CKD-MBD related publications in the ERA journals

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 important papers, providing a link to their abstracts.

From January to June 2021, 27 CKD-MBD related articles, including editorial comments and experimental studies, have been published; 17 in Nephrology Dialysis and Transplantation and 10 in the Clinical Kidney Journal.

1) Phosphate (P) is again the most frequent recurrent topic during this semester. Interactions with age, malnutrition and inflammation with serum P levels and survival were again described by **Ye X et al. et al** (Clin Kidney J 14(1):348) among 245,853 adult chronic hemodialysis (HD) patients treated in FMC North America clinics. Importantly, the U-shaped relationship between P levels and outcome persisted even for patients with low or high levels of serum albumin, creatinine, normalized protein catabolic rate (nPCR) and neutrophil–lymphocyte ratio (NLR). Real-world management of hyperphosphatemia with sucroferric oxyhydroxide (SO) was retrospectively analyzed in the VELREAL multicentre Spanish study by **Navarro-González J.F. et al.** (Clin Kidney J 14(2):681) and it was associated with an editorial where **Cozzolino M. et al** (Clin Kidney J 14(2):474) compared the different available P binders. Another real-world but European prospective observational study on the safety and effectiveness of SO in dialysis patients will be published by **Vervloet M.G. et al** in the July issue (Clin Kidney J 14(7):1770), in essence confirming the strong P binding capacity and favourable safety and tolerability profile of SO, consistent with results of the Phase 3 study. **Thiem U. et al.** (Clin Kidney J 14(2):631) demonstrated in a randomized, controlled, cross-over trial that SO improved serum calcification propensity. Importantly, **Neto R. and Frazão J.** (Clin Kidney J 14(2):550) described in a cohort of *normophosphatemic* CKD G3-G4 patients that treatment with calcium carbonate for 24 months (mean prescribed dose 1178±90 mg of elemental calcium) was associated with increased vascular calcification assessed by Kauppila and Adragão scores. **Fusaro M. et al.** (Nephrol Dial Transplant 36(3):405) discussed the central role of P in the pathogenesis of CKD-MBD and how it may be associated with fracture risk, both in hyper- and hypophosphatemia.

2) **Bouma-de Krijger A. et al.** (Clin Kidney J 14(3):891) analyzed *changes* in **fibroblast growth factor-23 (FGF23)** in 404 patients from the CONvective TRansport STudy (CONTRAST). They demonstrated that FGF23 declined in patients with hemodiafiltration, whereas it remained stable in patients on HD. Whereas *decrease* in FGF23 was *not* associated with improved survival, *increased* FGF23 was associated with a significantly higher mortality risk. **De Jong M.A. et al.** (Nephrol Dial Transplant 36(1):121) described that FGF23 was independently associated with new-onset CKD and an increased risk of all-cause mortality in the Prevention of Renal and Vascular Endstage Disease (PREVEND) prospective population-based cohort.

3) Regarding serum **levels of calcium and P**, these were retrospectively analyzed during the first 90 days after *kidney transplantion* by **Chevarria J. et al**. (Clin Kidney J 14(4):1106). Whereas hypophosphataemia and hypercalcaemia were common occurrences post-kidney transplant (86.3 and 36.1%, respectively), and risk factors for these derangements were described, the authors did *not* find differences in death-censored graft failure or all-cause mortality. In addition to describing a patient with sarcoidosis associated **hypercalcemia**, **Iwazu Y. et al**. (Clin Kidney J 14(1):421) described increased serum FGF23 and calciprotein particle levels, suggesting that a disturbed P metabolism may also be present in this disease. A *post hoc* analysis from a randomized controlled clinical trial by **Bressendorff I. et al.** (Nephrol Dial Transplant 36(4):713) described the effect of increasing *dialysate* **magnesium** on calciprotein particles, inflammation and bone markers. Clinical features and outcomes of patients from the Australian Calciphylaxis Registry was published by **Ruderman I. et al.** (Nephrol Dial Transplant 36(4):649).

4) An European Consensus Statement on the diagnosis and management of **osteoporosis (OP)** in CKD stages G4-G5D was published by **Evenepoel P. et al**. (Nephrol Dial Transplant 36(1):42) on behalf of the European Renal Osteodystrophy (EUROD) work subgroup, and the committee of Scientific Advisors and National Societies of the International Osteoporosis Foundation. In the report by **Aleksova J. et al.** (Nephrol Dial Transplant 36(3):543), the authors found, using advanced hip analysis, that patients with end-stage kidney disease (ESKD) had lower mean±SD cortical thickness at the femoral neck and shaft, and buckling ratios were higher, compared with controls, indicating greater femoral neck instability. Therefore, it was suggested that these parameters should be assessed for incident fracture prediction and targeting treatment. Interestingly, in a nested case-control study by **Song S.H. et al.** (Nephrol Dial Transplant 36(4):722), bisphosphonate users had a significantly reduced risk of *graft* failure than did non-users. Clinical practice points on the assessment of bone disease in children with CKD Stages G2-G5D were published by **Bakkaloglu S.A. et al** (Nephrol Dial Transplant 36(3):413) on behalf of the CKD-MBD and Dialysis working groups of the European Society for Paediatric Nephrology and the ERA-EDTA CKD-MBD working group. Finally, how and when to assess bone mineral density and bone quality in CKD patients was reviewed but **Khairallah P. et al.** (Nephrol Dial Transplant 36(5):774), and the need of revitalization of bone biopsies in CKD was stressed by **Mazzaferro S. and Pasquali M.** (Nephrol Dial Transplant 36(2):202).

5) Regarding **secondary hyperpathyroidism**, **Tabibzadeh N et al** (Nephrol Dial Transplant 36(1):160) demonstrated from the Dialysis Outcomes and Practice Patterns Study (DOPPS) (Phases 4–6 data) that increased PTH before HD start predicted a higher PTH level 9–12 months later, despite greater use of active vitamin D and calcimimetics. Authors concluded that more targeted PTH control during non-dialysis CKD may influence outcomes during HD. **Arenas M.D. et al.** (Clin Kidney J 14(3):840) described that the lack of adherence to cinacalcet is a possible cause of the apparent lack of response to oral calcimimetics and that the use of etelcalcetide ensures compliance and control of secondary hyperparathyroidism in both non-adherent and adherent patients. **Cavalier E.** (Nephrol Dial Transplant 36(3):426) wonders what a PTH of 300 pg/mL actually means. Finally, a correction to the 2016 article "Con: Nutritional vitamin D replacement in chronic kidney disease and end-stage renal disease" was published (Nephrol Dial Transplant 36(3):566). A minus sign was inadvertently omitted.

6) In **experimental studies**, noxious *additive* effects in rats fed with a both high-*fat* and high-*P* diets in structural and ultrastructural renal lesions were described by **Esquinas P. et al.** (Clin Kidney J 14(3):847). High fat intake was preferentially associated with glomerular lesions, while lesions related to high P intake were located mainly in the tubuli and interstitium. **Ichida Y. et al.** (Nephrol Dial Transplant 36(1):68) demonstrated in rats with CKD that contribution of NaPi-IIb to intestinal P absorption dramatically decreases, and that a low-affinity alternative to NaPi-IIb, in particular PiT-1, is upregulated in a compensatory manner. **Carrillo-López N. et al.** (Nephrol Dial Transplant 36(4):618) demonstrated that the receptor activator of nuclear factor κB ligand (RANKL) receptor leucine-rich repeat-containing G-protein-coupled receptor 4 (LGR4) contributes to parathyroid hormone-induced vascular calcification. **Schön A. et al.** (Nephrol Dial Transplant 36(3):442) described a discrepancy between the cardioprotective effects of active vitamin D in experimental uremia but not in children with CKD G3-G5, and provided potential explanations. **Martinez-Arias L. et al.** (Nephrol Dial Transplant 36(5):793) demonstrated distinct effects of *paricalcitol* vs calcitriol in attenuating renal interstitial fibrosis through a combination of several inhibitory actions. The role of *activin A* as an endocrine factor produced in the kidney during renal disease which participates in the development of CKD-MBD extensive derangements (skeleton, vasculature, heart) was reviewed by **Cianciolo G. et al.** (Nephrol Dial Transplant 36(6):966).

7) Finally, the abstracts submitted at the 58th ERA-EDTA Congress 2021 can be found in the 2021 Nephrol Dial Transplant Supplement # 1

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