A Serum 25 Hydroxy-vitamin D Concentration in Search of a Bone Disease

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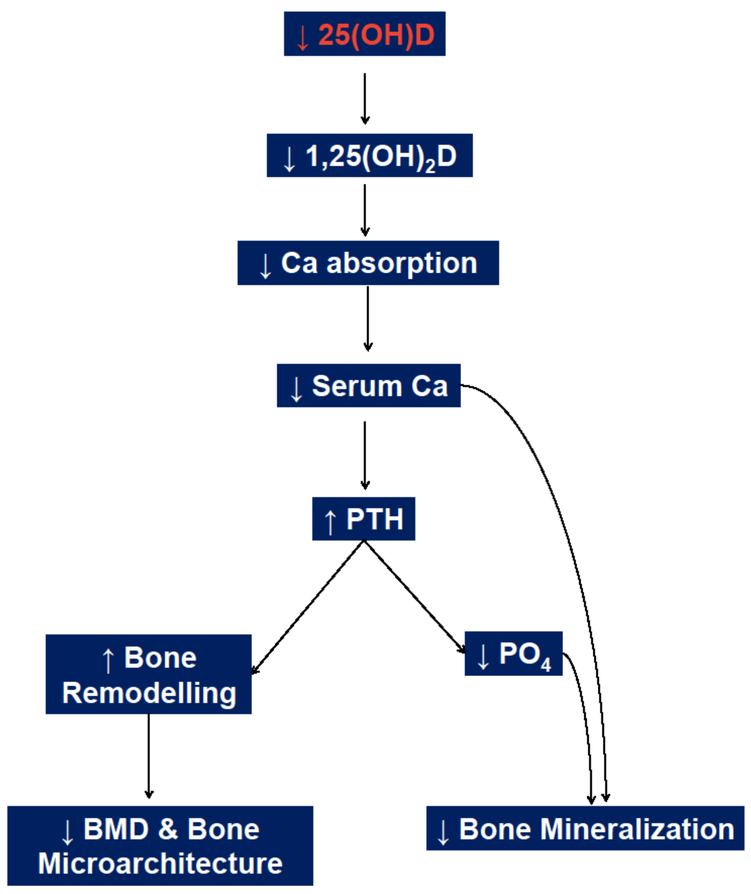
Background

Vitamin D insufficiency and deficiency are defined as a serum 25-hydroxy-vitamin D (25(OH)D) below 50 and 30 nmol/L respectively (1, 2). We aimed to determine whether there is a serum 25(OH)D level that signals a low serum calcium and phosphate, secondary hyperparathyroidism, high bone remodelling, reduced bone mineral density (BMD), and so, an increased risk for microstructural deterioration and bone fragility (figure 1).

Figure 1 Pathway of hypovitaminosis D leading to deleterious skeletal effects.



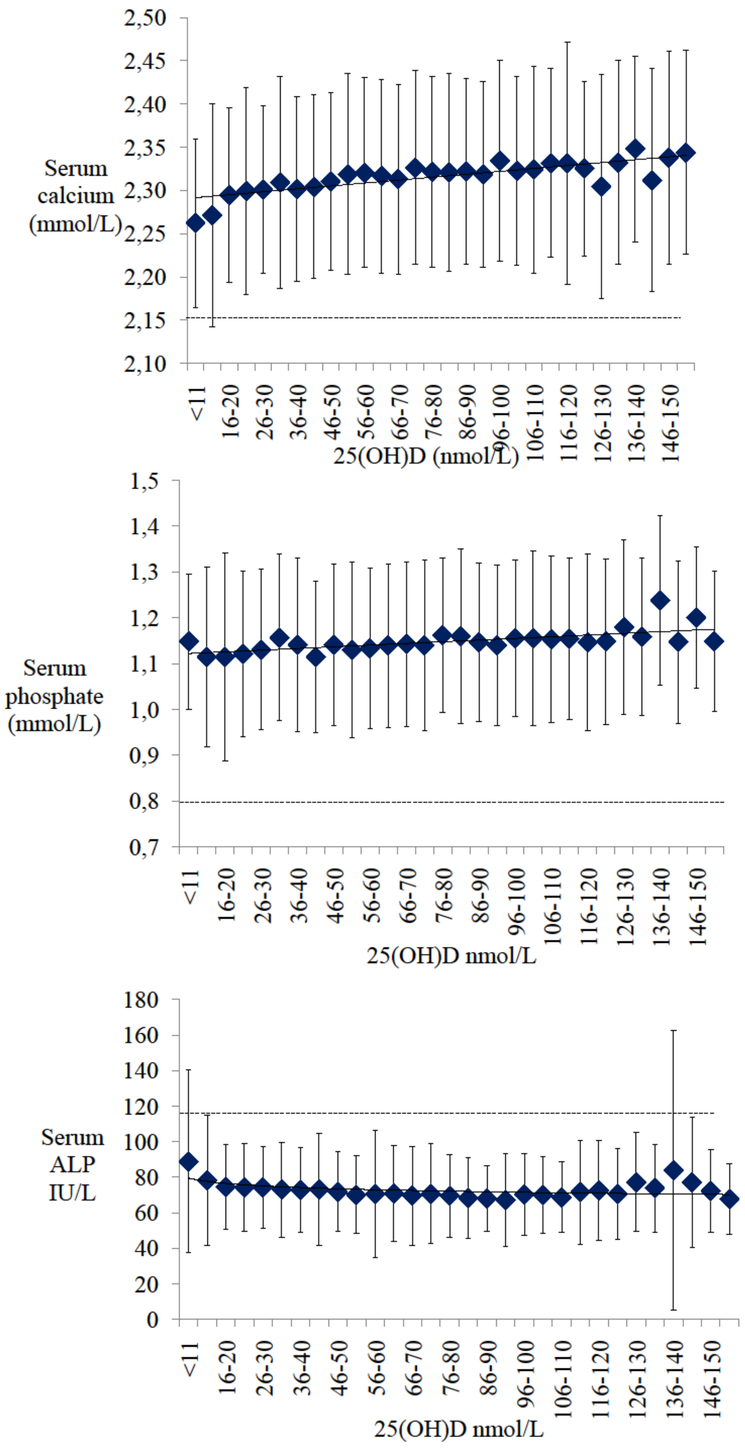
Methods

Concentrations of 25(OH)D, calcium, phosphate, creatinine and parathyroid hormone (PTH) were measured by Melbourne Pathology in the serum obtained from 11,855 subjects (8777 women, 3078 men. In a second cohort of 182 subjects from Austin Health, serum C-terminal telopeptide of type 1 collagen (CTX) and Procollagen type 1 N propeptide (P1NP) and areal bone mineral density (aBMD) at femoral neck and lumbar spine were measured. We excluded persons below 20 years of age, patients with hypercalcaemia, chronic kidney disease and a serum 25(OH)D ≥180nmol/L.

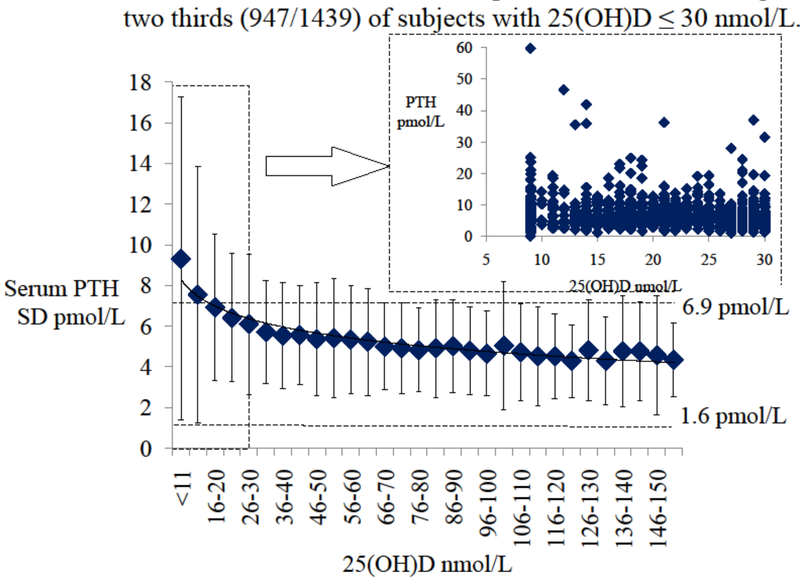
Results

Serum calcium and phosphate correlated positively with serum 25(OH)D. Serum PTH and alkaline phosphatase, but not CTX and P1NP, correlated negatively with serum 25(OH)D.

Figure 2 Mean corrected serum calcium, phosphate, alkaline phosphatase and parathyroid hormone (PTH) standard deviation versus serum 25(OH)D). Dashed line - lower or upper limit of the reference range.



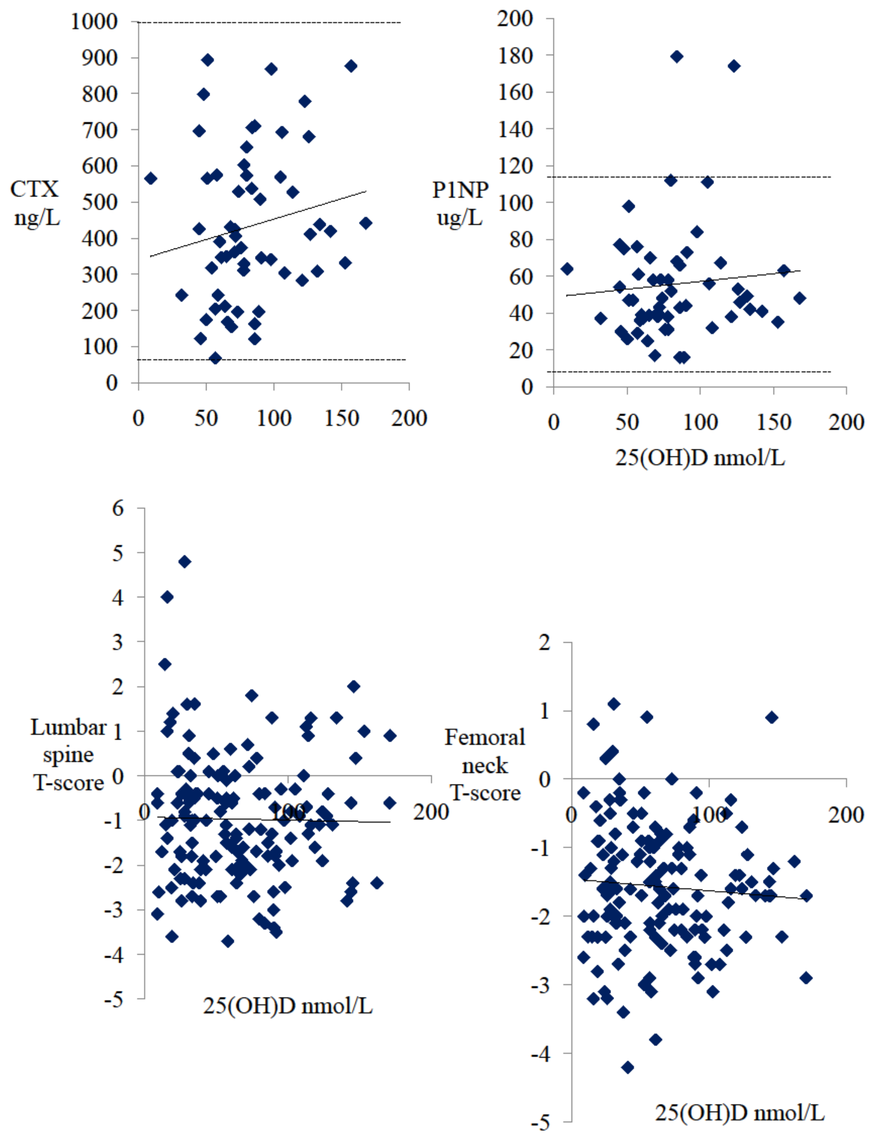
Inset : PTH was within the lower part of the reference range in two thirds (947/1439) of subjects with 25(OH)D ≤ 30 nmol/L.



Results

There was no threshold level of 25(OH)D that identified persons with deficits in serum calcium or phosphate or increased levels of PTH or remodelling markers; PTH was within the reference range in two thirds (947/1439) of subjects with 25(OH)D ≤ 30 nmol/L. PTH diminished as 25(OH)D increased, even when levels were above 50 nmol/l. There was no correlation between serum 25(OH)D and areal BMD.

Figure 3 Insignificant associations between CTX (R^2=0.03), P1NP (R^2=0.01), BMD mineral density T-score at Lumbar spine (R^2=0.00) and femoral neck (R^2=0.01) with 25(OH)D levels. Dashed line is the lower or upper limit of the reference range.



Conclusions

Diagnostic labelling of persons as having vitamin D 'deficiency' or 'insufficiency' based only on concentration of serum 25(OH)D is not evidence based. A diagnostic threshold level of serum 25(OH)D, and the duration of exposure at this level, predisposing to bone disease remain uncertain.

References

1. Institute of Medicine Dietary reference intakes for calcium and vitamin D. The National Academies Press, Washington, DC 2011
2. Holick MF et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011; 96: 1911–1930

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