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RACE AND ETHNICITY DISPARITIES (L. BREWER AND K. WATSON, SECTION EDITORS)

Racial and Ethnic Disparities in Cardiovascular Disease Risk Among Patients with Chronic Kidney Disease

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Abstract

Purpose of Review The purpose of this article is to critically appraise and summarize recent literature addressing racial and ethnic disparities in cardiovascular disease among adults with chronic kidney disease.

Recent Findings Despite advances in medical care, individuals with chronic kidney disease continue to bear a high burden of clinical and subclinical cardiovascular disease. Multiple racial and ethnic factors influence cardiovascular disease pathophysiology, burden, and clinical outcomes therein contributing to increased morbidity and mortality among racial and ethnic minority populations with chronic kidney disease.

Summary Racial differences in the prevalence of left ventricular hypertrophy, endothelial dysfunction, vascular calcification, and inflammation are observed in chronic kidney disease and contribute to increased morbidity and mortality. This review describes key pathophysiologic processes in addition to biologic and sociodemographic risk factors that impact observed cardiovascular disparities in racial and ethnic minority populations with chronic kidney disease. The review highlights factors impacting the relationship between chronic kidney disease and cardiovascular risk including diabetes, dyslipidemia, apolipoprotein L1 gene variants, dialysis, and kidney transplantation as well as drivers of racial and ethnic disparities including structural racism.

Keywords Cardiovascular disease · Disparities · Ethnicity · Kidney disease · Race · Risk factors

Introduction

The cardiovascular and renal systems are interdependent wherein factors affecting one system lead to downstream effects influencing the other. Chronic kidney disease (CKD), defined as functional or structural kidney impairment lasting more than 3 months, is an important contributor to morbidity and mortality with profound economic impacts [1, 2••, 3•]. CKD prevalence is estimated to range between 11 and 13% worldwide [4]. Among US Medicare recipients, CKD prevalence continues on an upward trend [3•] increasing to 29.3% from 1990 to 2017 [2••]. Despite advances in healthcare delivery, more than 746,000 US individuals in 2017 had end-stage kidney disease (ESKD) requiring either dialysis or kidney transplantation [3•]. The CKD progression rate to ESKD in the USA is one of the highest compared to other countries [3•]. Notably, race and ethnicity are associated with CKD risk, wherein progression is higher among underrepresented ethnic groups including persons of Black, Hispanic/Latinx, and Asian individuals [5•] with up to a threefold higher incidence of ESKD among Black patients [6, 7].

Cardiovascular disease (CVD) and cardiac imaging abnormalities are prevalent among patients with CKD [8•, 9, 10] with CVD being the leading cause of death in this patient population [11]. Up to 50% of all-cause mortality is attributed to CVD among individuals with CKD [8•]. Biologic changes in CKD such as uremia, microalbuminuria, anemia, chronic inflammation, and reduced estimated glomerular filtration rate (eGFR) accelerate

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premature CVD independently of conventional risk factors and older age [12]. Race-based estimates of GFR also propagate disparities in outcomes among patients with CKD which is discussed in more detail later in this review. Following cardiovascular events, the presence of CKD conveys poorer prognosis and the risk for recurrent cardiovascular events increases as CKD progresses. Compared to the non-CKD population, patients with CKD have up to a threefold increase in cardiovascular mortality risk [13]. Race and ethnicity influence cardiovascular risk such that Black and Hispanic/Latinx patients with CKD have an excess burden of CKD-associated CVD compared to non-Hispanic White [14]. CKD is also an independent risk factor for incident stroke and adverse vascular events among Black persons [15]. Multiple traditional and non-traditional factors influence cardiovascular risk among patients with CKD. This review summarizes the mechanisms of cardiovascular risk and CVD prevalence in patients with CKD while highlighting racial and ethnic differences (Fig. 1). Due to the volume of evidence available, this review focuses on disparities in Black and Hispanic/Latinx adults with CKD.

Pathophysiology of Cardiovascular Disease in Patients with Chronic Kidney Disease

Traditional risk factors such as hypertension, diabetes, and dyslipidemia contribute to the high cardiovascular risk in patients with CKD [8•]. These factors have a bi-directional relationship with CKD with the former increasing the risk for the latter and vice versa. The prevalence of these traditional risk factors is higher in Black individuals and discussed later in this review. In this section, we focus on mechanisms of cardiovascular risk that are independent of traditional cardiovascular risk factors (Fig. 2).

Left Ventricular Hypertrophy

Left ventricular hypertrophy (LVH) is common in CKD [16], and when eGFR is < 30 ml/min, the prevalence is estimated to be as high as 50% [17]. The etiology of LVH in CKD is related to a combination of factors including hypertension, anemia of CKD, and increased vascular stiffness [17]. LVH in CKD is associated with increased myocardial fibrosis which impairs myocardial contractility [18] leading

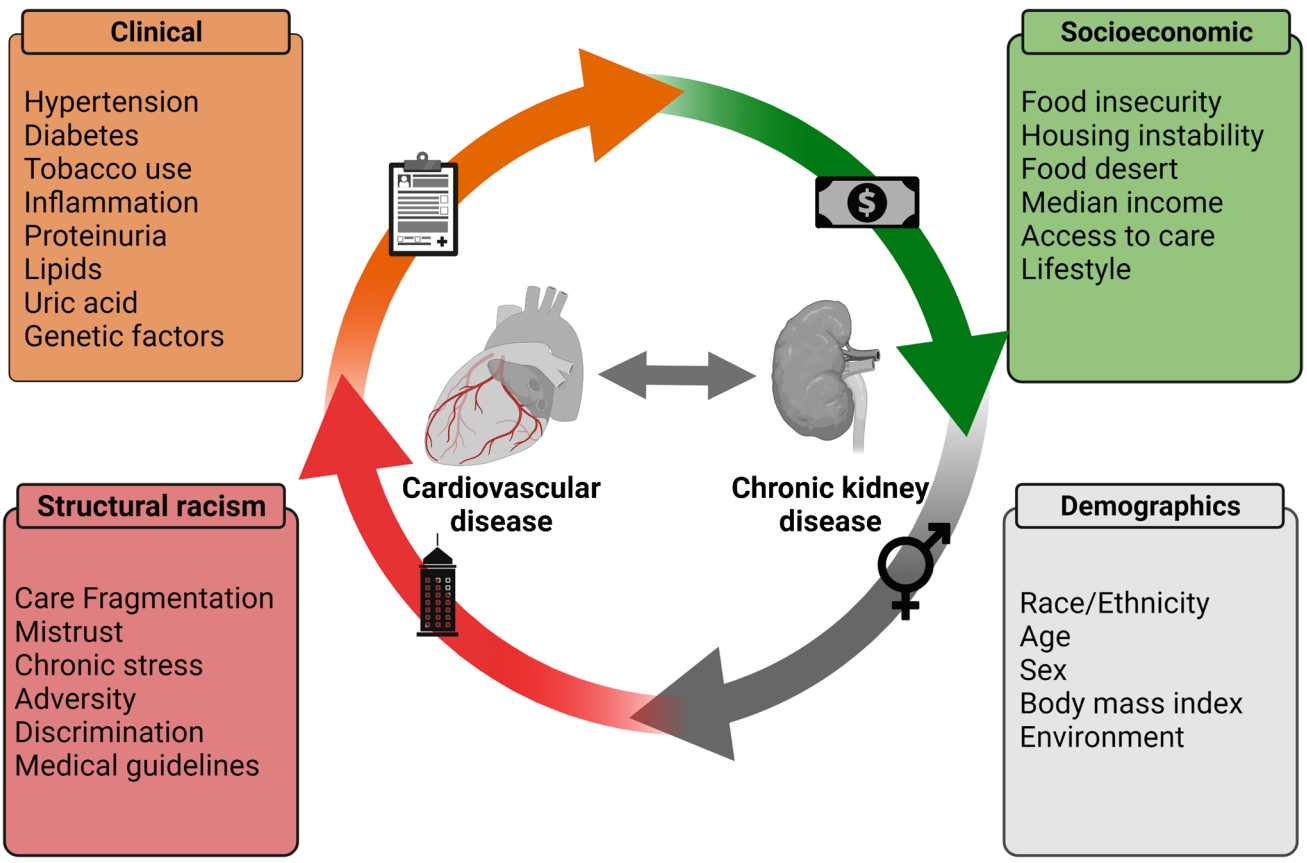

Fig. 1 Factors influencing cardiovascular disease risk among patients with chronic kidney disease. Several inter-related factors influence cardiovascular disease risk among racial and ethnic minority patients with chronic kidney disease

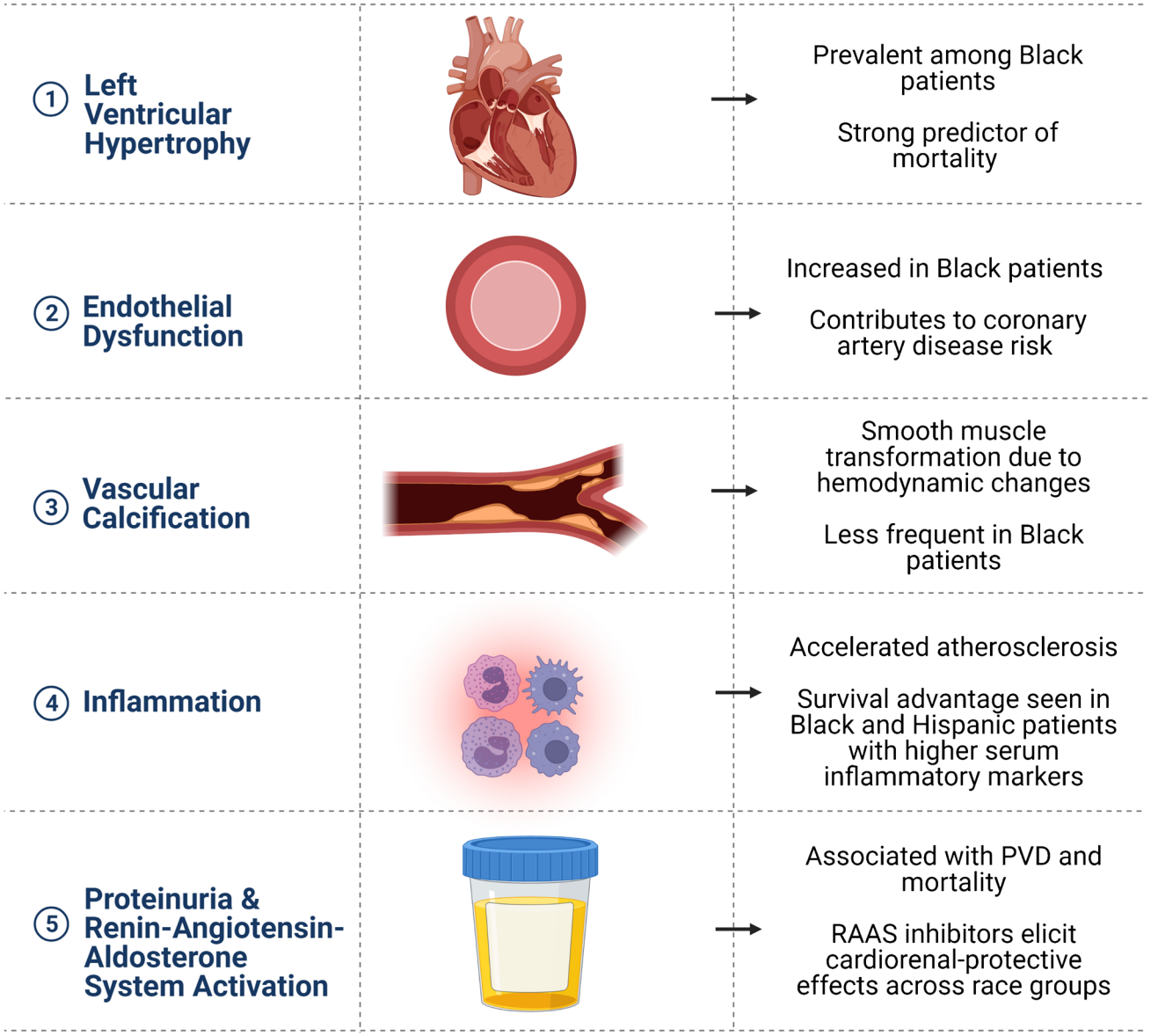

Fig. 2 Pathophysiology of cardiovascular disease in patients with chronic kidney disease. Key factors implicated in the pathophysiology of cardiovascular disease in patients with chronic kidney disease with emphasis on disparate factors in racial and ethnic minorities

to heart failure [19] and potentially explains the occurrence of cardiac rhythm abnormalities [20]. The development of LVH in patients with CKD can also lead to reduced coronary reserve. LVH is more prevalent among Black patients [21•] and is a stronger predictor of mortality than coronary artery disease and left ventricular ejection fraction [22].

Endothelial Dysfunction

Historically, racial differences in endothelial function have been observed with higher rates of impairment identified in Black persons compared to Whites [23]. A recent study found reduced levels of the cardioprotective endothelial nitric oxide in prehypertensive non-Hispanic Whites and in both prehypertensive and normotensive non-Hispanic Black adults [24]. Alterations in coronary endothelial nitric oxide due to increased oxidative stress in the vascular wall is a key mechanism for endothelial dysfunction in CKD [25]. Endothelial dysfunction is also associated with kidney abnormalities such as mild reductions in eGFR and microalbuminuria. A reduced cardiac capillary density and abnormal coronary dilation in CKD have been shown to contribute to coronary artery disease risk in animal studies [17]. A cross-sectional cohort of the Jackson Heart Study evaluating vascular function parameters as surrogates for endothelial function demonstrated that increased vascular stiffness and

loss of vascular bed pulsatility were associated with higher odds of reduced eGFR (or albuminuria) in Black participants [26•]. Overall, endothelial dysfunction is a contributor to both CVD and CKD and racial differences may modify its impact on associated clinical outcomes.

Vascular Calcification

Hemodynamic changes occurring in CKD lead to transformation of the smooth muscle cells within the medial layer of the vessel walls resulting in calcification [8•] which also affects the coronary vessels [27]. CKD-related factors (i.e., hyperphosphatemia, calcium dysregulation, uremia, inflammation) and the presence of co-occurring conditions such as diabetes enhance the progression of vascular calcification. Histologic exams demonstrated radial artery calcification prevalence to be 45 times higher in CKD compared to those without CKD [8•] and coronary artery calcification burden up to 3 times higher in patients with ESKD compared to age- and sex-matched controls [28]. Central vessel calcification leads to increased cardiac afterload and contributes to the development of LVH. We and others described outcomes in patients with widespread vascular medial calcification and pannicular thrombosis, called calcific uremic arteriolopathy, or calciphylaxis [29, 30], which is associated with high morbidity and mortality [8•]. Several mechanisms in CKD contribute to valvular calcification, particularly in the aortic valve, such as hyperparathyroidism and electrolyte abnormalities (hyperphosphatemia, elevated calcium-phosphate product, vitamin K, and magnesium) [8•, 31]. Paradoxically, arterial calcification is less frequent and of lesser severity in Black compared to White patients with CKD and in the general population [32], despite Black patients having a higher cardiovascular risk.

Inflammation

Chronic inflammation in CKD also contributes to the development of CVD. Increased inflammatory markers and oxidative stress as well as accumulation of toxins that would otherwise be cleared with intact kidney function all contribute to cardiovascular risk [17, 25, 33] and accelerated atherosclerosis [34]. Higher levels of c-reactive protein have been shown to be associated with cardiovascular risk [35], and results from the Canakinumab Anti-inflammatory Thrombosis Outcome (CANTOS) trial showed that the cardiovascular benefit of canakinumab was larger in patients with eGFR < 60 ml/min [36••]. However, an association between higher levels of inflammatory markers and improved survival has been found in Black and Hispanic/Latinx dialysis patients. This association is hypothesized to be related to greater resiliency in the presence of negative effects seen with inflammation [37].

Proteinuria and the Renin–Angiotensin–Aldosterone System

Increasing degrees of albuminuria are associated with higher cardiovascular risk and mortality in a linear fashion independent of eGFR [8•]. Albuminuria is also a risk factor for peripheral vascular disease and amputation [38]. Initiation of antiproteinuric measures, specifically renin–angiotensin–aldosterone system (RAAS) inhibitors, decreases the incidence of adverse cardiovascular outcomes and are considered first-line agents for CKD [17]. This mechanism of prevention is more strongly related to the prevention of CKD progression rather than direct cardiovascular protective effects [8•]. Racial differences in blood pressure control and autonomic regulation play a role in the risk for morbidity and mortality in patients with CKD [39], and there have been prior concerns about the effectiveness of RAAS blockade in Black CKD patients [40•]. However, the African American Study of Kidney Disease and Hypertension (AASK) trial demonstrated the beneficial effect of RAAS blockage in preventing CKD progression among Black adults [41].

Cardiovascular Disease in Patients with Chronic Kidney Disease

In this section, we discuss common cardiovascular conditions co-occurring with CKD (Fig. 3) and examine racial and ethnic differences in clinical outcomes.

Hypertension

Hypertension is an established risk factor for CVD-related morbidity and is more common among Black persons compared to all other racial groups [42]. Hypertension is more prevalent in patients with CKD compared to the general population [43]. Blood pressure values are also higher among Black adults with CKD, and higher rates of resistant hypertension and left ventricular hypertrophy have been observed [21•]. Despite awareness of a hypertension diagnosis and initiation of appropriate therapy, Black individuals are more likely to have poor blood pressure control compared to non-Hispanic Whites [42]. Likewise, hypertensive Black patients with CKD are less likely to have adequate blood pressure control compared to other race groups [44]. Among community-dwelling adults with hypertension, we found elevations in cardiac troponin T to be an independent predictor of CKD progression to ESKD among Black as well as in White patients [45]. Hypertension is, however, the most important risk factor for CVD in Black persons and represents the greatest potential for interventions to reduce CVD-related morbidity and mortality [46]. Intensive blood pressure control with a systolic blood pressure target < 130 mmHg

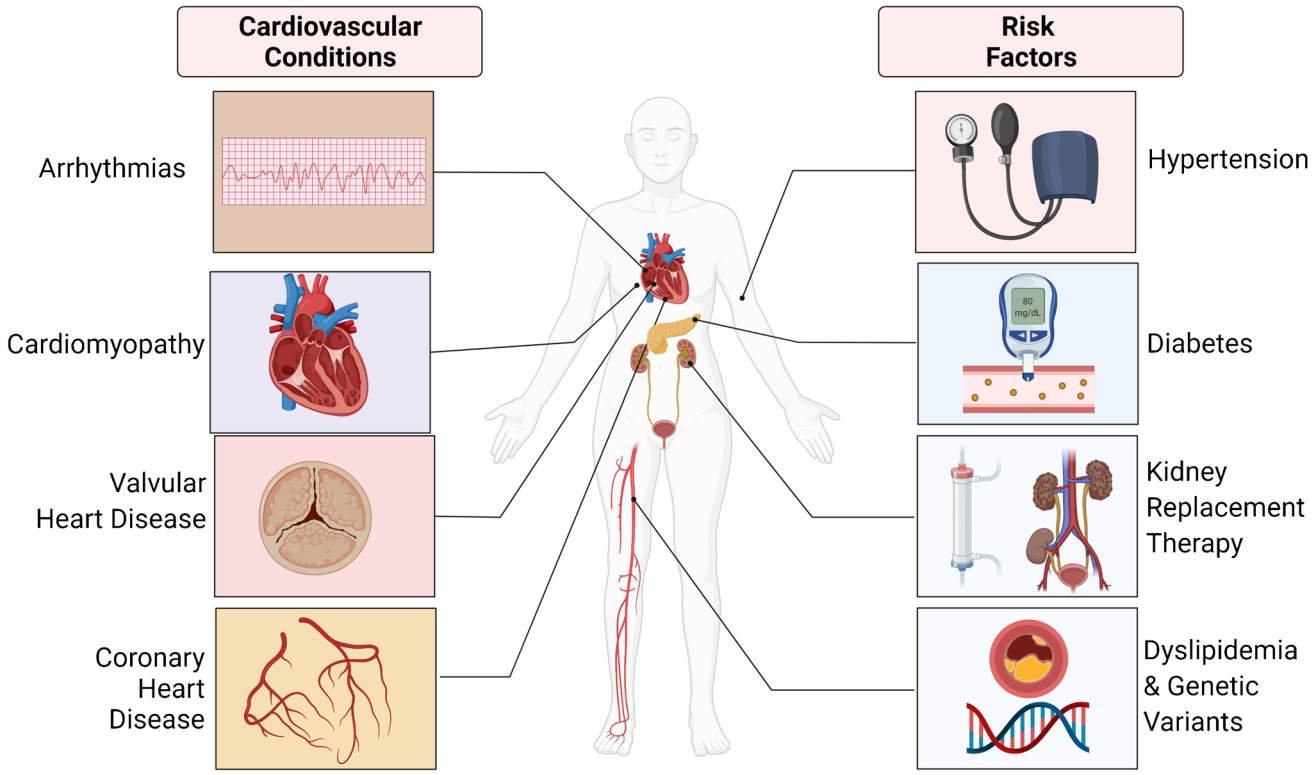

Fig. 3 Clinical cardiovascular conditions and risk factors in patients with chronic kidney disease. Common cardiovascular disorders and risk factors for cardiovascular disease in chronic kidney disease for which racial and ethnic differences have been observed

was associated with decreased all-cause mortality among patients with CKD based on a pooled analysis of four randomized control trials: AASK, ACCORD (Action to Control Cardiovascular Risk in Diabetes), MDRD (Modification of Diet in Renal Disease), and the SPRINT (Systolic Blood Pressure Intervention Trial) [43]. Self-reported perceptions of discrimination have also been recently demonstrated as one of several factors to be associated with poor hypertension control [47••].

Cardiomyopathy and Heart Failure

Global longitudinal strain measured with echocardiography, a subclinical marker of left ventricular systolic dysfunction, is significantly abnormal among Black patients with ESKD and is strongly associated with mortality [48]. LVH can occur as a consequence of adverse cardiovascular remodeling seen with longstanding hypertension and left ventricular outflow obstruction; or due to abnormal myocardial deposits related to infiltrative cardiomyopathies. This occurs more commonly among Black adults with CKD [21•] and is independently associated with adverse cardiovascular events [49]. Interestingly, systemic light chain (AL) amyloidosis, a plasma cell dyscrasia predominantly affecting the kidney and heart, is diagnosed at younger ages among Black and Hispanic/Latinx patients with Black patients having the poorest survival compared to non-Hispanic Whites [50]. Black men followed by Black women also have the highest mortality rate from cardiac amyloidosis (a type of restrictive cardiomyopathy), including light chain and transthyretin-related amyloidosis based on a national epidemiologic database [51]. Cardiorenal syndrome is a term used to describe the complex relation between cardiac and renal function in patients with heart failure. As CKD progresses, so does the risk for heart failure with near triple the risk among diabetic patients with CKD stages 4–5 compared to stages 1–2 [52]. In the general population, Black adults are disproportionately affected by heart failure, with a 20-fold higher rate of incident heart failure occurring before age 50 [46]. Similarly, among patients with CKD, Black and Hispanic/Latinx patients consistently have the highest risk for heart failure [14]. The most common type of heart failure identified in CKD patients is that with preserved ejection fraction for which therapeutic interventions remains limited [14]. Very recently, the EMPEROR-Preserved trial demonstrated for the first time a clinical benefit (reduction in the primary study endpoint – combined risk of cardiovascular death or hospitalization for heart failure) with empagliflozin, a sodium-glucose cotransporter

2 (SGLT2) inhibitor, among patients with heart failure with preserved ejection fraction [53•] including patients with renal dysfunction (eGFR < 60 ml/min/1.73 m^2). In the pre-specified sub-group analysis from the EMPEROR-Preserved trial, the effect estimates tended towards a positive clinical benefit with regard to the study's primary endpoint among Black study participants (4% of the study population), although this did not reach statistical significance. SGLT2 inhibitors reduced heart failure hospitalizations and slowed kidney disease progression among patients with heart failure with reduced ejection fraction regardless of diabetes status, and results from a meta-analysis of 2 large trials showed clinical benefit (a reduction in composite of first hospitalization for heart failure or cardiovascular death) in Black patients [54]. While the mechanism by which SGLT2 inhibitors exert cardiovascular and reno-protective benefits remains complex, potential pathways hypothesized include alterations in RAAS, blood pressure reduction through natriuresis, decreasing proteinuria, and lowering uric acid levels [55].

Valvular Heart Disease

Valvular heart disease is common among patients with CKD and is associated with poorer survival, with aortic stenosis and mitral regurgitation being more prevalent [56]. Among patients with CKD, mitral annular calcification and aortic valve calcification rates are higher, and also prevalent in younger patients due to accelerated disease progression. The pathophysiology of valve calcification is related to abnormal phosphate and calcium metabolism due to hyperparathyroidism as well as amyloid protein deposits [57]. The risk of infectious endocarditis also increases with CKD progression and is highest among those receiving hemodialysis, particularly those with prosthetic or structurally abnormal valves [57]. Black patients on dialysis had higher rates of hospital admission for endocarditis based on data from the US national inpatient sample (NIS) [58]. In contrast to other cardiovascular co-morbid conditions in patients with CKD, Black adults have been shown to have a lower prevalence of aortic valve calcification (values > 0 as detected by CT) compared to non-Hispanic Whites and a lower risk of progression to severe aortic stenosis [59].

Coronary Artery Disease

Coronary artery disease (CAD) is another common manifestation of CVD in patients with CKD with prevalence rates of significant coronary artery stenosis as high as 25–50% [60]. CAD etiology in CKD is attributed to multiple traditional risk factors such as diabetes and hypertension in addition to factors associated with CKD. Novel risk factors for CAD in the CKD population include anemia, oxidative stress, uremia-associated macrophage inflammation, and prothrombotic states [60, 61]. Black and Hispanic/Latinx adults with CKD have an excess burden of CAD [14], and the prevalence of high coronary calcium scores is more common among Hispanic/Latinx persons [62]. While cholesterol-lowering therapy is effective in the primary and secondary preventions of CAD in the general population, its effects are diminished in patients with ESKD [63]. In a retrospective analysis of data from US veterans, Black patients with ESKD were just as likely as White patients to have a mortality benefit from continuing statin therapy [64], whereas, a large observational study of Medicare patients showed that statins were not associated with a meaningful reduction in myocardial infarction and stroke events among dialysis-dependent patients [34]. However, racial disparities exist in use of statins in the CKD patient population. An analysis of OptumLabs data (which includes claims data, electronic health records, and laboratory data among insured persons in the US) showed that Black and White patients with the CKD had the lowest prevalence of statin use compared to Hispanic and Asian patients [44].

Arrhythmias and Sudden Cardiac Death

Sudden cardiac death due to ventricular arrhythmias occurs at a higher rate in CKD compared to the general population [65]. Atrial fibrillation is also highly prevalent in CKD [66] and tends to be higher among those receiving hemodialysis compared to peritoneal dialysis [60]. Contributing mechanisms for arrhythmias include cardiac structural changes, electrophysiological alterations, sympathetic overactivity [65], and electrolyte derangements. Notably, all these mechanisms appear to be more pronounced in Black patients [21•, 39, 67]. The management of atrial fibrillation-associated thromboembolic risk in patients with CKD is complicated by limited options as many non-vitamin K antagonist oral anticoagulants are dependent on renal clearance and hence are contraindicated in ESKD (with the exception of apixaban). Concerns remain in this patient population given increased bleeding risk [68] and accelerated vascular and valvular calcification with warfarin use [60]. Disparities in therapeutic interventions with anticoagulants have also been described with Black patients being less likely to receive non-vitamin k oral anticoagulants compared to White and Hispanic/Latinx patients independent of kidney function or other contraindications [69].

Factors Impacting the Relationship Between Chronic Kidney Disease and Cardiovascular Disease Risk and Drivers of Racial and Ethnic Disparity

In this section, we highlight key risk factors for CVD among patients with CKD (Fig. 3) and describe the impact of race and ethnicity on this relationship.

Diabetes Mellitus

Diabetes is an independent risk factor for CVD, thus conferring an incremental cardiovascular risk among patients with CKD. Approximately a third of patients with diabetes have CKD [70]. Moreover, diabetic kidney disease progresses more rapidly in racial and ethnic minorities [71]. Patients with diabetes experience varying degrees of hyperinsulinemia, insulin resistance, dyslipidemia, and glucose toxicity leading to a cascade of pro-inflammatory cytokines, endothelial dysfunction, macrophage activation, oxidative stress, cellular senescence burden, and promotion of a prothrombogenic state [72]. In a subgroup analysis of the blood pressure arm of the ACCORD trial, CKD patients with diabetes had more difficulty controlling blood pressure than those without CKD. Further, the secondary CVD benefits of intensive BP control were non-significant in patients with diabetes [73]. Select glucose-lowering therapies, SGLT-2 inhibitors and glucagon-like peptide-1 receptor agonist (GLP-1), induce beneficial effects in patients with CKD and CVD [74]. These classes of drugs have substantial reno-protective [75, 76] and cardiovascular benefits resulting in reduced risk of major adverse cardiac events, heart failure hospitalization, and cardiovascular mortality [77–79]. In the Jackson Heart Study, the co-occurrence of diabetes and CKD in Black patients was associated with a considerable increase in cardiovascular risk [80] beyond traditional cardiovascular risk factors. Regrettably, the incidence and prevalence of diabetes were noted to be on the upward trend between 1990 and 2008 among non-Hispanic Black and Hispanic/Latinx adults and the occurrence of ESKD attributed to diabetes was much higher among Black adults compared to non-Hispanic Whites [81]. An analysis of the National Health and Nutrition Examination Surveys between 1998 and 2014 showed Black and Mexican–American adults with diabetes were less likely to be on glucose-lowering therapies, RAAS inhibitors, or statins and were more likely to have higher hemoglobin A1c values compared to non-Hispanic Whites [82]. Similarly, in the general non-CKD population racial disparities were observed in the use of new glucose lowering medications (SGLT-2 inhibitors and GLP-1 receptor antagonists) with lower initiation rates among non-White men and women [83].

Dyslipidemia and Genetic Variants

Dyslipidemia with high triglycerides, high low-density lipoprotein cholesterol (LDL), and low high-density lipoprotein cholesterol (HDL) levels are associated with cardiovascular risk. However, lipid distribution in patients with CKD varies depending on type (nephrotic vs. non-nephrotic), disease stage (ESKD vs. non-ESKD), and continuous kidney replacement therapy options (hemodialysis vs. peritoneal dialysis) [84]. Variants in the apolipoprotein L1 gene (APOL1), which encodes an HDL-associated lipoprotein, occurs frequently in persons of African Ancestry. One subtype, hypothesized to have evolved as a protective mechanism against African trypanosomiasis, is associated with an increased risk of non-diabetic nephropathy [85]. An inverse relationship was demonstrated between HDL levels and eGFR in persons of African Ancestry, and variants in APOL1 modify this relationship leading to a larger inverse association between HDL and eGFR [85, 86]. CKD also contributes to alterations in HDL [87], and this mechanism likely influences the apparent increase in cardiovascular risk [84]. Data from the Atherosclerosis Risk in Communities (ARIC) study demonstrated that variants in APOL1 were associated with incident CKD and progression to ESKD among Black adults [88]. APOL1 variants are common among Black cohorts with a 13% prevalence of 2 risk alleles in the ARIC study [88]. Results from the Coronary Artery Risk Development in Young Adults (CARDIA) study also demonstrated an association between APOL1 variants and incident albuminuria as well as a decline in eGFR [89]. An analysis of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study showed variants in APOL1 to be associated with incident composite CVD (incident ischemic stroke and coronary artery disease) among Black participants without diabetes [90]. More recently, variants in APOL1 were associated with subclinical atherosclerosis in South African CKD patients [91], providing additional evidence of the effect of APOL1 variants in accelerating cardiovascular risk in patients with CKD.

Kidney Replacement Therapy

Health disparities have been observed in kidney replacement therapy. Studies have demonstrated that Black patients are less likely to be referred for a kidney transplant evaluation [92] and are more likely to experience premature allograft failure [93] with a 42% higher risk at 5 years post-transplant [94]. An analysis of the United Network for Organ Sharing (UNOS) database also demonstrated that Black kidney transplant recipients age 60 and older had a higher risk of graft failure compared to Whites [95]. Internalized,

personally mediated, and institutionalized racism have been described as potential barriers to kidney transplant access among Black patients [96]. A recent study analyzed data from 2 large academic medical centers and demonstrated that with removal of the race multiplier from the CKD-EPI equation for eGFR calculation, about a third of Black patients would be reclassified to higher degrees of kidney dysfunction (i.e., lower eGFR) therein negatively influencing early transplant referral among Black patients with CKD [97]. Notably, a newly proposed eGFR equation (utilizing creatinine and cystatin C) that does not account for race was more accurate in Black and non-Black persons than commonly used race-based eGFR calculations when compared to measured GFR [98]. In regard to transplant eligibility, another study demonstrated an improvement in referral rates for Black patients following the removal of the race coefficient from the eGFR equation [99••]. Other factors also contribute to lower transplantation rates among Black CKD patients. For example, due to higher rates of ESKD among Black persons, living kidney donation may be less frequently pursued by healthcare providers, particularly if risk factors for CKD are identified in the donor [100, 101]. Further, transplant selection committees may impose stringent criteria to avoid possible harm to at-risk individuals, turning potential Black donors away from kidney donation [102]. This makes community-based programs and efforts to promote awareness of living donation within at-risk communities less viable. In the kidney transplant population, cardiovascular risk factor control has been reported as poorer among Black persons compared to White. Lower adherence to cardiovascular medications, poorer diabetes control, APOL1 high-risk genotype (defined as carriage of 2 APOL1 risk alleles) kidney donors, and APOL1 high-risk recipients among Black kidney transplant recipients may explain these findings [94, 103–105]. Adjusting for cardiovascular risk factors and control reduces the negative influence of race on graft survival [103] suggesting that optimal control of cardiovascular risk factors in Black kidney transplant recipients can potentially improve graft survival. Disparities in health outcomes have also been observed in the dialysis-dependent patient population. Some studies previously demonstrated improved survival among Black and Hispanic/Latinx patients on dialysis compared to White, often referred to as the racial paradox [106, 107]. Others have suggested that the survival benefit seen among Black patients with ESKD on dialysis might be related to higher risk for death in early stages of CKD wherein only the more resilient individuals survive long enough for their CKD to progress to ESKD requiring dialysis [108]. Interestingly, two *APOL1* renal-risk variants (compared to one or none) were associated with longer survival in Black patients receiving chronic hemodialysis [109]. However, results from the Chronic Renal Insufficiency Cohort (CRIC) study demonstrated that the survival advantage seen with Black compared to White patients on dialysis was attenuated following multivariable adjustments and inclusion of deaths occurring prior to and following transition to dialysis [110]. Based on this study, it was inferred that White patients with more severe comorbid conditions were more likely to transition to dialysis compared to Black patients.

Systemic Racism and Social Determinants of Health

Systemic racism and social injustice are now clearly recognized by multiple healthcare/medical organizations and academic institutions as a public health crisis affecting Black and minority patients [111–113]. Health inequities date back to historical practices in medicine which supported differential healthcare allocation based on race, ethnicity, and social class, and these practices remain pervasive as a result of institutional and systemic racism [114]. In recognition of this issue, an increased number of studies and statements from the medical community have directly addressed racism with call-to-action documents aimed at educating the medical community and providing roadmaps and guidance to ensure health equity [111, 115–118]. Some medical organizations have also developed public action plans to address racial discrimination and health inequities. As part of the US Preventive Services Task Force's (USPSTF) commitment to health equity, race will be considered primarily as a social and not a biological construct in the development of its recommendations [114]. Psychosocial issues, racial discrimination, and social determinants of health are known to interact in a vicious cycle and play an important role in survival and quality of life among patients with CKD [40•]. In a study of Black patients with CKD, those randomized to recall of an acute race-related stressor had systolic and diastolic reactivity and higher rise in inflammatory cytokine interleukin-6 levels than those who recalled a general stressor suggesting the influence of race-related events on health status [119]. Among socioeconomically disadvantaged patients, preventive services of all kinds (including CVD prevention) are perceived as lower priority [40•]. Racial and ethnic minority groups are also more likely to be unaware of CKD risk and are less likely to receive appropriate preventive therapies, timely referral to nephrology care, home dialysis treatment, or kidney transplant [120]. In addition to the factors mentioned above, inadequate representation in clinical trials also contributes to disparate care in these vulnerable populations [121]. Continuous efforts must be directed at eliminating the systemic contributors to healthcare inequities that propagate disparities in CKD care.

Conclusion

In conclusion, multiple factors contribute to excess cardiovascular risk among racial and ethnic minority populations with CKD. We describe key pathophysiologic processes in addition to biologic and sociodemographic risk factors that impact observed cardiovascular disparities in these populations. Health systems are charged with the task of optimizing care for CKD patients in an equitable fashion including effective use of preventive services, providing patient education, and removal of systemic barriers to care for all CKD patients. This inevitably will require targeted efforts to improve CKD care through novel and transformative practice redesign and enhanced care coordination between specialists, internists, and primary care teams.

Early identification and treatment of CKD remain paramount so that efforts to reduce cardiovascular risk and appropriate management of CVD when present can be initiated in a timely manner. Optimization of patient education, social support structures, and care coordination is necessary to improve outcomes. Ultimately, industries outside of healthcare such as food, labor, mining, power generation, and waste management industries must also be held accountable for their role and contributions to socio-environmental factors that negatively impact health outcomes such as food insecurity, discriminative hiring practices, and environmental injustice. Policy and cultural changes that influence access to care and diminish racial and ethnic biases will also be required to ensure that all CKD patients have equal opportunities to achieve the best health outcomes possible which is the true definition of health equity.

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Declarations

Ethics Approval This is a review article, and no ethical approval is required.

Conflict of Interest DAA, IEP, ROW, and LJH have no relevant financial or non-financial interests to disclose.

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