Ethnicity and Peripheral Arterial Disease
The San Diego Population Study

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Background—Previous studies have indicated higher rates of peripheral arterial disease (PAD) in blacks than in non-Hispanic whites (NHWs), with limited information available for Hispanics and Asians. The reason for the PAD excess in blacks is unclear.

Methods and Results—Ethnic-specific PAD prevalence rates were determined in a randomly selected defined population that included 4 ethnic groups; NHWs, blacks, Hispanics, and Asians. A total of 2343 participants aged 29 to 91 years were evaluated. There were 104 cases of PAD (4.4%). In weighted logistic models with NHWs as the reference group and containing demographic factors only, blacks had a higher PAD prevalence than NHWs (OR = 2.30, \( P = 0.024 \)), whereas PAD rates in Hispanics and Asians, although somewhat lower, were not significantly different from NHWs. Blacks had significantly more diabetes and hypertension than NHWs and a significantly higher body mass index. Inclusion of these variables and other PAD risk factors in the model did not change the effect size for black ethnicity (OR = 2.34, \( P = 0.048 \)). A model containing interaction terms for black ethnicity and each of the other risk factors revealed no significant interaction terms, which indicates no evidence that blacks were more “susceptible” than NHWs to cardiovascular disease risk factors.

Conclusions—Black ethnicity was a strong and independent risk factor for PAD, which was not explained by higher levels of diabetes, hypertension, and body mass index. There was no evidence of a greater susceptibility of blacks to cardiovascular disease risk factors as a reason for their higher PAD prevalence. Thus, the excess risk of PAD in blacks remains unexplained and requires further study. (Circulation. 2005;112:2703-2707.)

Key Words: ankle-brachial index • epidemiology • ethnicity • risk factors • peripheral vascular disease

The prevalence of peripheral arterial disease (PAD) has been reported from several American and European populations. These data have consistently revealed a sharp increase in PAD prevalence with age and generally somewhat higher rates in men than in women.1–10 In addition, most studies have indicated significant associations between PAD and major cardiovascular disease (CVD) risk factors. Diabetes and cigarette smoking typically show the strongest CVD risk factor associations with PAD, and hypertension and dyslipidemia have usually shown a good correlation with PAD as well.3,11 PAD prevalence rates have been reported to vary somewhat by ethnicity, although published, direct ethnic comparisons within a study have been limited to non-Hispanic Whites (NHWs) and blacks in 2 studies3,7 and to these 2 ethnic groups plus the Mexican-American subset of Hispanic whites in a third study.10 Each of these studies also systematically underestimated PAD prevalence by not including prevalent PAD revascularized subjects who had normal ankle-brachial indexes (ABIs). The reason or reasons for significant ethnic differences in PAD rates are unclear. Possibilities include a greater burden of CVD risk factors or greater susceptibility to CVD risk factors in a given ethnic group (ie, a greater probability of developing PAD given 1 or more CVD risk factors).

We studied a defined multiethnic population of employees and retirees in southern California that included NHWs, blacks, Hispanics, and Asians. We evaluated the association between PAD and ethnicity and CVD risk factors and the degree to which ethnic-specific differences in CVD risk factor levels, or susceptibility to CVD risk factors, influenced ethnic differences in PAD prevalence.

Methods
Subjects
The population for this study was selected from current and retired employees of the University of California, San Diego (UCSD), who were invited to participate in a study of peripheral venous and arterial diseases. Details of the methodology including response rates have been reported previously.12 In brief, random selection was made...
within strata defined by age, sex, and ethnicity. For age, the categories were 29 to 49 years (predominately in men), 50 to 59 years, 60 to 69 years, and 70 to 91 years (predominately in men). Women were overrepresented compared with the general population, which allowed additional power for certain female-specific hypotheses, because rates of PAD in women are usually somewhat lower than in men. We attempted to recruit a population with 15% Hispanics, 15% blacks, and 15% Asians to allow statistical power for contrasts by ethnicity. The invited target population included the spouse or significant other of each randomly selected participant (n=588). We also enrolled a few volunteers (n=187) who had heard about the study and who asked to participate. By selecting persons from all levels of education and occupation, including working, unemployed, and retired individuals, we were able to study a broad-based population sample.

The study design was cross-sectional. At the study visit, each participant was interviewed by trained study personnel according to a standardized protocol for information on demographics, lifestyle questions, past personal and family medical history, and medication use, including use of antihypertensive and dyslipidemia medications. Age was calculated from reported birth date. Ethnicity, education, and occupation were self-reported. CVD history was defined as a past history of myocardial infarction (MI), PTCA, CABB, congestive heart failure, stroke, or carotid endarterectomy. Parental CVD history was defined as a history of MI, PTCA, CABB, stroke, carotid endarterectomy, or PAD in either parent. Diabetes was defined by medical history. Current and past cigarette smoking habits were assessed, and pack-years of smoking were calculated as the average number of cigarettes smoked per day over all the years cigarettes were smoked divided by 20, multiplied by the total number of years cigarettes were smoked. Hypertension was defined as a systolic pressure \( \geq 140 \) mm Hg or a diastolic pressure \( \geq 90 \) mm Hg measured with the subject sitting quietly. Height (in centimeters) and weight (in kilograms) were measured, and the body mass index (BMI) was calculated as kg/m\(^2\). A blood sample was drawn, and total and HDL cholesterol were measured with standardized laboratory assays (Beckman Coulter analyzer). Dyslipidemia was assessed by the ratio of total cholesterol to HDL cholesterol (TC/HDL), which has consistently been found to be the best single lipid/lipoprotein parameter in assessing CVD risk.\(^2\)\(^3\)

At the vascular examination, with the subject supine, systolic blood pressure (SBP) was measured in both arms. Continuous-wave Doppler ultrasound was used to measure SBP twice in each posterior tibial artery, or in the dorsalis pedis artery in the unusual case in which a signal could not be found at the posterior tibial artery, and to record a waveform tracing at the posterior tibial (or rarely, dorsalis pedis) artery. The ABI for each leg was calculated as the average SBP in the posterior tibial (or dorsalis pedis) artery divided by the higher of the 2 arm SBPs. The higher arm SBP was used because of the strong association between PAD and subclavian stenosis.\(^4\)\(^5\) PAD was defined by an ABI \( \leq 0.90 \) or an abnormal Doppler waveform (no negative component and broadened) at the posterior tibial (or rarely, dorsalis pedis) artery or by previous revascularization for PAD.

For all study procedures, participants provided signed informed consent after a detailed introduction to the study. The study was approved by the Committee on Investigations Involving Human Subjects of UCSD.

**Statistical Analysis**

The data required for these analyses were extracted from an Access database with DBMS Copy software and written into a file usable by SAS 8.1 for Windows, and all analyses were run in that program. Age, gender, and ethnic-specific frequencies of PAD were computed. Ethnic-specific prevalences of 9 potential CVD risk factors for PAD were calculated: education, occupation, diabetes, pack-years of cigarette smoking, hypertension, the TC/HDL ratio, BMI, (personal) CVD history, and parental CVD history. Multivariable logistic regression was first performed to determine the independent associations of age, gender, ethnicity, education, and occupation with PAD. To assess the degree to which ethnic-specific differences in CVD risk factors accounted for ethnic differences in PAD, a second multivariable logistic regression model included diabetes, pack-years of cigarette smoking, hypertension, the TC/HDL ratio, BMI, CVD history, parental CVD history, and variables for antihypertensive and dyslipidemia medication use. These 2 medication variables (hypertension medication use and lipid medication use) were included because they can alter blood pressure and the TC/HDL ratio, respectively. Height was also included in the model because the ethnic groups differ in height, and ABI is positively associated with height.\(^2\)\(^4\)

Finally, a model with interaction terms for ethnicity and each of the other risk variables was used to determine whether any ethnic-specific susceptibility to CVD risk factors could explain ethnic differences in PAD. All probability values reflect 2-tailed tests. No corrections were made for multiple comparisons, and exact probability values are provided for each contrast. Because our selected population was not strictly representative of the broader population of San Diego County residents, all logistic regression models were weighted to the gender and ethnic distribution in the comparable age groups of San Diego County in 1994, the year the study began.

**Results**

The mean ABI for normal legs in the cohort was 1.16 in men and 1.12 in women. We found 104 cases of PAD in the study population, for an overall prevalence rate of 4.4%. PAD was bilateral in 64 subjects and unilateral in 40 subjects, for a total of 168 affected legs. In legs with PAD, the average ABI was 0.78 in men and 0.82 in women. A plurality of legs (n=69) had both an abnormal ABI and abnormal waveform, including 7 limbs with previous revascularization. Sixty legs had an abnormal ABI alone, including 3 limbs with previous revascularization, and 33 had an abnormal waveform alone. The remaining 6 PAD limbs had normal findings after revascularization.

The average age was 60.1 years for men and 58.8 years for women (data not shown). Table 1 shows PAD rates for the study population by gender, age, and ethnicity. The overall PAD rate was higher in men (6.1%) than in women (3.6%). PAD prevalence increased sharply with age, roughly doubling each decade, from 1.2% at age \( <50 \) years to 10.2% in the group 70 years of age or older. The black group had the highest PAD rates (7.8%), followed by NHWs (4.9%), Hispanics (1.8%), and Asians (1.4%). Because these data were unadjusted, differences were not tested statistically.
Table 2 shows age- and sex-adjusted results by regression for education (percent with less than a college education), occupation (percent with less than a technical or administrative job classification), diabetes, pack-years of cigarette smoking, hypertension, the TC/HDL ratio, hypertension medication use, lipid medication use, height, BMI, CVD history, and parental CVD history by ethnicity. Compared with NHWs, blacks and Hispanics both had significantly more participants who were not college graduates, whereas Asians had significantly fewer. For occupational status, black and Hispanic participants were significantly more likely than NHWs to be in the less than technical or administrative job category.

For diabetes, the lowest rates were in NHWs (3.8%), and rates were 3 times higher in blacks (11.4%) and somewhat higher in Hispanics (6.5%) and Asians (6.0%). For pack-years of cigarette smoking, NHWs had the highest rates (10.2%), with significantly lower rates in Hispanics (7.1%) and Asians (4.0%). Hypertension rates were similar in NHWs, Hispanics, and Asians (31.9% to 34.5%) but were much higher in blacks (49.5%). The mean TC/HDL ratio was similar in NHWs, blacks, and Asians (4.33 to 4.35) but was significantly higher in Hispanics (4.60, compared with NHWs). Hypertension medication use was similar in NHWs, Hispanics, and Asians (25.3% to 26.2%) but was nearly twice as high in blacks (49.9%). Lipid medication use was significantly lower in Hispanics (7.6%) than in NHWs (11.7%). Height was the same in NHWs and blacks (169.2 cm) but was significantly lower in Hispanics (164.5 cm) and Asians (160.7 cm). BMI in blacks (29.9 kg/m²) and Hispanics (27.9 kg/m²) was significantly higher than in NHWs (26.7 kg/m²), and Asians had a significantly lower BMI (24.9 kg/m²). CVD history was similar by ethnicity, but both Hispanics and Asians had a significantly lower parental CVD history than NHWs.

Table 3 shows the results of the weighted multivariable logistic regression analysis. The numbers in Table 3 are slightly smaller than in Table 1 owing to missing data on some subjects for 1 or more variables. The first column shows ORs and probability values for model A, which was limited to age, sex, ethnicity, education, and occupation. Age, sex, occupational

### Table 2. Age- and Sex-Adjusted Risk Factor Levels by Ethnic Group

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>NHW</th>
<th>Black</th>
<th>Hispanic</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than a college education, %</td>
<td>40.0</td>
<td>59.3*</td>
<td>64.5*</td>
<td>30.6*</td>
</tr>
<tr>
<td>Less than an administrative or technical occupation, %</td>
<td>28.0</td>
<td>39.1*</td>
<td>44.8*</td>
<td>32.8</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>3.8</td>
<td>11.4*</td>
<td>6.5</td>
<td>6.0</td>
</tr>
<tr>
<td>Pack-years of smoking, mean</td>
<td>10.2</td>
<td>8.9</td>
<td>7.1*</td>
<td>4.0*</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>34.5</td>
<td>49.5*</td>
<td>33.2</td>
<td>31.9</td>
</tr>
<tr>
<td>Mean TC/HDL ratio</td>
<td>4.33</td>
<td>4.35</td>
<td>4.60*</td>
<td>4.35</td>
</tr>
<tr>
<td>Hypertension medication use, %</td>
<td>25.9</td>
<td>49.9*</td>
<td>25.3</td>
<td>26.2</td>
</tr>
<tr>
<td>Lipid medication use, %</td>
<td>11.7</td>
<td>10.5</td>
<td>7.6*</td>
<td>8.1</td>
</tr>
<tr>
<td>Height, cm, mean</td>
<td>169.2</td>
<td>169.2</td>
<td>164.5*</td>
<td>160.7*</td>
</tr>
<tr>
<td>BMI, kg/m², mean</td>
<td>26.7</td>
<td>29.9*</td>
<td>27.9*</td>
<td>24.9*</td>
</tr>
<tr>
<td>History of CVD, %</td>
<td>6.4</td>
<td>6.8</td>
<td>5.2</td>
<td>4.8</td>
</tr>
<tr>
<td>History of parental CVD, %</td>
<td>62.1</td>
<td>56.5</td>
<td>54.2*</td>
<td>50.3*</td>
</tr>
</tbody>
</table>

*P<0.05 with NHW as reference group.

### Table 3. Multivariable Predictors of PAD Prevalence: ORs

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Model A</th>
<th>P</th>
<th>Model B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10-y increase)</td>
<td>2.54</td>
<td>&lt;0.001</td>
<td>2.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>2.33</td>
<td>&lt;0.001</td>
<td>1.59</td>
<td>0.176</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHW</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>Black</td>
<td>2.30</td>
<td>0.024</td>
<td>2.34</td>
<td>0.048</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.80</td>
<td>0.498</td>
<td>1.08</td>
<td>0.836</td>
</tr>
<tr>
<td>Asian</td>
<td>0.60</td>
<td>0.411</td>
<td>0.62</td>
<td>0.471</td>
</tr>
<tr>
<td>Less than a college education</td>
<td>1.39</td>
<td>0.194</td>
<td>1.01</td>
<td>0.983</td>
</tr>
<tr>
<td>Less than an administrative or technical occupation</td>
<td>2.00</td>
<td>0.007</td>
<td>1.61</td>
<td>0.084</td>
</tr>
<tr>
<td>Diabetes</td>
<td>N/A</td>
<td>6.90</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Pack-years of smoking (20)</td>
<td>N/A</td>
<td>1.63</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>N/A</td>
<td>1.85</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td>TC/HDL ratio</td>
<td>N/A</td>
<td>1.17</td>
<td>0.042</td>
<td></td>
</tr>
<tr>
<td>Hypertension medication use</td>
<td>N/A</td>
<td>2.14</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Lipid medication use</td>
<td>N/A</td>
<td>1.34</td>
<td>0.324</td>
<td></td>
</tr>
<tr>
<td>Height (per 10 cm)</td>
<td>N/A</td>
<td>0.84</td>
<td>0.326</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>N/A</td>
<td>0.88</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>CVD history</td>
<td>N/A</td>
<td>3.02</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Parental CVD history</td>
<td>N/A</td>
<td>1.00</td>
<td>0.989</td>
<td></td>
</tr>
</tbody>
</table>

N/A indicates not applicable to this model.
status, and black ethnicity were all significant predictors of PAD. Model B included, in addition to the variables in model A, diabetes, pack-years, hypertension, the TC/HDL ratio, hypertension medication use, lipid medication use, height, BMI, CVD history, and parental CVD history. Age remained significant in model B, but sex did not. The associations for education and occupation were attenuated and nonsignificant in model B, which indicates some of the predictive value of these variables reflected an excess of other PAD risk factors at lower levels of education and occupation. Diabetes (OR=6.90), pack-years of cigarette smoking (OR=1.63 per 20 pack-years), the TC/HDL ratio (OR=1.17), hypertension (OR=1.85), BMI (OR=0.88), and CVD history (OR=3.02) were all independently and significantly associated with PAD prevalence. Hypertension medication use (OR=2.14) was also significant, which indicates this variable was an additional marker of PAD risk, possibly as a surrogate for hypertension severity. The lipid medication use association (OR=1.34) was not significant. In model A, the OR for black ethnicity for PAD was 2.30 (P=0.024). Despite lower levels of education and occupational status and higher levels of diabetes, hypertension, hypertension medication use, and BMI in blacks (Table 2), simultaneous adjustment for these (and other) risk factors barely changed the OR for black ethnicity, to 2.34 (P=0.048). Thus, the excess of PAD risk factors in blacks could not explain their excess risk of PAD. A model with product interaction terms for black ethnicity and each of the other demographic and cardiovascular risk factors revealed no statistically significant interactions. Separate analyses that excluded the 187 volunteers and additionally excluded the 588 spouses/significant others gave quite similar results.

Discussion

PAD prevalence rates have been reported in Native Americans from 13 tribes in the Dakotas, Oklahoma, and Arizona and in elderly Japanese American men in Hawaii. The Hawaii study showed somewhat lower age-specific rates in Japanese Americans than most population studies in NHWs, consistent with our findings for Asians. However, both of the above studies only evaluated 1 ethnic group. Selvin and Erlinger recently reported data from the National Health and Nutrition Examination Survey (NHANES) and showed no significant difference for PAD prevalence for Mexican-Americans compared with NHWs, consistent with our findings for Hispanics. A study in Texas reported an OR of 1.8 for PAD in Mexican-Americans compared with NHWs, but this excess was nonsignificant, and the study group was limited to subjects with type II diabetes.

To the best of our knowledge, direct ethnic comparisons of PAD prevalence within a study have only been reported in 3 previous general population-based studies. Each of these studies used ABI criteria alone to diagnose PAD, and none of these studies considered previous revascularization for PAD. Because ≈5% of prevalent PAD cases in the population are persons with previous revascularization who now have normal ABIs, these 3 studies likely both underestimated PAD prevalence and misclassified some PAD patients as normal. In the Atherosclerosis Research in Communities (ARIC) study, Zheng and colleagues reported on 4071 black men and women and 10 415 “white” men and women; information on Hispanic ethnicity was not reported. The authors noted an excess of hypertension and diabetes in blacks that was quite similar to the present data. Among blacks, 3.3% of the men and 4.0% of the women had an ABI ≤0.90 versus 2.3% of the white men and 3.3% of the white women. They did not further explore this ethnic difference in PAD. In addition to not considering revascularization, in ARIC, only 1 leg per participant was evaluated. Because about half the PAD cases in population studies have unilateral disease, this suggests that overall PAD prevalence rates were further underestimated by ≈25% in ARIC.

In addition to estimating PAD prevalence, the other 2 studies also explored whether the excess of PAD in blacks was independent of other CVD risk factors. In the Cardiovascular Health Study (CHS), Newman and colleagues reported on a population of 3372 subjects aged ≥65 years free of clinical CVD, 5.2% of whom were nonwhite (predominantly blacks). The authors did not report information on Hispanic ethnicity or ethnic-specific risk factor levels. PAD was defined as an ABI <0.90. Nonwhites in the CHS study showed an OR for PAD of 2.12 (P=0.002) compared with white participants in a logistic regression analysis that included age, diabetes, current smoking, pack-years of smoking, hypertension, TC, HDL, creatinine, BMI, and forced vital capacity in the logistic model. The NHANES study showed a higher PAD prevalence in blacks than in NHWs, with an OR for black ethnicity of 2.83 after adjustment for age and gender and an OR of 2.39 after further adjustment for other cardiovascular risk factors, which indicates only a modest attenuation of the risk for black ethnicity after adjustment for CVD risk factors. Although technically not population-based, a recent study based on a comparison of hypertensive sibships in Minnesota (NHWs) and Mississippi (blacks) showed elevated and statistically significant multivariate ORs for black ethnicity in men (4.7) and women (2.2). Similar to the above studies, revascularization for PAD was not considered.

The present study had the advantages of (1) evaluating 4 ethnic groups randomly selected from a defined population, (2) assessing all prevalent cases of PAD, including revascularized subjects, (3) adjusting for education and occupation, which could be linked to diagnostic and treatment differences, and (4) exploring the question of differential ethnic susceptibility to CVD risk factors for PAD by evaluating interaction terms. The present data concur that blacks have a significantly higher probability of PAD than NHWs and that this excess cannot be accounted for by the greater prevalence of diabetes and hypertension in blacks. Furthermore, we found no evidence of greater black susceptibility to CVD risk factors.

We considered whether a greater risk of PAD in blacks might represent less aggressive treatment of risk factors. As current and former employees of a large public university (and significant others), participants of all ethnicities had healthcare coverage. In addition, drug treatment of dyslipidemia in blacks was similar to NHWs, and drug treatment of hypertension was (appropriately) more common in blacks.

Findings of a greater PAD prevalence in black men are consistent with a clinical report of greater severity of PAD in blacks than in NHW older men. The reason for excess PAD prevalence in blacks is currently unknown. One possibility is higher levels of newer (or novel) risk factors. Some atherogen-
ic, inflammatory, and prothrombotic factors have been reported to be more prevalent in blacks than in NHWs. Another possibility is a greater genetic susceptibility to PAD in blacks. However, whereas 1 study has reported on possible genotype differences in PAD, no information is currently available on ethnic differences for these genotypes. Finally, unmeasured psychosocial variables such as depression or hostility might be relevant.

Limitations of the present study include an insufficient number of Hispanic and Asian subjects to definitively evaluate any ethnic difference compared with NHWs. Any differences, however, appear to be less pronounced than for blacks.

We conclude that black ethnicity can now be considered a consistent and independent risk factor for PAD at a magnitude similar to that of other established risk factors. The excess prevalence of PAD in blacks cannot be explained by the excess of diabetes, hypertension, or other CVD risk factors in blacks or by any greater susceptibility of blacks to CVD risk factors. Further research is indicated to determine whether novel CVD risk factors, such as newer atherogenic, inflammatory, and prothrombotic markers, can explain all or part of the excess of PAD in blacks.

Acknowledgments

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