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Perspective Article

Hylonome

Periosteal apposition and fracture risk

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Periosteal bone formation occurs throughout life. It is regulated by the growth hormone/IGF axis and by sex hormones. Throughout adulthood, men's skeletons undergo more periosteal apposition than women's. This sexual dimorphism is due mainly to the differential effects of sex hormones on the periosteum – estrogen suppresses periosteal bone formation whereas androgens stimulate the periosteum. Periosteal apposition reduces bone fragility in two ways: it adds more bone mass to the skeleton and it greatly increases the stiffness and strength of long bones by adding bone further from the neutral bending axis.

Estrogen suppresses periosteal bone formation throughout adult life in women. After the menopause, periosteal bone formation appears to increase and thus partially compensates for the bone loss experienced at trabecular and endocortical surfaces. Estrogen also preserves bone mass on bone surfaces near marrow. These dual effects of estrogen appear to be regulated by different molecular pathways. The suppressive effect of estrogen at the periosteum is largely due to signaling through the beta isoform of the estrogen receptor (ERβ) whereas the preservative effects of estrogen on trabecular and endocortical surfaces rely on signaling through estrogen receptor-α (ERα). In contrast androgens tend to enhance periosteal bone formation. The fact that estrogens and androgens have differential effects on periosteal bone formation may to a large extent explain why women have more age-related bone fragility. A proper treatment for bone fragility in women would preserve bone near marrow while enhancing periosteal apposition. Presumably a selective estrogen receptor modulator that acts as an agonist for ERα and an antagonist for ERβ would be ideally suited for this task.

Reference

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