OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Vitamin D receptor polymorphism is associated with fracture risk in older women

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The active form of vitamin D, calcitriol, is essential to bone turnover and remodeling and to calcium-phosphate homeostasis. Alterations in the vitamin D endocrine system may contribute to bone loss with aging. One hypothesis proposes that age-related bone loss results from decreased intestinal absorption of calcium, leading to increased PTH, which, in turn, increases the rates of bone remodeling and bone loss. Decreases in the production of 1,25(OH)2 vitamin D, intestinal responsiveness to 1,25(OH)2 vitamin D, and levels of 25(OH) vitamin D may all contribute to the decreased intestinal absorption of calcium and increased bone loss seen with aging.

Vitamin D's effects on bone are mediated through the vitamin D receptor (VDR), a nuclear transcription factor that regulates gene expression by interacting with vitamin D response elements within vitamin D target genes. VDR is regulated in an age-, tissue-, and cell-specific manner. A common and functional *C* to *T* polymorphism in exon 2 of the *VDR* gene introduces a translation start site and protein product that differs in length by three amino acids. The shorter receptor (424aa) encoded by the *C* allele seems to increase target gene expression.

Moffett et al [1] evaluated the association between the *VDR* translation start site polymorphism and osteoporotic phenotypes among 6698 older white women. There were 2532 incident nontraumatic, nonvertebral fractures during 13.6 years of follow-up, including 509 wrist and 703 hip fractures. Women with the C/C genotype had lower wrist bone mineral density (BMD) and an increased risk of wrist and all non-spine/low-trauma fractures, but not of hip fractures. The high frequency of this variant confers a population attributable risk that is similar to established risk factors for fracture such as maternal history of fracture, low body weight , corticosteroid use, and smoking.

The common and potentially functional *VDR* translation start site polymorphism confers a modestly increased relative risk of fracture among older white women. However, the high frequency of this variant confers a population attributable risk that is similar to or greater than several established risk factors for fracture.

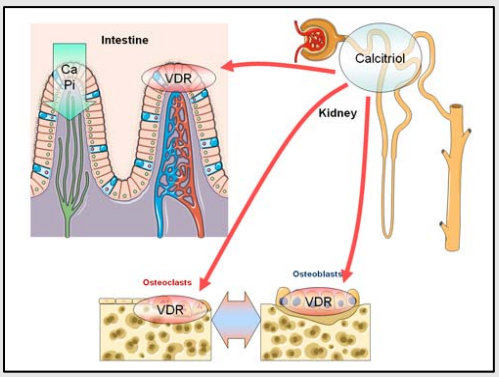
1. Moffett SP. et al. *J Bone Miner Res*. 2007;22:730-736.

Vitamin D modulates bone turnover

The active form of vitamin D, calcitriol, is synthesized in the kidney. It acts on the intestine, through vitamin D receptors (VDR) to increase calcium and phosphate absorption, which is mandatory for bone mineralization.

VDRs are present in bone cells, both osteoblasts and osteoclasts, which need calcitriol for differentiation and activity.

VDR polymorphisms may affect the efficiency of signal transduction triggered by calcitriol and reduce or enhance the responsiveness of target cells.



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