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RACE AND ETHNICITY DISPARITIES (M. ALBERT, SECTION EDITOR)

Peripheral Artery Disease and African Americans: Review of the Literature

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Abstract

Purpose of Review Peripheral artery disease (PAD) is a chronic, obstructive disease of the peripheral vasculature which is a coronary heart disease risk equivalent. African Americans (AA) are at the highest risk for developing this disease at every age group. The purpose of this review is to shed light on the risk factors for PAD and their implications for disease manifestation in AA, and to highlight ways to combat these known racial disparities in order to achieve cardiovascular health equity in this population.

Recent Findings Even after controlling for differences in the prevalence of known cardiovascular risk factors, AA are still significantly more likely to have PAD. In part, due to a disproportionate amount of cardiovascular risk factors and detrimental socioeconomic factors, AA with PAD have a worse prognosis and more unfavorable outcomes than other ethnic groups with PAD. AA with PAD are more likely to have limb loss with amputation and less likely to receive revascularization leading to limb salvage.

Summary Advanced age, cigarette smoking, diabetes, hypertension, hyperlipidemia, chronic kidney disease, and poor socioeconomic status or education level have all been associated with increased risk of PAD. AA have a higher likelihood of having many, but not all, of these conditions. Nevertheless, increased cardiovascular risk for PAD combined with a relative lack of awareness about the disease in the AA community leads to poor health outcomes. Targeted interventions that partner healthcare access and delivery in community-based, non-traditional health care settings as well as the traditional clinics and hospitals may prove to be a more successful means of outreach in this high-risk population.

Keywords African Americans · Peripheral artery disease · Racial disparities · Ethnic differences · Cardiovascular risk

Background

Peripheral artery disease (PAD) is a chronic, debilitating condition stemming from atherosclerotic, obstructive disease in the arteries of the peripheral vasculature, most notably of the lower extremities. It is a common cause of morbidity, mortality, and disability due to limb loss [1, 2]. It is also a marker of underlying atherosclerotic disease in other vascular beds reflecting an increased risk of ischemic stroke, myocardial infarction, and death due to cardiovascular disease [3–8]. As a result, PAD has been recognized as a coronary heart disease risk equivalent by major cardiovascular organizations [9, 10••, 11]. The purpose of this review is to shed light on the risk factors for PAD and their implications for disease manifestation in African Americans, and to highlight ways to combat these known racial disparities in order to achieve cardiovascular health equity in this population.

African Americans (AA) have the highest rates of PAD in the USA [12]. In fact, black race has been shown to be one of the strongest risk factors for the development of PAD. The prevalence of PAD among individuals aged 40 years or older in the USA is somewhere between 4% and 10% and has been shown to be increasing in recent years [12, 13•]. Strikingly, the rate for AA is about twice that of non-Hispanic whites (NHW) at any given age [12].

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Rates for Hispanics, Asian Americans, and Native Americans were similar to NHW. Even after adjusting for differences in the distribution of traditional cardiovascular risk factors among ethnic groups (e.g., cigarette smoking, diabetes, hypertension), PAD remains significantly more prevalent in AA [12–18]. The addition of novel inflammatory biomarkers associated with PAD, such as CRP, IL-6, D-dimer, fibrinogen, and homocysteine, to an adjusted multivariate model of traditional risk factors attenuated but failed to eliminate the excess prevalence of PAD in AA as they were still 1.5 times more likely to have PAD as compared with NHW [19].

The higher rate of PAD among AA confers an increased PAD-related morbidity and mortality. AA with PAD have greater ambulatory dysfunction, faster functional decline, and higher rates of mobility loss when compared with NHW as measured by serial walking tests [20, 21]. The age-adjusted mortality rate resulting from PAD is higher among AA men (24.8 per 100,000) than NHW (19.9 per 100,000), American Indian or Alaska Native (20.8 per 100,000), Hispanic (15.4 per 100,000), and Asian Pacific Islander (8.5 per 100,000) men [22, 23••]. Similar patterns of PAD mortality are observed for AA women (16.5 per 100,000) compared with NHW (13.8 per 100,000), American Indian or Alaska Native (16.1 per 100,000), Hispanic (10.7 per 100,000), and Asian or Pacific Islander (6.8 per 100,000) women [22, 23••].

Deaths attributed to PAD are often due to sequelae of critical limb ischemia (CLI). CLI is the most advanced form of PAD characterized clinically by ischemic rest pain, tissue loss, or gangrene in the presence of hypoperfusion of the lower extremity. It can often lead to limb loss as a result of total or subtotal arterial obstruction and subsequent tissue necrosis. AA with PAD have higher rates of limb loss as evidenced by the fact that they are two to four times more likely to undergo amputation compared with their NHW counterparts [24–27]. Despite higher rates of CLI, AA are less likely to be offered and less likely to undergo revascularization in an effort to salvage the limb and avoid amputation [28–34]. AA who do undergo surgical or endovascular revascularization have disproportionately higher total hospitalization costs and lower rates of successful limb salvage compared with their NHW peers [35–37].

In addition to CLI and limb loss, PAD represents an increased burden of clinical and subclinical cardiovascular disease. Among patients with coronary artery disease (CAD), those with comorbid PAD have worse cardiovascular outcomes than patients with CAD alone [38, 39]. In one prospective study of 1018 patients with stable CAD, incident PAD conferred a 70% increased risk of subsequent cardiovascular events after adjustment for traditional risk factors [40]. Thus, AA with PAD may be at an even greater risk of cardiovascular events than NHW counterparts. Since the earliest studies in the 1950s, stroke mortality rates in AA remain 4.5-fold higher than among NHW [23••]. AA men and women also have substantially higher rates of fatal MI than NHW (men HR, 2.18; 95% CI, 1.24–2.56; women HR, 1.63; 95% CI 1.02–2.62) [41]. Clearly, the burden of PAD and cardiovascular disease, in general, disproportionately falls on AA.

Risk Factors

Most risk factors for PAD are attributed to modifiable causes. These include cigarette smoking and diabetes, which show the strongest risk factor associations with PAD [13•]. Hypertension and hyperlipidemia also have a significant association with PAD. It is important to understand how the following risk factors affect the development of PAD in AA.

Age

Age is a non-modifiable risk factor that is closely linked with the incidence of PAD. The rate of PAD increases exponentially with age, while the racial disparities in prevalence remain constant expand. The prevalence of PAD in individuals less than 40 years of age is exceedingly rare. Among individuals > 60 years of age, 12–20% have evidence of PAD [42]. At age ≥ 80 years, AA have a prevalence of 59% which is nearly three times the 23% prevalence of PAD in NHW of this age [12].

Cigarette Smoking

Cigarette smoking is a major, modifiable risk factor for the development of arterial disease in all vascular beds. It causes endothelial dysfunction, impaired vasodilation, and increased inflammation within the blood vessel resulting in accelerated atherosclerosis [43]. Smoking has been shown to be linked with poor cardiovascular outcomes and smoking cessation has been shown to slow the progression of PAD [44–46]. The amount and duration of tobacco use correlate directly with the development and progression of PAD in AA [47]. At the biological level, it has been proposed that differential endothelial dysfunction and/or cardiovascular inflammation may account for a more severe phenotype of PAD in AAs, but this has failed to fully account for race-related disparities in PAD [48]. Although the prevalence of cigarette smoking among AA is similar or less than in the general population (~ 20%), smoking cessation remains the least successful risk factor modification in AAs with PAD [49–51].

AA are significantly more likely or just as likely to attempt to quit smoking as NHW, yet significantly less likely than NHW to be successful at quitting [52]. In the CARDIA study which had the longest follow-up period of 25 years, NHW had higher rates of smoking cessation (54.0%) compared with African Americans (33.2%) [53]. In prospective cohort studies, reasons for the racial disparity in smoking cessation include lack of home ownership, lower income, greater

neighborhood problems, higher baseline cotinine, and increased likelihood of using menthol cigarettes among AA [54, 55].

Diabetes

Diabetes mellitus (DM) is strongly associated with PAD and, unlike cigarette smoking, the prevalence of diabetes in the USA is increasing. The prevalence of type 2 DM is even higher among patients with PAD than CAD patients with an estimated 30% of PAD patients having type 2 DM [56, 57]. AA have the highest rates of type 2 DM in the country [58]. In one study, AA are 1.5–2 times more likely to develop DM over their lifetime than NHW [59]. DM has PAD-specific implications with regard to the distribution of lower limb atherosclerosis and likelihood of future limb events. DM confers an increased tendency towards infrapopliteal atherosclerosis which differs from PAD associated with cigarette smoking which predisposes toward an aortoiliac distribution [60–62]. Patients with DM and PAD are at much higher risk for lower extremity amputation and CLI than those without DM [63]. AA and Hispanics with DM have a higher prevalence of PAD than NHW, even after adjustment for other known risk factors [64].

While type 2 diabetes is a treatable and potentially reversible condition, AA are much less likely to be aware of their diabetes diagnosis and, when treated, are less likely to achieve adequate glycemic control. [65] Despite this, there have been no large-scale studies to show that aggressive glycemic control contributes to reduction in PAD outcomes or mortality due to PAD. While the promising SGLT-2 inhibitor drugs for DM were the first to show a reduction in cardiovascular mortality in all groups including those with PAD, this did not translate to a reduction in PAD or limb events [66, 67]. In fact, the CANVAS trial revealed that canagliflozin reduced the primary endpoint of cardiovascular death, nonfatal MI, and nonfatal stroke by 14%, but actually led to an increased amputation risk (6.3 cases per 1000 patient years; HR 1.97) [67]. Minor amputations of the toe and midfoot were most frequent; however, major amputations involving the leg were also observed. As a result, there is now a black box warning on using this medication in individuals with PAD. It is important to note that AA were underrepresented in this trial, comprising only 3.3% of all participants. More research is needed to determine what impact newer diabetic drugs will have on PAD outcomes in AA.

Hypertension

Elevated blood pressure (BP) leads to increased risk of CAD, PAD, and stroke [68]. Even gestational hypertension increases the risk of incident PAD [69]. AA experience the highest reported rates of hypertension worldwide at 44% [70]. This prevalence is likely an underestimate in the setting of new guidelines from the ACC/AHA which lowered the threshold for hypertension to a BP of ≥ 130/80 mmHg instead of ≥ 140/90 mmHg [71]. The prevalence of hypertension in patients with PAD is high, ranging from 30 to 80% in published series depending on age and sex [72, 73]. Current guidelines recommend treating patients with PAD to the same BP targets as the general population in order to reduce cardiac events and stroke [10••]. However, many hypertensive patients with PAD have poorly controlled BP. In a US-wide registry of individuals with PAD, those with hypertension were less often treated for their hypertension than those with other cardiovascular disease (84% vs 95%) [74]. Compounding this problem in AA is the fact that the rates for treatment of hypertension are lowest in AA than in any other ethnic group [75]. While under treatment is clearly the biggest issue, there is a theoretical concern that overtreatment (i.e., to cause a low BP) may result in an increase in PAD events. Recently, a secondary analysis of PAD-induced limb events in the ALLHAT trial suggested a U-shaped association between achieved SBP < 120 mmHg and > 160 mmHg having higher event rates than those with a reference BP of 120–129/70–79 [76, 77]. Overall, the findings were consistent with a U-shaped association for PAD events, where both higher and lower extremes of BP resulted in increased limb events.

Hyperlipidemia

It is well established that elevated lipids and lipoproteins including total cholesterol, non-HDL cholesterol, LDL-C, and triglycerides are associated with an increased risk of incident cardiovascular disease and stroke [78, 79]. The wealth of clinical research on statins, ezetimibe, and more recently PCSK-9 inhibitors has demonstrated that lowering lipids and, in particular, LDL-C to the lowest possible target greatly improves cardiovascular outcomes [80–82]. More recently, randomized controlled trials have shown that lowering LDL-C results in a reduction of limb events in patients with PAD [83, 84]. The current guidelines have a Class I recommendation that individuals with PAD should be on high-intensity statin for secondary prevention [9, 10]. These guidelines are consistent with emerging data suggesting that high-intensity statin use at the time of PAD diagnosis is associated with a significant reduction in limb loss and mortality in comparison with low-to-moderate-intensity statin users [85].

NHW have a higher prevalence of hypercholesterolemia at 26.9% compared with AA at 21.5% and Mexican Americans at 21.8% [86]. However, AA are just as likely to have inherited familial hypercholesterolemia as NHW and more likely to have the disorder than Hispanics and other races [87]. Despite this finding, AA are 50% less likely to achieve LDL-C goals compared with NHW and significantly less likely to receive guideline-appropriate statin therapy [88, 89].

Chronic Kidney Disease

AA are disproportionately more likely to suffer from chronic kidney disease (CKD) and end-stage renal disease (ESRD) representing over 1/3 of all CKD and ESRD patients [90–94]. The prevalence of both symptomatic and asymptomatic PAD is both greater among individuals with CKD compared with the general population [95–97]. In the NHANES database, after multivariable adjustment, individuals with CKD were twice as likely to have prevalent PAD than those without CKD [98]. Furthermore, CKD imposes a poor prognosis on individuals with PAD. CKD is an independent predictor of all-cause and cardiovascular mortality as well as limb-related events in patients hospitalized with PAD [99–102].

Socioeconomic Status and Awareness

Socioeconomic factors including low household income and low education level have been associated with the development of PAD in US adults [103]. Patients with lower socioeconomic status and those on Medicaid insurance are also more likely to receive amputation for CLI even after controlling for medical comorbidities [104]. There is conflicting data as to whether lack of access to high quality health care, at least in part, accounts for these differences [104, 105]. However, even after controlling for access to health care and traditional cardiovascular risk factors, low income and low education attainment were still potent predictors of PAD-related hospitalizations [106]. Awareness of PAD among the US population is estimated at 25% based on prior studies, which is the lowest recognition of all the cardiovascular diseases (e.g., stroke and myocardial infarction) [107]. Thus, there is a lack of awareness about PAD in the general population, but especially in the AA community. In a sample of 2501 adults over the age of 50, 15.2% of NHW and 12.1% of Hispanics know that PAD can lead to amputation, while only 6.2% of AA surveyed knew this [108]. As a result, AA may be less likely to recognize or pay attention to warning signs and symptoms of PAD including claudication, walking impairment, and ulceration.

Disparity Reduction Measures

Much work needs to be done to ensure that AA with PAD achieve better health outcomes. Medical management of PAD is a critical area that is ripe for improvement. AA are less likely to receive adequate treatment of PAD itself as well as the cardiovascular risk factors which predispose to PAD [109–111]. Since achieving equity in socioeconomic status is a complex and perhaps unrealistic goal, targeted interventions that seek to improve guideline-based medical adherence and healthy lifestyle changes offer a feasible and effective way to improve overall vascular outcomes in this population. In a comprehensive review of interventions to reduce risk factors for PAD in AA, interventions that offered treatment in both community and clinical settings were shown to have the strongest effectiveness [112]. Moving forward, it will be important to partner non-traditional and community-based healthcare settings such as barbershops and churches with traditional clinics and hospitals in order to promote equal access and quality health care to a vulnerable population.

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Compliance with Ethical Standards

Conflict of Interest Dr. White Solaru declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

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