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Fibroblast Growth Factor 23 and Kidney Disease Progression in Autosomal Dominant Polycystic Kidney Disease

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Abstract

Background and objectives Increases in fibroblast growth factor 23 precede kidney function decline in autosomal dominant polycystic kidney disease; however, the role of fibroblast growth factor 23 in autosomal dominant polycystic kidney disease has not been well characterized.

Design, setting, participants & measurements We measured intact fibroblast growth factor 23 levels in baseline serum samples from 1002 participants in the HALT-PKD Study A ($n=540$; mean eGFR = 91 ± 17 ml/min per 1.73 m^2) and B ($n=462$; mean eGFR = 48 ± 12 ml/min per 1.73 m^2). We used linear mixed and Cox proportional hazards models to test associations between fibroblast growth factor 23 and eGFR decline, percentage change in height-adjusted total kidney volume, and composite of time to 50% reduction in eGFR, onset of ESRD, or death.

Results Median (interquartile range) intact fibroblast growth factor 23 was 44 (33–56) pg/ml in HALT-PKD Study A and 69 (50–93) pg/ml in Study B. In adjusted models, annualized eGFR decline was significantly faster in the upper fibroblast growth factor 23 quartile (Study A: quartile 4, -3.62 ; 95% confidence interval, -4.12 to -3.12 versus quartile 1, -2.51 ; 95% confidence interval, -2.71 to -2.30 ml/min per 1.73 m^2 ; P for trend <0.001 ; Study B: quartile 4, -3.74 ; 95% confidence interval, -4.14 to -3.34 versus quartile 1, -2.78 ; 95% confidence interval, -2.92 to -2.63 ml/min per 1.73 m^2 ; P for trend <0.001). In Study A, higher fibroblast growth factor 23 quartiles were associated with greater longitudinal percentage increase in height-adjusted total kidney volume in adjusted models (quartile 4, 6.76; 95% confidence interval, 5.57 to 7.96 versus quartile 1, 6.04; 95% confidence interval, 5.55 to 6.54; P for trend = 0.03). In Study B, compared with the lowest quartile, the highest fibroblast growth factor 23 quartile was associated with elevated risk for the composite outcome (hazard ratio, 3.11; 95% confidence interval, 1.84 to 5.25). Addition of fibroblast growth factor 23 to a model of annualized decline in $\text{eGFR} \geq 3.0$ ml/min per 1.73 m^2 did not improve risk prediction.

Conclusions Higher serum fibroblast growth factor 23 concentration was associated with kidney function decline, height-adjusted total kidney volume percentage increase, and death in patients with autosomal dominant polycystic kidney disease. However, fibroblast growth factor 23 did not substantially improve prediction of rapid kidney function decline.

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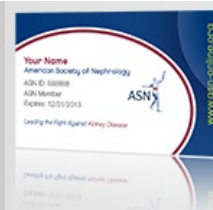
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