CRIC: studying the silent epidemic of kidney disease

Chronic kidney disease (CKD) is a public health problem affecting more than 20 million Americans, and far more worldwide. Although CKD typically begins with no noticeable symptoms, it is a progressive disease which if untreated often leads to kidney failure, also called end-stage renal disease (ESRD), requiring dialysis or kidney transplantation. CKD also leads to increased risk of cardiovascular disease (CVD). To advance our understanding of the epidemiology of CKD, the Chronic Renal Insufficiency Cohort (CRIC) Study was established in 2001. Since then, the CRIC Study has recruited a racially and ethnically diverse cohort of over 5000 participants with reduced kidney function from thirteen clinical recruitment sites across the US. Participants return for yearly clinic visits at which cognitive and behavioral health data, anthropometric data, electrocardiograms, samples of blood and urine, and updates on any medical events they have experienced are collected.

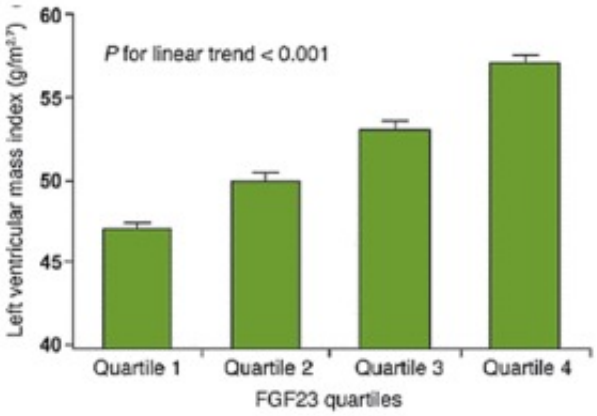

Fig. 1. Higher levels of FGF-23 were associated with significantly greater mean left ventricular mass index. (Bars show mean LV mass index and standard error of mean for each quartile of FGF-23.)

The original aims of CRIC were: (a) to identify novel predictors of CKD progression, and (b) to describe the types of CVD, and identify CVD risk factors, among individuals with CKD. One example of CRIC findings addressing these aims comes from a number of articles examining fibroblast growth factor 23 (FGF-23). FGF-23 is a chemical that stimulates the kidneys to remove phosphate from the blood, so when a person develops CKD and the kidneys start to have difficulty removing phosphate, the body starts to produce more FGF-23 to get the kidneys to work harder. CRIC investigators have found that a high level of FGF-23 in the blood is a good indicator of early-stage CKD. Compared to other related indicators of CKD, elevated FGF-23 levels occur earlier in the course of CKD, and are more common at all stages of CKD. Among participants with early-stage CKD (i.e., relatively well-functioning kidneys), the level of FGF-23 in the blood also predicted

the likelihood of developing ESRD. CRIC research has also shown FGF-23 to be a risk factor for CVD among CKD patients. For example, one analysis examined left ventricular hypertrophy (LVH), a common complication of CKD that contributes to CVD. The analysis demonstrated that elevated FGF-23 levels were associated both with prevalence of LVH at baseline (Fig. 1), and with increased risk of subsequently developing LVH, independently of other demographic, clinical, and laboratory characteristics. Another investigation found that higher baseline levels of FGF-23 were independently associated with greater risk of two other CVD outcomes – congestive heart failure (CHF) and atherosclerotic events.

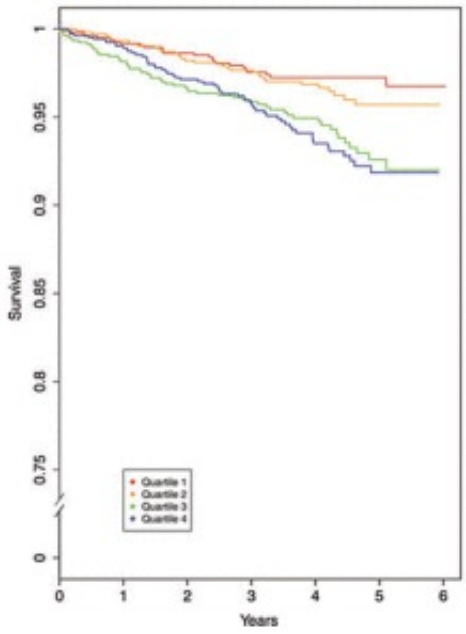

Fig. 2. Estimated rates (adjusted for demographic factors, known CVD risk factors, and inflammatory markers) of myocardial infarction-free survival over time for participants in each quartile of CXCL12

CRIC research has also examined numerous other risk factors for CVD among CKD patients. One example is CXCL12, a chemical produced by the body as part of the inflammatory response. A chronic state of inflammation is common in CKD, and increases the risk of CVD. CRIC was the first prospective study to examine the association of CXCL12 levels with subsequent clinical outcomes. High baseline levels of CXCL12 were found to be independently associated with prevalence of CVD at baseline, and were an independent risk factor for the subsequent occurrence of myocardial infarction (Fig. 2). Other examples include serum aldosterone, high-sensitivity troponin T, and NT-proBNP (found to be independent risk factors for heart failure).

Over time, CRIC has expanded into a national resource for the investigation of a broad array of

CKD-related topics. To date, it has produced nearly 100 published scientific manuscripts, promoted many young investigative careers in nephrology, and fostered international collaborations focused on understanding the global burden of CKD. The current phase of the CRIC Study is designed to answer high-priority questions regarding morbidity and mortality among individuals with mild to moderate CKD and to assess the burden of CKD in older persons.

Publication

Chronic Renal Insufficiency Cohort Study (CRIC): Overview and Summary of Selected Findings.
Denker M, Boyle S, Anderson AH, Appel LJ, Chen J, Fink JC, Flack J, Go AS, Horwitz E, Hsu CY, Kusek JW, Lash JP, Navaneethan S, Ojo AO, Rahman M, Steigerwalt SP, Townsend RR, Feldman HI; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators
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