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Review Article

The Vertebral Fracture Cascade: Etiology and Clinical Implications

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Abstract

A vertebral fracture is a marker of bone fragility and is associated with a downward spiral of recurrent fractures known as the vertebral fracture cascade. Etiology of this unfortunate cascade includes bone and muscle loss from immobility, changes in spinal mechanics causing increased loading on adjacent vertebrae, and the development of an increased thoracic kyphosis (hyperkyphosis [HK]). Degenerative disc disease, common in osteoporotic patients, can also cause HK. HK of any etiology has been associated with decreased thoracic extensor muscle strength, unstable gait, increased body sway, decreased physical and pulmonary functions, chronic pain, and increased spinal loads contributing to the vertebral fracture cascade.

Preventing this downward spiral requires a multidisciplinary approach that includes early identification, consideration of pharmacologic treatment, early mobilization of the fracture patient, appropriate exercise, and back protection. Exercise should include weight-bearing and muscle-strengthening activities, but caution is needed to avoid undue stress on the back. Physical therapy can be particularly helpful by teaching the patient how to safely perform daily activities and can assist the patient in establishing a safe exercise program that avoids flexion but promotes back extension and weight-bearing activities. Hopefully, these measures will decrease pain, prevent falls, improve posture, prevent additional bone and muscle loss, and potentially abort the devastating downward spiral of the vertebral fracture cascade.

Key Words: Bone strength; kyphosis; osteoporosis; physical therapy; vertebral fracture.

Introduction

Vertebral fractures are a hallmark of osteoporosis. The classic image of osteoporosis is that of an elderly female with height loss and a dowager's hump from multiple vertebral fractures. Even 1 vertebral fracture, if atraumatic, can diagnose osteoporosis. According to the National Osteoporosis Foundation, in their 2013 clinical guide, "A vertebral fracture is consistent with a diagnosis of osteoporosis, even in the absence of a bone density diagnosis, and is an indication for pharmacologic treatment with osteoporosis medication to reduce fracture risk" *(1)*.

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Vertebral fractures are not only diagnostic of osteoporosis but also highly predictive of future fractures. In a meta-analysis, the presence of a vertebral fracture increased the relative risk (RR) of a future wrist fracture by 1.4, hip fracture by 2.3, and a subsequent vertebral fracture by 4.4 *(2)*. The absolute fracture risk is significant for these individuals. In a US administrative claims database, the 5 yr risk of a fracture after a clinical vertebral fracture in patients aged 65–74 was 24.5% for men and 37.4% for women *(3)*. In Rochester, the cumulative risk of any fracture 10 yr after a vertebral fracture was 70% *(4)*. The risk is particularly large for subsequent vertebral fractures. In controlled clinical trials, Ettinger et al *(5)* documented a 20% incidence of a new vertebral fracture for more than 3 yr in placebo patients who entered the trial with a prevalent fracture, and Lindsay et al *(6)* documented a 19% incidence of a vertebral fracture 1 yr after an incident fracture. Finally, the increased fracture risk increases exponentially with an increased number and severity of vertebral

fractures. In the Study of Osteoporotic Fractures (7), in women older than 67 yr, with an average follow-up of 3.7 yr, the RR of a vertebral fracture was 3.2 (95% confidence interval [CI]: 2.43−4.18) in individuals with 1 fracture, 5.4 (95% CI: 3.82−7.57) with 2 fractures, and 10.6 (95% CI: 7.75−14.47) with 3 or more fractures (Fig. 1). In the Multiple Outcomes of Raloxifene Evaluation trial, the incidence of a new vertebral fracture in 3 yr was 10.5% in those who entered the trial with a mild vertebral fracture, 23.6% in those with a moderate fracture, and 38.1% in those with a severe fracture (8). This escalating risk has been called the vertebral fracture cascade (9). This article will review the possible reasons for the fracture cascade and discuss its clinical implications.

Etiology of the Vertebral Fracture Cascade

A Vertebral Fracture is a Marker of Bone Fragility

A fragility fracture is proof of decreased bone strength and is a marker of bone fragility independent of bone density. An early study by Ross et al (10) documented that a patient with just 1 vertebral fracture and a bone density in the highest tertile had a greater RR of future fracture than a patient with low bone density but no existing fracture (RR = 10.2 vs 7.4). Most patients who fracture do not have osteoporosis by World Health Organization criteria. In the study of osteoporotic fractures, only 39% of individuals with a vertebral fracture had a World Health Organization diagnosis of osteoporosis by dual-energy X-ray absorptiometry (DXA) at the spine, only 25% by DXA of the total hip (11). This means that there are factors beyond BMD that predispose individuals to fracture. Mechanical studies in cadaveric vertebrae have shown that BMD explains only 60%−80% of the strength of a vertebral body (12,13). Other factors affecting bone strength include crystal size and distribution, composition of collagen, microdamage, and viability of bone cells—all factors that cannot be measured clinically. Microarchitecture (e.g., cortical porosity, trabecular separation) and macroarchitecture or geometry (e.g., bone size and shape) are also important. Although we now have techniques that can evaluate architectural parameters (e.g., quantitative computed tomography, micromagnetic resonance imaging, finite element analysis, hip structural analysis, trabecular bone score), these are currently used only in research studies. Although BMD by DXA is a major risk for fracture and can diagnose osteoporosis, it is not the only risk factor. As shown in the aforementioned studies (2−8), the presence of a vertebral fracture is a marker of bone fragility and is an even better predictor of future fracture risk than BMD.

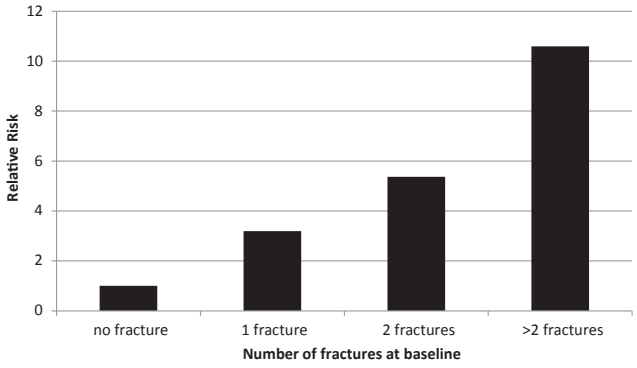

Fig. 1. Vertebral fractures predict future vertebral fractures. Relative risk of vertebral fracture, average follow-up of 3.7 yr, in the Study of Osteoporotic Fractures. Data from Black et al (7).

Bone and Muscle Loss After Fracture

Many patients after an acute vertebral fracture require a period of bed rest that can cause significant loss of bone and muscle. In 1 study, healthy males lost 3.9% of bone in the lumbar spine, 4.6% in the greater trochanter, and 3.6% in the femoral neck after 17 wk of bed rest with minimal recovery after 6 mo of ambulation (14). Bed rest also results in microarchitectural deterioration of bone. In another study, 6 wk of bed rest in surgical patients resulted in increased cortical porosity and detrimental changes in trabecular parameters and finite element analysis. Although trabecular architecture improved after return to weight bearing, little improvement was seen in cortical porosity or finite element analysis. In fact, BMD continued to decrease after 6 and 13 wk of weight bearing (15). Loss of muscle strength is also significant with bed rest: 10%−15% loss weekly in muscles at complete rest and nearly 50% loss of strength within 3−5 wk of immobilization (16). Muscle atrophy also occurs with up to 50% loss of muscle mass after 2 mo (16). Even if bed rest is not required, patients with vertebral fractures have significant morbidity, including chronic pain, depression, and decreased pulmonary function that causes disability and decreased activity that adds to the downward spiral of the vertebral fracture cascade.

Postural Change

As most osteoporotic vertebral fractures are anterior wedge deformities, an increased thoracic kyphosis (hyperkyphosis [HK]) is a common sequelae of vertebral fractures. Yet, HK itself is a risk factor for future fractures that is independent of prior fractures. In a clinical trial in elderly patients with osteoporosis (mean age: 73.3), the RR for subsequent fracture was 1.70 (95% CI: 1.32−2.21) in patients with high kyphosis vs those with low kyphosis (17). This difference persisted even after adjustment for age, body mass index, BMD, and prevalent fractures. Similar results were seen in another study in community-dwelling individuals with an odds ratio of 1.77 (95% CI: 1.02−3.05) for a new fracture in patients with HK adjusted for age, hip BMD, and prevalent fracture. In that study, even patients with mild HK were at risk—28% of those patients experienced a fracture over more than 4 yr compared with 16% in patients without HK (18).

Although 40% of older women have HK, only 1/3 of these individuals have radiographic fractures (19). The etiology of