



**Karolinska
Institutet**

**Institutionen för klinisk vetenskap, intervention och teknik
(CLINTEC), enheterna för Baxter Novum och Medicinska
Njursjukdomar**

Studies on Bone and Mineral Disorders in CKD: Determinants and Survival Implications

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
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av

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ABSTRACT

Disruptions in mineral metabolism occur already at an early stage of chronic kidney disease (CKD) and may eventually lead to a complex of CKD - mineral and bone disorders (CKD-MBD) characterized by alterations of the mass, turnover rate, mineralization and strength of bones, and high risk of vascular calcification, fractures and other complications resulting in worse survival. The aim of this thesis was to increase the understanding of some aspects of CKD-MBD with special emphasis on clinical and laboratory determinants and implications for clinical outcome.

In *Study 1*, we defined and tested a novel non-surgical, adjustable model of tubulointerstitial nephropathy in mice by adding adenine to a casein-based diet and showed that this model could induce and maintain a uremic phenotype with decline of renal function and initiation of alterations linked to CKD-MBD.

In *Study 2*, we investigated the impact of classical risk factors for osteoporosis such as age, body composition, and nutritional status in end-stage renal disease (ESRD) subjects, and how these factors influence the relationship between bone mineral density (BMD) and mortality in patients with ESRD. We found that low BMD is associated with low total fat mass, poor nutritional status and increased mortality risk in ESRD patients.

In *Study 3*, we studied determinants of the variability of two bone metabolic markers, fibroblast growth factor-23 (FGF23) and intact parathyroid hormone (PTH) in ESRD patients treated by peritoneal dialysis, hemodialysis or online hemodiafiltration. We found that baseline vitamin D status and serum phosphorous were independent determinants of the longitudinal variation in PTH and FGF23, respectively, and that the intra-subject variability of FGF23 was lower than the variability of PTH irrespective of dialysis mode.

In *Study 4*, we analyzed baseline serum insulin-like growth factor 1 (IGF-1) concentration and the longitudinal changes of IGF-1 over 1-year in CKD stage 5 patients starting on dialysis in relation to bone and mineral metabolism parameters including BMD, nutritional status, and mortality. We found that IGF-1 associates with markers of mineral and bone metabolism and that IGF-1 is a strong independent predictor of mortality risk in CKD stage 5 patients.