SIGNIFICANCE STATEMENT

Elevated fibroblast growth factor 23 (FGF23) levels, measured at a single time point, are strongly associated with mortality in CKD, but it is not known how FGF23 levels change over time or whether rising values predict risk of death. In this case-cohort study nested in the Chronic Renal Insufficiency Cohort (CRIC) Study, FGF23 levels rose rapidly over five annual time points in only a minority of participants. In fully adjusted analyses, this group was at >15-fold higher risk of death than the majority of participants whose levels remained stable. Participants with slowly rising FGF23 levels also were at approximately fourfold higher risk of death. FGF23 levels are stable over time in the majority of patients with CKD, but serial measurements identify smaller subpopulations with rising levels and exceptionally high risk of death.