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Response to ‘Adynamic Bone Disease and MICS’




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### Authors
Kalantar-Zadeh, K
Kopple, J-D



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# Response to 'Adynamic Bone Disease and MICS'

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**We appreciate the important thoughtful points raised by Dr Heaf[1] regarding adynamic bone disease (ABD). ABD may indeed be a secondary phenomenon and a consequence of the malnutrition–inflammation complex syndrome (MICS), which is also associated with hypoalbuminemia, increased serum levels of proinflammatory cytokines, protein–energy wasting, and poor outcome in maintenance dialysis patients.[2] A recent study in 44 chronic peritoneal dialysis patients showed that low serum albumin was associated with ABD.[3] Although we are not aware of any study that indicates a direct causal effect of inflammation on ABD in chronic kidney disease, *in vitro* parathyroid hormone (PTH) secretion is suppressed by interleukin-6,[4] a strong proinflammatory cytokine that is associated with poor outcome in maintenance-dialysis patients. Interleukin-1 beta (IL-1$\beta$), another proinflammatory cytokine, may also suppress PTH secretion. In another *in vitro* study, PTH secretion from cultured parathyroid tissue slices was significantly inhibited in media containing IL-1$\beta$.[5] This effect may be mediated through the specific IL-1 receptors that upregulate the calcium-sensing receptor mRNA leading to apparent low bone turnover.[5] Indeed in the foregoing study, the inhibitory effect of IL-1$\beta$ could be counteracted by the IL-1 receptor antagonist (IL-1ra),[5] indicating that the inflammation-induced suppression of PTH can potentially be overcome by treatment of MICS in individuals with chronic kidney disease. Hence, interventions that can improve hypoalbuminemia and kidney disease wasting by correcting malnutrition and/or by mitigating inflammation, for example, via IL-1ra *anakinra*, may be more promising approaches for the management of ABD rather than decreasing the dose of or withholding activated vitamin D analogs.**

**In our study, the MICS could indeed explain a large portion of the association between low PTH and increased death rate. However, in our epidemiologic study, inflammatory markers and cytokines were not measured. Hence, controlling for MICS was suboptimal, which may explain the existence of the residual association between low PTH and death after multivariate adjustment. Moreover, many patients with low PTH did not receive paricalcitol,[6] which may be another explanation for high mortality in this group. Nevertheless, any dose of paricalcitol is associated with better survival compared to no paricalcitol administration, including in those with low PTH levels.[6] As Dr Heaf suggested, we plan to perform additional subgroup analyses to examine more carefully the association of ABD and MICS in maintenance-dialysis patients.**

**K Kalantar-Zadeh has received honoraria from Abbott (manufacturer of calcitriol (calcijex) and paricalcitol (zemplar)).**

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K Kalantar-Zadeh[1,2] and JD Kopple[1,2,3]
[1]*Division of Nephrology and Hypertension, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California, USA;* [2]*David Geffen School of Medicine at UCLA, Los Angeles, California, USA and* [3]*UCLA School of Public Health, Los Angeles, California, USA*
**Correspondence:** *K Kalantar-Zadeh, Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, 1124 West Carson Street, Torrance, California 90502. E-mail: kamkal@ucla.edu*

# Don't be so BOLD: Potential limitations in the use of BOLD MRI for studies of renal oxygenation

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**To the Editor:** Blood oxygen level-dependent contrast magnetic resonance imaging is used for studies of intrarenal oxygenation[1] and has been touted as a useful non-invasive diagnostic tool in renal medicine. The validity of this technique as an indicator of parenchymal oxygenation, however, relies on the assumption that tissue oxygenation varies with blood oxygenation. We recently found that in both rabbits and rats renal cortical and medullary tissue $pO_2$ can remain remarkably stable in the face of changes in renal blood flow,[2] even if renal oxygen consumption does not change.[3] We also observed increased renal venous blood oxygen content with increasing renal blood flow, despite stable tissue $pO_2$.[3] These observations support the concept that diffusional shunting of oxygen from arteries to veins increases with increased renal blood flow and so contributes to dynamic regulation of renal oxygenation.[3] The possibility that similar mechanisms operate in the human kidney raises concerns over the reliability of clinical assessment of renal tissue oxygenation using blood oxygen level-dependent magnetic resonance imaging. Our data indicate that changes in the oxygen level of blood in the renal circulation, as evidence by altered renal venous $pO_2$, do not necessarily reflect changes in tissue $pO_2$. The possibility that kidney vascular oxygenation and tissue oxygenation may vary