

NEWSLETTER # 12 (2), 2019

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 summarise the content of several recent important papers, providing a link to their abstracts.

From July to December 2018, 21 CKD-MBD related articles, including several editorial comments and experimental studies, have been published; 18 in [Nephrology Dialysis and Transplantation](#) and 3 in [Clinical Kidney Journal](#).

- 1) A systematic review and meta-analysis on the effects of lower vs higher **phosphate** (P) diets on **FGF-23** levels was analyzed by **W.C. Tsai et al** ([Nephrol Dial Transplant 33 \(11\):1977](#)). The authors showed that short-term dietary phosphate restriction tends to reduce FGF-23 levels in patients with moderately decreased kidney function and that the FGF23-lowering effects tend to be more prominent when measured with the intact FGF-23 assay. **M. Vervloet** ([Nephrol Dial Transplant 33 \(7\):1091](#)) analyzed several aspects that should be taken into account when selecting, titrating and/or switching phosphate-binder therapy in CKD patients.
- 2) In **experimental studies**, and following important previous work, **M. Leifheit-Nestler et al** ([Nephrol Dial Transplant 33 \(10\):1722](#)) demonstrated that **FGF-23** is induced by an activated renin-angiotensin-aldosterone system in cardiac myocytes, promoting the pro-fibrotic cross-talk between cardiac myocytes and fibroblasts, contributing to myocardial fibrosis in CKD. On the other hand, **B. Fernández-Fernández et al** ([Nephrol Dial Transplant 33 \(10\):1712](#)) showed that albumin directly downregulates Klotho expression in tubular cells, which at least partially explains the decrease in Klotho and FGF-23 resistance in early CKD stages (lacking uremic toxin accumulation), as observed in preclinical and clinical proteinuric kidney disease. **B. Spoto et al** ([Nephrol Dial Transplant 33 \(10\):1764](#)) showed that circulating adiponectin strongly modifies the FGF-23 response to vitamin D receptor activation from the post hoc analysis of the results of a double-blind, randomized clinical trial, paricalcitol vs placebo in CKD.
- 3) **Y. Zhang et al** ([Nephrol Dial Transplant 33 \(10\):1742](#)) published a systematic review and meta-analysis of observational studies regarding **vitamin D** status and mortality risk among patients on dialysis. In their study, increased serum calcidiol level (i.e. relative risk per 10 ng/mL increase) was significantly associated with lower all-cause mortality and lower cardiovascular mortality in dialysis patients. **J. Bachetta and S. Pelletier** ([Nephrol Dial Transplant 33 \(10\):1679](#)) stated in their related editorial that the renal community should stop wondering whether the epidemiological link between calcidiol and mortality in dialysis is true, but should rather proceed with intervention trials.

C. Lerch et al ([Nephrol Dial Transplant 33 \(12\):2208](#)) reported the effects of nutritional vitamin D supplementation on markers of bone and mineral metabolism in *children* with CKD. Vitamin D supplementation normalized Klotho and sclerostin in children with mild to moderate CKD but further increased FGF23 in advanced CKD. On the other hand, **A. Teumer et al** ([Nephrol Dial Transplant 33 \(12\):2139](#)) ran a Mendelian randomization study based on three single nucleotide variants associated with calcidiol levels and suggested a potential negative effect of vitamin D on the glomerular filtration rate (no effect on albuminuria). **C.A. Wagner** ([Nephrol Dial Transplant 33 \(12\):2071](#)) comments on this study in an associated editorial.

- 4) Concerning **calciphylaxis**, the results of a multi-intervention management in 24 patients was published by **C. Harris et al.** ([Clin Kidney J 11 \(5\):704](#)), expanding their previous observations, and suggested that direct calciphylaxis-attributable mortality may be lower than historic reports. The successful use of a high-dose vitamin K supplementation and an increase in dialysis frequency in a female dialysis patient with calciphylaxis was reported by **D. Christiadi** and **R.F. Singer** ([Clin Kidney J 11 \(4\):528](#)).
- 5) **D. Fouque et al** ([Clin Kidney J 11 \(5\):710](#)) reported the poor achievement of 2009 and 2017 KDIGO mineral targets in a French cohort of 566 CKD stage 4 and 153 CKD non-dialysis stage 5. Authors found an increased mortality risk linked to older age and lower haemoglobin level, but not to serum calcium, phosphate or PTH targets.
- 6) With regards to **biomarkers**, **F. F. Wei et al** ([Nephrol Dial Transplant 33 \(7\):1122](#)) reported inactive desphospho-uncarboxylated matrix Gla protein (dp-uc MGP) as a novel circulating biomarker predicting deterioration of renal function in the general population. **S. Ferrè et al** ([Nephrol Dial Transplant 33 \(8\):1389](#)) described that low serum magnesium levels (1.4–1.9 mg/dL; 0.58–0.78 mM) were independently associated with all-cause death in patients with prevalent CKD in the Dallas Heart Study (DHS) cohort, and **W. Chen et al** ([Nephrol Dial Transplant 33 \(9\):1572](#)) did not observe an independent association of bicarbonate or arterialized venous pH with arterial stiffness measured by high pulse wave velocity or ankle-brachial index in community-living older individuals from the Health ABC study. **S. Sedaghat et al** ([Nephrol Dial Transplant 33 \(12\):2165](#)) observed in the Rotterdam study a graded association between lower kidney function and impaired gait, suggesting that individuals with decreased kidney function, even at an early stage, need to be evaluated and might benefit from fall prevention programs. **S. Benjamins et al** ([Nephrol Dial Transplant 33 \(12\):2253](#)) found an independent association between a high abdominal aortic calcification score, assessed by dual X-ray absorptiometry, and cardiovascular events in renal transplant patients. Finally, **P. Delanaye et al** ([Nephrol Dial Transplant 33 \(8\):1404](#)) found large differences in sclerostin concentrations with different assays (poor concordance) and their associations with clinical or other biochemical parameters.
D. Claramunt-Taberner et al ([Nephrol Dial Transplant 33 \(9\):1525](#)) described that **bone** impairment (a poorly described complication of nephropathic cystinosis is related to cystinosis-induced osteoclastic dysfunction. Finally, **S Mazzaferro et al** ([Nephrol Dial Transplant 33 \(12\):2092](#)) reviewed the relationship between bone, inflammation and the bone marrow niche in CKD, underlining the increasing importance of bone for different inter-organ communications that needs to be considered in patients with complex diseases.

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