller I, et al. Bone regeneration: stem cell therapies and clinical studies in orthopaedics and traumatology. J Cell Mol Med. 2011;15(6):1266–86.
44. Friedlander GE, Perry CR, Cole JD, et al. Osteogenic protein-1 (bone morphogenetic protein-7) in the treatment of tibial nonunions. J Bone Joint Surg Am. 2001;83A:S151–8.
45. Govender S, Csimma C, Genant HK, et al. Recombinant human bone morphogeneetic protein-2 for treatment of open tibial fractures: a prospective, controlled, randomized study of four hundred and fifty patients. J Bone Joint Surg Am. 2002;84A:2123–34.
46. Burkus JK, Transfeldt EE, Kitchel SH, et al. Clinical and radiographic outcomes of anterior lumbar interbody fusion using recombinant human bone morphogenetic protein-2. Spine. 2002;27:2396–408.
47. Kanayama M, Hashimoto T, Shigenobu K, et al. A prospective randomized study of posterolateral lumbar fusion using osteogenic protein-1 (OP-1) versus local autograft with ceramic bone substitute: emphasis of surgical exploration and histologic assessment. Spine. 2006;31:1067–74.
48. Vaccaro AR, Patel T, Fischgrund J, et al. A 2-year follow-up pilot study evaluating the safety and efficacy of OP-1 putty (rhBMP-7) as an adjunct to iliac crest autograft in posterolateral lumbar fusions. Eur Spine J. 2005;14:623–9.
49. Vaccaro AR, Anderson DG, Patel L, et al. Comparison of OP-1 putty (rhBMP-7) to iliac crest autograft for posterolateral lumbar arthrodesis: a minimul 2-year follow-up pilot study. Spine. 2005;30:2709–16.
50. Boden SD, Kang J, Sandju HS, et al. Use of recombinant human bone morphogenetic protein-2 to achieve posterolateral lumbar spine fusion in humans: a prospective, randomized clinical pilot trial: 2002 Volvo Award in clinical studies. Spine. 2002;27:2662–73.
51. Johnsson R, Stromqvist B, Aspenberg P. Randomized radiostereometric study comparing osteogenic protein-1 (BMP-7) and autograft bone in human noninstrumented posterolateral lumbar fusion: 2002 Volvo Award in clinical studies. Spine. 2002;27:2654–61.
52. Bono C, Lee C. Critical analysis of trends in fusion for degenerative disc disease over the last twenty years: influence of technique on fusion rate and clinical outcome. Spine J. 2002;2:47S–8.
53. Egerman M, Baltzer AW, Adamaszek S, et al. Direct adenoviral transfer of bone morphogenetic protein-2 cDNA enhances fracture healing in ostroporotic sheep. Hum Gene Ther. 2006;17:507–17.
54. Diwan AD, Leong A, Appleyard R, et al. Bone morphogenetic protein-7 accelerated fracture healing in osteoporotic rats. Indian J Orthop. 2013;47(6):540–6.
55. Park SB, Park SH, Kim NH, Chung CK. BMP-2 induced early bone formation in spine fusion using rat ovariectomy osteoporisis model. Spine J. 2013; 13(10):1273–80.
56. Zarrinkalam MR, Schultz CG, Ardern DW, et al. Recombinant human bone morphogenetic protein-type 2 (rhBMP-2) enhances local bone formation in the lumbar spine of osteoporotic sheep. J Orthop Res. 2013;31(9):1390–7.
57. Carragee EJ, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. Spine J. 2011;11(6): 471–91.
58. Fujita T, Inoue T, Morii H, et al. Effect of intermittent weekly dose of human parathyroid hormone (1-34) on osteoporosis: a randomized double-masked prospective study using three dose levels. Osteoporos Int. 1999;9(4):296–306.
59. Zhang D, Potty A, Vyas P, Lane J. The role of recombinant PTH in human fracture healing: a systematic review. J Orthop Trauma. 2014;28(1):57–62.
60. Aspenberg P, Genant HK, Johansson T, et al. Teriparatide for acceleration of fracture repair in humans: a prospective, randomized, double-blind study of 102 postmenopausal women with distal radius fractures. J Bone Miner Res. 2010;25(2):404–14.
61. Peichl P, Holzer LA, Maier R, Holzer G. Parathyroid hormone 1-84 accelerates fracture-healing in pubic bones of elderly osteoporotic women. J Bone Joint Surg Am. 2011;93:1583–7.
62. Sugiura T, Kashii M, Matsuo Y, et al. Intermittent administration of teriparatide enhances bone graft healing and adccelerates spinal fusion in rats with glucocorticoid-induced osteoporosis. Spine J 2015; 15(2): 298–306.
63. Qui Z, Wei L, Liu J, et al. Effect of intermittend PTH (1-34) on posterolateral spinal fusion with iliac crest bone graft in an ovariectomized rat mode. Osteoporos Int. 2013;24(10):2693–700.
64. Lehman Jr RA, Dmitriev AE, Cardoso MJ, et al. Effect of teriparatide [rPTH(1,340] and calcitonin on intertransverse process fusion in a rabbit model. Spine (Phila PA 1976). 2010;35(2):146–52.
65. Lina IA, Puvanesarajah V, Liauw JA, et al. Quantitative study of parathyroid hormone (1-34) and bone morphogenetic protein-2 on spinal fusion outcomes in a rabbit model of lumbar dorsolateral intertransverse process arthrodesis. Spine (Phila PA 1976). 2014;39(5):347–55.
66. Huang RC, Khan SN, Sandhu HS, et al. Alendronate inhibits spine fusion in a rat model. Spine. 2005; 30:2516–22.
67. Xue Q, Li H, Zou X, et al. The influence of alendronate treatment and bone graft volume on posterior lateral spine fusion in a porcine model. Spine. 2005; 30:1116–21.

68. Koo KH, Lee JH, Chang BS, Lee CK. Effects of alendronate on lumbar posterolateral fusion using hydroxyapatite in rabbits. Artif Organs. 2012;36(12): 1047–55.
69. Park SB, Park SH, Kang YK, Chung CK. The time-dependent effect of ibandronate on bone graft remodeling in an ovariectomized rat spinal arthrodesis model. Spine J. 2014;14(8):1748–57.
70. Park YS, Kim HS, Baek SW, et al. The effect of zolendronic acid on the volume of the fusion-mass in lumbar spinal fusion. Clin Orthop Surg. 2013;5(4):292–7.
71. Li C, Wang HR, Li XL, et al. The relation between zolendronic acid infusion and interbody fusion in patients undergoing transforaminal lumbar interbody fusion surgery. Acta Neurochir (Wein). 2012;154(4):731–8.
72. Nagahama K, Kanayama M, Togawa D, et al. Does alendronate disturb the healing process of posterior lumbar interbody fusion? A prospective randomized trial. J Neurosurg Spine. 2011;14(4):500–7.
73. Xue D, Li F, Chen G, et al. DO bisphosphonates affect bone healing? A meta-analysis of randomized controlled trials. J Orthop Surg Res. 2014;9:45.
74. Bassett CA, Becker RO. Generation of electric potentials by bone in response to mechanical stress. Science. 1962;137:1063–4.
75. Park P, Lau D, Brodt ED, Dettori JR. Electrical stimulation to enhance spinal fusion: a systematic review. Evid Based Spine Care J. 2014;5(2):87–94.
76. Abeed RI, Naseer M, Abel EW. Capacitively coupled electrical stimulation treatment: results from patients with failed long bone fracture unions. J Orthop Trauma. 1998;12:510–3.
77. Phieffer LS, Goulet JA. Delayed unions of the tibia. J Bone Joint Surg Am. 2006;88:206–16.
78. Johansson T, Jacobsson SA, Ivarsson I, et al. Internal fixation versus total hip arthroplasty in the treatment of displaced femoral neck fractures: a prospective randomized study of 100 hips. Acta Orthop Scand. 2000;71(6):597–602.
79. Ravikumar KJ, Marsh G. Internal fixation versus hemiarthroplasty versus total hip arthroplasty for displaced subcapital fractures of the femur – 13 year results of a prospective randomised study. Injury. 2000;31:793–7.
80. Miller BJ, Callaghan JJ, Cram P, et al. Changing trends in the treatment of femoral neck fractures: a review of the American Board of Orthopaedic Surgery database. J Bone Joint Surg Am. 2014; 96(17):e149.
81. Utrilla AL, Reig JS, Munoz FM, et al. Trochanteric Gamma nail and compression hip screw for trochanteric fractures: a randomized, prospective, comparative study in 210 elderly patients with a new design of the Gamma nail. J Orthop Trauma. 2005; 19:229–33.
82. Parker MJ, Bowers TR, Pryor GA. Sliding hip screw versus the Targon PF nail in the treatment of trochanteric fractures of the hip: a randomised trial of 600 fractures. J Bone Joint Surg Br. 2012;94(3):391–7.
83. Verettas DA, Ifantidis P, Chatzipapas CN, et al. Systematic effects of surgical treatment of hip fractures: gliding screw-plating vs intramedullary nailing. Injury. 2010;41(3):279–84.
84. Schlaich C, Minne HW, Bruckner T, et al. Reduced pulmonary function in patients with spinal osteoporotic fractures. Osteoporos Int. 1998;8:261–7.
85. Leidig-Bruckner G, Minne HW, Schlaich C, et al. Clinical grading of spinal osteoporosis: quality of life components and spinal deformity in women with chronic low back pain and women with vertebral osteoporosis. J Bone Miner Res. 1997;12:663–75.
86. Nguyen HV, Ludwig S, Gelb D. Osteoporotic vertebral burst fractures with neurologic compromise. J Spinal Disord Tech. 2003;16:10–9.
87. Korovessis P, Maraziotis T, Piperos G, et al. Spontaneous burst fracture of the thoracolumbar spine in osteoporosis is associated with neurological impairment: a report of seven cases and review of the literature. Eur Spine J. 1994;3:286–8.
88. Diamond TH, Champion B, Clark WA. Management of acute osteoporotic vertebral fractures: a nonrandomized trial comparing percutaneous vertebroplasty with conservative therapy. Am J Med. 2003;114(4):257–65.
89. Kasperk C, Hillmeier J, Noldge G, et al. Treatment of painful vertebral fractures by kyphoplasty in patients with primary osteoporosis: a prospective nonrandomized controlled study. J Bone Miner Res. 2005;20:604–12.
90. Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral compression fractures. N Engl J Med. 2009;361(6):557–68.
91. Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. N Engl J Med. 2009;361(6):569–79.
92. Bono CM, Heggenes M, Mick C, et al. North American Spine Society: newly released vertebroplasty randomized controlled trials: a tale of two trials. Spine J. 2010;10(3):238–40.
93. Buchbinder R, Kallmes DF. Vertebroplasty: when randomized placebo-controlled trials clash with common belief. Spine J. 2010;10(3):241–3.
94. Lindsey SS, Kalmes DF, Opatowsky MJ, et al. Impact of sham-comtrolled vertebroplasty trials on referral patterns at two academic medical centers. Proc (Bayl Univ Med Cent). 2013;26(2):103–5.
95. Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. JAMA. 2001;285:320–3.
96. Harrop JS, Prpa B, Reinhardt MK, et al. Primary and secondary osteoporosis' incidence of subsequent vertebral compression fractures after kyphoplasty. Spine. 2004;29:2120–5.
97. Huybregts JGJ, Jacobs WCH, Peul WC, Vleggeert-Lankamp LA. Rationale and design of the

INNOVATE Trial: an international cooperative study on surgical versus conservative treatment of odontoid fractures in the elderly. BMC Musculoskelet Disord. 2014;15:1471–8.
98. Schoenfeld AJ, Bono CM, Reichmann WM, et al. Type II odontoid fractures of the cervical spine: do treatment type and medical comorbidities affect mortality in elderly patients? Spine. 2011;36(11):879–85.
99. Chapman J, Smith JS, Kopjar B, et al. The AOSpine North America geriatric odontoid fracture mortality study. Spine. 2013;38(13):1098–104.
100. Smith JS, Kepler CK, Kopjar B, et al. Effect of type II odontoid fracture nonunion on outcome among elderly patients treated without surgery: based on the AOSpine North America geriatric odontoid fracture study. Spine. 2013;38(26):2240–6.
101. Chen CW, Huang TL, Su LT, et al. Incidence of subsequent hip fractures is significantly increased within the first month after distal radius fracture in patients older than 60 years. J Trauma Acute Care Surg. 2013;74(1):317–21.
102. Kannus P, Parkkari J, Sievanen H, et al. Epidemiology of hip fractures. Bone. 1996;18(Supplement):57S–63.
103. Moroni A, VAnnini F, Faldini C, et al. Cast vs external fixation: a comparative study in elderly osteoporotic distal radial fracture patients. Scand J Surg. 2004;93:64–7.
104. Hegeman JH, Oskam J, Vierhout PA, et al. External fixation for unstable intra-articular distal radial fractures in women older than 55 years. Acceptable functional end results in the majority of patients despite significant secondary displacement. Injury. 2005;36:339–44.
105. Ring D, Jupiter JB. Treatment of osteoporotic distal radius fractures. Osteoporos Int. 2005;16(Suppl): S80–4.
106. Gradl G, Gradl G, Wendt M, et al. Non-bridging external fixation employing multiplanar K-wires versus volar locked plating for dorsally displaced fractures of the distal radius. Arch Orthop Trauma Surg. 2013;133(5):595–602.
107. Sanchez-Sotelo J, Munuera L, Madero R. Treatment of fractures of the distal radius with a remodellable bone cement: a prospective, randomised study using Norian SRS. J Bone Surg Br. 2000;82-B: 856–63.
108. Arora R, Milz S, Sitte I, Blauth M, Lutz M. Behavior of ChronOS Inject in metaphyseal bone defects of the distal radius fractures: tissue reaction after 6-15 months. Injury. 2012;43(10):1683–8.
109. Fitzpatrick SK, Casemyr NE, Zurakowski D, et al. The effect of osteoporosis on outcomes of operatively treated distal radius fractures. J Hand Surg Am. 2012;37(10):2027–34.
110. Cabitza P, Tamin H. Occult fractures of tibial plateau detected employing magnetic resonance imaging. Arch Orthop Trauma Surg. 2000;210:355–7.
111. Luria S, Liebergall M, Elishoov O, et al. Osteoporotic tibial plateau fractures: an underestimated cause of knee pain in the elderly. Am J Orthop. 2005;34: 186–8.
112. Broome B, Mauffrey C, Statton J, et al. Inflation osteoplasty: in vitro evaluation of a new technique for reducing depressed intra-articular fractures of the tibial plateau and distal radius. J Orthop Traumatol. 2012;13:89–95.
113. Veitch SW, Stroud RM, Toms AD. Compaction bone grafting in tibial plateau fracture fixation. J Trauma. 2010;68(4):980–3.
114. Schandelmaier P, Stephan C, Krettek C, et al. Distal fractures of the femur. Unflallchirurg. 2000;103: 428–36.
115. Ali AM, El-Shafie M, Willett KM. Failure of fixation of tibial plateau fractures. J Orthop Trauma. 2002;16:323–9.