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Is there an association between the prevalence of atrial fibrillation and severity and control of hypertension? The REasons for Geographic And Racial Differences in Stroke (REGARDS) study

Hemal Bhatt, MD¹, Christopher M. Gamboa, MPH², Monika M. Safford, MD^{2,3}, Elsayed Z. Soliman, MD⁴, and Stephen P. Glasser, MD²

¹Division of Cardiovascular Disease, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama

²Division of Preventive Medicine, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama

³Division of General Internal Medicine, Weill Cornell Medical College, New York, NY

⁴Division of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, North Carolina

Abstract

Background—The association of atrial fibrillation (AF) with the severity and control of hypertension (HTN) remains unclear.

Methods—We analyzed data from the national biracial cohort of REasons for Geographic And Racial Differences in Stroke (REGARDS) study. The AF prevalence ratios were estimated and full multi-variable adjustment included demographics, risk factors, medication adherence, HTN duration and antihypertensive medication classes.

Results—Of the 30,018 study participants (8.6% with AF), 4,386 had normotension (4.3% with AF), 5,916 had prehypertension (4.3 with AF%), 12,294 had controlled HTN (11.2% with AF), 5,587 had uncontrolled HTN (8.1% with AF), 547 had controlled apparent treatment resistant hypertension (aTRH) (19.2% with AF), and 1288 had uncontrolled aTRH (15.5% with AF). Compared with normotension, the AF prevalence ratios for prehypertension, controlled HTN, uncontrolled HTN, controlled aTRH and uncontrolled aTRH groups in fully adjusted model were 1.01 (95% CI 0.84 – 1.21), 1.42 (1.18 – 1.71), 1.37 (1.14 – 1.65), 1.17 (0.86 – 1.58) and 1.42 (1.10 – 1.84) respectively ($p < 0.001$).

Corresponding Author: Hemal Bhatt, MD, Department of Vascular Biology and Hypertension, Division of Cardiovascular Disease, University of Alabama at Birmingham, Room 115, 933 19th Street South, Birmingham, AL 35294, Phone: 205-934-9281, cardiothorax@gmail.com.

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Conclusion—The prevalence of AF was similar among persons with HTN regardless of BP level and antihypertensive treatment resistance.

Keywords

Atrial fibrillation; treatment resistant hypertension; blood pressure; antihypertensive medications; beta-blockers

Introduction

Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, increases the risk of stroke, heart failure and all-cause mortality.^{1,2} Systemic hypertension (HTN) is a major modifiable risk factor for AF.^{3–8} Left ventricular diastolic dysfunction from long standing HTN leads to left atrial remodeling and dilation resulting in increased AF risk.^{3,4,9–11} Prehypertension, defined as systolic blood pressure (SBP) 120–139 mmHg and/or diastolic blood pressure (DBP) of 80–89 mmHg has been associated with the development of frank HTN and AF.^{12,13,14} Increased prevalence of prehypertension has been associated with aging and black race,¹⁵ but the impact of age, race, and gender on the association of prehypertension and AF remains unknown. Resistant HTN, an extreme phenotype of HTN, is defined as SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg on $\geq$ 3 antihypertensive medication classes.¹⁶ The term apparent treatment resistant HTN (aTRH) has been used in epidemiologic studies to describe cases of resistant HTN in which pseudoresistance (i.e., falsely labelled as having resistant HTN) is not reliably excluded.

Apparent TRH is further classified into controlled aTRH (SBP $<$ 140 mmHg and DBP $<$ 90 mmHg on $\geq$ 4 antihypertensive medication classes) and uncontrolled aTRH (SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg with $\geq$ 3 antihypertensive medication classes).^{17,18} In persons with HTN, the prevalence of AF has been reported to be higher among those with uncontrolled HTN compared to controlled HTN.⁸ Antihypertensive medications such as beta-blockers and angiotensin converting enzyme inhibitors (ACE-I) are associated with decreased AF risk.^{19–21} However, the prevalence of AF among hypertensive persons with treatment resistance based on the number of antihypertensive medications used and BP control remains unknown.

In this study, using data from the REasons for Geographic and Racial Disparities in Stroke (REGARDS) study, we determined the cross sectional association between AF and BP level and HTN severity (defined by the number of antihypertensive medication class used). We hypothesized that the prevalence of AF would increase with increasing HTN severity and poorer BP control; we further investigated differences in this association by age, gender, race and geographical region.

Methods

REGARDS is a longitudinal study designed to investigate factors contributing to excess stroke mortality across the southeastern United States (US) and among blacks. The details of REGARDS sample and study recruitment have been previously described.²² Briefly, the REGARDS study includes a cohort of 30,239 black and white adult's $\geq$ 45 years old

recruited from the 48 continental US states between January 2003 and October 2007. The study was designed to balance on gender and race, with oversampling from regions in the Southeastern US with high stroke incidence. The final cohort included 55% women, 42% blacks, and 55% in the stroke belt (defined as North Carolina, South Carolina, Georgia, Alabama, Mississippi, Arkansas, Tennessee and Louisiana). Briefly, participants were recruited via mail and telephone. Trained personnel using computer-assisted telephone interview obtained baseline demographic information and medical history. Anthropometric and BP measurements, venous blood samples, brief physical exam, electrocardiogram, and pill bottle review of medications were conducted during the in-home visit 3–4 weeks after the telephone interview. All participants provided written informed consent and the study protocol was approved by the participating Institutional Review Boards.

Blood pressure measurements

BP was taken by trained examiners using android sphygmomanometer. BP was measured twice following a standard protocol. All participants were asked to sit for 5 minutes with feet on floor prior to BP measurement, and there was a 30-second interval between measurements. The average of two readings was calculated. BP quality was monitored by central examination of digit preference and retraining of personnel as needed.

Definition of groups based on BP and antihypertensive treatment

We stratified the cohort into 6 mutually exclusive groups based on BP control and number of antihypertensive medications used. We defined normotension as SBP < 120 mmHg and DBP < 80 mmHg without antihypertensive medication use; prehypertension as SBP 120 – 139 mmHg and/or DBP 80 – 89 mmHg without antihypertensive medication use¹²; controlled HTN as SBP < 140 mmHg and DBP < 90 mm Hg on 3 classes of antihypertensive medications²³; uncontrolled HTN as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on none or < 3 classes of antihypertensive medications; controlled aTRH as SBP < 140 mmHg and DBP < 90 mm Hg on 4 classes of antihypertensive medications and uncontrolled aTRH as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on 3 classes of antihypertensive medications.

AF ascertainment

Details of AF ascertainment in REGARDS have been previously reported.²⁴ Briefly, baseline AF was determined using: 1) self-reported AF during computer-assisted telephone surveys based on history of physician diagnosis of AF; and 2) electrocardiogram (ECG) obtained during in-home visit that was centrally read by electrocardiographers blinded to clinical data.

Covariates

Demographics included age, race, and sex. Geographic regions of stroke prevalence (stroke belt, stroke buckle and non-belt) were also included. Measures of socioeconomic status included annual household income (< \$35,000 or ≥ \$35,000) and highest level of education attained (less than high school, high school completion or higher). Cardiovascular risk factors included exercise (any vs none), current smoking, heavy alcohol use (defined by National Institute on Alcohol Abuse and Alcoholism as: ≥ 7 drinks/week for women and

14 drinks/week for men),²⁵ diabetes (fasting glucose ≥ 126 mg/dl or non-fasting glucose ≥ 200 mg/dl or self-reported history of diabetes mellitus or use of diabetic medications), self-reported history of coronary heart disease, stroke or transient ischemic attack, renal function as urine albumin/creatinine ≥ 30 mg/g, waist circumference; serum low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides and total cholesterol levels and high-sensitivity C-reactive protein (CRP) levels. The presence of left ventricular hypertrophy (LVH) was determined based on the ECG Cornell LVH criteria. Medication adherence was determined based on the standard Morisky Medication Adherence Score.²⁶ HTN duration was determined based on the self-reported history of short, medium, and long-term (i.e., < 10 , $10 - 20$ and > 20 years respectively). Comorbidities and medication use were included as listed in Table 1.

Statistical analysis

Descriptive statistics included proportions, means and standard deviations, and medians and 25th and 75th percentiles where appropriate. Prevalence ratios (PR) for AF were calculated using Poisson regression with a robust variance estimator. Models were constructed among the 6 BP groups sequentially using an unadjusted model 1; model 2 adjusted for age, race, gender, income, education, and stroke region; model 3 adjusted for model 2 covariates and current smoking, exercise, alcohol use, diabetes mellitus, albumin-creatinine ratio, waist circumference, LVH, aspirin use, statin use, warfarin use, log-transformed CRP, and total cholesterol to HDL-C ratio; model 4 adjusted for model 3 covariates and HTN duration (short, medium and long); model 5 adjusted for model 4 and use of antihypertensive medication classes such as beta-blockers, calcium channel blockers, ACE-I/angiotensin receptor blockers, mineralocorticoid antagonists and diuretics. Additional model adjusting for model 5 and medication adherence, history of coronary heart disease (CHD), stroke or transient ischemic attack was assessed. Subgroup analyses were performed to evaluate effect modification by age (< 70 vs ≥ 70 years), race (white vs black), gender (female vs male) and geographic region (stroke belt vs non-stroke belt). Statistical significance was defined as $p < 0.05$ for all comparisons. SAS version V9.3 (Cary, NC) was used for all the analyses.

Results

From the overall sample of 30,183 participants, those with no data on AF, SBP or medication bottle count were excluded, resulting in a final sample size of 30,018 participants. Table 1 shows the baseline characteristics and demographics of the study cohort. The prevalence of AF was similar in the normotension and prehypertension groups. The prevalence of AF was higher in aTRH groups (controlled $>$ uncontrolled) compared with HTN groups. The prevalence of AF in blacks, those with less than high school education, and a higher albumin-to-creatinine ratio increased across the BP groups based on increasing HTN severity and BP level.

Table 2 shows the unadjusted and adjusted prevalence of AF across BP groups with normotension as the reference group. In the unadjusted model, the prevalence of AF was higher among persons with aTRH (controlled and uncontrolled) compared to those with prehypertension, controlled HTN, and uncontrolled HTN. Among persons with aTRH, those

with controlled aTRH had a higher prevalence of AF than uncontrolled aTRH. Among persons with HTN, those with controlled HTN had a higher prevalence of AF than uncontrolled HTN.

After adjusting for demographics, cardiovascular risk factors, and HTN duration in model 4, the magnitude of the differences in AF prevalence between HTN (controlled and uncontrolled) and aTRH (controlled and uncontrolled) groups attenuated. AF prevalence was similar in both the pre-HTN and normotension (reference) groups. The prevalence was also similar in controlled and uncontrolled aTRH groups (PR 2.37 and 2.39, respectively). We assessed the sequential impact of antihypertensive medications on the prevalence of AF when added one at a time to model 4 (Supplemental Table 1). Of all the antihypertensive medication classes, the use of beta-blockers (model 4a) had a substantial impact on decreasing AF prevalence, especially in the controlled and uncontrolled aTRH groups. After full adjustment (model 5), the prevalence of AF was similar in controlled HTN (PR 1.42), uncontrolled HTN (PR 1.37) and uncontrolled aTRH (PR 1.42). The prevalence of AF was lowest in controlled aTRH (PR 1.17) compared with other HTN groups, but was still higher than the normotension and prehypertension groups. AF prevalence was similar across all BP groups when adjusted for medication adherence and a history of CHD or stroke/transient ischemic attack (data not shown).

When stratified by age (< 70 years and ≥ 70 years), in an unadjusted model, AF prevalence was higher among all HTN groups, and AF prevalence was higher among aTRH groups compared with the other HTN groups. However, among persons ≥ 70 years, these differences attenuated after full adjustment (Supplemental table 2). There was no evidence of effect modification by age (Supplemental table 3).

When stratified by race in the unadjusted model among both whites and blacks, compared with normotension, the AF prevalence was higher in all HTN groups, especially aTRH. However, in blacks, these differences attenuated in the fully adjusted model. Among whites, AF prevalence was higher among HTN groups (both controlled and uncontrolled) compared to aTRH groups (Supplemental Table 4). In interaction testing, after full adjustment the AF prevalence was higher among blacks than whites in persons with aTRH ($p = 0.04$, Supplemental Table 3). There was no evidence of effect modification by gender or region.

Discussion

The current study shows that compared to normotension, prehypertension was not associated with increased AF prevalence. The prevalence of AF was higher in hypertensive persons compared to those without HTN, but the severity and control of HTN was not associated with AF prevalence. The combination of antihypertensive medications, and beta-blockers alone, had a significant impact on AF prevalence across all BP groups. Blacks with controlled aTRH had a higher prevalence of AF compared with whites. Gender, age and geographic region had no impact on the association of AF prevalence based on HTN severity and BP control.

In some studies, prehypertension has been associated with increased risk of incident AF,^{14,27,28} but the current study did not show an association between prehypertension and prevalent AF. These findings were consistent when stratified by age, race, gender, and region. One of the explanations for the current findings may be that in the current study, we did not assess the duration of prehypertension duration.

The association between HTN and AF is well-established. Long-standing HTN is associated with left ventricular hypertrophy and diastolic dysfunction and resultant left atrial remodeling.

Persistent activation of the renin angiotensin aldosterone system also contributes to left atrial hypertrophy and fibrosis resulting in left atrial remodeling.^{9–11} The association of AF and HTN based on both treatment resistance and BP level has not been previously investigated. Several studies have described a positive association of uncontrolled BP and AF.^{8,14,27,29} For example, Grundvold et al described higher AF risk among men with baseline uncontrolled SBP (≥ 140 mmHg) or DBP (≥ 80 mmHg) compared to those with controlled BP.¹⁴ Vyssoulis G et al reported increased prevalence of AF with increasing SBP in persons with essential HTN.²⁹ But, none of the aforementioned studies have stratified hypertensive persons based on antihypertensive treatment resistance and have not taken antihypertensive medication classes into account. In the current study, we stratified persons with HTN into distinct categories based on BP level and treatment resistance. This is important, because recent studies have reported an association of aTRH with cardiovascular risk factors and adverse cardiovascular events.^{30,31} Since aTRH is associated with an increased risk for incident stroke,¹⁸ determining the prevalence of AF, also a major stroke risk factor, among persons with aTRH could possibly explain part of the increased risk.

The current study found a higher AF prevalence in hypertensive persons compared to those with normotension or prehypertension. However, the AF prevalence was similar among persons with HTN and aTRH regardless of BP control (i.e., $\geq 140/90$ mmHg vs $< 140/90$ mmHg). The above findings were obtained after adjusting for demographics, cardiovascular risk factors, medication adherence, HTN duration, and number of antihypertensive medications. In contrast to the literature, we adjusted for antihypertensive medications classes, which are known to affect the risk for AF. For example, beta-blockers and ACEIs/ARBs are associated with decreased AF risk. Beta-blockers may reduce the risk for AF by attenuating the effect of sympathetic nervous system on atrial automaticity and by ameliorating left ventricular and atrial remodeling.^{19–21} ACEIs/ARBs inhibit the activation of renin angiotensin aldosterone system and thereby reduce left atrial dilation and fibrosis, left ventricular hypertrophy and remodeling.^{19,20} In this study, beta-blocker use significantly decreased the prevalence of AF across all groups, especially among those with controlled aTRH. The impact of calcium channel blockers, ACE-I/ARBs, diuretics, and mineralocorticoid antagonists on AF prevalence was not substantial. After adjusting for antihypertensive medication classes, the prevalence of AF was similar among controlled HT, uncontrolled HT, and uncontrolled aTRH, and was lowest in the controlled aTRH group. Compared to other BP groups, the use of beta-blockers was highest among the controlled aTRH group (96.9%), which could possibly explain the lower AF prevalence.

The progression from HTN to uncontrolled or controlled aTRH occurs over time. In hypertensive patients, antihypertensive medications are usually titrated gradually depending on BP response; consequently, it may take few office visits before establishing the diagnosis of treatment resistant HTN.¹⁶ One of the explanations for our findings could be that atrial remodeling process in patients with aTRH may occur in early stages of HTN,³² which may lead to AF even before establishing the diagnosis of treatment resistant HTN. Moreover, treatment with certain antihypertensive medication classes and consequent BP control may reverse atrial remodeling thereby decreasing the risk of AF.^{33–36} However, in the current study, we assessed prevalent AF and did not assess the duration of HTN control in persons treated for HTN. Therefore, the impact of HTN control on AF prevalence could not be reliably assessed in our study. The impact of HTN control on reversal of atrial remodeling and subsequent risk of recurrent AF warrants further investigation. The current study findings suggest that the prevalence of AF remains similar among persons with HTN regardless of BP control and treatment resistance. Thus, having treatment resistance may not identify persons with an increased AF risk.

Aging, male gender, and white race have been associated with increased AF risk,^{15,16,37–39} but their impact on the association of AF and HTN based on severity and BP level remains unclear. In the current study, among persons < 70 years, those with HTN had increased prevalence of AF. Interestingly, among persons ≥ 70 years, having HTN was not associated with increased AF prevalence. Given that both HTN and aging are risk factors for AF, the above findings may possibly suggest that after a certain age, HTN has no additional impact on prevalent AF. Moreover, familial causes, obesity, alcohol, sports and physical activity are associated with AF in young adults, which may partly explain increased AF prevalence among persons < 70 years.^{40–44} In terms of race, we found that after full adjustment blacks compared with whites with controlled aTRH had a significantly higher prevalence of AF, suggesting that racial differences persist in controlled aTRH even after adjusting for known confounding factors. These findings are in contrast to the previous studies, which showed increased prevalence of AF in whites compared with blacks; however, these studies either excluded persons with RHTN or were not stratified based on BP control and treatment resistance.^{37–39} The presence of racial disparities in extreme HTN phenotypes, such as aTRH, needs further investigation. In addition, among whites, the increased AF prevalence among persons with HTN compared with aTRH is probably due to the impact of medications, especially beta-blockers. The current study did not find significant differences in the association of AF prevalence and BP severity based on gender and geographical regions. The absence of gender and geographical differences in AF prevalence among more severe forms of HTN warrants further investigation.

The strengths of our study include a previously unstudied assessment of prevalent AF after adjusting for antihypertensive medication classes and based on BP level and severity; a large biracial national cohort; BP measurement and AF ascertainment by trained personnel; lower recall bias related to medication data owing to pill bottle review; adjustment for antihypertensive medication adherence and HTN duration; and assessment of AF prevalence by age, race, gender, and stroke region. Our findings should be interpreted in the context of several limitations. This was a cross-sectional analysis of baseline data; therefore, changes over time could not be assessed. We did attempt to assess the duration of prior HTN as short,

medium and long-term, but the duration of preceding HTN could not be precisely obtained for each participant. AF ascertainment based on self-reported and ECG data may have potentially missed cases of paroxysmal AF. Other classes of antihypertensive medications such as vasodilators and centrally acting agents were not included in our analysis, but use of these agents was relatively uncommon and the association of these agents with AF remains unknown. The evidence of effect modification by race on AF prevalence in controlled aTRH group and lack of similar trend in other BP groups should be interpreted in context of study limitations. Due to lack of baseline data we could not assess the impact of transthoracic echocardiogram derived atrial size and duration of HTN control on atrial fibrillation prevalence. Finally, as is true with any observational study, we cannot rule out residual confounding by unmeasured covariates.

In conclusion, our study of a biracial national cohort demonstrated that prehypertension was not associated with prevalent AF. Having aTRH did not confer an increased risk of prevalent AF compared with persons without aTRH. These findings suggest a threshold effect on AF prevalence among hypertensive persons. That is, once the diagnosis of HTN is established, the risk of AF may remain the same regardless of BP level and severity. Antihypertensive medications, especially beta-blockers, significantly impact the prevalence of AF and must be taken into account when determining the association of HTN and AF. Our study emphasizes the need for continued efforts focused on HTN prevention to minimize AF risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Atrial fibrillation prevalence is not associated with prehypertension.
- Atrial fibrillation prevalence is associated with hypertension.
- Atrial fibrillation prevalence is not associated with treatment resistance.
- Atrial fibrillation prevalence is not associated with BP control in hypertension.

Baseline characteristics of the study participants

Table 1

Characteristics	Blood Pressure Groups					
	Overall	Normotension	Prehypertension	Controlled HTN	Uncontrolled HTN	Uncontrolled aTRH
Sample size	30,018	4,386	5,916	12,294	5,587	1,288
Atrial fibrillation, n (%)	2582 (8.6)	190 (4.3)	257 (4.3)	1377 (11.2)	453 (8.1)	200 (15.5)
Age, mean $\pm$ SD	64.9 $\pm$ 9.4	60.7 $\pm$ 8.9	62.9 $\pm$ 9.2	66.3 $\pm$ 9.2	66.1 $\pm$ 9.4	67.6 $\pm$ 8.8
Black, n (%)	12430 (41.4)	1099 (25.1)	1948 (32.9)	5429 (44.2)	2829 (50.6)	820 (63.7)
Male, n (%)	13484 (44.9)	1652 (37.7)	2988 (50.5)	5258 (42.8)	2759 (49.4)	582 (45.2)
Stroke region, n (%)						
<i>Non-belt</i>	13358 (44.5)	1948 (44.4)	2766 (46.8)	5289 (43.0)	2543 (45.5)	579 (45.0)
<i>Belt</i>	10381 (34.6)	1467 (33.4)	1973 (33.4)	4292 (34.9)	2002 (35.8)	458 (35.6)
<i>Buckle</i>	6279 (20.9)	971 (22.1)	1177 (19.9)	2713 (22.1)	1042 (18.7)	251 (19.5)
Annual household income, n (%)						
\$35,000	13598 (45.3)	2562 (58.4)	3137 (53.0)	5193 (42.2)	2096 (37.5)	404 (31.4)
< \$35,000	12715 (42.4)	1314 (30.0)	2067 (34.9)	5518 (44.9)	2833 (50.7)	712 (55.3)
<i>Declined to report</i>	3705 (12.3)	510 (11.6)	712 (12.0)	1583 (12.9)	658 (11.8)	172 (13.4)
Education less than high school, n (%)	3771 (12.6)	252 (5.8)	522 (8.8)	1705 (13.9)	912 (16.3)	283 (22.0)
Current smoking, n (%)	4370 (14.6)	728 (16.7)	845 (14.3)	1582 (12.9)	986 (17.7)	154 (12.0)
Any exercise, n (%)	19387 (65.6)	3105 (71.9)	4238 (72.8)	7590 (62.6)	3449 (62.8)	716 (56.6)
Heavy alcohol use, n (%)	1181 (4.0)	185 (4.3)	265 (4.6)	418 (3.5)	264 (4.8)	33 (2.6)
Diabetes, n (%)	7591 (25.3)	396 (9.0)	763 (12.9)	3920 (31.9)	1595 (28.5)	622 (48.3)
History of CHD, n (%)	5288 (17.6)	292 (6.7)	465 (7.9)	2888 (23.5)	969 (17.3)	445 (34.5)
History of stroke/TIA, n (%)	3023 (10.1)	167 (3.8)	251 (4.2)	1605 (13.1)	628 (11.3)	263 (20.4)
Ratio of albumin to creatinine 30 mg/g, n (%)	4353 (15.2)	223 (5.3)	480 (8.4)	1797 (15.5)	1262 (23.8)	448 (36.4)
Waist circumference, mean $\pm$ SD	96.2 $\pm$ 15.5	86.9 $\pm$ 13.4	93.8 $\pm$ 13.7	97.9 $\pm$ 15.1	99.5 $\pm$ 15.8	103.6 $\pm$ 16.8
Presence of LVH, n (%)						
<i>No</i>	19986 (66.6)	3354 (76.5)	4073 (68.8)	8196 (66.7)	3276 (58.6)	724 (56.2)
<i>Yes</i>	1042 (3.5)	36 (0.8)	93 (1.6)	462 (3.8)	281 (5.0)	133 (10.3)
<i>Not available</i>	8990 (29.9)	996 (22.7)	1750 (29.6)	3636 (29.6)	2030 (36.3)	431 (33.5)
Aspirin use, n (%)	12994 (43.3)	1250 (28.5)	1883 (31.8)	6409 (52.2)	2344 (42.0)	747 (58.0)

Characteristics	Blood Pressure Groups						
	Overall	Normotension	Prehypertension	Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH
Statin use, n (%)	9450 (31.5)	718 (16.4)	1037 (17.5)	5219 (42.5)	1518 (27.2)	311 (56.9)	647 (50.2)
Warfarin use, n (%)	1106 (3.7)	51 (1.2)	73 (1.2)	680 (5.5)	165 (3.0)	61 (11.2)	76 (5.9)
High-sensitivity C-reactive protein (mg/L), median [25th, 75th percentiles]	2.2 [1.0, 5.1]	1.4 [0.7, 3.4]	1.9 [0.8, 4.1]	2.5 [1.1, 5.8]	2.7 [1.1, 5.9]	2.9 [1.3, 6.4]	3.0 [1.3, 6.6]
Total Cholesterol, mean $\pm$ SD	192.1 $\pm$ 40.1	197.8 $\pm$ 38.2	199.4 $\pm$ 38.5	185.8 $\pm$ 39.4	197.1 $\pm$ 41.8	172.6 $\pm$ 39.2	184.6 $\pm$ 39.8
High-density lipoprotein cholesterol, mean $\pm$ SD	51.8 $\pm$ 16.1	55.9 $\pm$ 16.9	52.4 $\pm$ 16.0	50.5 $\pm$ 15.6	51.9 $\pm$ 16.7	45.9 $\pm$ 14.1	49.1 $\pm$ 14.1
Low-density lipoprotein cholesterol, mean $\pm$ SD	113.9 $\pm$ 34.6	119.0 $\pm$ 33.4	121.3 $\pm$ 33.6	108.0 $\pm$ 33.5	117.7 $\pm$ 36.1	98.2 $\pm$ 33.6	107.6 $\pm$ 34.9
Triglycerides	111 [81, 158]	97 [72, 136]	107 [80, 153]	115 [84, 164]	115.5 [83, 163]	117 [89, 176]	118 [87, 168]
Anti-hypertensive medication use, n (%)							
<i>Beta-blockers</i>	6797 (22.6)	0 (0.0)	0 (0.0)	4334 (35.3)	1017 (18.2)	530 (96.9)	916 (71.1)
<i>Calcium-channel blockers</i>	6179 (20.6)	0 (0.0)	0 (0.0)	3717 (30.2)	1090 (19.5)	491 (89.8)	881 (68.4)
<i>ACEI/ARBs</i>	10826 (36.1)	0 (0.0)	0 (0.0)	7230 (58.8)	1890 (33.8)	541 (98.9)	1165 (90.5)
<i>Mineralocorticoid receptor antagonists</i>	387 (1.3)	0 (0.0)	0 (0.0)	203 (1.7)	11 (0.2)	106 (19.4)	67 (5.2)
<i>Diuretics</i>	9191 (30.6)	0 (0.0)	0 (0.0)	6137 (49.9)	1386 (24.8)	539 (98.5)	1129 (87.7)

All p-values testing differences across blood pressure groups are < 0.001 .

Abbreviations: HT - hypertension; aTRH - apparent treatment resistant hypertension; CHD - coronary heart disease; TIA - transient ischemic attack; LVH - left ventricular hypertrophy; ACEI/ARBs - angiotensin converting enzyme inhibitor/angiotensin receptor blockers; SD - standard deviation

Table 2

Prevalence ratios (95% CI) comparing atrial fibrillation across blood pressure groups.

	Normotension	Prehypertension	Blood Pressure Groups				Uncontrolled aTRH	Uncontrolled aTRH	p
			Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH			
Atrial fibrillation (n)	190	257	1377	453	105	200	-	-	-
Total (n)	4,386	5,916	12,294	5,587	547	1,288	-	-	-
Model 1	1 (ref)	1.00 (0.83, 1.20)	2.59 (2.23, 3.00)	1.87 (1.59, 2.21)	4.43 (3.55, 5.53)	3.58 (2.97, 4.33)	<0.001	<0.001	<0.001
Model 2	1 (ref)	0.97 (0.81, 1.17)	2.41 (2.07, 2.80)	1.78 (1.51, 2.11)	4.20 (3.35, 5.25)	3.44 (2.83, 4.18)	<0.001	<0.001	<0.001
Model 3	1 (ref)	0.99 (0.83, 1.18)	1.90 (1.63, 2.21)	1.59 (1.35, 1.89)	2.50 (1.98, 3.15)	2.54 (2.08, 3.10)	<0.001	<0.001	<0.001
Model 4	1 (ref)	1.00 (0.83, 1.20)	1.88 (1.58, 2.24)	1.59 (1.33, 1.90)	2.37 (1.85, 3.03)	2.39 (1.92, 2.98)	<0.001	<0.001	<0.001
Model 4a									
(beta-blockers)	1 (ref)	1.00 (0.83, 1.20)	1.56 (1.31, 1.86)	1.42 (1.19, 1.71)	1.57 (1.22, 2.03)	1.72 (1.38, 2.16)	<0.001	<0.001	<0.001
Model 5	1 (ref)	1.01 (0.84, 1.21)	1.42 (1.18, 1.72)	1.37 (1.14, 1.65)	1.17 (0.86, 1.58)	1.42 (1.10, 1.84)	<0.001	<0.001	<0.001

Model 1 is unadjusted.

Model 2 adjusts for age, race, gender, region, income, and education.

Model 3 adjusts for Model 2 covariates + smoking, exercise, heavy alcohol use, diabetes, ACR, waist circumference, LVH, regular aspirin use, statin use, and warfarin use, log-transformed CRP, and total cholesterol : HDL-C ratio.

Model 4 adjusts for Model 3 covariates + duration of hypertension (short, medium, long, none).

Model 4a adjusts for Model 4 covariates + specified medication class.

Model 5 adjusts for Model 4 covariates + use of anti-hypertensive medications, including beta-blockers, calcium channel blockers, ACEI/ARBs, mineralocorticoid receptor antagonists, and diuretics.

Abbreviations: HTN - hypertension; aTRH - apparent treatment resistant hypertension; CHD - coronary heart disease; LVH - left ventricular hypertrophy; CRP - C reactive protein; ACEI/ARBs - angiotensin converting enzyme inhibitor/angiotensin receptor blockers; ACR - albumin to creatinine ratio; HDL-C high density lipoprotein cholesterol.