Racial Differences in the Prevalence of Hypertensive Retinopathy

Tien Yin Wong, Ronald Klein, Bruce B. Duncan, F. Javier Nieto, Barbara E.K. Klein, David J. Couper, Larry D. Hubbard, A. Richey Sharrett

Abstract—Few population-based data support the hypothesis that hypertensive retinopathy is more common in African Americans than in whites. We examined racial differences in the prevalence of and risk factors for hypertensive retinopathy in a population-based sample of 1860 African Americans and 7874 white persons, aged 49 to 73 years, without diabetes. Retinal photographs were taken of one randomly selected eye and evaluated for the presence of retinopathy (flame and blot-shaped retinal hemorrhages, microaneurysms, and soft exudates) according to standardized protocols by graders masked to participant characteristics. The prevalence of retinopathy was 2 times higher in African Americans than in whites (7.7% versus 4.1%, age- and gender-adjusted odds ratio [OR] 2.03, 95% confidence intervals [CI] 1.65, 2.49). After controlling for 6-year mean arterial blood pressure, use of antihypertensive medications and left ventricular hypertrophy by ECG criteria, the excess prevalence of retinopathy in African Americans was reduced by 40% (adjusted OR 1.61, 95% CI 1.26, 2.06). Further adjustment for other vascular risk factors, common carotid artery intima-media thickness, and serum creatinine levels reduced the excess prevalence in African Americans by another 13% (adjusted OR 1.48, 95% CI 1.08, 2.03). We conclude that hypertensive retinopathy is twice as frequent in African Americans compared with whites without diabetes and that the excess prevalence of retinopathy in African Americans is associated with blood pressure and severity of hypertension. (Hypertension. 2003;41:1086-1091.)

Key Words: hypertension, genetic • blacks • race • microcirculation • retinopathy • blood pressure

The higher prevalence of hypertension in African Americans compared with white persons in the United States is well documented.1–3 Studies show that African Americans are more likely to develop hypertensive-related complications (eg, left ventricular hypertrophy,4,5 hypertensive kidney disease,6–8 and stroke9), to have higher mortality rates,10 and to have poorer access to antihypertensive treatment.3

An important clinical marker of hypertensive end-organ damage is the presence of retinopathy, a spectrum of lesions seen in the retina resulting from hypertensive injury to the microvasculature (eg, retinal hemorrhages, microaneurysms).11,12 Black people of African descent have long been suggested to have an excess risk of hypertensive retinopathy.13–16 However, the few existing studies available that suggest possible racial differences have important limitations. First, most studies were based on highly selected clinic samples not representative of the general population.13,14 Second, the majority has relied on the use of clinical ophthalmoscopy to detect retinopathy,13–15 an unreliable method.17 Finally, older studies were conducted before the widespread use of antihypertensive treatment.13–16 Thus, whether hypertensive retinopathy is more common in African Americans in contemporary United States communities, and whether this is related to racial difference in blood pressure or other factors remains uncertain.

In the current study, we describe the prevalence of hypertensive retinopathy in community-based samples of African American and white persons living in the United States and examine risk factors that may account for possible racial differences in the prevalence of retinopathy.

Methods

Study Population
The Atherosclerosis Risk In Communities (ARIC) study is a population-based study that included 15 792 women and men 45 to 64 years of age at recruitment in 1987–1989.14 Population samples were selected from four US communities: Forsyth County, North Carolina; Jackson, Mississippi (blacks only); and suburbs of Minneapolis, Minnesota; and Washington County, Maryland. More than 90% of the African American participants were from Jackson. Of those examined at baseline, 14 346 (93% of survivors) returned for a second examination approximately 3 years later (1990–1992) and 12 887 (86% of the survivors) returned for a third examination approximately 6 years later (1993–1995).
Retinal photographs were taken at the third examination when the participants were 51 to 72 years of age. Of 12,887 participants who returned for this examination, we excluded those whose race was not African American or not white, 42 nonwhite residents in Minneapolis and Maryland, and 1,012 with no photographs, ungradable photographs, or retinal vascular occlusions. Because diabetes may complicate the definition of hypertensive retinopathy, we also excluded 1,674 persons with diabetes (defined as a fasting glucose \( \geq 7.0 \) mmol/L, a nonfasting glucose \( \geq 11.1 \) mmol/L, or a self-reported history of treatment for diabetes at any examination), and 387 with missing blood pressure or diabetes data at any examination. These exclusions left 9,734 persons available for this analysis.

Institutional review boards at each study site and the Retinal Reading Center approved the study. Informed consent was obtained from all participants.

**Definition of Retinopathy**

The retinal photography procedure and its assessment have been reported. Briefly, after 5 minutes of dark adaptation, a 45-degree retinal photograph was taken of one randomly selected eye, centered on the optic disc and macula. Trained graders who were masked to participant identity evaluated the retinal photographs, according to a standardized protocol, for the presence or absence of retinal changes. In each quadrant, the following retinopathy lesions were evaluated: microaneurysm, cotton wool spot, dot or blot hemorrhages, maculopathy, cotton wool spots (soft exudates), and disk swelling. Each lesion was classified as definite, probable, or none in each quadrant. Retinopathy was defined as “present” if any of these lesions were definite or probable in any of the 4 quadrants. Reliability of the grading has been previously reported. In general, intra- and inter-grader kappa statistics of specific retinal lesions ranged from 0.76 to 1.00, respectively.

**Definition of Risk Factors**

Participants underwent a standardized interview, clinical examination, and laboratory investigations in the ARIC study. At each visit, blood pressures were taken with a random-zero sphygmomanometer, and the mean of the last 2 measurements was used for analyses. Hypertension was defined as systolic blood pressure \( \geq 140 \) mm Hg, diastolic blood pressure \( \geq 90 \) mm Hg, or use of antihypertensive medication during the previous 2 weeks. Mean arterial blood pressure was also computed as 2/3 of the diastolic plus 1/3 of the systolic value. Current blood pressure was defined as measurements at the time of retinal photography (third ARIC examination), whereas 3- and 6-year past blood pressures were defined as measurements taken 3 and 6 years before retinal photography (first and second ARIC examinations). The 6-year mean arterial blood pressure (average of the 3 examinations) was used as a covariate to adjust for the effects of blood pressure. Left ventricular hypertrophy was defined from electrocardiographic criteria, described previously.

Blood collection and processing followed a standard protocol. Total plasma cholesterol was measured by enzymatic methods, HDL cholesterol was measured after dextran-magnesium precipitation of the non-HDL lipoproteins, and glucose was assessed by a modified hexokinase/glucose-6-phosphate dehydrogenase procedure. Serum creatinine level was measured using a modified kinetic Jaffe method. Technicians measured height and weight with participants in standing position, and body mass index (BMI) was calculated as weight/height\(^2\) (kg/m\(^2\)). Physical activity, education, occupation, cigarette smoking, and alcohol consumption were ascertained from interview. Physical activity was characterized by a sports index, with values ranging from 1 to 5. Coronary heart disease (CHD) at baseline was defined on the basis of a medical history, and incident CHD events were defined using symptoms, ECG, and biomarker levels. The cumulative prevalence (prevalence CHD and incident CHD up to the third ARIC examination) was used to define absence versus presence of CHD. Measurement of common carotid artery intima-media thickness (IMT) by ultrasound followed a standard protocol. All variables were based on data from the third examination, except for IMT and left ventricular hypertrophy (first examination), serum creatinine (second examination), and 6-year mean arterial blood pressure (average of 3 examinations).

**Statistical Methods**

We compared participant characteristics and the prevalence of retinopathy in African Americans and whites using analysis of covariance models or logistic regression models to adjust for age and gender. We used logistic regression models to calculate odds ratios (OR) for retinopathy associated with race (African Americans versus whites) and specific risk factors (eg, presence versus absence of hypertension or a 10 mm Hg difference in current or past mean arterial blood pressure), adjusting for age and gender.

To evaluate the extent that blood pressure and other risk factors might explain the excess prevalence of retinopathy in African Americans compared with whites, we estimated the percentage reduction in odds associated with adjustment for these factors according to the following formula: \((r_a - r_b)/r_a \times 100\), where \(r_a\) is the OR of retinopathy in African Americans compared with whites, adjusted for age and gender only (reference Model 1), and \(r_b\) is the OR after additional adjustment in Models 2 to 4. These were grouped as follows: Model 2: age-, gender-, and hypertension-related factors (6-year mean arterial blood pressure, antihypertensive medications use, and left ventricular hypertrophy); Model 3: variables in Model 2 plus other cardiovascular risk factors (total and HDL cholesterol, fasting glucose, BMI, sports index, smoking and alcohol consumption status, education, occupation); and Model 4: variables in Model 3 plus indices of subclinical macrovascular and renal microvascular disease (common carotid IMT and serum creatinine).

**Results**

Table 1 shows participant characteristics of African Americans and whites. African Americans were slightly younger than whites and less likely to be men. After adjusting for age
TABLE 3. Associations of Race and Other Potential Risk Factors With Retinopathy

<table>
<thead>
<tr>
<th>Potential Risk Factors</th>
<th>All Persons</th>
<th>African Americans</th>
<th>Whites</th>
<th>OR (95% CI)*</th>
<th>P</th>
<th>OR (95% CI)*</th>
<th>P</th>
<th>OR (95% CI)*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>African Americans vs Whites</td>
<td>2.03 (1.65,2.49)</td>
<td>&lt;0.001</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Present vs absent</td>
<td>1.66 (1.37, 2.00)</td>
<td>&lt;0.001</td>
<td>1.56 (1.09, 2.25)</td>
<td>0.02</td>
<td>1.43 (1.13, 1.80)</td>
<td>0.002</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Current MABP</td>
<td>10 mm Hg increase</td>
<td>1.22 (1.13, 1.32)</td>
<td>&lt;0.001</td>
<td>1.27 (1.22, 1.44)</td>
<td>&lt;0.001</td>
<td>1.09 (0.99, 1.20)</td>
<td>0.08</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>3-year past MABP</td>
<td>10 mm Hg increase</td>
<td>1.19 (1.10, 1.29)</td>
<td>&lt;0.001</td>
<td>1.25 (1.10, 1.42)</td>
<td>&lt;0.001</td>
<td>1.07 (0.97, 1.18)</td>
<td>0.20</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>6-year past MABP</td>
<td>10 mm Hg increase</td>
<td>1.16 (1.07, 1.25)</td>
<td>&lt;0.001</td>
<td>1.19 (1.05, 1.34)</td>
<td>0.008</td>
<td>1.01 (0.91, 1.12)</td>
<td>0.80</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LV hypertrophy</td>
<td>Present vs absent</td>
<td>1.92 (1.03, 3.60)</td>
<td>0.03</td>
<td>1.79 (0.83, 3.86)</td>
<td>0.14</td>
<td>1.17 (0.36, 3.75)</td>
<td>0.48</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Education</td>
<td>High school vs less</td>
<td>0.71 (0.57, 0.89)</td>
<td>0.003</td>
<td>0.83 (0.58, 1.20)</td>
<td>0.33</td>
<td>0.84 (0.62, 1.14)</td>
<td>0.25</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Occupation</td>
<td>Professional vs others</td>
<td>0.87 (0.69, 1.09)</td>
<td>0.22</td>
<td>0.78 (0.51, 1.20)</td>
<td>0.26</td>
<td>0.91 (0.70, 1.19)</td>
<td>0.51</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Per SD increase</td>
<td>0.99 (0.90, 1.08)</td>
<td>0.77</td>
<td>1.07 (0.91, 1.26)</td>
<td>0.41</td>
<td>0.96 (0.85, 1.08)</td>
<td>0.95</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Per SD increase</td>
<td>0.98 (0.88, 1.05)</td>
<td>0.65</td>
<td>0.86 (0.71, 1.03)</td>
<td>0.10</td>
<td>1.00 (0.89, 1.14)</td>
<td>0.11</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>Per SD increase</td>
<td>1.09 (1.00, 1.20)</td>
<td>0.06</td>
<td>0.92 (0.78, 1.09)</td>
<td>0.35</td>
<td>1.15 (1.03, 1.29)</td>
<td>0.01</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Body mass index</td>
<td>Per SD increase</td>
<td>1.11 (1.01, 1.21)</td>
<td>0.02</td>
<td>0.97 (0.83, 1.13)</td>
<td>0.71</td>
<td>1.10 (0.98, 1.23)</td>
<td>0.11</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Sports index</td>
<td>Per unit increase</td>
<td>0.84 (0.75, 0.95)</td>
<td>0.004</td>
<td>0.84 (0.66, 1.07)</td>
<td>0.15</td>
<td>0.88 (0.77, 1.02)</td>
<td>0.08</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>Ever vs never</td>
<td>1.15 (0.94, 1.40)</td>
<td>0.17</td>
<td>1.43 (0.99, 2.05)</td>
<td>0.05</td>
<td>1.10 (0.87, 1.39)</td>
<td>0.45</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Ever vs never</td>
<td>0.79 (0.63, 0.98)</td>
<td>0.03</td>
<td>1.02 (0.70, 1.48)</td>
<td>0.93</td>
<td>0.83 (0.63, 1.09)</td>
<td>0.17</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Carotid IMT</td>
<td>Per mm increase</td>
<td>1.70 (1.00, 2.88)</td>
<td>0.05</td>
<td>1.43 (0.54, 3.80)</td>
<td>0.48</td>
<td>1.77 (0.93, 3.37)</td>
<td>0.08</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>Per SD increase</td>
<td>1.03 (0.97, 1.09)</td>
<td>0.37</td>
<td>1.00 (0.87, 1.14)</td>
<td>0.93</td>
<td>1.15 (0.94, 1.41)</td>
<td>0.18</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

MABP indicates mean arterial blood pressure; LV hypertrophy, left ventricular hypertrophy.

*Odds ratio (95% confidence interval) of retinopathy, comparing presence vs absence or difference in risk factors, adjusted for age and sex.
African American race (age- and gender-adjusted OR of 2.03, Model 1) was reduced by 40% after controlling for 6-year mean arterial blood pressure, use of antihypertensive medications, and left ventricular hypertrophy (adjusted OR of 1.61, Model 2). Further adjustment for other vascular risk factors, common carotid artery IMT, and serum creatinine reduced the excess prevalence of retinopathy in African Americans marginally (Models 3 and 4). In people with hypertension, the OR of retinopathy associated with African American race (age- and gender-adjusted OR of 1.89, Model 1) was reduced by 45% after adjustment for 6-year mean arterial blood pressure, antihypertensive medication use, and left ventricular hypertrophy (adjusted OR of 1.49, Model 2), which was reduced by a further 25% with additional adjustment for other factors (adjusted OR of 1.26, Model 4). In contrast, in persons without hypertension, the OR of retinopathy associated with African American race (age- and gender-adjusted OR of 1.77, Model 1) was not altered substantially in models controlling for blood pressure and other factors (Models 2 to 4). Results were essentially similar in analyses adjusting for systolic or diastolic blood pressure (data not shown).

Because most of the African Americans were from Jackson and only one site (Forsyth County) had both racial groups, we repeated the analysis limited to Forsyth County participants only (n=2445 whites and n=214 African Americans). The prevalence of retinopathy was 2 times higher in African Americans (9.3%) than in whites (4.3%) living in Forsyth County.

Finally, we conducted subsidiary analyses for specific retinopathy lesions (ie, retinal hemorrhages, microaneurysms, and soft exudates), in men and women separately, including people with diabetes (n=1674). The results were not qualitatively different (data not shown).

**Discussion**

Hypertensive retinopathy reflects microvascular damage resulting mainly from elevated blood pressure, is a marker of subclinical cerebral disease, and is associated with risk of stroke and higher mortality in people with hypertension. Thus, both the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the British Society of Hypertension have recommended that retinopathy is an indication for initiating antihypertensive drug therapy, even in persons with mild hypertension (systolic/diastolic blood pressures of 140 to 159/90 to 99 mm Hg).

In the current study, we showed that hypertensive retinopathy, as assessed from retinal photographs, is twice as frequent in African Americans as in whites living in the United States, with the excess prevalence occurring in people with and without hypertension. We further showed that the higher prevalence of retinopathy in African Americans is substantially diminished after controlling for 6-year average arterial blood pressure and severity of hypertension (as indexed by use of antihypertensive medications and left ventricular hypertrophy). Additional adjustment for other cardiovascular risk factors, common carotid artery disease, and serum creatinine reduced the racial difference in retinopathy prevalence only marginally.

Our findings provide the first documentation of higher prevalence of hypertensive retinopathy in African Americans in contemporary, community-based populations in the United States. This is consistent with previous smaller studies in the literature, mostly conducted in the 1960s and 1970s, that show black people of African descent have a higher prevalence of hypertensive retinopathy than white people of European ethnicity. In a study in England, the prevalence of hypertensive retinal changes, as defined from retinal photographs, was higher in the 299 participants of Afro-Caribbean origin than in the 384 participants of European origin. The study noted that differences in resting blood pressure between Afro-Caribbean and Europeans could not fully account for the racial difference in retinopathy prevalence, although no data on other possible cardiovascular risk factors that may explain the excess prevalence of retinopathy in Afro-Caribbean people were available.

There are several possible explanations for the excess prevalence of retinopathy in African Americans. First, differences in the blood pressure and severity of hypertension (as reflected by the use of antihypertensive medications and the presence of left ventricular hypertrophy) explained almost
half of the excess prevalence of retinopathy in African Americans. Racial differences in other vascular risk factors, socioeconomic status, and subclinical macrovascular (as reflected by common carotid artery IMT) and microvascular (serum creatinine) disease explained some of the remaining racial difference in retinopathy. It is likely that we were unable to adequately control for racial differences in the cumulative exposure to elevated blood pressure or other risk factors, so that residual confounding from these may still contribute to the racial differences observed. Second, the retinopathy lesions may reflect pathogenic processes involving the endothelium and microvasculature not measured here. Thus, differences in the frequency of these conditions or processes may contribute to the racial difference in retinopathy prevalence. The fact that blood pressure and standard vascular risk factors did not explain the racial difference in retinopathy prevalence in the subgroup of people without a history of hypertension lends support to this latter hypothesis (Table 4). Third, poorly understood differences in the susceptibility to retinal vascular damage from elevated blood pressure may contribute to the higher prevalence of retinopathy in African Americans.3,29,30

We note that “normotensive” participants also had retinal signs traditionally classified as “hypertensive retinopathy” (Table 2). This is partly related to measurement error in our definition of hypertension (ie, single blood pressure measurements only partially reflect a person’s lifetime history of “exposure” to hypertension) and partly to the fact that some retinal signs are related to aging (eg, arteriosclerosis) and other nonhypertensive processes (eg, ocular ischemia from carotid artery disease).11,12

Our study may have important public health and clinical implications. The higher prevalence of retinopathy in middle-aged African Americans with hypertension is disturbing (9.1%) because retinopathy is associated with an increased risk of cerebrovascular disease and mortality.12,20,24 These findings reemphasize the importance of current public health approaches to tackling hypertension in this racial group. Additionally, the higher prevalence of retinopathy in African Americans supports the growing literature that this racial group is more likely to have cerebral microvascular disease such as lacunar stroke31 and white matter lesions (which are thought to be microvascular in nature),26 but less likely to have extracranial macrovascular disease such as carotid artery atherosclerosis.32,33

The strengths of the current study include its population-based nature, the quantitative and masked evaluation of retinopathy, standardized assessment of blood pressure, and data on other risk factors. Study limitations should be highlighted. First, because retinal photographs were taken 6 years into the ARIC study, selection biases may have attenuated or accentuated some findings. If African Americans with retinopathy were more likely to die before photography, these associations could be attenuated. Second, the ARIC study did not employ pharmacological pupillary dilation before photography, and therefore, a high percentage of photographs was ungradable. We have previously found that African Americans were more likely to have ungradable retinal photographs than whites.19 In addition, only one eye was photographed. Although hypertensive retinopathy is often symmetrical between eyes, it is possible that some retinopathy was missed because of the possibility of the involved eye not being photographed. However, we have no reason to believe these factors would lead to a differential detection of retinopathy between African Americans and whites. Fourth, we cannot exclude the possibility that geographical differences contribute to the disparity in retinal prevalence. Nonetheless, the results were not substantially different in analyses restricted to one site with both African Americans and whites (Forsyth County). Finally, because diabetes complicates the assessment of hypertensive retinopathy, we excluded persons with diabetes from these analyses. In a subsidiary analysis with diabetics included, we found a higher OR of hypertensive retinopathy associated with African American race (age- and gender-adjusted OR of 2.44 compared with an OR of 2.03, as shown in Table 4). Thus, we may have underestimated the racial differences in hypertensive retinopathy.

Perspective
Hypertensive retinopathy is twice as common in middle-aged African Americans as in whites. Racial difference in the prevalence of retinopathy is closely linked to racial differences in blood pressure levels and hypertension severity, suggesting that appropriate strategies to control hypertension in African Americans may reduce this disparity.

Acknowledgments
This study was supported by contracts N01-HC-35125, N01-HC-35126, N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022 from the National Heart, Lung, and Blood Institute, Bethesda, Md. The authors thank the staff and participants in the ARIC study for their important contributions.

References


Racial Differences in the Prevalence of Hypertensive Retinopathy
Tien Yin Wong, Ronald Klein, Bruce B. Duncan, F. Javier Nieto, Barbara E.K. Klein, David J. Couper, Larry D. Hubbard and A. Richey Sharrett

Hypertension. 2003;41:1086-1091; originally published online March 24, 2003;
doi: 10.1161/01.HYP.0000064181.63546.53
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/41/5/1086

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/