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Association of black race with recurrent stroke risk

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ABSTRACT

Background: The significantly higher risk of primary stroke in Black vs. Whites is very well established. However, very few studies have specifically examined the presence of this racial disparity in recurrent stroke risk.
Methods: We conducted an analysis of a clinical trial dataset comprising 3470 recent non-cardioembolic stroke patients aged ≥35 years and followed for 2 years. Subjects were categorized by race into Whites and Blacks. Cox regression analysis was used to evaluate the associations between Black (vs. White) and ischemic stroke (primary outcome); and stroke/coronary heart disease (CHD)/vascular death as major vascular events (secondary outcome) with and without adjustment for comorbid conditions associated with stroke.
Results: Among participants (2925 Whites and 545 Blacks), a total of 287 (8.3%) incident stroke and 582 (16.8%) major vascular events occurred. Compared with Whites, Blacks had higher frequencies of prior stroke, hypertension, diabetes mellitus, and smoking; but were younger with lower prevalence of CHD. Frequency of stroke was higher in Blacks vs. Whites (11.4% vs. 7.7%; $P = 0.004$), but there was no difference in major vascular events (16.9% vs. 16.8%). Compared with Whites, Blacks experienced a significantly higher risk of recurrent stroke (HR 1.58; 95% CI, 1.19–2.09), but the stroke risk was not significant after multivariable adjustment (1.13; 0.81–1.59).
Conclusion: Blacks are ~60% more likely to experience a recurrent stroke within 2 years than their Whites, but this risk is likely mediated via stroke risk factors. These results underscore a need to optimize and sustain risk factor control in Black stroke populations.

1. Introduction

Several population-based studies have shown that people of Black race are at significantly higher risk of a first-time stroke compared to people of White race [1,2]. However, there is a relative paucity of studies that have specifically examined whether this racial disparity exists for recurrent stroke risk. A single hospital study of 299 patients (110 black and 132 white) found an unadjusted relative risk of stroke recurrence for blacks relative to white to 2.0 (95% CI: 0.9–4.4) [3], and another single site study (135 Whites and 177 Blacks) demonstrated that Whites had a higher risk of stroke recurrence than Blacks [4]. Data covering bigger numbers of participants and more sites are needed to better determine the nature of secondary stroke risk among Blacks vs. Whites, and assess potential mitigating factors. The objective of this study was to compare the risk of recurrent stroke in Black vs. White patients with a recent ischemic stroke.

2. Methods

2.1. Database

We reviewed data from the Vitamin Intervention for Stroke Prevention (VISP) trial [5]. VISP study was a multicenter, double blind, randomized controlled clinical trial performed at 56 centers across the United States, Canada, and Scotland. The study enrolled 3680 patients aged ≥35 years to determine whether high doses of multivitamin (folic acid, pyridoxine, and cobalamin) given to lower total homocysteine levels would reduce the risk of recurrent stroke and major vascular events in patients with a recent (<120 days) non-cardioembolic stroke [5]. In VISP trial, high-dose vitamin therapy had no effect on the outcome measures of stroke, composite of vascular events, or death [5]. Details of methods and main results of the trial have been reported previously. Demographic, physical, neurological examination including stroke scales, medication use assessment, and laboratory data collected at randomization, with subsequent information obtained at follow-up visits of 1, 6, 12, 18, and 24 months. Physicians were instructed to provide best available background medical and surgical management to prevent recurrent stroke, which included risk factor control education

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and, usually, administration of aspirin, 325 mg/d [5]. For each patient, presence of hypertension and diabetes were documented not only by history, but also if newly diagnosed at the first visit. We reviewed data on medication use, which was collected at every 6-month interval follow-up visit. We utilized secondary prevention drug information including antihypertensive, antithrombotic (antiplatelet or anticoagulant), and lipid-lowering therapy (statin mostly) that was provided at the last follow-up visit, because the number and type of such medications can vary during the post-discharge follow-up setting [6] and our preliminary evaluation indicated that several hundred patients had their baseline prescriptions modified to include more therapeutic drug classes at the time of their 2nd or 3rd (and further) follow-up visits. Last follow-up visit was defined as the last documented study encounter that preceded either a vascular outcome event or end of the trial. Furthermore, we retrieved information on mini-mental state examination (MMSE) score, since cognitive impairment has been implicated as a potential predictor for stroke risk [7]. Study subjects were categorized into White race and Black race. The trial was approved by the ethics committee or institutional review board at each national or local site, and all participants provided written informed consent before enrolment [5].

2.2. Outcome measure

The primary outcome for this analysis was time to recurrent ischemic stroke. Secondary outcome was time to the first stroke, coronary heart disease (CHD) including myocardial infarction, coronary revascularization, cardiac resuscitation, and fatal CHD, or vascular death as major vascular events. Recurrent stroke was diagnosed only with evidence of sudden onset of focal neurologic deficit lasting at least 24 h accompanied by an increased National Institutes of Health Stroke Scale (NIHSS) score in an area that was previously normal [5]. When the sudden onset of symptoms lasting at least 24 h was not accompanied by an increased NIHSS score in an area that was previously normal, then recurrent stroke was diagnosed using cranial CT or MRI evidence of new infarction consistent with the clinical presentation [5].

2.3. Statistical analysis

Data are summarized as mean ± standard deviation (SD) or number of subjects (percentage), as appropriate. Comparisons across the groups were examined using the χ^2 test for categorical variables and Student *t*-test for continuous variables. Whites were the control group for purposes of comparison. Baseline demographic and clinical covariates were preselected based on previous studies of factors that influence vascular events after ischemic stroke. Cox proportional hazard regression analyses were performed to estimate the risk of outcome events during 2 years after adjusting for baseline covariates (age, sex, systolic blood pressure, hypertension, diabetes mellitus, smoking, stroke severity, history of stroke (before VISP qualifying stroke), history of CHD, history of congestive heart failure (CHF), history of carotid endarterectomy, history of alcohol use, body mass index (BMI), serum levels of triglycerides, high-density lipoprotein cholesterol (HDL-C) and creatinine, mini-mental state examination (MMSE) score, antihypertensive medication, antithrombotic therapy, and lipid modifier use; all $P < 0.10$). Participants not having outcome events were censored at last follow-up examination, or last visit. Participants lost to follow-up during the course of the study were included in the Cox model until the last contact. Results are given by hazard ratio (HR) and its 95% confidence interval (CI). All analyses were conducted using IBM SPSS Version 22.0 (IBM Corp., Armonk, NY) and a probability value of <0.05 was considered statistically significant.

3. Results

3.1. Subjects characteristics by race

Of 3680 participants in the trial, 210 non-White and non-Black persons were excluded from the final analysis, yielding a total of 3470 (94.3%) subjects. Among 3470 participants, mean age was 66.5 ± 10.8 years, 62.5% were men, and 15.7% were Black. Baseline demographic and clinical characteristics between white and black races are provided in Table 1. Compared with Whites, Blacks had higher systolic blood pressure, higher BMI, higher serum levels of HDL-C and creatinine, higher National Institutes of Health Stroke Scale (NIHSS) score, higher frequencies of male, hypertension, diabetes mellitus, smoker and antihypertensive medication, higher histories of prior stroke and CHF, whereas age, serum triglycerides levels, MMSE score, frequencies of male, history of CHD, carotid endarterectomy and alcohol use, antithrombotic and lipid-lowering medication were lower.

3.2. Comparison of vascular outcomes between whites and blacks

During 2-years of follow-up, a total of 287 (8.3%) incident stroke and 582 (16.8%) major vascular events were recorded. Results of the unadjusted and adjusted associations between Blacks (vs Whites) and vascular events appear in Table 2. Occurrence of stroke was higher in Blacks vs Whites (11.4% vs 7.7%; $P = 0.004$), whereas that of major vascular events was not (16.9% vs 16.8%). When referenced to white group, Blacks were significantly linked to risk of recurrent stroke (HR 1.58; 95% CI, 1.19–2.09), but not of major vascular events (HR 1.07; 95% CI, 0.86–1.34). The adjusted HR for stroke for Blacks was however, attenuated and non-significant after multivariable

Table 1
Baseline characteristics of study patients between Whites and Blacks.

	Whites (n = 2925)	Blacks (n = 545)	*P*
Age, years	67.3 ± 10.6	62.2 ± 10.9	<0.001
Systolic blood pressure, mm Hg	140.4 ± 18.6	143.7 ± 19.0	<0.001
BMI, kg/m^2	28.0 ± 5.5	29.9 ± 6.7	<0.001
Total cholesterol, mg/dL	202.1 ± 45.9	200.1 ± 46.1	0.358
LDL-C, mg/dL	121.8 ± 39.4	123.6 ± 40.2	0.349
Triglycerides, mg/dL	179.8 ± 166.6	143.2 ± 91.0	<0.001
HDL-C, mg/dL	45.3 ± 15.7	46.9 ± 14.2	0.034
Creatinine, mg/dL	1.11 ± 0.60	1.19 ± 0.56	0.004
Homocystein, μmol/L	14.1 ± 6.1	14.5 ± 5.2	0.148
Baseline MMSE score	27.1 ± 3.2	25.9 ± 3.6	<0.001
Male	1871 (64.0)	299 (54.9)	<0.001
Hypertension	2418 (82.7)	502 (92.1)	<0.001
Diabetes mellitus	788 (26.9)	218 (40.0)	<0.001
Smoker	445 (15.2)	146 (26.8)	<0.001
Qualifying stroke NIHSS			<0.001
0	1064 (36.4)	122 (22.4)	
1–4	1653 (56.5)	356 (65.3)	
≥5	208 (7.1)	67 (12.3)	
History			
Prior stroke[a]	639 (21.9)	175 (32.1)	<0.001
Coronary heart disease[b]	789 (27.0)	116 (21.3)	0.005
Congestive heart failure	143 (4.9)	42 (7.7)	0.008
Carotid endarterectomy	236 (8.1)	10 (1.8)	<0.001
Alcohol use	1804 (63.0)	227 (44.0)	<0.001
Medication			
Antihypertensive	2346 (80.2)	472 (86.6)	<0.001
Antithrombotic	2754 (94.2)	490 (89.9)	<0.001
Lipid-lowering	1648 (56.3)	237 (43.5)	<0.001
High-dose B vitamin	1473 (50.4)	259 (47.5)	0.224

Values provided are number (%) or mean ± SD, as appropriate, otherwise stated. BMI indicates body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; MMSE, mini-mental state examination; NIHSS, National Institutes of Health Stroke Scale.

[a] Before VISP qualifying stroke.

[b] Defined as history of myocardial infarction, angina, coronary angioplasty/stenting, or coronary artery bypass graft surgery.