



NEWSLETTER # 7 (1), 2017

CKD-MBD related publications in the ERA-EDTA journals

The ERA-EDTA acknowledges the high clinical and scientific relevance of the CKD-MBD syndrome, reflected by several key publications in the journals of our society. We hereby summarize the content of several recent important papers, providing a link to their abstracts.

From July to December 2016, **19 CKD-MBD related articles**, including several editorial comments and experimental studies, have been published; 16 in [Nephrology Dialysis and Transplantation](#) and 3 in [Clinical Kidney Journal](#).

- 1) Regarding **FGF-23**, an important study by **M. Leifhert-Nestler et al** ([Nephrol Dial Transplant 31 \(7\): 1088](#)) provided clear evidence that connect previous findings in animal studies to humans, and an editorial comment by **O.M. Gutiérrez** ([Nephrol Dial Transplant 31 \(7\): 1031](#)) underlined the importance of research connecting the dots on FGF-23 and left ventricular hypertrophy (LVH). In the original study, a strong association was shown between LVH and enhanced expression of FGF-23, FGFR4 and calcineurin activation of nuclear factor of activated T-cells (NFAT) (as well as reduced levels of circulating Klotho) in the myocardium of autopsies from *pediatric* patients with CKD compared with matched deceased controls. Moreover, the quantity of FGF-23 expression in cardiac myocytes was shown to be determined at least in part by the degree of myocyte hypertrophy. Furthermore, FGFR4, FGF-23, calcineurin and NFAT expression were all lower in cases with functioning renal transplants than in cases who were undergoing dialysis at the time of death.

FGF-23 was also shown by **N. Prasad N et al** ([Clin Kidney J 9 \(5\): 669](#)) to be associated with early post-transplant hypophosphatemia, normalizing faster than iPTH in a longitudinal follow-up study of living donor renal transplant recipients . An editorial comment by **G. Cianciolo and M. Cozzolino** ([Clin Kidney J 9 \(5\): 665](#)) underlined the major importance of the post-transplant period to investigate this pathway. On the other hand, **S. Goto et al** ([Clin Kidney J 9 \(5\): 677](#)) described the *absence* of association of serum FGF-23 levels with serum P and calcitriol levels in four patients with Fanconi syndrome–induced hypophosphatemia, suggesting the existence of other FGF-23 regulatory novel factors. **Humalda J.K. et al** ([Nephrol Dial Transplant 31 \(9\): 1494](#)) described the association of FGF-23 with volume status in hemodialysis (HD) patients, suggesting in this observational post-hoc analysis that optimization of volume status may also benefit mineral homeostasis. However, a single dialysis session did not lower FGF-23 levels.

- 2) **Phosphate (P)** metabolism in peritoneal dialysis (PD) and HD patients was reviewed by **P. Evenepoel et al** ([Nephrol Dial Transplant 31 \(9\): 1508](#)). Despite higher residual renal

function, total P clearance was significantly lower in PD. Total P mass removal, conversely, was significantly higher in PD. Time-averaged P concentrations in patients treated with PD were higher as compared with patients treated with HD. Despite a better preserved renal function, total P clearance was lower in patients treated with PD. However, additional studies are needed to confirm these findings in different populations. On the other hand, oral iron intake was revisited by **T. Nakanishi et al** ([Nephrol Dial Transplant 31 \(9\): 1588](#)) in relation to the unexpected efficacy of novel iron-containing P binders such as ferric citrate in improving intestinal iron-absorption.

- 3) **S. Tanaka et al** ([Nephrol Dial Transplant 31 \(7\): 1152](#)) prospectively reported (Q-Cohort Study) that intravenous **vitamin D receptor activator** (VDRA) more effectively reduced the incidence of mortality from infection than oral VDRA in HD patients. Oral VDRA did not significantly reduced this risk compared with those who did not receive VDRA. The rationale and study protocol of the ViRTUE study by **C.A. Keyzer** ([Nephrol Dial Transplant 31 \(7\): 1081](#)) will analyze whether combination of VDRA treatment and sodium restriction (paricalcitol vs placebo, with or without sodium restriction) will additionally reduce residual albuminuria in non-diabetic CKD patients on top of RAAS blockade. The initial results of this study have just been published in another journal ([J Am Soc Nephrol](#)).
- 4) In regard to **vascular calcification**, **S.G. Hold and E.R. Smith** ([Nephrol Dial Transplant 31 \(10\): 1583](#)) reviewed the issue of fetuin-A-containing calciprotein particles in mineral trafficking and vascular disease. In ageing and disease, ectopic calcium crystal deposition impairs tissue function and it is frequently accompanied by simultaneous loss of mineral from sites where it is useful (i.e. bone). **V. Brandenburg on behalf of ERA-EDTA Working Group on CKD-MBD and EUCALNET** ([Nephrol Dial Transplant 31 \(8\): 1211](#)) provided some guidance for clinicians who face patients with calciphylaxis in the current setting of absence of evidence-based medicine (lack of evidence does not justify neglect). In an interesting experimental study, **D. Zickler et al** ([Nephrol Dial Transplant 31 \(10\): 1706](#)) incubated calcifying human coronary vascular smooth muscle cells (VSMCs) with patient's serum samples. They showed that the use of high cut-off (HCO) dialysis membranes in chronic dialysis patients reduces the procalcific effects of serum on VSMC *in vitro*. **S. Chand et al** reported ([Nephrol Dial Transplant 31 \(7\): 1140](#)) that a CAV1 single-nucleotide polymorphism rs4730751 (CC genotype) was associated with lower arterial pulse wave velocity in two different populations (CRIB and RIISC), even following adjustment for other important confounders. This study suggests potential utility of this polymorphism as a genetic biomarker in CKD, and a role for CAV1 in the development of arteriosclerosis in this setting. **J Chen et al** ([Nephrol Dial Transplant 31 \(7\): 1145](#)) analyzed traditional and non-traditional risk factors for incident peripheral arterial disease (PAD) among patients with CKD and found that inflammation, prothrombotic state, oxidative stress, glycated hemoglobin, insulin resistance and alkaline phosphatase are associated with an increased risk of PAD, independent of traditional risk factors.

- 5) **D. Hansen et al** ([Nephrol Dial Transplant 31 \(10\): 1654](#)) confirmed that patients on dialysis or living with a transplanted kidney had a significantly higher risk of **fracture** than the general population in a Dutch study. **P. Messa** ([Nephrol Dial Transplant 31 \(10\): 1554](#)) provided insights, in an editorial comment, on several points needed to fill in the gaps in the current knowledge on this issue. On the other hand, **J.C. Ayus et al** ([Nephrol Dial Transplant 31 \(10\): 1662](#)) reported on the association between mild prolonged chronic hyponatremia (two consecutive measurements of serum sodium <135 mmol/L lasting >90 days; mean 132 mmol/L) and the 4.5 times higher relative risk of hip fracture in an elderly population. Only 0.9% subjects had prolonged chronic hyponatremia (low absolute risk). However, proof that correcting hyponatremia will result in a reduction of hip fractures is lacking (associated editorial by **B. Zietse and W. Van Biesen**) ([Nephrol Dial Transplant 31 \(10\): 1556](#)).

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