A Review and Clinical Perspective of the Impact of Osteoporosis on the Spine

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Abstract
Introduction: Osteopenia and osteoporosis are common conditions in the United States. The health consequences of low bone density can be dire, from poor surgical outcomes to increased mortality rates following a fracture. Significance: This article highlights the impact low bone density has on spine health in terms of vertebral fragility fractures and its adverse effects on elective spine surgery. It also reviews the clinical importance of bone health assessment and optimization. Results: Vertebral fractures are the most common fragility fractures with significant consequences related to patient morbidity and mortality. Additionally, a vertebral fracture is the best predictor of a subsequent fracture. These fractures constitute sentinel events in osteoporosis that require further evaluation and treatment of the patient’s underlying bone disease. In addition to fractures, osteopenia and osteoporosis have deleterious effects on elective spine surgery from screw pullout to fusion rates. Adequate evaluation and treatment of a patient’s underlying bone disease in these situations have been shown to improve patient outcomes. Conclusion: With an increased understanding of the prevalence of low bone mass and its consequences as well as an understanding of how to identify these patients and appropriately intervene, spine surgeons can effectively decrease the rates of adverse health outcomes related to low bone mass.

Keywords
geriatric medicine, geriatric trauma, geriatric nursing, nonoperative spine, physical therapy

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Introduction
Osteopenia and osteoporosis (low bone density) are common conditions in the United States that are increasing in prevalence as the population ages. As of 2010, there were 10.3 million Americans over the age of 50 years with osteoporosis and there were 43.4 million Americans with low bone mass (ie, osteopenia). Over the next 20 years, these numbers are expected to increase by 32%. As the population continues to age, so too will the burden of diminished bone quality and its clinical sequelae. As the vertebral column represents the most common anatomic site of osteoporosis-related fractures, spine surgeons are uniquely positioned to help with the detection, evaluation, and management of low bone density. Moreover, diminished bone quality plays a large role in the ultimate success of elective spine surgery. The purpose of this review article is 3-fold: first, we will review the impact low bone density has on the spine; second, we will review the negative consequences of low bone density on clinical outcomes following elective spine surgery; third, we will review the clinical importance of bone density assessment and optimization. Our intent is to provide a concise summary of the literature regarding the impact of low bone density and the importance of bone health optimization in patients with spinal disease.

Methods
A review of the literature pertaining to osteopenia and osteoporosis and its relation to vertebral fractures and elective spine surgery was performed. Using PubMed, a combination of the search terms “osteoporosis,” “osteopenia,” “fragility
### Basic Concepts in Osteoporosis

Bone density is a critical component of a patient’s bone health status. The most common method for diagnosing osteoporosis is densitometric assessment. To classify a patient’s bone density, dual energy X-ray absorptiometry (DXA) is used to determine an individual’s bone mineral density (BMD). The subject’s BMD is then compared to a reference standard, specifically the BMD of a 20- to 30-year-old adult race-matched subject’s BMD is then compared to a reference standard, spine specific an individual’s bone mineral density (BMD). The densitometric assessment. To classify a patient’s bone density status, these criteria do not adequately determine the risk of fragility fracture. In fact, the majority of patients who sustain fragility fractures do not have osteoporosis based on the WHO criteria. In light of this deficiency, the AACE and the ACE developed clinical practice guidelines in 2016 that added clinical criteria to the definition of osteoporosis (Table 3). These standards recognize that the presence of a spine or hip fragility fracture, regardless of BMD, confirms the diagnosis of osteoporosis. Further, AACE/ACE clinical practice guidelines indicate that patients with osteopenia (T score −1 to −2.5) and a fragility fracture of the pelvis, wrist, or shoulder should be diagnosed with osteoporosis.

### Table 1. Literature Summary by Topic.

| Topic                                             | References |
|---------------------------------------------------|------------|
| Fragility fracture and osteoporosis epidemiology   | 1,2,7,21   |
| Treatment strategies and treatment deficiencies following fragility fracture | 22-36      |
| Bone health and elective spine surgery outcomes    | 3,5,6,36,59|
| Osteoporosis treatment and elective spine surgery outcomes | 8,39,60-68 |

### Table 2. Indications for Bone Mineral Density Testing.

1. All women ≥65 years old
2. All postmenopausal women:
   a. With a history of fracture(s) without major trauma
   b. With osteopenia identified radiographically
   c. Starting or taking long-term systemic glucocorticoid therapy (≥3 months)
3. Other peri- or postmenopausal women with risk factors for osteoporosis if willing to consider pharmacologic interventions:
   a. Low body weight (<127 lb or body mass index <20 kg/m²)
   b. Long-term systemic glucocorticoid therapy (≥3 months)
   c. Family history of osteoporotic fracture
   d. Early menopause (<40 years old)
   e. Current smoking
   f. Excessive alcohol consumption
4. Secondary osteoporosis

### Table 3. 2016 AACE Diagnosis of Osteoporosis in Postmenopausal Women.

1. T-Score of −2.5 or below in the lumbar spine, femoral neck, total, and/or 33% (one-third) radius
2. Low-trauma spine or hip fracture (regardless of BMD)
3. Osteopenia or low bone mass (T-score between −1 and −2.5) with a fragility fracture of proximal humerus, pelvis, or possibly distal forearm
4. Low bone mass or osteopenia and high FRAX fracture probability based on country-specific thresholds

Abbreviations: AACE, American Association of Clinical Endocrinologists; BMD, bone mineral density.

### Vertebral Fragility Fracture

Fragility fracture is the sentinel event in osteoporosis and the most morbid effect of low bone mass on the spine. Fragility fractures represent a major burden to the health-care system in the United States with over 2.1 million patients sustaining a fragility fracture at any anatomic location in 2011, a number greater than the occurrence of breast cancer, myocardial infarction, and stroke combined. In the United States, there were over 4.9 million hospitalizations as a result of fragility fractures with an estimated cost of $17 billion per year between 2000 and 2012. Over 260,000 patients are hospitalized annually for vertebral fracture; however, this is only the tip of the iceberg as 2 in 3 vertebral fragility fractures are clinically silent and a majority of these fractures are treated in an outpatient setting. Vertebral fractures are the most common type of fragility fracture and the incidence of these fractures increases with age and also varies by gender, with females having a 4 to 5 times higher risk of fracture than men.

While many view vertebral fragility fractures as benign, requiring mostly comfort care, they are often associated with significant pain and disability. Tosteson et al assessed long-term, health-related quality-of-life outcomes at 5 years in 215 patients who presented with hip and vertebral fractures compared to 200 control patients. They found that 25% of patients with vertebral fractures reported limitations in

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*Note: Table 1 and Table 2 are not included in the text.*
activities of daily living and over two-thirds of patients reported limitations if they had a combined hip and spine fracture.\textsuperscript{14} Chen et al, in a study assessing options for management of vertebral compression fractures, reported an average baseline pain of 7.8 on the visual analog scale which significantly improved following conservative treatment, but still remained 3.4 at 6 months.\textsuperscript{22} While the pain improved, the persistence highlights the long-term significance of this injury.

Patients with symptomatic vertebral fragility fractures are also at an increased risk of mortality, with studies showing a 2 to 8 times increased risk of age-matched mortality following a symptomatic vertebral fracture.\textsuperscript{13} Patients have the highest risk of mortality within the first 6 months following a vertebral fracture.\textsuperscript{13} Lau et al assessed Medicare claims and found that the mortality following vertebral fracture was 46.1\%, 68.1\%, and 89.5\% at 3, 5, and 8 years, respectively.\textsuperscript{15} They then adjusted for comorbidities and found that vertebral fracture alone was associated with a hazard ratio of 1.83 for mortality.\textsuperscript{15} Surprisingly, mortality following a vertebral fragility fracture approaches that following a hip fracture which has been shown to be 28.3\% at 1 year.\textsuperscript{16} Further, surviving patients are significantly more likely to require long-term nursing care and to drop to a lower income status following the hip fracture.\textsuperscript{16} Chen et al identified similar losses in independence after vertebral fracture.\textsuperscript{22}

Another cost of vertebral fracture is related to emotional changes. Svensson et al performed a structured questionnaire on octogenarians who had a prior vertebral fragility fracture. They found that fear and anxiety was a dominant complaint. Patients experienced fear of recurrent pain, struggled to understand their deceiving body, and experienced loss of independence as well as fear of an uncertain future.\textsuperscript{17} Thus, pain and deformity is not the only clinically significant impact of vertebral fragility fracture.

Fragility fractures are the strongest predictor of subsequent fragility fractures. Hodson et al reported that at 5 and 10 years following a vertebral fracture, secondary fractures had occurred in 16.3\% and 25.7\% of patients, respectively.\textsuperscript{18} A meta-analysis performed by Anderson et al found that 18\% of patients with nonoperatively treated vertebral fractures sustained secondary fractures within 12 months.\textsuperscript{26} Another meta-analysis showed that a previous fracture history was associated with a significantly increased risk of any fracture when compared to individuals without prior fracture.\textsuperscript{19} Further, Lindsay demonstrated that patients with more than one vertebral fracture had double the risk of secondary fracture.\textsuperscript{20}

Given the morbidity and mortality associated with fragility fractures as well as the significantly increased risk of subsequent fracture, a fragility fracture must be considered a sentinel event by all providers attending to the fracture. It should prompt a clinical diagnosis of osteoporosis and a process of management (typically led by the primary care provider or a bone health specialist, such as an endocrinologist, rheumatologist, geriatrician, or a fracture liaison service) that includes evaluating bone density and bone health. In addition to subsequent medical treatment, fall prevention and counseling regarding calcium and vitamin D usage, regular exercise, and smoking cessation play a critical role in preventing subsequent fractures. However, over the last decade, fewer than 20\% to 30\% of patients have received adequate bone health evaluation, follow-up, and treatment after sustaining a fragility fracture.\textsuperscript{27-29} Bawa et al assessed osteoporosis care after fragility fracture in over 31 000 patients and found that only 10.6\% of patients were treated with anti-osteoporotic medications following the index fracture.\textsuperscript{30} In the 10.6\% of patients that did receive anti-osteoporotic therapy, there was a 40.6\% reduction in subsequent fractures.\textsuperscript{30} Hawley et al assessed the results following governmental recommendations that hip fracture patients were prescribed bisphosphonates for secondary fracture prevention in Great Britain and found that 3 years after the initiation of the intervention, there was a 22\% reduction in subsequent hip fracture and a 14\% reduction in major osteoporotic fracture (including vertebral fractures).\textsuperscript{31}

The recommendations for assessing and managing osteoporosis are not vague or difficult to find; compliant implementation of these measures results in >40\% to 80\% reduction in subsequent fragility fracture of the spine.\textsuperscript{30} Thus, the missing link is not the need of a better means for diagnosing or treating this disease, rather it is simply the need to initiate the process.\textsuperscript{21} While spine specialists may not have the extended patient contact required to manage the prescription and surveillance of anti-osteoporotic therapy, we certainly know the impact that osteoporosis has on spine health. It should be the aim of all spine specialists consulted for vertebral fragility fracture to not only treat the fracture, but also to have an informative bone health-care discussion with the patient. This conversation, at a minimum, should include informing the patient that they have osteoporosis, recommending DXA scanning, and instructing the patient to follow-up with their primary care provider or with a bone health specialist to initiate anti-osteoporotic therapy. The Own the Bone (OTB) initiative described below provides a roadmap for a successful strategy to prevent subsequent fragility fractures.

Given the impact of fragility fractures, in 2004, the United States Surgeon General issued a report stating that bone health was among the most important health issues facing Americans. In response to this report, the American Orthopaedic Association (AOA) created the OTB Program.\textsuperscript{32} The program focuses its efforts on the prevention of secondary fractures.\textsuperscript{33,34}

As of June 2016, there were 147 enrolling institutions.\textsuperscript{35} Of the 33 158 enrolled patients, 27.8\% of patients presented with an axial fracture involving the spine or pelvis.\textsuperscript{35} It should be noted that over 99\% of the participating OTB sites enroll patients in the in-patient setting, which skews the proportion of fracture types seen. A vertebral compression fracture is the most common fragility fracture occurring in the general population but a majority are clinically silent or managed nonoperatively.\textsuperscript{28} Roughly 36\% of the enrolled patients had a previous fracture after the age of 50.\textsuperscript{35}

Dirschl and Rustom report that within the OTB program, 72.8\% of patients had anti-osteoporosis treatment recommended and in this same cohort, 12.1\% of patients were started
Bone Fragility and Its Impact on Elective Spine Surgery

Many aspects of bone health have been shown to have an impact on spine surgery. For instance, vitamin D deficiency has been shown to be a prevalent issue that can adversely impact elective spine surgery.6,37,38 Ravindra et al found that 30.0% of patients undergoing elective spine fusion surgery had vitamin D deficiency; Stoker et al similarly found that 27.0% of patients undergoing spine fusion surgery had vitamin D deficiency.39,40 Subsequent studies have shown that vitamin D deficiency has a negative impact on spine fusion outcomes. Ravindra et al showed that vitamin D deficiency was an independent predictor of nonunion and that the time to fusion in patients with vitamin D deficiency was significantly longer.38 A literature review performed by Kerezoudis et al found that patients presenting with vitamin D deficiency achieved lower fusion rates and had higher rates of persistent low back pain following spinal fusion.5 Kim found that functional outcome as measured by Oswestry Disability Index inversely correlated with baseline 25(OH) Vit D after spine surgery.37 Thus, in order to maximize patient outcomes following elective spine surgery, it is important to fully investigate a patient’s bone health, which includes DXA and laboratory assessment.

In addition to vitamin D deficiency, low bone density is associated with poor outcomes in spine surgery. Investigations have shown an association between low BMD and poor pedicle screw purchase, demonstrating that patients with osteoporosis are at increased risk of screw loosening, hardware failure, and interbody cage subsidence.5,36,41-45,46 The diminished bone density of cancellous bone and the associated increase in bone porosity in patients with osteopenia or osteoporosis contributes to implant failure by changing the vertebrae’s ability to load share.47 In a synthetic bone model, Varghese et al assessed pedicle screw pullout strength at different bone densities, finding significantly reduced pullout strength in the severely osteoporotic model.48 Similarly, Halvorson et al found that decreased BMD was significantly correlated with pedicle screw axial pull-out with pullout force averaging 206 ± 159 N in osteoporotic spines compared to 1540 ± 361 N in normal spines.49 Clinically, studies by Sakai et al and Bredow et al have shown that low Hounsfield Units on computed tomography scans, a marker of low BMD, are predictive of pedicle screw loosening.43,44 Bjerke et al compared osteoporotic, osteopenic, and normal patients undergoing thoracolumbar fusion.3 They found that “osteoporosis-related complications” (such as proximal junctional fracture or kyphosis and screw pullout) occurred in 50% of osteoporotic, 34% of osteopenic, and in 23% of patients with normal bone.5 Bernstein et al also found that, when compared to patients without rheumatoid arthritis, patients with rheumatoid arthritis had a significantly higher implant-related complication rate; osteoporosis was significantly more prevalent in this cohort of patients.45 Additionally, Formby et al and Tempel et al both report that low BMD is associated with significantly increased cage or graft subsidence in patients undergoing transforaminal lumbar interbody fusions or lateral lumbar interbody fusions, respectively.36,46

Nonunion is another complication seen more commonly in patients with osteoporosis.3,50,51 In the study by Bjerke et al, nonunion occurred in 46% of osteoporotic patients compared to 19% of patients with normal bone.3 Cho et al found that patients with osteoporosis undergoing a one-level posterior lumbar interbody fusion had a significantly higher rate of screw loosening which was associated with a significantly lower fusion rate.50 DeWald et al, in a case series of patients over the age of 65 years undergoing spinal fusion involving a minimum of 5 levels, found a pseudarthrosis prevalence of 11%.51 Patients with osteoporosis are also at increased risk of proximal junctional failure following spinal fusion surgery.3 Yagi et al investigated risk factors for proximal junctional kyphosis (PJK) following long instrumented spinal fusion and found that patients who developed PJK were significantly more likely to have low bone density.52 Uei et al found that low bone density was significantly associated with increased rates of revision surgery for PJK and postoperative vertebral fractures.53 O’Leary et al similarly found that decreased bone density was a risk factor for fractures at the most proximal end of long pedicle screw constructs.54 The most proximal end of a fusion construct is not the only area at risk in patients with low bone density. Kwon et al describe a case series of 13 patients presenting with caudal junctional failure and found that 79% of these patients had low bone density.55 Furthermore, Meredith et al found that osteoporosis is a significant risk factor for sacral fractures following multilevel spinal arthrodesis.56 Papadopoulos et al similarly found that osteoporosis places patients at increased risk of sacral fracture following thoracolumbar fusion to the sacrum.57

Finally, rates of revision surgery are higher in patients with low BMD with studies by Bjerke et al, Sheu et al, and Puvanesarajah et al all demonstrating higher revision rates following spinal fusion surgery in patients with low BMD.3,58,59 These studies illustrate the high prevalence of poor bone health in spine patients and that variations from normal bone density (ie, low bone mass or osteoporosis) result in a significant increase in bone fragility-related complications and failure of fusion following spinal surgery.

Bone Health Assessment Prior to Elective Spine Surgery

Given the potential influence of bone health status on the risk of future fragility fracture and on the outcomes of elective spine
If Vitamin D level is less than 15 ng/mL consider consulting endocrinology.

Any fusion patient with vitamin D below 30 ng/mL is supplemented for up to 2 years. It can take months for DXA scan values to change, but even prior to that, insertional torques for pedicle screws can increase; likewise, perioperative administration of these agents is associated with increased fusion rates.

The ultimate goal of bone health optimization prior to elective spine surgery is to limit osteoporosis-related complications. The recognition of low bone mass and its subsequent treatment with an anabolic agent, such as teriparatide or abaloparatide, which stimulates osteoblastic activity, has been shown to enhance fusion rates while also helping to increase overall BMD. While some studies in animals have shown that bisphosphonates, which inhibit osteoclasts and catabolic bone metabolism, may limit fusion, the highest level of clinical information to date demonstrates that continuation of these agents in the perioperative period leads to higher fusion rates.

**Table 4. Preoperative Vitamin D Supplementation.**

1. All fusion patients have vitamin D levels checked preoperatively.
2. Vitamin D levels between 30 and 60 ng/mL are considered normal.
3. Any fusion patient with a vitamin D below 30 ng/mL is supplemented for 1 year as follows:
   - If more than 4 weeks before surgery:
     - Vitamin D level of 25 to 30 ng/mL then recommend cholecalciferol 1000 IU daily
     - Vitamin D level of 15 to 24 ng/mL then recommend cholecalciferol 2000 IU daily
   - If less than 4 weeks before surgery:
     - Vitamin D level of 25 to 30 ng/mL then recommend cholecalciferol 50 000 IU daily ×4 days followed by cholecalciferol 1000 IU daily
     - Vitamin D level of 15 to 24 ng/mL then recommend cholecalciferol 50 000 IU daily ×7 days followed by Cholecalciferol 2000 IU daily
4. If Vitamin D level is less than 15 ng/mL consider consulting endocrinology.

Vitamin D = total 25-hydroxyvitamin D.

**Conclusions**

The health consequences of low bone mass can be dire, from poor surgical outcomes to increased mortality rates following a fracture. Spine surgeons are uniquely positioned to identify patients with low bone mass given its impact on all facets of their practice. With an increased understanding of the prevalence of low bone mass and its consequences as well as understanding of how to identify these patients and appropriately intervene, we can decrease the rates of adverse health outcomes related to low bone mass. While the focus of this review is on the impact of low bone density on bone health, it is important to recognize that other factors such as medical comorbidities, medications, tobacco use, a patient’s fall risk, and overall nutritional status play a crucial role in a patient’s overall bone health. With an array of successful treatment strategies available, it is crucial to identify patients who require low bone mass treatment. Ultimately, the imaging modalities and clinical assessment routinely used to diagnosis spinal disease are rich in information related to bone health. Spine care providers must learn to look beyond the spinal disease and detect and respond to the coexistent diminished bone quality.

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