Osteoporosis and the risk of fracture

Bone quality framework – Science writer guide (Courtesy of Sanofi-Aventis)

Correspondence: enquiries@medpharm.co.za

Abstract

Osteoporosis is a skeletal disease characterised by low bone mass and a deterioration of the microarchitecture of bone tissue, leading to an increase in bone fragility and a greater risk of fracture. It is a life-threatening disease, with mortality following hip fracture exceeding mortality after myocardial infarction.[1] For women, the risk of dying from the consequences of a hip fracture is greater than that of dying from breast cancer.[2] Moreover, the morbidity associated with hip fracture, in particular, has an overwhelming impact on patients' quality of life and places an undue burden on caregivers and the healthcare system.[3] The goal of osteoporosis treatment is to prevent fractures and the subsequent morbidity and mortality associated with them. More than 90% of all hip and spine fractures in elderly women result from osteoporosis.[4] About 20% of patients will die in the following year as an indirect consequence of hip fracture.[5] One-third of women who survive hip fracture will need constant care.[6]

(SA Fam Pract 2005;47(9): 34-36)

Introduction

Common fracture sites in patients with osteoporosis are the spine, hip, and wrist. The gold standard for the diagnosis of osteoporosis is based on the measurement of bone mineral density (BMD) with dual energy X-ray absorptiometry (DXA). Bone mass is determined per projected area, and the BMD score obtained correlates with whole-bone strength.[7,8] A diagnosis of osteoporosis is made if the T-score is below –2.5 at the spine, femoral neck, or wrist.

The risk of osteoporotic fractures is not only reflected by low BMD, however. A range of other factors exist that, independent of BMD, increase the risk of fracture (Table I). These factors are age, female sex, high bone turnover, low body weight, lifestyle factors, risk of falls, smoking and excessive alcohol consumption, medical history of a prior fracture or family history, and the use of certain medications such as corticosteroids,[11] as well as some secondary causes of osteoporosis. The incidence of fractures increases with diminishing BMD. However, fractures frequently occur in women who have normal BMD, but other risk factors.[12]

Table I: Risk factors for fractures, independent of BMD

Age

Measurable
- High bone turnover
- Low body weight

Lifestyle
- Risk of falls
- Smoking
- Excessive alcohol consumption

Medical history
- Prior Fracture
- Family history

Medication use
- Corticosteroids

Secondary causes of osteoporosis

Understanding bone strength: The bone quality framework

To answer the question 'why do bones break?', we need to look at a number of factors that affect bone strength. As with any structure, the strength of bone depends on its structural and material properties. Bone tissue undergoes continuous renewal through the process of bone turnover or remodelling. This process affects both structural and material properties of bone tissue and has an impact on bone strength. A fracture occurs when the applied load to a bone is greater than its strength. Bone strength results from a combination of 3 key factors (Figure 1):

- structural properties
- material properties
- bone turnover rate

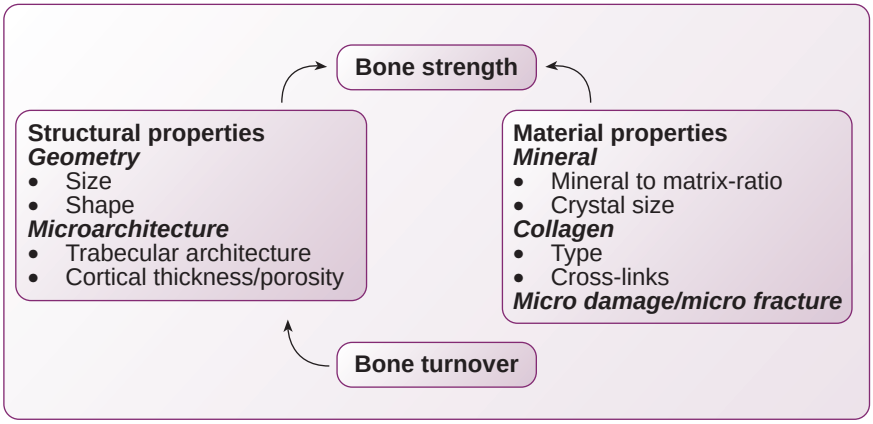
To understand the nature of bone strength, and the Bone Quality Framework, it is necessary to take all 3 factors into account.

Structural properties

Bone strength is partly determined by its structural properties: the shape and size of the bone as well as its microarchitecture, including trabecular structures and cortical thickness and porosity. In osteoporosis, changes in the trabecular bone architecture weaken the bone and increase fracture risk. Patients with hip fracture show a deterioration of the trabecular architecture of bone tissue, and the concomitant loss of cross-connections is associated with an increased risk of fracture.[13]

Of particular importance to women is the observation that dramatic changes in the trabecular architecture occur over the period of a year during the first years after menopause.[13] In one study, vertebral bodies from young healthy individuals were compared with those of elderly individuals with osteoporosis.[14] In the young individuals, there was a greater than 2-fold difference in the amount of trabecular bone in the vertebral column compared with the elderly individuals. Cortical shell thickness in the elderly individuals was also greatly reduced. The amount of force required to break the vertebrae of

Figure 1: Understanding bone strength



an elderly individual with osteoporosis was nearly 10 times less than that required to break the vertebrae of a young, healthy person.

Material properties

In addition to bone structure, the materials that make up bone tissue are vital to bone strength. Bone is a composite of the calcium-containing mineral hydroxyapatite and the protein collagen. Cells called osteoblasts produce the organic matrix component in its primary form. Collagen obtains its final conformation outside the osteoblasts, where cross-links between collagen fibres are formed. The collagen fibres provide a matrix upon which hydroxyapatite crystals are deposited, creating a strong composite material. The degree of mineralization influences bone strength,[15] and the cross-links between collagen fibres affect the ability of bone to absorb energy – during a fall, for example.

Bone turnover

Like any other material exposed to everyday stresses, bone material will weaken over time. Fortunately, bone is a complex living tissue that undergoes constant renewal to repair the microdamage that occurs on a daily basis. In the bone renewal cycle, bone resorption is initiated by cells called osteoclasts that are recruited to the bone surface. Once on the bone surface, osteoclasts erode the bone by creating a resorption cavity. Bone-lining cells differentiate into osteoblasts that secrete an unmineralized matrix into the cavity. The matrix eventually mineralizes, first by a rapid phase, followed by a more prolonged phase of mineralization. If the renewal process proceeds as it should, the resorption cavity will be completely refilled with new bone and the bone surface will be restored. This process of renewal is called bone remodelling.

Clinical studies have shown that remodelling increases with age and reduced oestrogen production. After menopause, when oestrogen production ceases, an increase in bone turnover results in a decrease in mineral density, because osteoblasts do not completely fill the resorption cavities created by the osteoclasts. The increase in bone remodelling results in a greater number of resorption cavities, which act as weak points on the surface of the trabeculae. When bone turnover does not occur at all, however, microdamage and microfractures in trabecular bone cannot be efficiently repaired. Deterioration of bone microarchitecture is found in individuals with high bone turnover, but not in those with low turnover.[16] Strong bones, therefore, result from an optimal bone turnover rate.

Future perspectives

The primary targets for the treatment of osteoporosis are the cells involved in bone remodelling. Many of the structural and material properties of bone are influenced in different ways by treatments, depending on the nature of their physiological effects. Not all the treatment effects on bone strength are equally reflected by a measurement of BMD.

For example, antiresorption treatments that increase BMD by 1–7% lead to a decrease in vertebral fracture risk of 40–60%.[17] From clinical trials we know that the increase in BMD accounts for less than 30% of the reduction in fracture risk.[18,19,20]

Understanding the bone quality factors that contribute to bone strength will help us better appreciate the concept that treatment effects on bone strength have multiple facets. Therefore, the evaluation of treatments should be done on the basis of fracture efficacy data, and not on the basis of one surrogate end-point such as an increase in BMD.

Currently, some new technologies in the experimental stage may help measure the components of bone quality and how they contribute to bone strength. These technologies are quantitative computed tomography (QCT), high-resolution magnetic resonance imaging (MRI), and finite element analysis (FEA). Three-dimensional QCT provides information on bone geometry, including trabecular and cortical bone density, and high-resolution MRI can be used to carry out an in vivo 'virtual bone biopsy' that reveals information about the trabecular architecture of bone. FEA is a computer model designed to predict bone strength. It integrates material and structural information and uses imaging data to create a strength map of the bone. Some of these techniques hold promise for future clinical applications. The goal of osteoporosis treatment is to prevent fracture and subsequent mortality and morbidity. Strong bones fracture less. Treatment approaches, therefore, should focus on increasing bone strength. In accordance with the Bone Quality Framework, strong bones are a reflection of good bone quality, in which there is a carefully maintained balance of structure and material, and bone turnover occurs at an optimal rate. Selection of treatments should be based on available fracture data and not on BMD measurement alone, as BMD response does not adequately reflect the effect of treatment on all the components of bone strength. A better understanding of the Bone Quality Framework and the components that contribute to bone strength may help improve the diagnosis and management of patients at risk for osteoporotic fracture.

References

1. Cummings SR, Black DM, Rubin SM. Lifetime risks of hip, Colles', or vertebral fracture and coronary heart disease among white postmenopausal women. Arch Intern Med 1989;149:2445-8.
2. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. J Women's Health 1997;6:49-62.
3. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet 2002;359:1761-7.
4. Melton LJ III, Thamer M, Ray NF, et al. Fractures attributable to osteoporosis: report from the National Osteoporosis Foundation. J Bone Miner Res 1997;12:16-23.
5. Center JR, Nguyen TV, Schneider D, et al. Mortality after all major types of osteoporotic fracture in men and women: an observational study. Lancet 1999;353:878-82.
6. Jensen JS, Bagger J. Long-term social prognosis after hip fractures. Acta Orthop Scand 1982;53:97-101.
7. Prince RL, Smith M, Dick IM, et al. Prevention of postmenopausal osteoporosis. A comparative study of exercise, calcium supplementation, and hormone-replacement therapy. N Engl J Med 1991;325:1189-95.
8. Consensus Development Conference. Diagnosis, prophylaxis and treatment of osteoporosis. Am J Med 1993;94:646-50.
9. Cooper C, Melton LJ III. Epidemiology of osteoporosis. Trends Endocrinol Metab 1992;3:224-9.
10. Ross PD, Davis JW, Epstein RS, Wasnich RD. Pre-existing fractures and bone mass predict vertebral fracture incidence in women. Ann Intern Med 1991;114:919-23.
11. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet 2002;359:1929-36.
12. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. Lancet 1993;341:72-5.
13. Dufresne TE, Chmielewski PA, Manhart MD, et al. Risedronate preserves bone architecture in early postmenopausal women in 1 year as measured by three-dimensional microcomputed tomography. Calcif Tissue Int 2003;73:423-32.
14. Mosekilde L. The effect of modelling and remodelling on human vertebral body architecture. Technol Health Care 1998;6:287-97.
15. Follet H, Boivin G, Rumelhart C, Meunier PJ. The degree of mineralization is a determinant of bone strength: a study on human calcanei. Bone 2004;34:783-9.
16. Borah B, Dufresne TE, Chmielewski PA, et al. Risedronate preserves bone architecture in postmenopausal women with osteoporosis as measured by three-dimensional microcomputed tomography. Bone 2004;34:736-46.
17. Delmas PD. Treatment of postmenopausal osteoporosis. Lancet 2002;359:2018-26.
18. Cummings SR, Karpf DB, Harris F, et al. Improvement in spine bone density and reduction in risk of vertebral fractures during treatment with antiresorptive drugs. Am J Med 2002;112:281-9.
19. Li Z, Meredith MP, Hoseyni MS. A method to assess the proportion of treatment effect explained by a surrogate endpoint. Stat Med 2001;20:3175-88.
20. Sarkar S, Mitlak BH, Wong M, et al. Relationships between bone mineral density and incident vertebral fracture risk with raloxifene therapy. J Bone Miner Res 2002;17:1-10.
21. Wehrli FW, Gomberg BR, Saha PK, et al. Digital topological analysis of in vivo magnetic resonance microimages of trabecular bone reveals structural implications of osteoporosis. J Bone Miner Res 2001;16:1520-31.