High Prevalence of Stroke Symptoms Among Persons Without a Diagnosis of Stroke or Transient Ischemic Attack in a General Population

The REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

Virginia J. Howard, MSPH; Leslie A. McClure, PhD; James F. Meschia, MD; LeaVonne Pulley, PhD; Sean C. Orr, MD; Gary H. Friday, MD

Background: A substantial portion of the general population has clinically silent stroke on brain imaging. These lesions may cause symptoms. This study assessed the prevalence of stroke symptoms in a stroke- and transient ischemic attack (TIA)–free population and the association of symptoms with risk factors indexed by the Framingham Stroke Risk Score.

Methods: We performed a cross-sectional analysis from a randomly sampled national cohort enrolled from January 25, 2003, through November 30, 2005, with oversampling from the southeastern stroke belt and African American populations. The main outcome measure was stroke symptoms assessed by validated questionnaire.

Results: The study included 18,462 (41% African American; 51% female; mean age, 65.8 years) participants who reported no stroke or TIA. The prevalence of stroke symptoms was 5.8% for sudden painless hemibody weakness, 8.5% for sudden hemibody numbness, 4.6% for sudden painless loss of vision in one or both eyes, 3.1% for sudden hemifield visual loss, 2.7% for sudden inability to understand speech, and 3.8% for sudden inability of linguistic expression. The prevalence of 1 or more symptoms was 17.8%. Relative to the first quartile of the Framingham Stroke Risk Score, the adjusted odds ratio for 1 or more stroke symptoms increased from 1.0 (95% confidence interval [CI], 0.90-1.2) in the second quartile to 1.2 (95% CI, 1.1-1.5) and 1.5 (95% CI, 1.3-1.6) in successive quartiles. Symptoms were more prevalent among African American compared with white participants and among those with lower income, lower educational level, and fair to poor perceived health status.

Conclusions: The general population without prior diagnosed stroke or TIA has a high prevalence of stroke symptoms. The relationship between symptoms and risk factors suggests that some symptomatic individuals may have had clinically undetected cerebrovascular events and may benefit from aggressive stroke prophylaxis.

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SUBSTANTIAL PORTION OF the population has clinically undiagnosed stroke. Silent infarctions have been documented by magnetic resonance imaging (MRI) in 11% of community-dwelling adults aged 55 to 64 years in the Atherosclerosis Risk in Communities (ARIC) cohort; this incidence increased from 22% at the age of 65 to 69 years to 43% for individuals older than 85 years in the Cardiovascular Health Study. In both studies, MRI-detected silent infarctions were in individuals who had not been told by a physician that they had had a stroke or transient ischemic attack (TIA), but these same individuals could have experienced stroke symptoms that failed to reach a threshold required for clinical diagnosis. It is possible that many subclinical strokes are nonetheless symptomatic.

Evaluating persons with symptoms of stroke or TIA is an important part of stroke prevention owing to the high risk of stroke. Such evaluation requires that the public and health care professionals recognize and initiate prompt action when major stroke symptoms are reported. A 1999 survey by the National Stroke Association found that 2.3% of a random sample of 10,112 US residents had been told by a physician that they had had a TIA, but only 64% had seen a physician within 24 hours of the event. An additional 3.2% reported TIA symptoms but had not sought medical attention. A report on 61,019 adults surveyed across 17 states and the US Virgin Islands found that only 17.2% could correctly
classify all stroke symptoms and would call 911 if they thought someone was having a stroke.7

Few studies have looked at the association of stroke symptoms with stroke risk factors in a general population. The ARIC study reported a higher prevalence of risk factors, including diabetes mellitus, current smoking, and hypertension, among those with stroke symptoms.8 The REasons for Geographic And Racial Differences in Stroke (REGARDS) study provides an opportunity to assess self-reported stroke symptoms and the association of these symptoms with well-established stroke risk factors in a national population sample that included a large African American population.

**METHODS**

Beginning in January 2003, a national cohort of community-dwelling individuals older than 45 years were recruited, with approximately equal representation of white and African American individuals and men and women.9 Twenty percent of the sample was randomly selected from the “buckle” of the stroke belt (coastal plain region of North Carolina, South Carolina, and Georgia), 30% from the stroke belt states (remainder of North Carolina, South Carolina, and Georgia plus Alabama, Mississippi, Tennessee, Arkansas, and Louisiana), and the remaining 50% from the other 42 contiguous states. Individuals were identified from commercially available lists of residents and recruited using an initial mailing followed by telephone contact. Using a computer-assisted telephone interview, trained interviewers obtained demographic information, medical history, and indexes of quality of life. Consent was obtained verbally and later in writing. A brief physical examination, including blood pressure measurements, blood samples, and an electrocardiogram (ECG), was conducted in person 3 to 4 weeks after the telephone interview. The institutional review boards of the University of Alabama at Birmingham, University of Vermont and State Agricultural College (Burlington), Wake Forest University School of Medicine (Winston-Salem, NC), Alabama Neurological Institute (Brookwood Medical Center), and University of Alabama at Birmingham, University of Vermont and State Agricultural College (Burlington) approved the study methods. Additional methodological details are provided elsewhere.9

Participants were asked if a health care professional had ever told them that they had had a stroke or TIA and whether they had ever experienced the sudden onset of each of 6 stroke symptoms using the Questionnaire for Verifying Stroke-Free Status (QVSFS) (Table 1).10-12 The QVSFS is a validated questionnaire proposed as a quick screening instrument for identification of stroke-free individuals in a general population. This instrument was shown to be sensitive (sensitivity, 0.97), although specificity is only modest (specificity, 0.60).13 Prevalent stroke symptoms were defined as answering yes to 1 or more symptoms vs no to all symptoms. The Framingham Stroke Risk Score (FSRS), which estimates the 10-year probability of stroke given the participant’s demographic and risk factor profile, was used as a summary index of the stroke risk factor burden for each participant. This risk score includes age, sex, systolic blood pressure, use of antihypertensive medications, current smoking status, history of heart disease, diabetes, left ventricular hypertrophy, and atrial fibrillation.14-16 Systolic blood pressure was defined as the average of 2 measurements obtained by a trained technician using a standard protocol and regularly tested aneroid sphygmomanometer, measured after the participant was seated for 5 minutes. History of heart disease was defined as any self-reported myocardial infarction or “heart attack,” coronary artery bypass surgery, coronary angioplasty or stenting, or evidence of myocardial infarction from ECG. Diabetes was defined as a fasting glucose level greater than 126 mg/dL (7.0 mmol/L), nonfasting glucose level greater than 200 mg/dL (11.1 mmol/L), or self-reported medication use for glucose control. Left ventricular hypertrophy was defined by centrally adjudicated ECG. Atrial fibrillation was assessed by self-report or the study ECG. Age, race, sex, use of antihypertensive therapy, educational level, annual family income, health insurance, and perceived health status were defined on the basis of interview data.

Between January 25, 2003, and November 30, 2005, 191 028 telephone numbers called to recruit participants had a final disposition. Defined according to standards recommended by Morton et al,13 the response rate (percentage agreeing to be interviewed among known eligible candidates contacted plus an adjustment for estimate of likely eligible participants among unknown eligible participants) was 40.7% (31 356/77 526). At the time of this analysis, 20 677 participants completed both the telephone survey and in-person component; in-person examinations were pending for 2314, and 8565 participants could not or did not complete the in-home examination. Participants who self-reported either stroke or TIA were excluded (2215), resulting in an analysis cohort of 18 462 participants.

Logistic regression was used to establish the association of prevalent stroke symptoms with age, sex, race, region (stroke belt, stroke buckle, or other), and the FSRS. Along with these factors, the potential confounders of educational level, annual family income, health insurance, and perceived health status were evaluated using multivariate analysis. The FSRS includes items that reflect both age and traditional stroke risk factors. Because we anticipated that the prevalence of stroke symptoms would increase with age, it would not have been clear whether an association between stroke symptoms and the FSRS would be attributable to an association with age or to the other risk factors that are included in the FSRS. In multivariate analysis, the association with the FSRS was assessed after adjustment for age, allowing these associations to be attributable to the risk factors independent of age (since association with age was removed by covariate adjustment).

Table 1 gives the baseline characteristics, stroke risk factors, and FSRSs. A total of 7567 (41.0%) of the participants were African American, 9463 (51.3%) were women,
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pants, with the most common symptom being “a sud-
tremely significant difference that was only partially mediated by the adjustment for other factors in the multivariate model. In both the univariate and multivariate models, the presence of symptoms was not significantly different between the stroke belt and the rest of the United States. The odds of 1 or more symptoms was 1.2 times greater among women than men in the univariate model; however, multivariate adjustment mediated this difference. The likelihood of symptoms was not associated with age in the univariate model but was lower among older par-
ticipants in the multivariate model (notably the FSRS, which also includes age in the formulation). In univariate analysis, the prevalence of 1 or more stroke symp-
toms was more common among participants in lower socio-
economic status strata, as indexed by an income of less than $25,000, educational level of less than a high school diploma, or the absence of health insurance. In multivariate analysis, this association persisted for both income and educational level but not for health insurance. In both analyses, those with fair or poor perceived general health were more likely to have 1 or more stroke symptoms than those with excellent, very good, or good perceived general health.

Table 3 provides a description of the prevalence of each of the stroke symptoms overall and by race and sex strata, age strata, and region. One or more stroke symp-
toms were reported by 3292 (17.8%) of 18,462 partici-
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toms was significantly higher among those in the stroke belt for 2 of the 6 symptoms. Table 4 provides the dis-
tribution of the total number of symptoms, with 11.0% having 1 symptom, 5.0% having 2, 1.0% having 3, and less than 1% having 4 or more symptoms.

Results of the univariate and multivariate logistic regres-
sion models predicting 1 or more symptoms are provided in Table 5. In the univariate model, there was a higher likelihood of the presence of symptoms among participants with higher FSRSs, a relationship that was maintained in the multivariate model. Additionally, the odds of 1 or more symptoms was 1.6 times greater among African American than white participants, a statistically significant difference that was only partially mediated by the adjustment for other factors in the multivariate model. In both the univariate and multivariate models, the presence

Abbreviations: ECG, echocardiography; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; REGARDS, Reasons for Geographic And Racial Differences in Stroke.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113.

*Data are presented as number (percentage) of participants unless otherwise indicated; continuous variables are expressed as mean (SD).
†Variables included in the Framingham Stroke Risk Score.
‡Calculated as weight in kilograms divided by the square of height in meters.
§History of heart disease is defined as self-reported myocardial infarction, coronary bypass surgery, coronary angioplasty or stenting, or evidence of myocardial infarction from ECG.

and 6534 (35.4%) resided in the stroke belt. The overall mean (SD) age was 65.8 (9.0) years, with a range of 45 to 96 years.

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ralysis, numbness or tingling, and dizziness or loss of balance. Of 12,205 participants, 47% reported the sudden onset of at least 1 stroke symptom during their lifetime. In the Renfrew/Paisley Study, 15,113 participants were asked if they had ever experienced, without warning, any of the following 4 symptoms, assumed to be indicative of TIA: suddenly lost power of an arm, suddenly lost power of a leg, suddenly been unable to speak properly, or suddenly lost consciousness. Table 6 contrasts the prevalence of stroke and TIA symptoms in these 3 studies. Although the prevalence of several symptoms was comparable across studies, differences in the wording of some questions make comparisons problematic. Each study asked about speech problems, with 3.8% of REGARDS participants reporting a sudden loss of ability to express yourself verbally or in writing and 2.6% of ARIC participants reporting a speech dysfunction compared with only 1.8% of the Renfrew/Paisley Study participants reporting the inability to speak properly. The prevalence of weakness was 5.8% in REGARDS, weakness or paralysis prevalence was 2.3% in ARIC, and the prevalence of lost power of an arm or leg was 2.3% and 2.4%, respectively, in the Renfrew/Paisley Study; however, REGARDS specified unilateral symptoms and did not ask about painless numbness or tingling, whereas ARIC did not restrict symptoms to unilateral events and included paralysis. Both REGARDS and ARIC asked about numbness, reporting an 8.5% prevalence in REGARDS and about twice that in ARIC; however, REGARDS specified unilateral symptoms, whereas ARIC did not. In addition, REGARDS asked about “numbness or a dead feeling,” whereas ARIC asked about “numbness or tingling.” Tingling is a symptom that connotes a peripheral neuropathic process rather than focal cerebral ischemia. Both ARIC and REGARDS asked about visual symptoms; however, the format of these questions makes the results difficult to contrast. Additionally, the presence of 1 or more symptoms was higher in ARIC, largely from the question asking about dizziness (not asked in REGARDS or the Renfrew/Paisley Study); however, it is uncertain whether this finding represents a true difference between the populations or differences in the questions.

The ARIC investigators have further classified symptoms into TIA or stroke or not, based on a validated TIA or stroke algorithm, and found a prevalence of 12.9%. Although the same algorithm cannot be applied to REGARDS because the stroke symptom questions were not the same, it can be projected that some of the REGARDS participants who reported at least 1 stroke symptom either had a mild stroke or TIA that was not diagnosed or they do not recall the physician diagnosis. The strong association with the FSRS supports the theory that these are likely to be stroke events in at least a subset of the population with symptoms.

Certainly, many of the symptoms assessed in this study do not reflect stroke. For example, in REGARDS, during follow-up, the same QVSFS is administered semi-annually, with the retrieval of medical records for any participant who answers positively to any of the 6 symptom questions and reports going to a physician or being hospitalized for the symptom. During the tracking process, many nonstroke causes for these symptoms were identified. For “sudden painless weakness” or “sudden numbness or a dead feeling,” some participants have potential alternative explanations for the symptoms, such as surgery or a condition related to the hip or spine. For “sudden painless loss of vision,” some participants reported ocular conditions or procedures that could explain the symptoms, including cataracts, glaucoma, eye surgery, and eye examinations. This experience is consistent with prior validation studies of the QVSFS that showed it to have high sensitivity but modest specificity with regard to detecting stroke symptoms.
mimics are excluded, physicians may wish to control vas-
lar validation has been performed for the FSRS.
creased risk. We have also assumed that the FSRS is a
strokes. A 2003 national random sample of 1024 women 25 years and older found
that correct identification of the warning signs of stroke was low across all racial/ethnic and age groups; knowl-
edge of warning signs ranged from 2% to 8% for the symp-
tom of disorientation to 11% to 23% for sudden dim-
ness or loss of vision to 29% to 39% for sudden unilateral weakness or numbness of the face or limb.

Strengths of this work include the use of a national general population sample with a large African American population; however, it is always possible that those choosing to participate in any study could be nonrepresentative of the general population. An unknown number of eligible individuals may have been missed because of the inability to determine eligibility in some of the households contacted. A potential bias also exists in that approximately 27% of the participants who initially consented by telephone could not or did not continue to the in-person examination. Although this would affect the estimate of the prevalence of stroke symptoms, it plays a minor role in the association of symptoms with stroke risk factors. The use of the QVSFS, a validated instrument for the identification of stroke-free individuals, is a strength of the study. Although we can only speculate that some proportion of those reporting symptoms have actually experienced a stroke, this link will be strengthened in the future as neurologist-adjudicated incident stroke events become available through the follow-up of the REGARDS cohort. In ARIC, participants with these self-reported stroke symptoms had a 2.8-fold greater risk of a subsequent clinically diagnosed stroke. Similarly, in the Renfrew/Paisley Study, men with 2 or more stroke symptoms had a 2.3-fold increased risk for clinically diagnosed stroke, whereas women had a 2.4-fold increased risk. We have also assumed that the FSRS is a valid index of stroke risk in a biracial national cohort. Although the Framingham Coronary Heart Disease Risk Score has been validated in multiethnic groups, no similar validation has been performed for the FSRS.

When evaluating a person who screens positively for stroke symptoms but is not otherwise known to have had either stroke or TIA, it may be appropriate to evaluate the person with head imaging for evidence of prior cerebral infarction or an alternative origin for the symptoms. If stroke mimics are excluded, physicians may wish to control vascular risk factors in accordance with secondary stroke prevention guidelines and even consider screening for symptomatic cervical carotid stenosis that might warrant revascularization. However, as yet no evidence exists that screening for stroke symptoms is associated with improved stroke or other outcomes on a population basis.

In this article, we have demonstrated a strong association between the presence of stroke symptoms and the stroke risk factor burden as indexed by the FSRS. Coupled with previous reports showing a substantially increased risk of a subsequent stroke in those with stroke symptoms and a substantial prevalence of silent stroke according to MRI, our findings suggest that these commonly reported symptoms may be mild strokes that failed to reach the threshold for clinical diagnosis. Targeted education on the warning signs of stroke and risk factor reduction efforts for individuals who report stroke symptoms may be helpful in improving early recognition and in the prevention of stroke.

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Correspondence: Virginia J. Howard, MSPH, Department of Epidemiology, University of Alabama at Birmingham School of Public Health, 1665 University Blvd, Birmingham, AL 35294-0022 (vjhoward@uab.edu).

Author Contributions: Ms Howard and Dr McClure had access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Howard. Acquisition of data: Howard, McClure, and Pulley. Analysis and interpretation of data: Howard, McClure, Meschia, and Friday. Drafting of the manuscript: Howard, McClure, and Meschia. Critical revision of the manuscript for important intellectual content: Howard, McClure, Meschia, Pulley, Orr, and Friday. Statistical analysis: McClure. Obtained funding: Howard. Administrative, technical, and material support: Howard, Meschia, and Pulley. Study supervision: Howard.

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