Relative risks of chronic kidney disease for mortality and end-stage renal disease across races are similar

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Some suggest race-specific cutpoints for kidney measures to define and stage chronic kidney disease (CKD), but evidence for race-specific clinical impact is limited. To address this issue, we compared hazard ratios of estimated glomerular filtration rates (eGFR) and albuminuria across races using meta-regression in 1.1 million adults (75% Asians, 21% Whites, and 4% Blacks) from 45 cohorts. Results came mainly from 25 general population cohorts comprising 0.9 million individuals. The associations of lower eGFR and higher albuminuria with mortality and end-stage renal disease (ESRD) were largely similar across races. For example, in Asians, Whites, and Blacks, the adjusted hazard ratios (95% confidence interval) for eGFR 45–59 versus 90–104 ml/min per 1.73 m^2 were 1.3 (1.2–1.3), 1.1 (1.0–1.2), and 1.3 (1.1–1.7) for all-cause mortality, 1.6 (1.5–1.7), 1.4 (1.2–1.7), and 1.4 (0.7–2.9) for cardiovascular mortality, and 27.6 (11.1–68.7), 11.2 (6.0–20.9), and 4.1 (2.2–7.5) for ESRD, respectively. The corresponding hazard ratios for urine albumin-to-creatinine ratio 30–299 mg/g or dipstick 1+ versus an albumin-to-creatinine ratio under 10 or dipstick negative were 1.6 (1.4–1.8), 1.7 (1.5–1.9), and 1.8 (1.7–2.1) for all-cause mortality, 1.7 (1.4–2.0), 1.8 (1.5–2.1), and 2.8 (2.2–3.6) for cardiovascular mortality, and 7.4 (2.0–27.6), 4.0 (2.8–5.9), and 5.6 (3.4–9.2) for ESRD, respectively. Thus, the relative mortality or ESRD risks of lower eGFR and higher albuminuria were largely similar among three major races, supporting similar clinical approach to CKD definition and staging, across races.

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Chronic kidney disease (CKD) is a global public health problem,[1–3] affecting 10–16% of the adult population in several continents[4–7] and increasing the risk of adverse outcomes.[8–12] The definition and staging of CKD is based on the level of glomerular filtration rate (GFR) and the presence of kidney damage, usually ascertained as albuminuria.[1,11,13] However, the comparability of GFR and albuminuria measures across racial groups and their relationship with risk have not been fully explored,[14] although some have suggested race-specific thresholds for GFR and albuminuria to define and stage CKD.[15] The primary objective of this study was to quantify the associations of GFR and albuminuria with risk for all-cause and cardiovascular mortality, and end-stage renal disease (ESRD) among Asians, Whites, and Blacks, three major races in the world, and assess whether there are any substantial differences across the races.

RESULTS

Study populations

A total of 1,130,472 individuals were studied, including 75% Asians (mostly Eastern Asians), 21% Whites, and 4% Blacks. Majority of the study population, 83% or 940,366

individuals, were from 25 general population cohorts, with the remaining 13% or 151,494 individuals from 7 high-risk cohorts, and 3% or 38,612 individuals from 13 CKD cohorts (Table 1). Thus, our primary analyses were conducted in the general population cohorts, and results for the high-risk cohorts and CKD cohorts were shown in Supplementary Materials separately. Asians comprised the majority of the general population cohorts (87%), but not the high-risk (6%) or CKD (12%) cohorts, and mainly came from cohorts based on data from comprehensive health screening programs for the healthy population. Accordingly, Asians tended to have a lower risk profile (younger age and lower prevalence of comorbid conditions) as compared with Whites and Blacks. Although most Asians were from Asian cohorts, most Blacks were from US cohorts. There were differences in the methods for ascertainment of albuminuria among the general population cohorts: only 1% of Asians had albumin-to-creatinine ratio (ACR) data, whereas ACR data were available in 73% of Whites and 100% of Blacks included in the meta-analysis, reflecting different medical and research settings.

Estimated glomerular filtration rate and albuminuria distributions by race

In the general population cohorts, the crude prevalence of reduced estimated glomerular filtration rate (eGFR; <60 ml/min per 1.73 m^2) in Asians, Whites, and Blacks was 5.1, 15.8, and 9.4%, respectively (Supplementary Figure S1A online). The prevalence of elevated albuminuria ($\geqslant 30$ mg/g by ACR or $\geqslant 1+$ by urine dipstick) in the three races was 2.8, 9.9, and 16.6%, respectively (Supplementary Figure S1B online). The difference in prevalence of reduced eGFR and elevated albuminuria across racial groups was attenuated after age standardization, particularly for reduced eGFR (Supplementary Figure S1C and D online). In the high-risk cohorts, the crude prevalence of decreased eGFR and high albuminuria were 11.6 and 24.0% in Asians, 18.7 and 20.6% in Whites, and 10.4 and 13.5% in Blacks, respectively (Supplementary Figure S2 online).

Incidence rates of mortality and ESRD by race

We observed 38,696 all-cause deaths and 9065 cardiovascular disease (CVD) deaths in Asians (mean follow-up of 9.2 years), 20,079 and 7325 cases in Whites (mean follow-up of 8.4 years), and 2485 and 436 cases in Blacks (mean follow-up of 6.6 years; Supplementary Table S1 online). Crude rates for all-cause and CVD mortality in the general population cohorts were 5.9 and 1.4 per 1000 person-years in Asians, 24.1 and 10.4 in Whites, and 18.7 and 5.5 in Blacks, respectively (Supplementary Figure S3 online). After age standardization, mortality rates were higher in Blacks compared with that in Whites, whereas the lower rates in Asians persisted. The variation in mortality rates was as great among studies within races as among races within studies. Among the studies with data on ESRD, crude incidence rates of ESRD per 1000 person-years were 0.3 in Asians, 0.8 in Whites, and 2.8 in Blacks.

Independent relationships of eGFR and albuminuria with clinical risk by race

Figure 1 shows hazard ratios (HRs) for all-cause mortality, CVD mortality, and ESRD in the general population cohorts by race for eGFR from 15 to 120 ml/min per 1.73 m^2 compared with the reference point at eGFR 95 ml/min per 1.73 m^2. The patterns for each outcome were qualitatively similar among three races across most of the range of eGFRs, with higher risk at lower eGFR. For all-cause and CVD mortality, although there was variation across races in the eGFR thresholds below which the HRs were significantly greater than the reference point, partially owing to difference in the precision of estimates across races, the HR reached significance at eGFR between 60 and 75 ml/min per 1.73 m^2 in most analyses and did not differ significantly for a given eGFR among races, except for small ranges noted at the bottom of Figure 1. For ESRD, the threshold eGFR varied from 65 to 83 ml/min per 1.73 m^2 for all three races, although the pattern was least steep in blacks for eGFR <30 ml/min per 1.73 m^2.

Figure 2 shows HRs for all three outcomes by races according to albuminuria categories (ACR <10, 10–29, 30–299, and $\geqslant 300$ mg/g or urine dipstick levels negative, trace, $1+$ and $\geqslant 2+$, respectively; Supplementary Figure S4 online shows the association for ACR as a continuous variable). Again, the patterns for each outcome were similar among races, with higher HRs for higher albuminuria. The only significant difference was higher CVD mortality in Blacks with ACR 30–299 mg/g. In all races, the threshold category above which the HRs for mortality outcomes was significantly greater than the reference category was ACR $\geqslant 10$ mg/g or dipstick $\geqslant$ trace. Although data were limited, the independent associations of low eGFR and high albuminuria with three outcomes were largely similar across three races in both high-risk and CKD cohorts (Supplementary Figures S5–S8 online).

Combined relationships of eGFR and albuminuria with clinical risk by race

Figure 3 shows the adjusted HRs for all-cause mortality, CVD mortality, and ESRD in the general population cohorts by eGFR and albuminuria categories compared with the reference categories of eGFR 90–104 ml/min per 1.73 m^2 and ACR <10 mg/g or dipstick negative. Consistent with the results in Figures 1 and 2, all-cause mortality risks for eGFR categories and albuminuria categories (marginal rows and columns in Figure 3) were similar for Asians, Whites, and Blacks. For example, in Asians, Whites, and Blacks, compared with eGFR 90–104 ml/min per 1.73 m^2, the HR (95% confidence interval) for eGFR 45–59 ml/min per 1.73 m^2 was 1.25 (1.20–1.31), 1.09 (0.97–1.22), and 1.33 (1.07–1.65) for all-cause mortality, 1.59 (1.45–1.74), 1.40 (1.17–1.68), and 1.44 (0.72–2.86) for cardiovascular mortality, and 27.6 (11.1–68.7), 11.2 (6.01–20.9), and 4.05 (2.18–7.51) for ESRD, respectively. The corresponding HRs for ACR 30–299 mg/g or dipstick $1+$ compared with ACR <10 mg/g or dipstick negative were 1.61 (1.41–1.84), 1.68 (1.50–1.88), and 1.84 (1.65–2.06) for all-cause mortality, 1.66 (1.37–2.01), 1.76 (1.49–2.09), and