CKD-MBD – An Official ERA-EDTA Working Group
ERA-EDTA Operative Headquarters
Strada dei Mercati 16/A, 43126 Parma, Italy
Tel: +39 0521 989078
Mob. +39 370 3538784
Email: ckd-mbd@era-edta.org
www.era-edta.org

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 2020**, **24 CKD-MBD related articles**, including several editorial comments and experimental studies, have been published; 14 in Nephrology Dialysis and Transplantation and 10 in Clinical Kidney Journal.

1) Regarding **phosphate (P) and parathyroid hormone (PTH) control**, **D.S. Fuller et al** (Clin Kidney J 13(6):1056) confirmed, in another DOPPS study from Europe, Canada and USA, that simultaneous consideration of calcium (Ca), P and PTH outside certain target levels may help in identifying dialysis patients with a higher risk of major clinical outcomes. As in many other studies, the mortality association was stronger for patients ≥ 65 years of age. In another study derived from DOPPS, **M. Barreto-Lopes et al** (Nephrol Dial Transplant 35 (10):1794) reported that worse P control over a 6-month long period was strongly associated with cardiovascular (CV) mortality. Moreover, the more P values not exceeding 4.5 mg/dL the better was survival, and that P-area under the curve was a better predictor of CV death than the single most recent P level. These data support KDIGO recommendation for the need of serial assessments to guide clinical decisions. Other unusual serum biomarkers (such as osteopontin, osteoprotegerin, matrix metalloproteinase-9 and vascular endothelial growth factor) could improve CV risk prediction in high-risk individuals, as reported by a machine learning analysis performed by **C. Forné et al** (Clin Kidney J 13(4):631). **D.A. Bushinsky et al** (Nephrol Dial Transplant 35 (10):1769) described the one-year safety and efficacy of intravenous etelcalcetide in patients on hemodialysis with secondary hyperparathyroidism (SHPT). Etelcalcetide effectively lowered PTH levels sustainably and no new safety concerns emerged over this period. Finally, **J. Bover et al** (Clin Kidney J 13(4):513) underlined the poor level of evidence present not only in CKD-MBD guidelines but also in other areas of nephrology, emphasizing the importance of individualization of treatments and shared decision-making.

2) **Cardiovascular calcification**-related articles were numerous. **P. Ureña-Torres et al** (Nephrol Dial Transplant 35 (12):2046) summarized the current knowledge on the pathophysiology and relevance of valvular calcifications in CKD patients, highlighting specific clinical consequences and potential therapeutic implications. **P. Kouis et al** (Clin Kidney J 13 (5):842) performed a systematic review and meta-analysis of non-invasive measures of atherosclerosis and arterial stiffening [such as carotid intima–media thickness (cIMT), coronary artery calcium (CAC) score and pulse wave velocity (PWV)], and concluded that they are associated with all-cause and CV mortality as well as CV events among patients with all stages of CKD, supporting the study of interventions on them. **H. Mukai et al** (Nephrol Dial Transplant 35 (7):1202) described in CKD 5 that mortality increased linearly with higher CAC score and CAC volume whereas for CAC density an inverse J-shaped pattern was observed, with the crude mortality rate being highest for the middle tertile of CAC density. **T. Saritas et al** (Clin Kidney J 13 (4):571) reported that epicardial adipose tissue (EAT) is a modifiable risk factor in patients with CKD, and although EAT correlates with CV calcifications, these relations depend on CV risk factors. **S. Menez et al** (Nephrol Dial Transplant 35 (11):1878) reported from the ARIC (Atherosclerosis Risk in Communities) cohort that lower magnesium was independently associated with incident peripheral artery disease (PAD), but this association was significantly weaker in those with reduced kidney

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function. In contrast, high PTH levels was significantly related to PAD only in those with eGFR <60 mL/min/1.73 m^2. Therefore, **M.H. de Borst and JHF de Baaij** (Nephrol Dial Transplant 35 (11):1831) stated in their editorial that more CKD-specific data are needed to reach a final verdict on low serum magnesium as a risk factor for PAD and other CV outcomes in CKD patients. Dietary zinc intake, but not supplemental, total intake or serum zinc levels, were associated with severe abdominal aortic calcification among noninstitutionalized US adults according to **W. Chen et al** (Nephrol Dial Transplant 35 (7):1171). However, **L.F.M.F. Cardozo and D. Mafra** (Nephrol Dial Transplant 35 (7):1094) emphasized in their associated editorial that no association was found between zinc intake and aortic abdominal calcification in the fully adjusted model in CKD patients. Nevertheless, in view of all the important functions zinc is involved in, they consider that we should not forget this mineral in our patients' diet.

3) Klotho remains as a hot topic. **S. Sembray et al** (Clin Kidney J 13 (6):1017) described the association of a single nucleotide polymorphism combination pattern of the Klotho gene with non-cardiovascular death in patients with CKD. **C. Lanzani et al** (Clin Kidney J 13 (6):926) reviewed in an associated editorial that Klotho genetic polymorphisms may influence Klotho clinical and prediction relationship with both cardiovascular and non-cardiovascular mortality, representing a bridge between inflammation, salt sensitivity, hypertension and mortality. **M. Vila-Cuenca et al** (Nephrol Dial Transplant 35 (9):1478) reviewed the distinct endothelial alterations mediated by non-traditional risk factors such as α-klotho, vitamin D, disturbances in mineral metabolism, uremic factors, oxidative stress or inflammation, and describe therapeutic strategies that may promote restoration of endothelial abnormalities in CKD patients.

4) Regarding **fractures**, **B. Runesson et al** (Nephrol Dial Transplant 35 (11):1908) highlighted the commonness of fractures and the increased risk for subsequent adverse outcomes in CKD patients at the Stockholm CREAtinine Measurement project. Moreover, **L-C. Desbiens et al** (Nephrol Dial Transplant 35 (10):1712) reported in the CARTaGENE population that even early CKD increases fracture incidence, especially in younger individuals and in men. Consequently, **P. Khairallah and T.L. Nickolas** (Nephrol Dial Transplant 35 (10):1649) highlighted in the associated editorial that those observations should compel nephrologists to focus on the skeletal complications of early CKD and the need to implement strategies that mitigate risk as well as to investigate mechanisms that underpin associations between early CKD and fractures. Finally, **P. Anastasio et al** (Clin Kidney J 13 (5):873) showed data, from 12 patients with central diabetes insipidus, supporting the intriguing new relationship between vasopressin and osteoporosis in ageing and microgravity/bed rest.

5) Excepcional cases: R.A. Plasse et al (Clin Kidney J 13 (4):710) described an exceptional case where a biotin supplement interfered with immunoassays for PTH and 25-hydroxyvitamin D in a patient with metabolic bone disease on maintenance hemodialysis. **P-E. Cailleaux et al** (Clin Kidney J 13 (5):897) described a dialysis patient with a loosening hip prosthesis secondary to a hypophophatemic osteomalacia due to low P intake.

6) Experimental studies on iron-based P-binders described the route of intestinal absorption (distal colon) and tissue distribution of iron contained in ferric citrate [**N.D. Vaziri et al** (Nephrol Dial Transplant 35 (7):1136)] and renoprotective effects of sucroferric oxyhydroxide [**E. Neven et al** (Nephrol Dial Transplant 35 (10):1689)].

Dr Jordi Bover and Sandro Mazzaferro

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