Vitamin D levels and early mortality among incident hemodialysis patients

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To the Editor: We greatly appreciate the large study of Wolf *et al.*[1] pointing a link between low serum 25-OH vitamin D levels and early mortality among incident hemodialysis patients who did not beneficiate of active vitamin D. The inverse link between higher all-cause mortality and lower 25-OH vitamin D levels in these patients strongly suggests that vitamin D deficiency is a mortality risk factor that may be reversed by its correction. Unfortunately, the fact that the patients who eventually received 1αOH vitamin D were previously better treated (with higher arteriovenous fistula prevalence and at lower risk (lower heart failure prevalence)) skews the evidence that the survival benefit was only due to active vitamin D administration. Therefore, it is interesting to recall that the risk of cancer was significantly reduced by native vitamin D increasing serum 25-OH vitamin D above 80 nmol/l (by a placebo-controlled randomized trial performed in post-menopausal patients in whom 50 cases of new cancer was observed).[2] Therefore, we suggest that newer 1αOH vitamin D derivatives survival benefit should be proven by a placebo-controlled trial in patients with 25-OH vitamin D levels $\geqslant$70 nmol/l as recommended by the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) for the CKD grades 3–4 patients.

1. Wolf M, Shah A, Gutierrez O *et al.* Vitamin D levels and early mortality among incident hemodialysis patients. *Kidney Int* 2007; **72**: 1004–1013.
2. Lappe JM, Travers-Gustafson D, Davies KM *et al.* Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr* 2007; **85**: 1586–1591.

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Response to 'Vitamin D levels and early mortality among incident hemodialysis patients'

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We thank the authors for their comments regarding deficiency of 25-hydroxyvitamin D (25D) as a novel risk factor for mortality.[1] Although we attempted to adjust for baseline factors at the initiation of dialysis including certain quality of care indicators such as fistula prevalence, we agree with the authors that residual confounding remains a limitation in this and other observational studies. We also agree with the authors that the benefits of maintaining normal 25D levels observed in other clinical settings such as cancer prevention lend further evidence in support of the importance of the vitamin D axis in health.

We do recommend caution, however, when attempting to infer the relative importance of 25D versus calcitriol (1,25D) deficiency based on our study. Although it is tempting to conclude that 25D deficiency is more important than 1,25D deficiency given that the greatest risk of mortality was observed in the group with the lowest 25D levels, it is important to recognize that virtually all patients in this study were profoundly 1,25D deficient. Thus, the group of patients with severe 25D deficiency also had severe 1,25D deficiency: they were globally deficient in the vitamin D axis.

Although we strongly agree with the suggestion that randomized controlled trials are needed to test the benefits of active vitamin D preparations on survival in patients with kidney disease, we also believe that trials are needed to test the effects of correction of 25D deficiency either alone or in combination with active vitamin D.

1. Wolf M, Shah A, Gutierrez O *et al.* Vitamin D levels and early mortality among incident hemodialysis patients. *Kidney Int* 2007; **72**: 1004–1013.

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Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease

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To the Editor: Levin *et al.*[1] have documented that serum calcitriol decrease with glomerular filtration rate decline is independent of calcidiol. As low calcitriol is associated with coronary calcification, they speculate that hypocalcitriolemia favors vascular calcification and hyperparathyroidism, and propose to perform randomized trial with activated vitamin D against placebo, but not against ergocalciferol, because, according to their citation of our cohort study,[2] vitamin D2 would not effectively suppress parathyroid hormone.