



Apparent Treatment-resistant Hypertension Among Individuals with History of Stroke or Transient Ischemic Attack

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ABSTRACT

BACKGROUND: Blood pressure control is a paramount goal in secondary stroke prevention; however, high prevalence of uncontrolled blood pressure and use of multiple antihypertensive medication classes in stroke patients suggest this goal is not being met. We determined the prevalence and factors associated with apparent treatment-resistant hypertension in persons with/without stroke or transient ischemic attack.

METHODS: Data came from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national, population-based cohort of 30,239 black and white adults aged ≥ 45 years, enrolled 2003-2007, restricted to 11,719 participants with treated hypertension. Apparent treatment-resistant hypertension was defined as (1) uncontrolled blood pressure (systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg) with ≥ 3 antihypertensive medication classes, or (2) use of ≥ 4 antihypertensive medication classes, regardless of blood pressure level. Poisson regression was used to calculate characteristics associated with apparent treatment-resistant hypertension.

RESULTS: Among hypertensive participants, prevalence of apparent treatment-resistant hypertension was 24.9% (422 of 1694) and 17.0% (1708 of 10,025) in individuals with and without history of stroke or transient ischemic attack, respectively. After adjustment for cardiovascular risk factors, the prevalence ratio for apparent treatment-resistant hypertension for those with versus without stroke or transient ischemic attack was 1.14 (95% confidence interval, 1.03-1.27). Among hypertensive participants with stroke or transient attack, male sex, black race, larger waist circumference, longer duration of hypertension, and reduced kidney function were associated with apparent treatment-resistant hypertension.

CONCLUSIONS: The high prevalence of apparent treatment-resistant hypertension among hypertensive persons with history of stroke or transient ischemic attack suggests the need for more individualized blood pressure monitoring and management.

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KEYWORDS: Predictors; Prevalence; Resistant hypertension; Secondary prevention; Stroke; Transient ischemic attack

Funding: The REasons for Geographic And Racial Differences in Stroke (REGARDS) research project is supported by cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, U.S. Department of Health and Human Services. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health. Representatives of the funding agency have been involved in the review of the manuscript but not directly involved in the collection, management, analysis or interpretation of the data. The authors thank the other investigators, the staff, and the participants of the

REGARDS study for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at <http://www.regardsstudy.org>.

Conflict of Interest: None.

Authorship: VJH, RMT, and PM had access to the data. All authors had a role in writing the manuscript.

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Hypertension is considered to be the most important risk factor for primary and secondary stroke prevention.^{1,2} In persons with history of stroke, the prevalence of hypertension is high, with estimates ranging from 70% to 82%.³⁻⁷ Although there have been few clinical trials examining blood pressure (BP) treatment in secondary prevention, meta-analyses of such trials show that risk of recurrent stroke is reduced with antihypertensive medications.⁸⁻¹⁰ American Heart Association/American Stroke Association guidelines recommend BP reduction for prevention of recurrent stroke as well as prevention of other vascular events in persons who have had an ischemic stroke or transient ischemic attack (TIA).^{1,2}

Control of BP after stroke is a substantial challenge. Reports of risk factor management in stroke survivors have described low prevalence of BP control.^{5,7,11-16} Among 2830 black and white participants in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study who reported a physician diagnosis of stroke or TIA, 2200 (78%) were being treated for hypertension, but 732 (33.3%) had uncontrolled BP (ie, systolic blood pressure [SBP] ≥ 140 mm Hg or diastolic blood pressure [DBP] ≥ 90 mm Hg).¹² Uncontrolled hypertension among black stroke survivors is a particular challenge.^{12,15,16} Reasons for this are multifactorial and include medication nonadherence/nonpersistence/nonfulfillment due to costs, side effects, complexity of treatment regimen, not receiving regular medical care, treatment-resistant hypertension, and lack of healthy behaviors such as physical activity.¹⁷⁻¹⁹ Because stroke is considered a cardiac risk equivalent, such a comorbid condition increases the complexity of treating hypertension.^{20,21}

Apparent treatment-resistant hypertension is defined as uncontrolled BP on 3 or more antihypertensive medication classes or, regardless of BP, being on 4 or more antihypertensive medication classes.¹⁹ There are few studies on the burden of apparent treatment-resistant hypertension in secondary stroke prevention. The objective of this study was to determine the prevalence and factors associated with apparent treatment-resistant hypertension among those with a history of stroke or TIA in the REGARDS cohort.

METHODS

REGARDS is a national, population-based cohort study of 30,239 community-dwelling individuals, aged ≥ 45 years at enrollment in 2003-2007. Details of methods have been previously described.^{22,23} REGARDS was designed to

investigate causes of regional and black-white disparities in stroke mortality with oversampling of blacks and residents of the “buckle” of the Stroke Belt²⁴ (coastal plain region of North Carolina, South Carolina, and Georgia), and the rest of the Stroke Belt²⁵ (remainder of North Carolina, South Carolina, and Georgia, plus Alabama, Mississippi, Tennessee, Arkansas, and Louisiana). Individuals were randomly selected from a commercially available list and contacted by mail, followed by telephone for recruitment and verbal consent. Exclusion criteria included self-reported medical conditions (such as cancer) that would prevent long-term participation, or being on a waiting list for a nursing home. The final sample comprised 21% from the stroke buckle, 35% from the rest of stroke belt area, and 44% from the other 40 contiguous states, and was 42% black, 55% female. Using a computer-assisted telephone interview, trained interviewers obtained demographics, medical history, and risk factors. A brief physical examination including

BP measurements, blood and urine samples, and an electrocardiogram was conducted during an in-home visit 3 to 4 weeks after the telephone interview. Participants were asked to provide all prescription and nonprescription medications they had taken in the past 2 weeks, and medication names (but not dosages) were recorded during the in-home visit. Written consent was obtained during the in-person evaluation. Biological samples were stored and analyzed at the central laboratory at the University of Vermont, and electrocardiograms were read centrally by electrocardiographers at Wake Forest University who were blinded to clinical data. The institutional review boards of participating institutions approved the study methods. The primary analysis for this report was limited to participants who reported history of hypertension with concurrent use of antihypertensive medication determined from medication inventory ($n = 15,004$.) We excluded participants missing data on SBP or DBP ($n = 87$), history of stroke or TIA ($n = 221$), or self-reported antihypertensive medication use ($n = 23$), reducing the number to 14,673. The primary analysis cohort consisted of 11,719, excluding participants with uncontrolled hypertension who were taking 1 or 2 antihypertensive medications ($n = 2954$) because they did not meet criteria for apparent treatment-resistant hypertension; however, these individuals were included in secondary analysis described below.

During the in-person examination, 2 BP measurements were taken by a trained technician using a standard protocol and regularly tested aneroid sphygmomanometer (American

CLINICAL SIGNIFICANCE

- Among hypertensive participants with stroke/transient ischemic attack, after multivariable adjustment, male sex, black race, larger waist circumference, longer duration of hypertension, and reduced kidney function were associated with higher prevalence of apparent treatment-resistant hypertension.
- Sensitivity analysis of only those participants with a stroke or transient attack whose medications included a diuretic resulted in attenuation of the increased risk of apparent treatment-resistant hypertension for blacks but not whites.

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