# Vitamin-D & osteoporosis in CKD

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Vitamin D is required for normal bone formation and normal mineralization, which play a critical role in bone biology. Altered vitamin D metabolism plays a crucial role in secondary hyperparathyroidism along with other mineral metabolism changes. Increased bone turnover, bone loss, and mineralization defects have been noted with serum 25-(OH) D levels <50 nmol/L. Mucsi et al. demonstrated a positive relationship between 25 (OH) vitamin D levels and radial bone BMD in HD patients. Lower 25 (OH) vitamin D levels have been determined to be associated with subperiosteal resorption and reduced BMD in ESRD patients. Vitamin D deficiency also causes frailty because of muscle weakness, nonvertebral and hip fractures, and all-cause mortality.

CKD patients receive high 1,25(OH)2D doses that suppress 25-hydroxylase in the liver and 1-α-hydroxylase in the kidney through feedback inhibition. Thus, the greater the 1,25(OH)2D dose is, the lower the 25(OH)D production. Consequently, administering a high 1,25(OH)2D dose exacerbates the 25(OH)D shortage in the kidney, pancreas, bone, prostate, breast, and immune cells. In CKD patients with secondary hyperparathyroidism, the proliferation of oxyphil cells in the parathyroid gland elevates 1-α-hydroxylase production, facilitating the 25(OH)D to 1,25(OH)2D conversion. In addition, 24-hydroxylase expression is elevated in the uremic kidney. Therefore, native vitamin D (cholecalciferol) supplements convert to 25(OH)D, then occupy 24-hydroxylase. In addition, native vitamin D supplements increase 1,25(OH)2D production in the PTH gland through an autocrine or paracrine mechanism to suppress PTH production by chief cells.

On the other hand, $1,25(OH)_2D$ overuse, total parathyroidectomy, and immunosuppression after kidney transplantation lower serum PTH levels and lead to low bone turnover disorders or adynamic bone disorder. The characteristic feature of adynamic bone disorder is the low viability of osteoblasts and osteoclasts. Therefore, providing native vitamin D may recover the viability of osteoblasts and improve bone turnover and bone quality.

However, in CKD patients with acceptable PTH levels, the KDOQI guidelines recommended that 25(OH)D be measured once a year in CKD patients at all stages, and the levels should be >30 ng/mL. Furthermore, early vitamin D supplementation can prevent or delay the onset of secondary hyperparathyroidism.

Vitamin D deficiency is well known to lead to rickets in children and

osteomalacia or osteoporosis in adults. Previous studies approve that vitamin D supplement cures weakened bone mineralization. Osteoporosis is a systemic metabolic bone disease of multiple causes, which have the characters of impaired bone strength and increasing fragility fracture risk. Bone strength is reflected equally by both BMD, which is determined by peak bone mass and amount of bone loss and bone quality, which refers to architecture, turnover, and mineralization.

Mounting evidence indicates most bone cells possess 1α-hydroxylase to perform the intracrine/paracrine activities of vitamin D. 1,25(OH)2D produced by bone cells can diminish bone resorption through an intracrine/paracrine function resulting in increased bone mass. Vitamin D deficiency will increase the risks of fracture, which not only impairs bone mineralization but also numerous pathological alterations. Vitamin D deficiency increases both the beginning and extension of fragility fracture. Thus, vitamin D deficiency is associated with both diminished bone mass and worsen bone quality. Appropriate vitamin D levels are the key to preserve the structural integrity of bone. Although several meta-analyses show no influence of vitamin D treatment alone on fracture risk, the emerging evidence shows that cholecalciferol combined with calcium has the greatest advantage to reduce the risk of non-vertebral and hip fractures.

This talk emphasizes the role of native vitamin D replacements in CKD patients, reviews vitamin D biology, and summarizes the present literature regarding native vitamin D replacement especially in the osteoporotic CKD population.

**References**


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