

**Perspective Article**

Bone quality: Understanding what matters

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Introduction

Although bone strength and fracture risk are generally assessed by measuring bone mineral density (BMD), the mechanical properties of bone are in fact determined not only by bone mass, but also by the architecture/geometry of the bone and by the intrinsic material properties of the tissue.

Fracture risk increases with age, partly as a function of changes in BMD. However, the risk of fracture in a 75-year-old woman is 4-7 times that in a 45-year-old woman with an identical bone mass¹. This demonstrates that there is a component to bone fragility that is independent of bone mass, and determined by bone quality. This has been emphasized recently by the observation that anti-resorptive treatments for osteoporosis all have about the same fracture efficacy, though there is a seven-fold difference in their effect on BMD.

Bone quality is defined by at least four factors: (1) the rate of bone turnover; (2) properties of the collagen/mineral matrix; (3) microdamage accumulation; (4) architecture/geometry of cancellous and cortical bone.

Bone turnover

Vertebral fracture risk is determined by both BMD and turnover rate². Rapid turnover accelerates osteoclastic resorption on trabecular surfaces that can reduce their resistance to buckling and make failure more likely³. Resorption lacunae on trabecular surfaces are responsible for larger decreases in bone stiffness than in trabecular thinning⁴. Additionally, the resorption bays create stress concentrations that may promote the initiation of microcracks. More rapid turnover also increases the probability for perforation and elimination of trabecular struts.

A 50% reduction in turnover can result in a 4-fold reduction in trabecular perforation⁵. However, agents such as teriparatide that increase turnover also may lower fracture risk by increasing net bone formation on trabecular surfaces.

Matrix mineralization

The amount of energy that can be absorbed before fracture is reduced by either hypo- or hypermineralization of the bone tissue^{6,7}. Suppression of remodeling increases tissue mineralization by lengthening the period of time over which secondary mineralization can occur⁸⁻¹². This may increase the tendency for microcracks to initiate. As importantly, remodeling suppression increases tissue homogeneity, possibly making crack growth easier as well. However, the magnitude of the effect is probably determined by the amount of suppression. On the other hand, teriparatide stimulates increased bone turnover and increases the heterogeneity of the tissue matrix.

Collagen

The collagen matrix has a profound effect on bone's mechanical properties¹³. The risk of vertebral fracture is significantly increased in subjects with the Sp1 polymorphism of the COL1A1 gene¹⁴. Changes in collagen with aging are known to affect the amount of energy required to cause fracture¹⁵. This may have to do either with the amount of collagen in the matrix, or with the extent or nature of its cross-linking. Anti-resorptive treatments probably increase the amount of cross-linking, but whether this is a positive or a negative change is unclear at this time.

Microdamage

Microdamage accumulation reduces bone's strength, stiffness and toughness¹⁶. Bone from older women is more susceptible to the initiation of microcracks¹⁷ and must be inherently more fragile than bone from younger women. This may

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be why there is a significant accumulation of microdamage at several anatomical sites with age¹⁸⁻²¹. Suppression of remodeling pharmaceutically also increases damage accumulation^{22,23}; the extent of this increase is probably dependent on the magnitude of the suppression²⁴.

Architecture/Geometry

Cancellous bone that is more plate-like, with thicker and more trabeculae, enhances strength. Trabecular architecture that is more isotropic, having similar mechanical properties in all directions, may lower fracture risk further. This could provide a rationale for the clinical observation that fracture risk decreases by 50-60% in the first year of bisphosphonate therapy with only a 5% increase in bone mineral density. Teriparatide increases trabecular number and connectivity via longitudinal tunneling, converting thickened trabeculae to multiple struts of normal thickness²⁵. Although it increases cortical porosity, the porosity is located close to the marrow cavity where its mechanical effect is small^{26,27}. Simultaneously, teriparatide allows periosteal apposition, which maintains or improves cortical bone strength²⁸.

Conclusion

It is quite clear that the assessment of bone quality as defined here, in addition to BMD measurement, is important to determine fracture risk, but techniques to measure these properties are nascent. Development of new non-invasive techniques will be necessary to provide better pre-fracture evaluations of tissue quality. These will need to be made accessible and convenient for the health practitioner.

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