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Prevalence of electrocardiographic abnormalities based on hypertension severity and blood pressure levels: 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

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—We evaluated the prevalence of major and minor electrocardiographic (ECG) abnormalities based on blood pressure (BP) control and hypertension (HTN) treatment resistance.

Methods—We analyzed data from the REGARDS study of 20,932 participants who were divided into presence of major (n = 3,782), only minor (n = 8,944) or no (n = 8,206) ECG abnormalities. The cohort was stratified into normotension (n = 3,373), prehypertension (n = 4,142), controlled HTN (n = 8,619), uncontrolled HTN (n = 3,544), controlled apparent treatment resistant HTN (aTRH n = 400) and uncontrolled aTRH (n = 854) groups and the prevalence ratios (PR) of major and minor ECG abnormalities were assessed separately for each BP group. The full multi-variable adjustment included demographics, risk factors and HTN duration.

Results—Compared with normotension, the PRs of major ECG abnormalities for prehypertension, controlled HTN, uncontrolled HTN, controlled aTRH and uncontrolled aTRH groups were 1.01 (0.90 – 1.14), 1.30 (1.16 – 1.45), 1.37 (1.23 – 1.54), 1.42 (1.22 – 1.64) and 1.44 (1.26 – 1.65) respectively (p < 0.001), whereas, the PRs of minor ECG abnormalities among each of the above BP groups were similar.

Corresponding Author: Hemal Bhatt, MD, 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—Detection of major ECG abnormalities among hypertensive persons with poor control and treatment resistance may help improve their cardiovascular risk stratification and early intervention.

Keywords

Blood pressure; electrocardiographic abnormalities; apparent treatment resistant hypertension; hypertension severity

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Introduction

The presence of major and minor ECG abnormalities has been associated with an increased risk for coronary heart disease (CHD), stroke, cardiovascular (CV) mortality and sudden cardiac death.¹⁻¹² Given its relatively low cost and widespread availability, ECG serves as a valuable adjunctive tool to facilitate CV risk stratification and predict adverse CV outcomes, especially in asymptomatic individuals.^{1-4,9,11} The Minnesota coding system, commonly used to codify ECG abnormalities in epidemiologic studies, was classified into major and minor abnormalities.¹³⁻¹⁵ Black race and male gender has been associated with a greater prevalence of ECG abnormalities.^{8,16-20} The association of both major and minor ECG abnormalities with traditional CV risk factors, including hypertension (HTN), has been previously reported.^{17,21,24}

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 adverse CV events.²⁵⁻²⁸ However, the association of prehypertension and ECG abnormalities remains unknown. Resistant HTN, an extreme phenotype of HTN, is defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg on ≥3 antihypertensive medication classes.²⁹ 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 ≥4 antihypertensive medications) and uncontrolled aTRH (SBP ≥140 mmHg and/or DBP ≥90 mmHg with ≥3 antihypertensive medications).^{30,31} Although elevated SBP has been associated with a greater prevalence of ECG abnormalities, the prevalence of ECG abnormalities among hypertensive persons based on treatment resistance and BP control has not been previously reported.

In this study, using data from the REasons for Geographic and Racial Disparities in Stroke (REGARDS) study, we determined the cross sectional association between major and minor ECG abnormalities and BP levels and HTN severity (defined by the number of antihypertensive medication used). We hypothesized that the prevalence of ECG abnormalities would be greater with increasing HTN severity and poorer BP control; we further investigated the interaction of age, gender, race and geographical region on this association.

Methods

REGARDS is a longitudinal study designed to investigate factors contributing to excess stroke mortality across the southeastern US and among blacks. The REGARDS study includes a cohort of 30,239 black and white adults ≥ 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). The details of REGARDS sample and study recruitment have been previously described.³² Briefly, the participants were recruited via mail and telephone. Baseline demographic information and medical history were obtained by trained personnel using computer-assisted telephone interview. The anthropometric and BP measurements, venous blood samples, brief physical exam, ECG, and pill bottle review was conducted during the in-home visits 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 an 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

The presence of HTN was determined based on self-reported history and in-home review of antihypertensive medication bottles. We stratified our 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 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.

ECG abnormalities

A standard 12-lead ECG was obtained during the in-home visit. All ECGs were centrally read and coded by trained physician electrocardiographers and all abnormalities were over-read by a second physician electrocardiographer. The ECG variables including Minnesota codes have been described previously.¹³⁻¹⁵ We defined major ECG abnormalities as: major Q waves (MC 1.1, 2.12), minor Q waves and STT abnormalities (MC 1.3 + 4.1 or 4.2 or 5.1 or 5.2), major isolated STT abnormalities (MC 4.1 or 4.2 or 5.1 or 5.2), left ventricular

hypertrophy (LVH) and major STT abnormalities (MC 3.1 + 4.1 or 4.2 or 5.1 or 5.2), major atrioventricular (AV) conduction abnormalities (MC 6.1, 6.2, 6.4 or 6.8), artificial pacemaker (MC 6.8), ventricular conduction defects (MC 7.1, 7.2, 7.4 or 7.8), other major arrhythmias (MC 8.2 or 8.4), presence of atrial fibrillation or atrial flutter and major QT prolongation (QTc 116). Minor ECG abnormalities included: minor isolated Q/QS waves (MC 1-3), minor STT abnormalities (MC 4.3, 4.4, 5.3 or 5.4), high R waves (MC 3.1, 3.2, 3.3 or 3.4), ST segment elevation (MC 9.2), incomplete right and left bundle branch block (MC 7.3, 7.6 and 7.7) and all other minor abnormalities. Participants with the presence of only major or only minor ECG abnormalities were grouped separately. Participants with the presence of both major and minor ECG abnormalities were included in the major ECG abnormalities group.

Covariates

Variables on demographics and geographic regions of stroke prevalence (stroke belt, stroke buckle and non-belt) were included. Measures of socioeconomic status included annual household income (< \$35,000 or ≥ \$35,000) and the highest level of education attained (less than high school, high school completion or higher). Cardiovascular risk factors included exercise (any vs none), heavy alcohol use (defined by National Institute on Alcohol Abuse and Alcoholism as: ≥ 7 drinks/week for women and ≥ 14 drinks/week for men),³³ current smoking, diabetes (fasting glucose ≥ 126mg/dl or non-fasting glucose ≥ 200mg/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 ≥ 30mg/g, waist circumference; serum low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides and total cholesterol levels, current smoking status and high-sensitivity C-reactive protein (CRP) levels. Medication adherence was determined based on the standard Morisky Medication Adherence Score.³⁴ 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 and 2.

Statistical analysis

Descriptive statistics included proportions, means and standard deviations, and medians and 25th and 75th percentiles where appropriate. Prevalence ratios (PR) for major and minor ECG abnormalities were calculated separately in each of the above BP groups using Poisson regression with a robust variance estimator. Models were constructed among the 6 BP groups sequentially using an unadjusted model (model 1); model 2 adjusted for age, race, gender, income, education, and stroke region; model 3 adjusted for model 2 covariates and exercise, alcohol use, current smoking, diabetes mellitus, albumin-creatinine ratio, waist circumference, aspirin use, statin use, nitrate use, medication adherence, log-transformed high sensitivity (hs) CRP, and total cholesterol to HDL-C ratio; model 4 adjusted for model 3 covariates and HTN duration (short, medium and long), history of CHD, stroke or transient ischemic attack. Additionally, 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 and non-stroke belt) comparing models with and without interaction terms. SAS version V9.4 (Cary, NC) was used for all the analyses.

Results

From the overall sample of 30,183 participants, those without 12-lead ECG, SBP or data obtained from pill bottle review were excluded, resulting in a final sample size of 20,932 participants. The cohort was divided into presence of major (n = 3782), only minor (n = 8944) or no (n = 8206) ECG abnormalities (Figure 1). The cohort was stratified into normotension (n = 3,373), prehypertension (n = 4,142), controlled HTN (n = 8,619), uncontrolled HTN (n = 3,544), controlled aTRH (n = 400) and uncontrolled aTRH (n = 854) groups. Table 1 shows the baseline characteristics and demographics of 11,988 participants with normal ECG or major ECG abnormalities. The prevalence of blacks, education less than high school, albumin to creatinine ratio ≥ 30 mg/g and waist circumference was higher across BP groups with increasing BP severity. Table 2 shows the baseline characteristics and demographics of 17,150 participants with normal ECG or minor ECG abnormalities. The prevalence of blacks, persons with household income $< \$35,000$, education less than high school, elevated hs-CRP levels and albumin to creatinine ratio ≥ 30 mg/g was higher across the BP groups with greater BP severity.

Table 3 shows the unadjusted and adjusted prevalence of major ECG abnormalities across BP groups with normotension as a reference group. In the unadjusted model, the prevalence of major ECG abnormalities was higher among persons with prehypertension and HTN. In addition, among persons with HTN, those with aTRH (controlled and uncontrolled) had a higher prevalence of major ECG abnormalities compared to those with controlled and uncontrolled HTN, whereas, the prevalence was similar among controlled and uncontrolled aTRH groups (PR 3.94 vs 3.95). After adjusting for demographics, CV risk factors and HTN duration in model 4, there was higher prevalence of major ECG abnormalities with any higher BP and a further trend with greater BP severity; however, the magnitude of these differences between HTN (controlled and uncontrolled) and aTRH (controlled and uncontrolled) groups attenuated. The prevalence of major ECG abnormalities was similar in both pre-HTN and normotension groups.

When stratified by age (< 70 years and ≥ 70 years), in an unadjusted model, the prevalence of major ECG abnormalities was higher among aTRH groups compared with HTN groups (supplemental Table 1). Among persons < 70 years, after full adjustment, the differences in prevalence among aTRH and HTN groups attenuated with trend towards higher prevalence with increasing BP severity and treatment resistance; whereas among persons ≥ 70 years, after full adjustment, the prevalence of major ECG abnormalities remained similar across all the BP groups. Prehypertension was not associated with an increased prevalence of major ECG abnormalities in both the age groups. With interaction testing, after adjusting for model 3, the prevalence of major ECG abnormalities was greater among uncontrolled HTN, controlled and uncontrolled aTRH groups in persons < 70 years compared with those ≥ 70 years; however, these differences attenuated after full adjustment. There was no evidence of effect modification by gender, race and region on the prevalence of major ECG abnormalities among individuals based on HTN severity and BP control (data not shown).

Table 4 shows the adjusted and unadjusted prevalence of minor ECG abnormalities across the BP groups. In the unadjusted model the prevalence of minor ECG abnormalities was

higher among persons with HTN with a trend towards higher prevalence with increasing BP severity. However, after full adjustment the prevalence of minor ECG abnormalities was similar among both HTN and aTRH groups with no trend with greater HTN severity. The prevalence was also similar among prehypertension and normotensive groups. We conducted secondary analyses to assess the impact of antihypertensive medications on prevalence ratios of major and minor ECG abnormalities across BP groups (Supplemental tables 3 and 4 respectively). Significant impact was seen in aTRH groups, probably due to multiple antihypertensive medication use among the participants with aTRH.

When stratified by race, among whites, there were no significant differences in the prevalence of minor ECG abnormalities across the BP groups. Among blacks, the prevalence of minor ECG abnormalities was significantly higher among HTN and aTRH groups compared with normotension group, with the highest prevalence in uncontrolled aTRH group (supplemental table 2). In the interaction testing, blacks with uncontrolled HTN and uncontrolled aTRH had significantly higher prevalence of minor ECG abnormalities compared with whites (1.27 vs 1.09, $p = 0.02$ and 1.34 vs 1.04, $p = 0.006$ respectively). There was no evidence of effect modification by gender, age and region on the prevalence of minor ECG abnormalities among individuals based on HTN severity and BP control (data not shown). Additional secondary analyses report the unadjusted and adjusted prevalence of LVH among participants with major ECG abnormalities (supplemental table 5) and prevalence of major and minor ECG abnormalities in participants with prior MI or stroke (supplemental table 6).

Discussion

The current study shows that compared with normotension, prehypertension was not associated with a greater prevalence of major or minor ECG abnormalities. The prevalence of major but not minor ECG abnormalities was associated with higher BP levels and HTN severity. Among persons < 70 years, the prevalence of major ECG abnormalities was higher with increasing HTN severity and treatment resistance. Blacks with uncontrolled HTN and uncontrolled aTRH had a higher prevalence of minor ECG abnormalities compared with whites.

The association of prehypertension and ECG abnormalities has not to our knowledge, been previously reported. Since prehypertension is associated with incident CHD and adverse CV events,^{27,28} identifying ECG abnormalities early may help improve risk stratification. In our study, prehypertension was not associated with major or minor ECG abnormalities. Using the REGARDS study cohort, Prineas et al reported a weak association of SBP (including normotension and prehypertension range) with prevalent major ECG abnormalities (OR 1.05);¹⁷ however, in contrast to the current study, they did not adjust for a history of CHD, CV and lifestyle risk factors and HTN duration. One of the explanations for our current findings may be that the association of SBP with ECG abnormalities may only manifest at SBP levels above the prehypertension range. In addition, knowing the duration of prehypertension may help to determine the temporal association with ECG abnormalities.

Long standing HTN leads to left atrial and ventricular remodeling, which contributes to left ventricular hypertrophy, left atrial enlargement and repolarization ECG abnormalities.³⁵⁻³⁹ The association of major and minor ECG abnormalities and HTN has been previously reported. Ohira T et al, in a cohort of 10,741 persons, reported a higher prevalence of HTN and elevated SBP among persons with major and minor compared with no ST T abnormalities.²¹ Sutherland S et al, using 993 participants, reported a higher age-adjusted baseline SBP and DBP among persons with major and minor ECG abnormalities compared with normal ECG.²² Prineas et al reported that HTN, determined based on the use of antihypertensive medications, was independently associated with major ECG abnormalities (OR 1.35).¹⁷ However, none of the studies have assessed the prevalence of ECG abnormalities based on BP control and HTN severity.

In this study, we stratified hypertensive persons into 4 groups based on their BP control and treatment resistance (based on the number of antihypertensive medication classes). This is important, because aTRH has been associated with a higher prevalence of CV risk factors and increased risk of CHD and all-cause mortality.^{30,31,40,41} Among persons with aTRH, those with uncontrolled aTRH have a higher risk for CHD.³¹ In our study, the prevalence of major ECG abnormalities was higher among hypertensive persons compared with normotensives. There was trend towards a higher prevalence of major ECG abnormalities with greater HTN severity and poorer control. The prevalence was highest among persons with uncontrolled aTRH. These findings are significant, because we adjusted for all traditional CV and life-style risk factors, HTN duration, medication adherence and history of CHD. Therefore, early detection of major ECG abnormalities among hypertensive persons, especially in those with extreme HTN phenotypes, may help identify person with increased CV risk and may help intervene early to improve their CV risk profile.

The prevalence of minor ECG abnormalities was higher among persons with HTN compared with normotension. However, among those with HTN, the prevalence was similar regardless of BP control and treatment resistance. One of the explanations for these findings could be that ST T abnormalities, commonly associated with HTN, are part of both major and minor ECG abnormalities and may present concurrently. In our study, we grouped persons with both minor and major ECG abnormalities in the major ECG abnormality group, which may have underestimated the prevalence of minor ECG abnormalities. The above findings suggest that the presence of only minor ECG abnormalities may not help identify high-risk hypertensive persons based on treatment resistance and poor control.

Compared to whites blacks have a higher prevalence of ECG abnormalities.^{17,19,20,42} Sellers MB et al, in a cohort 635 black persons, reported a 37% baseline prevalence of minor ECG abnormalities.⁴² Vitelli LL et al, using the Atherosclerosis Risk in Communities study cohort, reported, after adjusting for traditional CV risk factors, a higher prevalence of minor ECG abnormalities among blacks compared with whites (46% vs 25%, $p < 0.001$).²⁰ However, none of the studies have investigated the impact of race on the association of HTN and the prevalence of ECG abnormalities. In our study, race had no impact on the prevalence of major ECG abnormalities among persons with HTN. However, among blacks compared with whites, having HTN was associated with an increased prevalence of minor ECG abnormalities. After full adjustment, compared with whites, blacks with uncontrolled HTN

and uncontrolled aTRH had a significantly higher prevalence of minor ECG abnormalities (by 18% and 30% respectively). These findings suggest that ECG based risk stratification could be useful in blacks with HTN, especially among those with poor control and treatment resistance.

Aging has been associated with a higher prevalence of ECG abnormalities.^{17,43} In our study, among persons < 70 years old, the prevalence of major ECG abnormalities was significantly higher among those with HTN with a trend towards greater prevalence with poor BP control and treatment resistance; whereas, among persons ≥ 70 years old, the prevalence was similar across all BP groups. In the interaction testing, the differences in the prevalence of major ECG abnormalities in both age groups attenuated after adjusting for HTN duration and a history of CHD. In terms of minor ECG abnormalities, among persons <70 years old, there was trend towards increased prevalence with poorer BP control and treatment resistance, whereas, among persons ≥ 70 years, the prevalence was similar among all HTN groups. These findings suggest that beyond a certain age, the impact of aging supersedes the impact of HTN on the prevalence of ECG abnormalities. Our study did not find significant differences in the association of the prevalence of ECG abnormalities and HTN severity and control based on gender and geographical region. The absence of gender and geographical disparities in prevalence of ECG abnormalities among more severe forms of HTN warrants further investigation.

The current study's strengths include the assessment of a previously unstudied association; that is the prevalence of major and minor ECG abnormalities based on BP level and severity with adjustment for demographics, CV risk factors and HTN duration. Additionally, the study includes a large biracial national cohort enrolled from 48 continental US states; BP measurement and ECG ascertainment by trained personnel; and assessment of the prevalence of ECG abnormalities by age, race, gender and stroke region. Our findings should be interpreted in the context of several limitations. REGARDS is a longitudinal cohort study and the BP measurements were obtained only at baseline, therefore, the impact of BP changes on incident ECG abnormalities was not 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 determined. Subjective recall of the duration of HTN likely involves bias, which was evident when a small number of participants with normotension and prehypertension reported having a history of HTN, and conversely when a small number of participants with HTN (and aTRH) reported not having history of HTN. As discussed previously, the prevalence of minor ECG abnormalities could have been underestimated because those with concurrent major and minor ECG abnormalities were included in the major ECG abnormality group. Finally, as is true with any cohort study, we cannot rule out residual confounding by unmeasured covariates.

In conclusion, the current study of a biracial national cohort demonstrates that prehypertension was not associated with prevalent ECG abnormalities. Having aTRH was associated with a higher prevalence of major but not minor ECG abnormalities. Racial disparities exist in the prevalence of minor ECG abnormalities. Thus, detection of ECG abnormalities could help identify population at higher CV risk, and improve risk

stratification and early intervention among persons with extreme HTN phenotypes beyond the traditional CV risk factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Prevalence of major ECG abnormalities is associated with hypertension severity.
- Prevalence of minor ECG abnormalities is not associated with hypertension severity.
- Prevalence of major/minor ECG abnormalities is not associated with prehypertension.

Figure 1.
Inclusion and exclusion cascade of study participants.

Table 1

Baseline characteristics of REGARDS participants by blood pressure group among participants with normal ECG or major ECG abnormalities. All p-values testing differences across blood pressure groups are < 0.01.

Variables	Overall	Normotension	Prehypertension	Blood Pressure Group			
				Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH
Sample size	11,988	2,099	2,438	4,816	1,917	240	478
Major ECG abnormalities	3782 (31.5)	323 (15.4)	448 (18.4)	1832 (38.0)	743 (38.7)	146 (60.8)	290 (60.6)
Socio-demographic factors							
Age, mean $\pm$ SD	63.6 $\pm$ 9.8	59.1 $\pm$ 8.8	61.5 $\pm$ 9.5	65.5 $\pm$ 9.5	65.1 $\pm$ 9.9	67.1 $\pm$ 9.0	67.5 $\pm$ 9.5
Black, n (%)	4759 (39.7)	529 (25.2)	801 (32.9)	2073 (43.0)	947 (49.4)	124 (51.7)	285 (59.6)
Male, n (%)	4680 (39.0)	666 (31.7)	1051 (43.1)	1825 (37.9)	843 (44.0)	102 (42.5)	193 (40.4)
Stroke region, n (%)							
<i>Non-belt</i>	4947 (41.3)	902 (43.0)	1084 (44.5)	1888 (39.2)	788 (41.1)	99 (41.3)	186 (38.9)
<i>Belt</i>	4123 (34.4)	685 (32.6)	793 (32.5)	1691 (35.1)	687 (35.8)	89 (37.1)	178 (37.2)
<i>Buckle</i>	2918 (24.3)	512 (24.4)	561 (23.0)	1237 (25.7)	442 (23.1)	52 (21.7)	114 (23.8)
Annual household income, n (%)							
\$35,000	5780 (48.2)	1267 (60.4)	1363 (55.9)	2150 (44.6)	757 (39.5)	96 (40.0)	147 (30.8)
< \$35,000	4705 (39.2)	581 (27.7)	793 (32.5)	2037 (42.3)	924 (48.2)	113 (47.1)	257 (53.8)
<i>Declined to report</i>	1503 (12.5)	251 (12.0)	282 (11.6)	629 (13.1)	236 (12.3)	31 (12.9)	74 (15.5)
Education less than high school, n (%)	1281 (10.7)	100 (4.8)	190 (7.8)	602 (12.5)	265 (13.8)	39 (16.3)	85 (17.9)
Lifestyle and biometric factors							
Current smoking, n (%)	1768 (14.8)	359 (17.2)	355 (14.6)	617 (12.9)	342 (17.9)	35 (14.6)	60 (12.5)
No exercise, n (%)	4107 (34.8)	576 (27.8)	686 (28.5)	1816 (38.3)	702 (37.3)	118 (49.8)	209 (44.2)
Heavy alcohol use*, n (%)	475 (4.0)	96 (4.6)	121 (5.0)	152 (3.2)	83 (4.4)	9 (3.8)	14 (2.9)
Diabetes, n (%)	2860 (23.9)	176 (8.4)	305 (12.5)	1497 (31.1)	532 (27.8)	123 (51.3)	227 (47.5)
Waist circumference, mean $\pm$ SD	95.1 $\pm$ 15.8	85.8 $\pm$ 13.3	93.2 $\pm$ 13.9	97.6 $\pm$ 15.6	98.5 $\pm$ 15.6	102.9 $\pm$ 17.7	103.2 $\pm$ 17.4
Aspirin use, n (%)	4914 (41.0)	567 (27.0)	701 (28.8)	2427 (50.4)	796 (41.6)	157 (65.4)	266 (55.6)
Statin use, n (%)	3774 (31.5)	348 (16.6)	413 (16.9)	2106 (43.7)	516 (26.9)	142 (59.2)	249 (52.1)
Nitrate use, n (%)	138 (1.2)	2 (0.1)	2 (0.1)	84 (1.7)	18 (0.9)	15 (6.3)	17 (3.6)
Not medication-adherent, n (%)	3223 (29.7)	501 (28.5)	529 (26.9)	1419 (30.3)	534 (31.0)	73 (30.8)	167 (35.7)
Ratio of albumin to creatinine	1595 (14.1)	108 (5.4)	190 (8.2)	657 (14.5)	404 (22.6)	67 (30.7)	169 (37.1)
30 mg/g, n (%)							

Variables	Overall	Normotension	Prehypertension	Blood Pressure Group			
				Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH
High-sensitivity C-reactive protein (mg/L), median [25th, 75th percentiles]	2.1 [0.9, 5.0]	1.4 [0.7, 3.3]	1.9 [0.9, 4.1]	2.5 [1.1, 5.9]	2.7 [1.1, 5.8]	3.0 [1.3, 6.5]	2.9 [1.1, 7.5]
Total Cholesterol, mean $\pm$ SD	191.8 $\pm$ 40.4	198.3 $\pm$ 38.4	200.2 $\pm$ 38.6	185.0 $\pm$ 39.3	195.8 $\pm$ 43.2	169.7 $\pm$ 42.4	182.1 $\pm$ 40.0
High-density lipoprotein cholesterol, mean $\pm$ SD	53.2 $\pm$ 16.6	57.3 $\pm$ 17.4	53.8 $\pm$ 16.3	51.8 $\pm$ 16.1	53.3 $\pm$ 17.3	45.5 $\pm$ 13.6	49.9 $\pm$ 13.9
Blood-pressure-related factors							
Duration of hypertension (years), n (%)							
> 20	2931 (25.0)	106 (5.1)	242 (10.0)	1865 (39.8)	582 (31.3)	39 (17.0)	97 (21.1)
10 - 20	1913 (16.3)	42 (2.0)	98 (4.1)	1156 (24.7)	384 (20.7)	82 (35.7)	151 (32.8)
< 10	1625 (13.8)	30 (1.4)	45 (1.9)	906 (19.3)	341 (18.3)	96 (41.7)	207 (45.0)
No hypertension	5268 (44.9)	1903 (91.4)	2033 (84.1)	762 (16.3)	552 (29.7)	13 (5.7)	5 (1.1)
History of CHD, n (%)	2450 (20.4)	158 (7.5)	244 (10.0)	1286 (26.7)	434 (22.6)	120 (50.0)	208 (43.5)
History of stroke/TIA, n (%)	1111 (9.3)	66 (3.1)	100 (4.1)	582 (12.1)	210 (11.0)	54 (22.6)	99 (20.8)
Anti-hypertensive medication use, n (%)							
<i>Beta-blockers</i>	2641 (22.0)	-	-	1681 (34.9)	373 (19.5)	236 (98.3)	351 (73.4)
<i>Calcium-channel blockers</i>	2235 (18.6)	-	-	1361 (28.3)	352 (18.4)	209 (87.1)	313 (65.5)
<i>ACEI/ARBs</i>	4170 (34.8)	-	-	2852 (59.2)	649 (33.9)	237 (98.8)	432 (90.4)
<i>Aldosterone receptor antagonists</i>	176 (1.5)	-	-	94 (2.0)	6 (0.3)	45 (18.8)	31 (6.5)
<i>Diuretics</i>	3537 (29.5)	-	-	2404 (49.9)	479 (25.0)	238 (99.2)	416 (87.0)

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

Table 2

Baseline characteristics of REGARDS participants by blood pressure group among participants with normal ECG or minor ECG abnormalities. All p-values testing differences across blood pressure groups are < 0.01 .

Variables	Overall	Normotension	Prehypertension	Blood Pressure Group			
				Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH
Sample size	17,150	3,050	3,694	6,787	2,801	254	564
Minor ECG abnormalities	8944 (52.1)	1274 (41.8)	1704 (46.1)	3803 (56.0)	1627 (58.1)	160 (62.9)	376 (66.6)
Socio-demographic factors							
Age, mean $\pm$ SD	63.1 $\pm$ 9.5	59.3 $\pm$ 8.8	61.5 $\pm$ 9.3	64.7 $\pm$ 9.2	64.5 $\pm$ 9.7	66.4 $\pm$ 8.4	66.3 $\pm$ 8.7
Black, n (%)	6979 (40.7)	763 (25.0)	1220 (33.0)	3070 (45.2)	1424 (50.8)	146 (57.5)	356 (63.1)
Male, n (%)	6037 (35.2)	932 (30.6)	1531 (41.4)	2182 (32.1)	1099 (39.2)	90 (35.4)	203 (36.0)
Stroke region, n (%)							
<i>Non-belt</i>	6985 (40.7)	1288 (42.2)	1620 (43.9)	2638 (38.9)	1126 (40.2)	103 (40.6)	210 (37.2)
<i>Belt</i>	5950 (34.7)	1012 (33.2)	1234 (33.4)	2344 (34.5)	1055 (37.7)	89 (35.0)	216 (38.3)
<i>Buckle</i>	4215 (24.6)	750 (24.6)	840 (22.7)	1805 (26.6)	620 (22.1)	62 (24.4)	138 (24.5)
Annual household income, n (%)							
\$35,000	8232 (48.0)	1825 (59.8)	2017 (54.6)	3017 (44.5)	1096 (39.1)	94 (37.0)	183 (32.4)
< \$35,000	6708 (39.1)	849 (27.8)	1214 (32.9)	2865 (42.2)	1353 (48.3)	125 (49.2)	302 (53.5)
<i>Declined to report</i>	2210 (12.9)	376 (12.3)	463 (12.5)	905 (13.3)	352 (12.6)	35 (13.8)	79 (14.0)
Education less than high school, n (%)	1842 (10.7)	151 (5.0)	281 (7.6)	854 (12.6)	407 (14.6)	43 (16.9)	106 (18.8)
Lifestyle and biometric factors							
Current smoking, n (%)	2506 (14.7)	524 (14.4)	529 (14.4)	861 (12.7)	492 (17.6)	32 (12.6)	68 (12.1)
Any exercise, n (%)	5682 (33.6)	823 (27.4)	992 (27.2)	2484 (37.0)	1029 (37.3)	115 (46.0)	239 (43.2)
Heavy alcohol use*, n (%)	678 (4.0)	129 (4.3)	174 (4.8)	230 (3.5)	125 (4.6)	6 (2.4)	14 (2.5)
Diabetes**, n (%)	3919 (22.9)	251 (8.2)	452 (12.2)	2078 (30.6)	741 (26.5)	129 (50.8)	268 (47.5)
Waist circumference, mean $\pm$ SD	94.9 $\pm$ 16.1	85.9 $\pm$ 14.0	93.2 $\pm$ 14.0	97.2 $\pm$ 15.8	99.1 $\pm$ 16.6	104.0 $\pm$ 18.2	104.3 $\pm$ 17.4
Aspirin use, n (%)	6774 (39.5)	824 (27.1)	1042 (28.2)	3368 (49.6)	1062 (38.0)	166 (65.6)	312 (55.3)
Statins use, n (%)	4970 (29.0)	471 (15.4)	632 (17.1)	2774 (40.9)	699 (25.0)	131 (51.6)	263 (46.6)
Nitrate use, n (%)	119 (0.7)	1 (0.0)	4 (0.1)	72 (1.1)	15 (0.5)	12 (4.7)	15 (2.7)
Medication adherence, n (%)	4522 (29.3)	707 (28.0)	781 (25.9)	1972 (29.9)	815 (32.5)	63 (25.5)	184 (33.4)
Ratio of albumin to creatinine	2011 (12.4)	148 (5.1)	280 (7.9)	819 (12.8)	551 (20.6)	53 (22.6)	160 (29.7)
30 mg/g, n (%)							

Variables	Overall	Normotension	Prehypertension	Blood Pressure Group			
				Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH
High-sensitivity C-reactive protein (mg/L), median [25th, 75th percentiles]	2.2 [0.9, 5.0]	1.4 [0.6, 3.3]	1.9 [0.9, 4.2]	2.5 [1.1, 5.9]	2.7 [1.1, 6.0]	2.8 [1.3, 6.3]	2.9 [1.2, 6.3]
Total Cholesterol, mean $\pm$ SD	193.5 $\pm$ 39.9	197.3 $\pm$ 37.4	200.4 $\pm$ 38.4	187.4 $\pm$ 39.7	198.2 $\pm$ 42.0	173.6 $\pm$ 40.7	184.9 $\pm$ 40.4
High-density lipoprotein cholesterol, mean $\pm$ SD	53.7 $\pm$ 16.4	57.2 $\pm$ 16.9	53.8 $\pm$ 16.1	52.4 $\pm$ 15.9	54.2 $\pm$ 17.3	47.5 $\pm$ 14.1	50.9 $\pm$ 14.5
Blood-pressure related factors							
Duration of hypertension (years), n (%)							
> 20	4244 (25.2)	142 (4.7)	377 (10.3)	2711 (40.9)	844 (31.0)	40 (16.5)	130 (23.8)
10 - 20	2689 (16.0)	61 (2.0)	159 (4.3)	1655 (25.0)	542 (19.9)	91 (37.6)	181 (33.2)
< 10	2217 (13.2)	34 (1.1)	80 (2.2)	1274 (19.2)	491 (18.0)	106 (43.8)	232 (42.5)
No hypertension	7691 (45.7)	2795 (92.2)	3053 (83.2)	986 (14.9)	849 (31.1)	5 (2.1)	3 (0.5)
History of CHD, n (%)	1569 (9.1)	96 (3.1)	126 (3.4)	924 (13.6)	239 (8.5)	68 (26.8)	116 (20.6)
History of stroke/TIA, n (%)	1389 (8.1)	92 (3.0)	144 (3.9)	733 (10.8)	268 (9.6)	54 (21.3)	98 (17.4)
Anti-hypertensive medication use, n (%)							
<i>Beta-blockers</i>	3290 (19.2)	-	-	2185 (32.2)	471 (16.8)	246 (96.9)	388 (68.8)
<i>Calcium-channel blockers</i>	3088 (18.0)	-	-	1996 (29.4)	475 (17.0)	240 (94.5)	377 (66.8)
<i>ACEI/ARBs</i>	5674 (33.1)	-	-	4007 (59.0)	895 (32.0)	253 (99.6)	519 (92.0)
<i>Aldosterone receptor antagonists</i>	161 (0.9)	-	-	93 (1.4)	3 (0.1)	36 (14.2)	29 (5.1)
<i>Diuretics</i>	4852 (28.3)	-	-	3411 (50.3)	695 (24.8)	249 (98.0)	497 (88.1)

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

Table 3

Prevalence ratios (95% CI) comparing major ECG abnormalities to normal ECG across blood pressure groups.

Models	Normotension	Prehypertension	Blood Pressure Group				P value
			Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH	
Major ECG abnormalities (n)	323	448	1,832	743	146	290	-
Total (n = 11,988)	2,099	2,438	4,816	1,917	240	478	-
Model 1	1 (ref)	1.19 (1.05, 1.36)	2.47 (2.22, 2.75)	2.52 (2.24, 2.83)	3.95 (3.43, 4.56)	3.94 (3.48, 4.46)	<0.001
Model 2	1 (ref)	1.04 (0.92, 1.18)	1.84 (1.65, 2.04)	1.85 (1.65, 2.08)	2.75 (2.39, 3.17)	2.65 (2.34, 3.01)	<0.001
Model 3	1 (ref)	1.02 (0.90, 1.16)	1.62 (1.45, 1.80)	1.64 (1.46, 1.84)	2.12 (1.83, 2.45)	2.09 (1.83, 2.38)	<0.001
Model 4	1 (ref)	1.01 (0.90, 1.14)	1.30 (1.16, 1.45)	1.37 (1.23, 1.54)	1.42 (1.22, 1.64)	1.44 (1.26, 1.65)	<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, waist circumference, regular aspirin use, statin use, nitrate use, medication adherence, ACR, log-transformed hs-CRP, and total cholesterol : HDL-C ratio.

Model 4 adjusts for Model 3 covariates + duration of hypertension (short, medium, long, none), history of CHD or stroke/TIA.

HTN - hypertension; aTRH - apparent treatment resistant hypertension; CHD - coronary heart disease; TIA - transient ischemic attack; ACR - albumin-to-creatinine ratio; hs-CRP - high sensitivity C reactive protein; HDL-C - high density lipoprotein to total cholesterol ratio

Table 4
Prevalence ratios (95% CI) comparing minor ECG abnormalities to normal ECG across blood pressure groups.

Models	Normotension	Prehypertension	Blood Pressure Group				P value
			Controlled HTN	Uncontrolled HTN	Controlled aTRH	Uncontrolled aTRH	
Minor ECG abnormalities (n)	1,274	1,704	3,803	1,627	160	376	
Total (n = 17,150)	3,050	3,694	6,787	2,801	254	564	-
Model 1	1 (ref)	1.10 (1.05, 1.17)	1.34 (1.28, 1.41)	1.39 (1.32, 1.46)	1.51 (1.36, 1.67)	1.60 (1.48, 1.71)	<0.001
Model 2	1 (ref)	1.07 (1.01, 1.12)	1.22 (1.16, 1.28)	1.26 (1.20, 1.33)	1.33 (1.20, 1.47)	1.40 (1.30, 1.51)	<0.001
Model 3	1 (ref)	1.05 (1.00, 1.11)	1.18 (1.12, 1.24)	1.22 (1.15, 1.28)	1.24 (1.12, 1.38)	1.31 (1.22, 1.42)	<0.001
Model 4	1 (ref)	1.05 (1.00, 1.11)	1.12 (1.06, 1.18)	1.17 (1.10, 1.24)	1.13 (1.01, 1.26)	1.20 (1.11, 1.31)	<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, waist circumference, regular aspirin use, statin use, nitrate use, medication adherence, ACR, log-transformed CRP, and total cholesterol : HDL-C ratio.

Model 4 adjusts for Model 3 covariates + duration of hypertension (short, medium, long, none), history of CHD or stroke/TIA.

HTN - hypertension; aTRH - apparent treatment resistant hypertension; CHD - coronary heart disease; TIA - transischemic attack; ACR - albumin-to-creatinine ratio; hs-CRP - high sensitivity C reactive protein; HDL-C - high density lipoprotein to total cholesterol ratio