



## Noninvasive methods for diagnosis of chronic kidney disease related bone diseases; help or hindrance?

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**C**hronic Kidney Disease (CKD) -related bone disease is caused by a complex combination of hyperphosphatemia, hypocalcemia, hyperparathyroidism, decreased 25-(OH)vitamin D, decreased renal synthesis of 1,25-(OH)<sub>2</sub>-vitamin D, metabolic acidosis and hypogonadism (1,2).

Bone biopsy with tetracycline labeling is the gold standard but not practical in all centers. There are great interest to find novel imaging and biochemical methods to diagnose and typifying the CKD -related bone diseases. Osteoporosis is a reduction of bone strength, and WHO defines it as a bone density that falls below 2.5 standard deviation for young healthy adults, measured by dual energy x-ray absorptiometry (DEXA). The role of DEXA to classify fracture risk in CKD is controversial. Elevated parathyroid hormone (PTH) levels in CKD patients, could be anabolic for trabecular and catabolic for cortical bone, but DEXA cannot discriminate these two components. Peripheral computerized tomography (pCT) measures the true density mass of bone tissue per unit volume, and analysis the cortical and trabecular bone separately. Peripheral quantitative computed tomography (pQCT) and high-resolution pQCT (HR-pQCT) could measures volumetric density and geometry more precisely. By those methods it has been shown that cortical deficits is predominate in CKD patients and predicts the fracture risk. All these measurements enable clinician to stratify the fracture risk but does not specify the type of bone disease (1-3).

Secondary hyperparathyroidism is a major problem in CKD patients and accurate measurement of serum parathyroid hormone (PTH) is essential. PTH assay using different commercial kits creates different results which related to their ability to detect the intact circulation PTH. A significant proportion of circulating PTH is oxidized PTH that does not have biologic activity. The ability to recognize and immune-extract the oxidized PTH is very important for better measurement of biologically active compartment (4,5).

Bone formation markers, such as bone specific alkaline

### ■ Implication for health policy/practice/research/ medical education

Chronic Kidney Disease (CKD) -related bone disease is a complex combination of different disease conditions. Up to know even modern measurement could not fill the place of bone biopsy, but with wise combination of noninvasive measurement, and understanding the limitations we could be approximate to the conditions.

phosphatase (BSAP), osteocalcin and procollagen type 1 N-terminal propeptide (PINP), are markers of osteoblast function and bone adsorbtion markers such as tartrate-resistant acid phosphatase 5b and C-terminal telopeptides of type I collagen (CTX), show osteoclast activity. Reference ranges for those markers in CKD populations are not well defined. Markers such as osteocalcin, PINP monomer, and CTX are cleared by kidney and their concentrations are increased in renal dysfunction. In clinical practice, PTH and bone-specific alkaline phosphatase (BSAP) are the most commonly used markers of bone turn-over in CKD patients. Low vitamin D levels and low levels of PTH with high levels of BSAP are correlated with osteomalacia. Finally, very high and very low levels of PTH predict the underlying bone disease, but most uncertainty dose exist in the mid-ranges (5,6). In fact fracture risk is higher in patients with either low (150 pg/ml) or high (300 pg/ml) PTH levels (7). PTH level greater than 130 pg/ml at three month after transplantation also predicts higher incidence of fracture (8).

CKD-related bone disease is a complex combination of different conditions. Up to know even modern measurement could not fill the place of bone biopsy, but with wise combination of noninvasive measurement, and understanding the limitations we could be approximate to the conditions.

### Author's contribution

MRA is the single author of the paper.

### Conflict of interests

The author declared no competing interests.

### Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the author.

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