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Hylonome

Perspective Article

Summary – Osteoporosis and fracture risk: bone matrix quality session

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Fracture risk increases with age, partly as a function of changes in bone mineral density. However, the risk of fracture in a 75-year-old woman is 4-7 times that of a 45-year-old woman with an identical bone mass, demonstrating a bone quality component to fragility that is independent of bone mass. Bone quality is determined by at least four factors: (1) properties of the collagen/mineral matrix; (2) microdamage accumulation; (3) architecture/geometry of cancellous and cortical bone, and (4) the rate of bone turnover. Collagen, mineral and architecture changes with age, osteoporosis and therapeutic treatment. Bone active agents have specific effects on each of these, and may affect cortical and cancellous bone compartments differently.

In this session, three aspects of bone matrix quality were considered: (1) collagen effects **Dr. Bailey**; (2) mineral effects **Dr. Boskey**; (3) architectural effects independent of bone mineral **Dr. Weinans**. The role that anti-resorptive therapies play in altering mineral and how these might be responsible for the greater than expected reduction in fracture incidence were addressed by **Dr. Boivin**. **Dr. Turner** began the session by defining fragility from a biomechanical perspective.

Aging is associated with a reduction in collagen content. In osteoporosis, there is an increase in both synthesis and degradation of collagen, and an increase in the number of immature cross-links. Osteoporotic bone may be more fragile due to fewer collagen fibers and weaker cross-linking. It was clear that the rate of collagen turnover has a significant effect on bone quality. The more rapid rate of collagen turnover may in itself affect the quality of the collagen in osteoporosis.

Although changes in bone mineral content are widely recognized to occur in aging and osteoporosis, the physicochemical properties of the mineral crystal may also be changed. Mineral crystallinity increases with age, and this in itself may make the tissue more brittle.

Anti-resorptive therapies increase tissue mineralization by increasing the mean tissue age. Whether this is beneficial or deleterious is not yet clear. However, the increase in mineralization never achieves the level of mineral in normal nonosteoporotic age-matched controls, so it is likely to be a positive change. However, anti-resorptive therapies also have a tendency to make the tissue mineralization more uniform; from a fracture mechanics standpoint, this would make it more likely for cracks that are introduced into the matrix to grow. In addition, tiludronate has been shown to increase crystal width, apart from their effect on bone mineral content.

Architectural changes, some of which are independent of bone mass, also occur in osteoporosis. In osteoporosis, there is a tendency to convert to a more rod-like and more anisotropic structure, whereas bisphosphonate treatments tend to make the bone more plate-like and more isotropic. Complete trabecular perforations increase as the remodeling space, or remodeling rate, increase. These may weaken the structure more than expected based on the loss of bone mass alone. Increased mineral content but reduced tissue modulus following anti-resorptive therapies may be explained by the accumulation of matrix microdamage.

Many questions remain to be answered:

Collagen:

- How do therapeutic treatments for osteoporosis alter collagen quality (content, cross-linking, turnover rate)?
- How does increased turnover alone affect collagen quality?

Mineral:

- How is bone crystallinity affected by long-term anti-resorptive therapies?
- What is the relationship between mineral crystallinity and brittleness?
- What is the mechanical effect of reduced variability in bone mineral distribution (i.e. increasing homogeneity of tissue properties)?
- What role do osteocytes play in matrix mineralization?

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Architecture:

- To what extent do resorption bays in trabeculae weaken bone?
- Does maintenance of isotropy reduce fracture risk?
- What is the relative role of trabecular and cortical bone in vertebral and hip fracture risk?

Once we have a better understanding of how these features of bone matrix vary in aging, disease, and therapeutic treatment, the next frontier will be to determine how to measure these aspects of bone quality in patients.