Iron deficiency and FGF 23 in chronic kidney disease

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INTRODUCTION AND AIMS: Chronic kidney disease patients are affected by a high burden of cardiovascular morbidity and mortality. Chronic kidney disease - mineral and bone disorder (CKD-MBD) with high levels of intact FGF23 and c-terminal FGF23 may contribute to this elevated cardiovascular risk. Recently, it has been shown that iron deficiency, which is very prevalent in CKD patients, up-regulates plasma FGF23. We now hypothesize that iron deficiency rather than direct FGF23 effects pathophysiologically explains the high cardiovascular event rate among CKD patients with highest plasma FGF23 levels. Therefore we investigated in the following the independent contribution of plasma intact FGF23, c-terminal FGF23 and ferritin on cardiovascular morbidity in CKD patients.

METHODS: In the ongoing CARE FOR HOMe study which recruited CKD KDIGO stages G2 to G4 patients, we analyzed ferritin, intact FGF23 and c-terminal FGF23 at baseline. The participants were consecutively followed annually for the occurrence of atherosclerotic cardiovascular events and all-cause mortality.

RESULTS: Ferritin correlated negatively with c-terminal FGF23 (r = -0.207; p < 0.001) but not with intact FGF23 (r = -0.016; p = 0.699). Participants in KDIGO stage G4 and ferritin levels lower than 30 ng/ml had the highest c-terminal FGF23 levels. During follow up of 5.1 ± 2.1 years, 123 had atherosclerotic cardiovascular events, and 98 participants died from any cause, in multivariate Cox regression analyses after adjustment for multiple confounders (including ferritin and intact FGF23), only c-terminal FGF23 remained significantly associated with cardiovascular events all-cause death. In contrast, neither intact FGF23 nor ferritin predicted adverse outcome in multivariate analyses.

CONCLUSIONS: In this study, we observed a close correlation between iron deficiency - indicated by low plasma ferritin - and c-terminal FGF23 among CKD patients. C-terminal FGF23 was independently associated significantly with all-cause mortality even after adjustment for ferritin and other confounders, whereas ferritin did not predict cardiovascular events.