

SIGNIFICANCE STATEMENT

Medial vascular calcification promoted by hyperphosphatemia is considered to play an important role in the high cardiovascular mortality of patients with CKD. Reduced serum zinc levels have frequently been observed in patients with CKD. This article provides evidence that zinc supplementation strongly blunts phosphate-induced vascular osteoinductive signaling and calcification *in vitro* in primary vascular smooth muscle cells, and *in vivo* in mouse models. Zinc supplementation may be a simple, yet highly effective clinical approach to reduce progression of vascular calcification and cardiovascular disease in CKD.