J Musculoskel Neuron Interact 2003; 3(4):417

Hylonome

Perspective Article

Summary – Bone turnover and fracture risk

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Bone fragility in osteoporosis is a product of bone mass, bone geometry, and tissue quality. Tissue quality is typically defined by four features of the tissue matrix: (1) rate of bone turnover; (2) properties of the mineral and collagen; (3) microdamage burden and (4) architecture. Although the role of the latter three quality measures has been discussed in some detail in the literature, the role played by bone turnover rate has received less attention.

Apart from increasing the remodeling space, the increased rate of turnover may further weaken trabeculae by creating deep "notches" in the trabecular struts, making them more prone to failure. Although the actual amount of bone loss caused by a single resorption event may be small, it may selectively weaken the structure by increasing the propensity of the strut to buckle. The reverse would occur under the influence of anti-resorptive therapies. Indeed, one model indicates that a 50% suppression of remodeling would over time reduce the number of trabecular perforations by 4-fold. Because of this, a reduction in remodeling rate may account for at least 50% of the reduction in fracture risk in patients on these therapies.

Perhaps not as well recognized, cortical bone has a significant influence on fracture risk. Expansion of the periosteal surface can compensate for losses of bone from the endosteal surface by increasing the cross-sectional moment of inertia and the section modulus, which are related to rigidity in bending. Current data suggest that signaling through the estrogen receptor-b (ER-β) pathway can suppress both endosteal resorption and periosteal apposition of new bone; when this receptor is knocked-out, both the marrow cavity width and total diameter of the bone expand (in females, but not in males), resulting in a larger and stronger bone. This may in fact be one reason that trabecular bone loss and expansion of the endosteal bone surface are accompanied by periosteal expansion in postmenopausal women (even though the expansion often is not sufficient to offset the effects of bone losses). Signaling through the estrogen receptor-α (ER-α) seems to affect the response of bone to a mechanical stimulus; apposition of new bone periosteally is suppressed in response to mechanical load when the ER-α is knocked out. Therefore, these receptors seem to work somewhat at odds to each other

The increased remodeling rate in the femoral neck allows clustering of Haversian canals and development of composite osteons may preferentially weaken some cortices of the neck more than expected based on changes in bone mass alone. These changes are localized to specific regions of the femoral neck, with the anterior aspect of the neck affected to the greatest degree. Endothelial nitric oxide synthase (eNOS) may play a role in this process as fracture cases may have a 50% reduction in osteocyte expression of eNOS; this implicates the vascular system in the development of cortical thinning and increased porosity in the femoral neck.

In combination, changes at both cancellous bone sites and cortical bone sites attributable to increased bone turnover, apart from loss of bone mass, may contribute significantly to fracture risk. The contribution of bone turnover as a contributor to increased fracture risk deserves greater study.

The author has served as a consultant for Eli Lilly Co. and Procter & Gamble Pharmaceuticals and owns stock in Eli Lilly Co.

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Accepted 15 August 2003