CKD-MBD
Chronic Kidney Disease Mineral and Bone Disorder

CKD-MBD related publications in the ERA journals
From July to December 2023

The ERA 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 papers, providing a link to their abstracts, full texts or electronic publications (Epub) ahead of print.

From July to December 2023, 26 CKD-MBD related articles have been published, including editorial comments and E-pubs ahead of print; 15 in Nephrology Dialysis and Transplantation and 11 in the Clinical Kidney Journal.

1) **Control of secondary hyperparathyroidism (SHPT) and parathyroid hormone (PTH)** were the topics dealt with in many reports. As previously mentioned, **A.Y-M. Wang et al** (Nephrol Dial Transplant 38 (8):1823-1835) described from a pilot prospective study (PROCEED) that both cinacalcet and parathyroidectomy (PTX) effectively improved biochemical abnormalities of CKD-MBD, and stabilized but did not reduce several intermediate end-points regarding left ventricular mass, calcification or patient-centered measures in *peritoneal* dialysis patients with advanced SHPT. **P. Evenepoel and H.S. Jørgensen** (Nephrol Dial Transplant 38 (8):1777-1779) wrote an associated editorial stating that, while awaiting for the results of additional studies, both treatment options should be considered not exclusive but rather complementary. Also in *peritoneal* dialysis patients, **M. Murashima et al** (Clin Kidney J 16 (11):1957-1964) reported associations of corrected calcium (Ca), phosphate (P) and iPTH with mortality, residual kidney function and technical failure.

2) Regarding **Ca and P control**, **S. Goto et al** (Nephrol Dial Transplant, gfad213) described from a 9-year prospective cohort Japanese study that transient *hypo*calcemia (corrected calcium <8.4 mg/dL) was associated with an increased risk of cardiovascular (CV) events in both cinacalcet users and all patients. **P. Evenepoel and H.S. Jørgensen** (Nephrol Dial Transplant, gfad210) published an associated editorial. A European consensus statement on the recommended Ca intake in adults and children with chronic kidney disease (CKD) was published by **P. Evenepoel et al.** (Nephrol Dial Transplant, gfad185). On the other hand, **C. A. Wagner** (Nephrol Dial Transplant, gfad188) addressed the basics of P metabolism and provided an integrated overview of the biology of P in mammals; **M. Wang et al** (Nephrol Dial Transplant, gfad256) published a P balance calculator for treatment of hyperphosphatemia in hemodialysis patients; **P. Barrera-Baena et al** (Nephrol Dial Transplant, gfad190) described from the COSMOS project (Current management Of Secondary hyperparathyroidism: a Multicentre Observational Study) that *hyper*phosphatemia (P > 6.1 mg/dL) was independently and consistently associated with an increased bone fracture risk in hemodialysis patients; and **L. Xue et al** (Nephrol Dial Transplant, gfad247) reported that in patients with autosomal dominant polycystic kidney disease (ADPKD), P *wasting* is prevalent and associated with more rapid disease progression. Moreover, **M. Bargagli et al** (Nephrol Dial Transplant 38 (7):1645-1654) described that chronic *tolvaptan* treatment was associated with *increased* femoral bone mineral density (BMD) and significant changes in both mineral metabolism (lower PTH and calcitriol, higher plasma and lower urinary fractional excretion of magnesium), and acid–base parameters (higher plasma bicarbonate and urine pH) in ADPKD patients.

3) **Fibroblast growth factor 23 (FGF-23), Klotho** and related issues were described in several articles. **A. Michon-Colin et al** (Clin Kidney J 16 (12):2472-2481) reported that baseline *intact* FGF23 concentrations (but not copeptin) were independently associated with the composite outcome including kidney failure (KF) (dialysis initiation, pre-emptive transplantation or a 57% decrease of measured

GFR) or death before KF, after multiple adjustments. **D. Egli-Spichtig et al** (Clin Kidney J 16 (10):1622-1633) analysed in a post-hoc analysis of the NOPHOS cohort, that *intact* FGF23 was a better predictor of changes in serum P induced by nicotinamide modified-release and P-binder treatment compared with cFGF23, and that markers of inflammation and iron metabolism had only a minor impact in predicting FGF23. In a related editorial, **L. Magagnoli et al** (Clin Kidney J 16 (10):1543-1549) discussed the main insights of the study, with particular attention given to evidence-based peculiarities of the intact and the C-terminal assays available for measuring FGF-23 levels. The absence of an effect of 12 weeks of *roxadustat* on intact, cFGF-23 levels and mineral parameters in patients undergoing peritoneal dialysis was published in a letter to the editor by **Z. Wang et al** (Clin Kidney J 16 (10):1703-1705). **D. Mattinzoli et al** (Clin Kidney J 16 (10):1555-1562) analysed the potential role for FGF-23 and klotho in *acute* kidney injury. **A.R. Martins et al** (Clin Kidney J 16 (12):2587-2596) published data supporting α-Klotho and lean mass as novel CV risk factors in hemodialysis patients. **C. Tanriover et al** (Clin Kidney J 16 (11):1751-1765) reviewed the topic of early aging and premature vascular aging in CKD, including key molecular pathways and molecules (potential therapeutic targets) such as klotho and nuclear factor erythroid 2-related factor 2 (Nrf-2), AMP-activated protein kinase (AMPK), and sirtuin1. Finally, **M. Kanbay et al** (Clin Kidney J 17 (1): sfad276) published a comprehensive review from our ERA CKD-MBD working group suggesting that Klotho could open the door to novel interventions aimed at addressing the challenges of aging and neurodegenerative disorders.

4) Regarding **vitamin K (VK) and/or vascular calcification**, the results of the RenaKvit trial were published by **K. Levy-Schousboe et al** (Nephrol Dial Transplant 38 (10):2131-2142). Menaquinone-7 supplementation was associated with an accelerated BMD loss of the distal *radius* after 2 years, whereas a decline in lumbar spine BMD was prevented. In aggregate, these results do not support this supplementation to preserve bone. In a related editorial, **M. Fusaro and P. Evenepoel** (Nephrol Dial Transplant 38 (10):2105-2108) consider that these results should help in designing the ideal trial of whether VK supplementation prevents bone fractures and/or attenuates the progression of vascular calcification. A systematic review and meta-analysis on VK supplementation impact in dialysis patients was performed by **T. Andrian et al** (Clin Kidney J 16 (12):2738-2749) and showed that vitamin K had no significant impact on mortality and proved no benefit in reducing vascular calcification, although supplementation with vitamin K_1 improved calcification biomarkers and vitamin K status. **M. Vervloet** (Clin Kidney J 16 (11):1766-1775) wondered in an editorial whether we can reverse arterial stiffness by intervening on CKD-MBD biomarkers, stressing that there are contributors to arterial stiffness in CKD other than calcification.

5) Miscellany: **L. Magagnoli et al** (Nephrol Dial Transplant 38 (11):2562-2575) reported that PTH and P were independently associated with all-cause mortality in patients aged ≥65 years with an estimated glomerular filtration rate ≤20 mL/min/1.73 m^2 (EQUAL study). While PTH level was only associated with CV mortality, P seemed to be associated with both CV and non-CV mortality. **B. Martin-Carro et al** (Nephrol Dial Transplant 38 (11):2589-2597) described (from the COSMOS study) a different association of PTH levels with the relative risk of mortality in diabetic and non-diabetic patients on hemodialysis (higher risk for diabetics with PTH higher than 9X normal). **E. Arroyo et al** (Nephrol Dial Transplant gfad168) described that baseline 3-epi-25(OH) vitamin D_3 was associated with V02 peak in transplanted and waitlisted patients, and **P. Matias et al** (Clin Kidney J 16 (11):1776-1785) underlined hypomagnesemia as a potential cause of persistent vitamin D deficiency in CKD.

6) Finally, contents of the 60th ERA Congress 2023 can be found in the 2023 Nephrol Dial Transplant Supplement # 1.

Jordi Bover and Sandro Mazzaferro on behalf of the CKD-MBD Working Group
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