Serum FGF23 and Klotho are associated with long term renal outcomes in autosomal dominant polycystic kidney disease (PKD)

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BACKGROUND PKD is a slowly progressive disease with end stage renal disease (ESRD) occurring late in life, so early-stage prognostic biomarkers are urgently needed. Blood levels of FGF23 are elevated in PKD out of proportion to kidney function, and circulating levels of its receptor, Klotho, are decreased, but whether these are associated with long-term renal outcomes is uncertain.

METHODS CRISP is an observational cohort study of 241 PKD patients. Intact FGF23 and soluble Klotho concentrations were measured on 191 available baseline serum samples and dichotomized into high vs low FGF23 groups (cutoff 50 pg/ml) and high vs low Klotho groups (cutoff 1000 pg/ml). The association of baseline FGF23 and Klotho level with follow-up log-transformed height-adjusted total kidney volume (htTKV) and GFR, measured by iothalamate clearance, was tested using linear mixed models with random slopes, with adjustment for age, gender, hypertension and htTKV (for GFR). The risk of ESRD and death was evaluated using a Cox model.

RESULTS Baseline serum FGF23 was 58 ± 29 pg/ml and Klotho 918 ± 925 pg/ml (mean ± SD). Median follow-up was 13 years. High FGF23 (vs low) was associated with faster growth of htTKV over time ($p<0.01$) after adjustment for age, gender, hypertension and PKD genotype, and faster decline in GFR ($p<0.01$) even after adjustment for Irazabal class. Similarly, low Klotho (vs high) was associated with faster decline in iGFR ($p<0.01$). Higher serum FGF23 and lower Klotho were each associated with increased risk of ESRD/death.

CONCLUSION Higher serum FGF23 and lower Klotho are associated with faster kidney growth, faster decline in kidney function, and increased risk of ESRD or death in PKD patients. FGF23 and Klotho are useful prognostic biomarkers in PKD.