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ORIGINAL RESEARCH

Differences in Left Atrial Size and Function and Supraventricular Ectopy Between Black and White Participants in the ARIC Study

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BACKGROUND: Black Americans have more atrial fibrillation risk factors but lower atrial fibrillation risk than White Americans. Left atrial (LA) enlargement and/or dysfunction, frequent atrial tachycardia (AT), and premature atrial contractions (PAC) are associated with increased atrial fibrillation risk. Racial differences in these factors may exist that could explain the difference in atrial fibrillation risk.

METHODS AND RESULTS: We included 2133 ARIC (Atherosclerosis Risk in Communities) study participants (aged 74±4.5 years[mean±SD], 59% women, 27% Black participants) who had echocardiograms in 2011 to 2013 and wore the Zio XT Patch (a 2-week continuous heart monitor) in 2016 to 2017. Linear regression was used to analyze (1) differences in AT/day or PAC/hour between Black and White participants, (2) differences in LA measures between Black and White participants, and (3) racial differences in the association of LA measures with AT or PAC frequency. Compared with White participants, Black participants had a higher prevalence of cardiovascular risk factors and disease, lower AT frequency, greater LA size, and lower LA function. After multivariable adjustments, Black participants had 37% (95% CI, 24%–47%) fewer AT runs/day than White participants. No difference in PAC between races was noted. Greater LA size and reduced LA function are associated with more AT and PAC runs; however, no race interaction was present.

CONCLUSIONS: Differences in LA measures are unlikely to explain the difference in atrial fibrillation risk between Black and White individuals. Despite more cardiovascular risk factors and greater atrial remodeling, Black participants have lower AT frequency than White participants. Future research is needed to elucidate the protective mechanisms that confer resilience to atrial arrhythmias in Black individuals.

Key Words: arrhythmia ■ atrial tachycardia ■ echocardiogram ■ epidemiology ■ race and ethnicity

There is a notable racial difference in the risk of atrial fibrillation (AF): Black individuals have lower risk of AF than White individuals[1–4] despite having a higher prevalence of risk factors for AF.[1,4] Many studies have attempted to elucidate this racial paradox with explanations ranging from underascertainment of AF in Black individuals attributed to racial disparities in health care usage and care,[5,6] differences in genetic susceptibility to AF[7,8] or left atrial (LA) size,[9–11] and variability in supraventricular ectopy (SVE) frequency (ie, premature atrial contraction [PAC] or atrial tachycardia [AT] frequency). Frequent AT and PAC are well-established precursors to AF.[12–14] Racial differences related to SVE have been reported, but the data are conflicting. The Cardiovascular Heart Study found that White participants had more PAC on a 24-hour Holter monitor than Black participants, partially explaining the higher risk of incident AF among White participants as compared with Black participants.[4] Although the REGARDS (Reasons for Geographic and Racial

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CLINICAL PERSPECTIVE

What Is New?

- In this large, community-based cohort, Black participants had lower atrial tachycardia frequency than White participants, despite having more cardiovascular risk factors and greater atrial remodeling.
- Larger left atrial size and impaired left atrial function are associated with more runs of atrial tachycardia and premature atrial contractions; however, no racial difference was noted.

What Are the Clinical Implications?

- Differences in left atrial measures likely do not explain the difference in atrial fibrillation risk between Black and White individuals.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis Risk in Communities
AT	atrial tachycardia
LA	left atrial
MESA	Multi-Ethnic Study of Atherosclerosis
PAC	premature atrial contraction
SVE	supraventricular ectopy

Differences in Stroke) study found that the presence of PAC (detected on a standard 12-lead ECG) was associated with an increased risk of AF and that there was no race-based difference in the association, whether there was a difference in PAC frequency between Black and White participants was not reported.[15] The latter underscores a major limitation in prior studies: the use of 12-lead ECGs or short-term 24 to 48-hour Holter monitoring, which fail to capture the day-to-day variability in SVE frequency and potentially misclassify SVE frequency.

LA enlargement and impaired LA function are substrates that promote AF genesis,[16] and both are associated with an increased AF risk.[9,17–21] When assessing differences in LA size between Black and White individuals, the Cardiovascular Heart Study found that LA diameter was greater in White men than in Black men, but no difference by race was noted among women.[10] The CARDIA (Coronary Artery Risk Development in Young Adults) study reported that LA diameter was significantly larger in Black participants than White participants in an unadjusted analysis; however, with further adjustments for demographics and comorbidities, White participants showed a significantly larger LA diameter.[9] Although racial differences in LA size may explain differences in AF risk in Black and White individuals, these prior studies have produced conflicting results. Of note, few studies have evaluated racial differences in LA function, which provides greater prognostic information than LA size alone.[21,22]

Therefore, to address the limitations of prior studies, we characterized racial differences in SVE frequency and LA size and function in the community-based and prospective ARIC (Atherosclerosis Risk in Communities) study. At the ARIC study visit 6 (2016–2017), participants wore the Zio XT Patch—a leadless, ambulatory ECG recording device—for up to 2 weeks. Owing to a longer monitoring time than a traditional Holter monitor,[23] the Zio XT Patch can provide a more precise estimate of SVE burden.[24] In addition, at the ARIC study visit 5 (2011–2013), 2-dimensional echocardiograms with speckle tracking were performed, allowing the measurement of LA function by strain analysis. The availability of SVE frequency and LA function data in the ARIC study allow us to evaluate the following 3 hypotheses: (1) Black participants will have lower AT and PAC frequency than White participants, (2) White participants will have larger LA size and lower LA function compared with Black participants, and (3) larger LA size and decreased LA function will be associated with higher AT and PAC frequency and an interaction by race will be present.

METHODS

The data, analytic methods, and study materials will be made available to other researchers for purposes of reproducing the results or replicating the procedure in accordance with ARIC study policies. Data are maintained by ARIC study and can be accessed, with appropriate approvals, through the National Heart, Lung, and Blood Institute's Biospecimen and Data Repository Information Coordinating Center (https://biolincc.nhlbi.nih.gov/home/) or by contacting the ARIC Coordinating Center.

Study Population

The ARIC study is a population-based cohort that began in 1987 to 1989. At inception, 15 792 participants aged 45 to 64 years were selected by probability sampling from 4 US communities: Forsyth County, NC; Jackson, MS; Washington County, MD; and the northwest suburbs of Minneapolis, MN.[25] Households were identified by area sampling in Forsyth County, whereas other communities sampled age-eligible individuals from lists to identify their households.[25] White participants were recruited from the Forsyth County, Washington County, and Minneapolis centers, and Black participants were recruited from the Forsyth County and Jackson centers. Among potentially

eligible participants, 67% of White and 46% of Black participants attended and completed the baseline clinic visit.[26] After the initial visit, participants have been followed continuously for hospitalizations and have been invited to take part in numerous in-person clinic visits. Relevant to this article, visit 5 took place in 2011 to 2013 and visit 6 in 2016 to 2017. Overall, the response rate among survivors for visits 5 and 6 were 65% and 49%, respectively. When stratified by race, response rates were similar: 60% of White survivors and 58% of Black survivors attended visit 5, whereas 50% and 49% of Black and White survivors attended visit 6, respectively.

Participants who attended visit 6 were invited to wear a Zio XT Patch for 14 days. Exclusion criteria for wearing the Zio XT Patch included history of cardio electronic device implantation or skin allergic reaction to adhesive tape. After the recording period, participants removed and mailed the device to iRhythm Technologies Inc. The recorded ECG data were then processed using an US Food and Drug Administration–approved proprietary algorithm developed by iRhythm. A certified cardiographic technician reviewed the data and generated a report. Of the 4003 participants who attended visit 6, 3680 participants were eligible to wear the Zio XT Patch, and 2650 of the eligible participants agreed to participate. Of the 2650 devices, 34 (1.3%) were lost or returned without data. Therefore, there were 2616 Zio XT Patch devices with analyzable data.

Exclusion criteria for hypothesis 1 included those whose race was other than Black or White as well as non-White participants in the Minneapolis and Washington County centers because of small numbers, those who wore the Zio XT Patch for <2 days, those with AF seen on their Zio XT Patch at visit 6 or on ECGs or hospitalizations before visit 6, and those with missing covariates. After all exclusions, the analytic sample for hypothesis 1 consisted of 2133 participants. For hypothesis 2, we included all participants who had 2-dimensional echocardiographic data at visit 5 (n=4344). For hypothesis 3, of the 2133 participants in the analytic sample for hypothesis 1, we excluded 416 with missing echocardiogram measures, resulting in a sample of 1717 participants. Figure 1A shows the flow of study participants for hypotheses 1 and 3. Figure 1B shows the flow of study participants for hypothesis 2. Institutional review boards at each participating center approved the study, and participants provided written informed consent.

Echocardiographic Measurements

At visit 5, transthoracic 2-dimensional echocardiograms were performed as previously described.[27] Briefly, echocardiograms were performed using dedicated Philips iE33 Ultrasound systems with Vision 2011. Studies were acquired, stored digitally, and transferred to a secure service at the Echocardiography Reading Center (Brigham and Women's Hospital, Boston, MA) from each field center. LA analysis was performed using a speckle tracking vendor-dependent software with an auto-strain algorithm (QLAB Advanced Quantification Software 13.0, Philips Ultrasound, Andover, MA), which identifies cardiac motion by tracking multiple chamber reference points over time. LA endocardial borders were automatically traced at the end-diastolic frame, defined by the QRS complex or the frame after mitral valve closure, of 2-dimensional images from the apical 4-chamber views, and speckles were tracked during a cardiac cycle frame by frame. LA phasic function was measured using volumes and strain indexes calculated as the average of the segments obtained. From LA strain analysis, LA phasic function was estimated using peak strain during systole to assess reservoir function, early peak strain during diastole to assess conduit function, and late peak strain during diastole to assess contractile function. Using the Simpson method, LA time–volume curves were generated by calculating LA volume at each phase of the cardiac cycle (LA maximal and LA minimum volumes). LA maximum and minimum volume index were derived by indexing to body surface area. LA pre-atrial (pre-A) contraction volume is defined as the LA volume before atrial contraction. LA function was estimated using the following equations:

$$\text{LA emptying fraction (reservoir function)} = [(\text{LA maximum volume} - \text{LA minimal volume}) / \text{LA maximum volume}] \times 100$$

$$\text{LA passive emptying fraction (conduit function)} = [(\text{LA maximum volume} - \text{LA pre - A volume}) / \text{LA maximum volume}] \times 100$$

$$\text{LA active emptying fraction (pump function)} = [(\text{LA pre} - \text{A volume} - \text{LA minimal volume}) / \text{LA pre - A volume}] \times 100.$$

Intra-reader and inter-reader variability for LA reservoir strain were assessed in a sample of 40 randomly selected participants. The intraclass correlation coefficients for inter-reader and intra-reader variability were 0.91 and 0.98, respectively.

AT and PAC Ascertainment

AT and PAC frequency measures were derived from the Zio XT Patch. PACs were detected and classified by iRhythm's proprietary algorithm based on prematurity and ectopic morphology. PAC detection performance was validated against the Massachusetts Institute of Technology-Beth Israel Hospital (MIT-BIH) Arrhythmia Database, as required by the US Food and Drug Administration. PAC frequency was calculated based on the number of isolated, couplet, and triplet PACs per

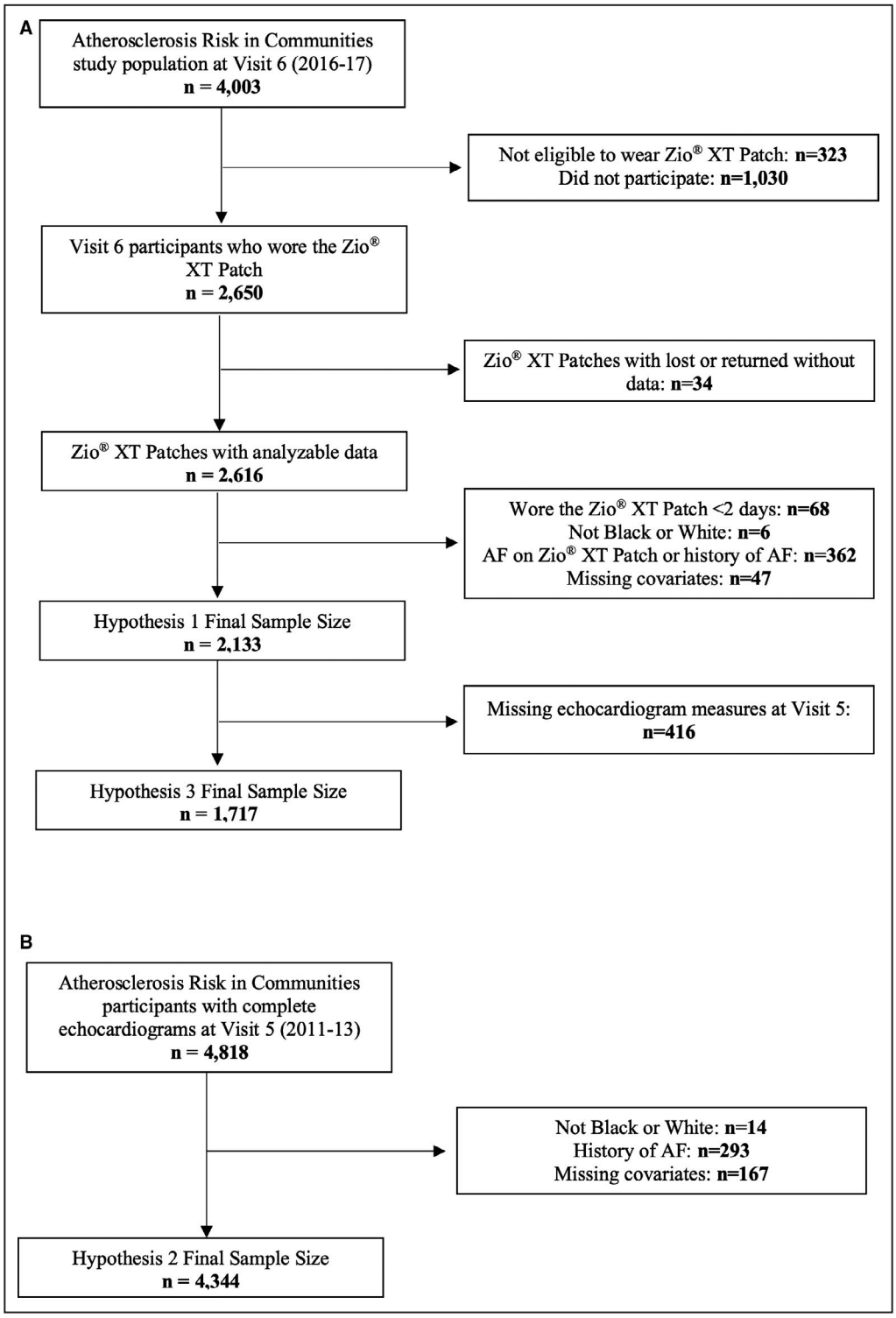

Figure 1. Study sample exclusions flowchart.
A, Flow of study participants for hypotheses 1 and 3. **B**, Flow of study participants for hypothesis 2. AF indicates atrial fibrillation.

day using the following equation: PAC count per day=# isolated PAC+2×(# couplet PAC)+3×(# triple PAC). PAC frequency was then analyzed as the average number of episodes per hour. AT was identified using iRhythm's proprietary algorithm and confirmed by a certified cardiographic technician. AT, which is defined by narrow regular complex tachycardia >4 beats with a rate >100 bpm, was differentiated from sinus tachycardia

based on p-wave morphology as well as a rapid onset of increased heart rate. For our analysis, AT was analyzed as the average number of episodes per day.

Covariate Measurements

Covariates were obtained from visit 6 for hypothesis 1 and from visit 5 for hypotheses 2 and 3. Participants self-reported their age, sex, race (Black race, White race), cigarette smoking status, and drinking status. Technicians at each field center measured each participant's height and weight to calculate body mass index. Educational attainment was obtained from visit 1.

Coronary heart disease was defined by self-reported physician diagnoses at visit 1, history of myocardial infarction on ECG, or adjudicated cases after visit 1.[28,29] Heart failure was identified by the Gothenburg criteria (visit 1 only) by self-report of heart failure medication use within the past 2 weeks or by the presence of heart failure *International Classification of Diseases, Ninth and Tenth Revisions* (*ICD-9* and *ICD-10*) codes in any hospitalization during follow-up.[28,30] Before visit 1, stroke was defined as self-reported history of a physician diagnosis of a stroke. After visit 1, stroke cases were adjudicated using criteria adapted from the National Survey of Stroke.[31] Participants brought all medication bottles to clinic visits, and medication use was recorded by technicians. Diabetes was defined as a fasting glucose ≥126 mg/dL, a nonfasting glucose ≥200 mg/dL, use of antidiabetic medication in the past 2 weeks, or a self-reported physician diagnosis of diabetes. Hypertension was defined as systolic blood pressure >140 mm Hg and diastolic blood pressure >90 mm Hg or antihypertensive medication use.

Statistical Analysis

Baseline characteristics of participants who wore the Zio XT Patch were described using frequencies and percentages for categorical variables and mean±SD for continuous variables and stratified by race. Statistical significance for categorical variables was tested using the chi-square method, whereas the Student *t* test was used for continuous variables. Runs of PAC per hour and AT per day were both highly skewed; therefore, natural log transformations of these variables were performed. Before log transformation was performed, the smallest observed value of PAC per hour (0.01) and AT per day (0.07) were added to participants with no PAC or AT. Linear regression was used for all 3 hypotheses in this analysis: (1) difference in AT or PAC frequency between Black and White participants, (2) difference in LA size and function between Black and White participants, and (3) racial difference in the association between LA size or function and AT or PAC frequency. For analyses in which the outcome was AT or PAC frequency (hypotheses 1 and 3), these associations were expressed as the ratio of geometric means, which can be interpreted as a percent difference. LA size and function parameters were assessed in 1-SD increments.

Multivariable models were adjusted as follows: model 1 was adjusted for age and sex; model 2 was further adjusted for education, smoking status, alcohol consumption, body mass index, diabetes, hypertension, coronary heart disease, heart failure, and stroke; model 3 was additionally adjusted for β-blockers and calcium-channel blockers. In hypothesis 1 (association of race with AT and PAC frequency), we further adjusted for LA minimum volume index and LA reservoir strain in model 4. As echocardiography measures were obtained from visit 5, inverse probability weighting was used for prospective analyses (hypothesis 3) involving LA size and function to account for attrition attributed to death, visit 6 nonattendance, or not wearing the Zio XT Patch.[32] Logistic models were used to model the estimated probabilities of being alive at visit 6, attending visit 6 (conditional on being alive at the time of visit 6), and agreeing to wear the Zio XT Patch at visit 6 (conditional on being alive and attending visit 6). Weights for each participant were the inverse of the estimated probabilities. For hypothesis 3, multiplicative interactions by race were analyzed by including cross-product terms in the models. We considered an interaction to be present when an interaction term was significant at $P<0.10$. All analyses were conducted using SAS software (version 9.4; SAS Institute Inc., Cary, NC).

RESULTS

A total of 2133 ARIC study participants who wore the Zio XT Patch were included in this analysis. On average (mean±SD), participants were 74±4.5 years at visit 5; 59% were women, and 27% were Black. Mean±SD wear time of the Zio XT Patch was 12.6±2.6 days. Participant characteristics at visit 5, stratified by race, are presented in Table 1. Black participants had a higher prevalence of cardiovascular risk factors and disease, larger LA size, and worse LA function parameters.

Association of Race With AT and PAC

Multivariable adjusted associations of race with runs of AT per day and PAC per hour are shown in Table 2. Black participants had 37% (95% CI, 24%–47%) fewer runs of AT per day than White participants after multivariable adjustment for cardiovascular risk factors and echocardiogram measures. Black participants also had fewer runs of PAC per hour than White participants; however, this association was not significant.

Association of Race With LA Size and Function

The associations of race with LA size and function parameters are shown in Figure 2. After multivariable

Table 1. Participant Characteristics by Race: The Atherosclerosis Risk in Communities Study, 2011 to 2013

	Black participants, n=584	White participants, n=1549	*P* value
PAC frequency, runs per h*	8.5 (2.2, 35.5)	8.2 (2.8, 31.5)	0.42
AT frequency, runs per day*	0.44 (0.14, 1.23)	0.79 (0.29, 2.12)	0.15
Demographics			
Age, y	73.8±4.6	74.1±4.5	0.12
Male sex	183 (31.3)	694 (44.8)	<0.001
Less than a high school education	133 (22.8)	129 (8.3)	<0.001
Current drinkers	107 (18.3)	904 (58.4)	<0.001
Current smokers	34 (5.8)	76 (4.9)	0.39
Clinical characteristics			
Body mass index, kg/m^2	30.7±6.4	27.9±4.7	<0.001
Diabetes	203 (34.8)	310 (20.0)	<0.001
Hypertension	473 (81.0)	976 (63.0)	<0.001
Coronary heart disease	36 (6.2)	170 (11.0)	0.001
Heart failure	74 (12.7)	80 (5.2)	<0.001
Stroke history	26 (4.5)	33 (2.1)	0.004
Medications			
β-blockers	127 (21.7)	392 (25.3)	0.09
Calcium channel blockers	204 (34.9)	225 (14.5)	<0.001
Echocardiogram measures†			
LA maximum volume index, mL/m^2	34.8±9.9	32.1±9.4	<0.001
LA minimum volume index, mL/m^2	15.0±6.1	13.0±5.5	<0.001
LA reservoir strain, %	33.1±6.5	34.6±7.0	<0.001
LA contractile strain, %	17.9±4.4	18.8±5.4	<0.001
LA conduit strain, %	15.3±5.3	15.8±5.5	0.08
LA emptying fraction, %	57.9±8.0	60.4±8.1	<0.001
LA passive emptying fraction, %	26.1±9.1	27.9±10.1	0.001
LA active emptying fraction, %	42.9±8.8	44.8±9.6	<0.001

Data are expressed as mean±SD, number (percentage), or median (25th percentile, 75th percentile). AT indicates atrial tachycardia; LA, left atrial; and PAC, premature atrial contraction.

*PAC and AT measures are obtained from the Zio XT Patch at visit 6 (2016–2017). Data are expressed as median (25th percentile, 75th percentile) because of skewness.

†Among participants with echocardiogram measures (n=1717).

adjustments, LA maximum and minimum volume indexes were both significantly greater in Black participants than in White participants. In addition, Black participants had significantly lower LA reservoir, LA contraction, LA emptying fraction, LA passive emptying fraction, and LA active emptying fraction than White participants.

Table 2. Percent Differences in Atrial Tachycardia and Premature Atrial Contraction Frequency (Black Versus White Participants): The Atherosclerosis Risk in Communities Study, 2016 to 2017 (n=2133)*

	AT per day	PAC per h
	Ratio of geometric means† (95% CI)	
Model 1	0.64 (0.55–0.74)	0.98 (0.83–1.16)
Model 2	0.67 (0.57–0.78)	0.92 (0.76–1.11)
Model 3	0.65 (0.55–0.76)	0.92 (0.76–1.11)
Model 4‡	0.63 (0.53–0.76)	0.92 (0.74–1.15)

Model 1 was adjusted for age and sex. Model 2 was adjusted for model 1 plus education, smoking status, alcohol consumption, body mass index, diabetes, hypertension, coronary heart disease, heart failure, and stroke. Model 3 was adjusted for model 2 plus β-blockers and calcium channel blockers. Model 4 was adjusted for model 3 plus LA minimum volume index, LA reservoir. AT indicates atrial tachycardia; LA, left atrial; and PAC, premature atrial contraction.

*Reference is White participants.

†AT and PAC burden were log-transformed because of the right-skew distribution. The ratio of geometric means refers to the exponentiated β coefficient from the linear regression and can be interpreted as a percent difference. For example, in model 4, Black participants have 37% fewer runs of AT per day than White participants.

‡Among participants with echocardiogram measures at visit 5 (2011–2013; n=1663).

Association of LA Size and Function With AT and PAC

Figure 3 depicts the association of LA size and function parameters with runs of AT per day in the entire cohort as well as stratified by race. In the entire cohort, greater LA size and lower LA function (reservoir strain, contractile strain, emptying fraction, and active emptying fraction) were associated with more runs of AT per day. No significant interactions by race (P>0.10) were present. For all LA size and function parameters, effect estimates for Black and White participants were similar, although estimates were more imprecise in Black participants. After full model adjustments, greater LA size was significantly associated with more runs of AT per day in both Black and White participants. In White participants, each 1-SD higher LA reservoir and LA contraction were associated with 13% (95% CI, 6%–20%) and 16% (95% CI, 9%–22%) fewer runs of AT per day, respectively. In Black participants, associations of LA reservoir or contraction with runs of AT were of similar magnitude to that of White participants, although estimates were more imprecise. Significantly fewer runs of AT were noted with each 1-SD increase in LA emptying fraction and active emptying fraction in both Black and White participants. There were no significant associations between LA conduit or passive emptying fraction and runs of AT in the entire cohort or when stratified by race.

The associations of LA size and function parameters with runs of PAC per hour are presented in Figure 4. Among all participants, greater LA size and lower LA

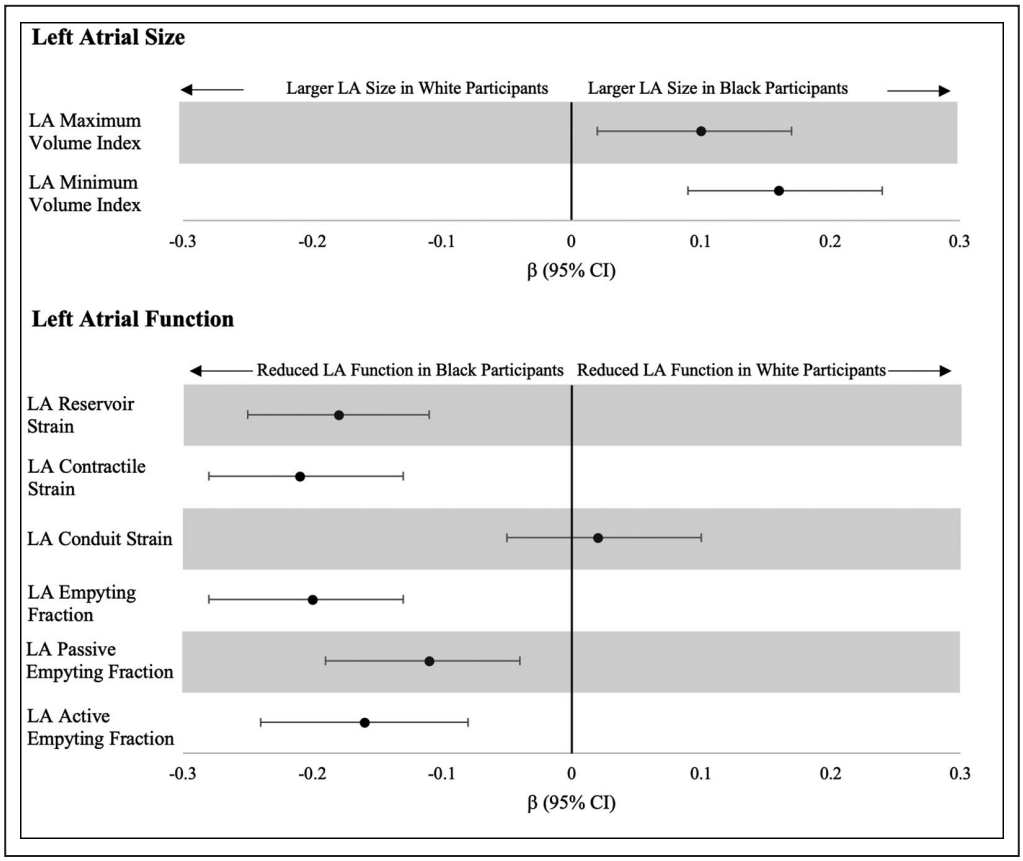

Figure 2. Differences in left atrial (LA) size and function between Black and White participants: the Atherosclerosis Risk in Communities study, 2011 to 2013 (n=4344; adjusted for age, sex, education, smoking status, alcohol consumption, body mass index, diabetes, hypertension, coronary heart disease, heart failure, stroke, β-blockers, and calcium channel blockers).
LA parameters were evaluated per 1-SD increment. Following is the definition of 1-SD: LA maximum volume index 11.1 mL/m^2, LA minimum volume index 7.4 mL/m^2, LA reservoir strain 7.7%, LA contractile strain 5.6%, LA conduit strain 5.6%, LA emptying fraction 9.4%, LA passive emptying fraction 10.3%, and LA active emptying fraction 10.6%.

function (reservoir strain, contractile strain, emptying fraction, and active emptying fraction) were associated with more runs of PAC per hour. An interaction by race (*P*=0.08) was observed when LA contractile strain was the exposure. Each 1-SD greater contractile strain was associated with 33% (95% CI, 17%–45%) and 20% (95% CI, 12%–27%) fewer runs of PAC in Black and White participants, respectively. No other significant interactions by race were noted (*P*>0.10). After multivariable adjustments, each 1-SD higher LA minimum volume index was associated with 35% (95% CI, 13%–61%) more runs of PAC per hour among Black participants and 37% (95% CI, 24%–51%) more runs of PAC per hour among White participants. Similar associations were noted for LA maximum volume index. When assessing LA function, each 1-SD higher LA reservoir was associated with 22% (95% CI, 5%–36%) fewer runs of PAC per hour for Black participants, whereas White participants had 18% (95% CI, 10%–26%) fewer runs. Black and White participants both had fewer runs of PAC per hour with similar magnitudes of association for each 1-SD higher LA emptying fraction and active emptying fraction. No significant associations between LA conduit or LA passive emptying fraction and runs of PAC were noted in the entire cohort or stratified by race.

DISCUSSION

In this multicenter prospective cohort study, we evaluated whether (1) PAC and AT frequency and (2) LA size and function were different between Black and White participants. In addition, we characterized the relationship of LA size and function to AT and PAC frequency, stratified by race. Our main findings were (1) Black participants had a higher prevalence of cardiovascular risk factors and disease than White participants, (2) Black participants had lower AT frequency than White

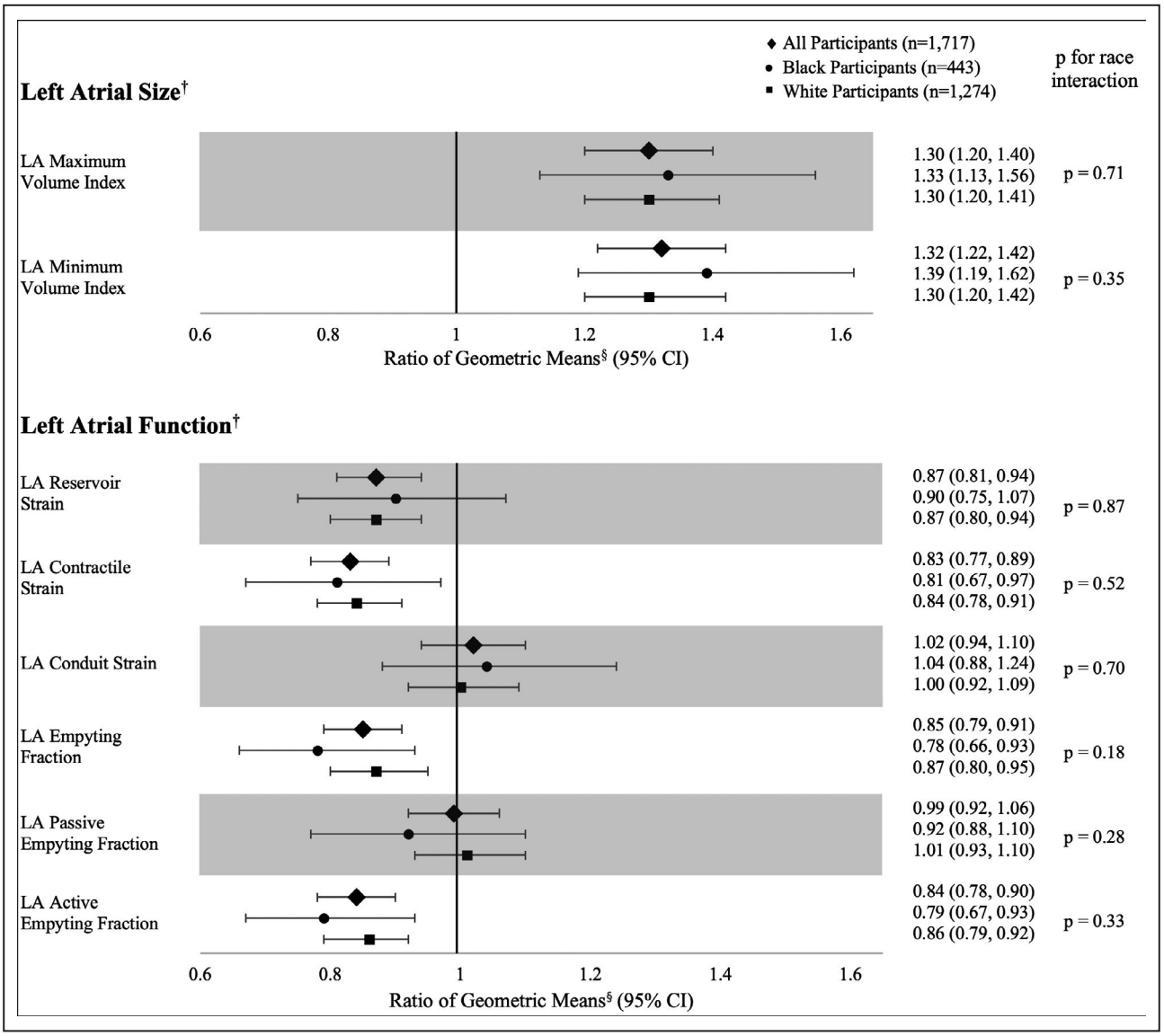

Figure 3. Association of left atrial (LA) size and function with atrial tachycardia (AT) runs per day by race: the Atherosclerosis Risk in Communities study, 2011 to 2017 (adjusted for age, sex, education, smoking status, alcohol consumption, body mass index, diabetes, hypertension, coronary heart disease, heart failure, stroke, β-blockers, and calcium channel blockers). Inverse probability weighting was used.†LA parameters were evaluated per 1-SD increment. Following is the definition of 1-SD: LA maximum volume index 9.8 mL/m^2, LA minimum volume index 5.9 mL/m^2, LA reservoir strain 6.9%, LA contractile strain 5.2%, LA conduit strain 5.5%, LA emptying fraction 8.2%, LA passive emptying fraction 9.9%, and LA active emptying fraction 9.5%. §AT burden was log-transformed because of the right-skew distribution. The ratio of geometric means refers to the exponentiated β coefficient from the linear regression and can be interpreted as a percent difference.

participants, (3) Black participants had greater LA size and reduced LA function compared with White participants, and (4) greater LA sizes and lower LA functions were associated with greater AT and PAC frequency among Black and White participants and only the association of LA contractile strain with PAC frequency indicated an interaction by race. Our results indicate that despite having a higher prevalence of cardiovascular risk factors and greater atrial remodeling than White participants, Black participants are less susceptible to atrial arrhythmias. Protective mechanisms that confer resilience to atrial arrhythmias in Black individuals remain elusive.

Frequent SVE have been associated with an increased risk of AF and/or stroke,[12–14,33,34] but few studies have assessed racial differences in SVE. In our study of community-based participants, Black participants had lower frequency of AT than White participants. Prior studies assessing racial differences in SVE have reported varying results. Consistent with our results, the MESA (Multi-Ethnic Study of Atherosclerosis) found that Black participants had fewer runs of AT than White

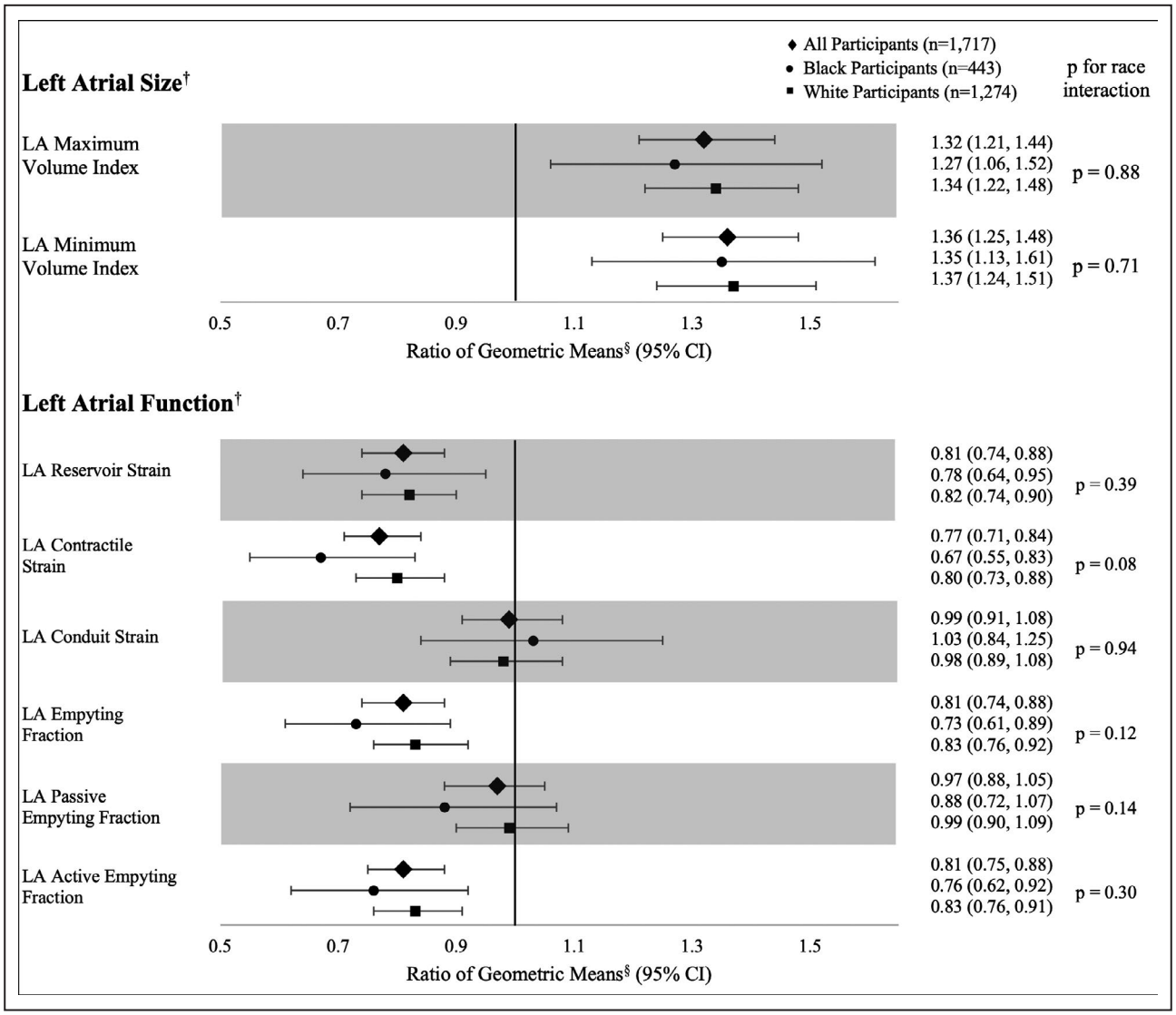

Figure 4. Association of left atrial (LA) size and function with premature atrial contraction runs per hour by race: the Atherosclerosis Risk in Communities study, 2011 to 2017 (adjusted for age, sex, education, smoking status, alcohol consumption, body mass index, diabetes, hypertension, coronary heart disease, heart failure, stroke, β-blockers, and calcium channel blockers).

Inverse probability weighting was used. †LA parameters were evaluated per 1-SD increment. Following is the definition of 1-SD: LA maximum volume index 9.8 mL/m^2, LA minimum volume index 5.9 mL/m^2, LA reservoir strain 6.9%, LA contractile strain 5.2%, LA conduit strain 5.5%, LA emptying fraction 8.2%, LA passive emptying fraction 9.9%, and LA active emptying fraction 9.5%. §Premature atrial contraction burden was log-transformed because of the right-skew distribution. The ratio of geometric means refers to the exponentiated β coefficient from the linear regression and can be interpreted as a percent difference.

participants.[35] By contrast, in a study using electronic health records from Kaiser Permanente Northern California, Black individuals had higher burdens of symptomatic episodes of paroxysmal AT (identified through *ICD-9* and *ICD-10* codes) than White participants and Asian/Pacific Islanders.[36] The Cardiovascular Heart Study reported Black participants had significantly fewer PAC (measured via 24-hour ECG Holter monitor) than White participants and suggested that this finding may partially explain the reduced risk of incident AF in Black individuals.[4] However, the REGARDS study reported that although atrial ectopy (detected on a 12-lead ECG) is associated with an increased risk of AF, it does not account for the differential risk of AF between White and Black individuals.[15] Compared with previous studies, which relied on *ICD-9* and *ICD-10* codes or shorter monitoring periods, we used 2-week continuous heart rhythm monitoring in our study, obtaining a more precise estimate of SVE burden in our study, hence clarifying the discrepancy in prior findings.[24]

Besides frequent SVE, LA abnormalities have been associated with an increased risk of AF.[17,18,37] Herein,

we found that greater LA size and lower LA function were associated with greater AT and PAC frequency. In addition, we report that Black ARIC study participants had greater LA volume and reduced LA function than White participants. Our findings were corroborated by MESA, in which they found that LA enlargement and reduced LA function were associated with more PAC/hour.[35] However, we also found that LA abnormalities were associated with greater AT frequency, which was not observed in MESA. Prior studies assessing racial differences in LA size have produced mixed results, and few have analyzed LA function. A study of 3 pooled cohorts reported LA diameter to be greater in White than Black individuals, but no difference in atrial volume or function were noted.[11] The Cardiovascular Heart Study found that White men had greater LA diameter than Black men.[10] The CARDIA study reported that White participants had significantly larger LA diameter than Black participants after multivariable adjustments[9]; however, Black participants had larger LA volume than White participants,[9] which are consistent with the present ARIC study findings. In addition, we found that Black participants had lower LA function than White participants. We note that the prevalence of cardiovascular risk factors and disease (except coronary heart disease) were higher in Black participants than in White participants, which likely explains the greater adverse atrial remodeling that we observed in Black participants than in White participants. Despite the higher prevalence of cardiovascular risk factors and greater atrial remodeling in Black participants, the frequency of AT was lower—a conundrum that underscores resilience to atrial arrhythmogenesis in Black individuals.

Racial differences in AF risk may be related to genetic, biological, or social factors. In this regard, a genetic admixture study of Black participants using 2 population-based cohorts reported that Black participants with a lower percentage of European ancestry had a lower risk of AF.[7] Another study consisting of 3 community-based cohorts found the minor allele of the rs10824026 single-nucleotide polymorphism, which is known to be protective against AF, was significantly more common in Black individuals than in White individuals.[8] In this study, it was suggested that the rs10824026 single-nucleotide polymorphism may account for up to 31% of the reduced AF risk in Black individuals when compared with White individuals.[8] It is also possible that NT-proBNP (N-terminal pro–brain natriuretic peptide) or inflammatory biomarkers may mediate the association between race and AF risk.[38,39] The Health, Aging, and Body Composition (Health ABC) study reports that approximately 40% of the increased risk of AF in White participants may be explained by racial differences in inflammation, as assessed via concentrations of adiponectin, TNF-α (tumor necrosis factor α), TNF-α soluble receptor I, and TNF-α soluble receptor II.[38] In addition, Black individuals have been shown to have lower NT-proBNP levels than White individuals.[39,40] A study using data from the ARIC study and the Cardiovascular Heart Study indicated that NT-proBNP explained approximately 25% of the elevated risk of incident AF in White participants.[39] In the ARIC study, each 10% greater percent European ancestry in Black participants was associated with 7% higher NT-proBNP levels.[40] Collectively, the foregoing studies suggest that in Black individuals, underlying genetic and biological factors mitigate the predilection to atrial arrhythmias conferred by greater atrial remodeling. In addition to these factors, social constructs may play a role in the observed racial differences in AF risk. Racial differences in self-advocacy have been noted in which Black women were less likely to mention health information to their physicians than White women.[41] Furthermore, the racial difference in patients' engagement in their health care may be mediated by health literacy.[42] Differences in health care self-advocacy and health literacy may result in underdiagnosed AF cases in Black individuals. Additional research is warranted to further identify factors that may explain the racial difference in AF risk.

The strengths of this study include the prospective design when assessing the association between LA measures and SVE burden; the use of 2-week continuous heart rhythm monitoring, which provided greater precision of SVE burden; high percentage of analyzable time; and the representation of Black and White men and women. Importantly, in addition to LA volume, we evaluated LA function. Prior research has suggested that reservoir function of the left atrium may indicate more advanced LA remodeling and underlying left ventricular dysfunction than LA enlargement alone.[43] LA function also may provide prognostic information over LA volume as a predictor of AF.[19,37] Several limitations should be noted. First, as the majority of Black participants were recruited from the Jackson, MS, site, the generalizability of our results to all Black Americans may be limited. In addition, because all Black participants in our study were recruited from 2 field centers (Forsyth County and Jackson), confounding by center cannot be adequately addressed given our study design. Moreover, we are unable to separate the effects of race from regional differences. Despite these limitations, race-specific findings have been previously published from the ARIC study.[1,3,44–46] Furthermore, differences between respondent and nonrespondent patterns were similar for Black participants at both the Jackson center, which recruited only Black participants, and the Forsyth County center, which recruited Black and White participants.[26] Second, given the limited number of Black participants in our study, our estimates are less precise in Black participants than in White participants. Third, although we accounted for

selection bias by using inverse probability weighting in our prospective analyses, selection bias may have occurred as a result of participants not agreeing to wear the Zio XT Patch or visit nonattendance. However, response rates in attending study visits and agreeing to wear the Zio XT Patch were similar between races. Fourth, the proprietary algorithm used by iRhythm to detect arrhythmias is US Food and Drug Administration approved; however, this software is not in the public domain. Finally, similar to other observational studies, residual confounding may exist.

CONCLUSIONS

In this population-based study, although Black participants have a higher prevalence of cardiovascular risk factors and greater abnormalities in LA size and function than White participants, Black participants have a lower susceptibility for AT than White participants. Greater LA size and impaired LA function are associated with more runs of AT and PAC in both Black and White participants without any racial differences. Future research is needed to unravel this racial paradox of AF and elucidate the protective mechanisms that confer resilience to atrial arrhythmias in Black individuals.

ARTICLE INFORMATION

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REFERENCES

1. Alonso A, Agarwal SK, Soliman EZ, Ambrose M, Chamberlain AM, Prineas RJ, Folsom AR. Incidence of atrial fibrillation in whites and African-Americans: the Atherosclerosis Risk in Communities (ARIC) Study. *Am Heart J*. 2009;158:111–117. doi: 10.1016/j.ahj.2009.05.010
2. Amponsah MKD, Benjamin EJ, Magnani JW. Atrial fibrillation and race - a contemporary review. *Curr Cardiovasc Risk Rep*. 2013;7:336–345. doi: 10.1007/s12170-013-0327-8
3. Mou L, Norby FL, Chen LY, O'Neal WT, Lewis TT, Loehr LR, Soliman EZ, Alonso A. Lifetime risk of atrial fibrillation by race and socioeconomic status: ARIC Study (Atherosclerosis Risk in Communities). *Circ Arrhythm Electrophysiol*. 2018;11:e006350. doi: 10.1161/CIRCEP.118.006350
4. Christensen MA, Nguyen KT, Stein PK, Fohtung RB, Soliman EZ, Dewland TA, Vittinghoff E, Psaty BM, Heckbert SR, Marcus GM. Atrial ectopy as a mediator of the association between race and atrial fibrillation. *Heart Rhythm*. 2017;14:1856–1861. doi: 10.1016/j.hrthm.2017.09.034
5. Eberly LA, Garg L, Yang L, Markman TM, Nathan AS, Eneanya ND, Dixit S, Marchlinski FE, Groeneveld PW, Frankel DS, et al. Racial/ethnic and socioeconomic disparities in management of incident paroxysmal atrial fibrillation. *JAMA Netw Open*. 2021;4:e210247. doi: 10.1001/jamanetworkopen.2021.0247
6. Nelson A. Unequal treatment: confronting racial and ethnic disparities in health care. *J Natl Med Assoc*. 2002;94:666–668.
7. Marcus GM, Alonso A, Peralta CA, Lettre G, Vittinghoff E, Lubitz SA, Fox ER, Levitzky YS, Mehra R, Kerr KF, et al. European ancestry as a risk factor for atrial fibrillation in African Americans. *Circulation*. 2010;122:2009–2015. doi: 10.1161/CIRCULATIONAHA.110.958306
8. Roberts JD, Hu D, Heckbert SR, Alonso A, Dewland TA, Vittinghoff E, Liu Y, Psaty BM, Olgin JE, Magnani JW, et al. Genetic investigation into the differential risk of atrial fibrillation among black and white individuals. *JAMA Cardiol*. 2016;1:442. doi: 10.1001/jamacardio.2016.1185
9. Dewland TA, Bibbins-Domingo K, Lin F, Vittinghoff E, Foster E, Ogunyankin KO, Lima JA, Jacobs DR, Hu D, Burchard EG, et al. Racial differences in left atrial size: results from the Coronary Artery Risk Development in Young Adults (CARDIA) study. *PLoS One*. 2016;11:e0151559. doi: 10.1371/journal.pone.0151559
10. Manolio TA, Gottdiener JS, Tsang TSM, Gardin JM; Cardiovascular Health Study Collaborative Research Group. Left atrial dimensions determined by M-mode echocardiography in black and white older (> or =65 years) adults (The Cardiovascular Health Study). *Am J Cardiol*. 2002;90:983–987.
11. Marcus GM, Olgin JE, Whooley M, Vittinghoff E, Stone KL, Mehra R, Hulley SB, Schiller NB. Racial differences in atrial fibrillation prevalence and left atrial size. *Am J Med*. 2010;123:375.e1–375.e7. doi: 10.1016/j.amjmed.2009.05.019
12. Dewland TA, Vittinghoff E, Mandyam MC, Heckbert SR, Siscovick DS, Stein PK, Psaty BM, Sotoodehnia N, Gottdiener JS, Marcus GM. Atrial ectopy as a predictor of incident atrial fibrillation: a cohort study. *Ann Intern Med*. 2013;159:721–728. doi: 10.7326/0003-4819-159-11-201312030-00004
13. Binici Z, Intzilakis T, Nielsen OW, Køber L, Sajadieh A. Excessive supraventricular ectopic activity and increased risk of atrial fibrillation and stroke. *Circulation*. 2010;121:1904–1911. doi: 10.1161/CIRCULATIONAHA.109.874982

14. Chong B-H, Pong V, Lam K-F, Liu S, Zuo M-L, Lau Y-F, Lau C-P, Tse H-F, Siu C-W. Frequent premature atrial complexes predict new occurrence of atrial fibrillation and adverse cardiovascular events. *Europace*. 2012;14:942–947. doi: 10.1093/europace/eur389
15. O'Neal WT, Kamel H, Judd SE, Safford MM, Vaccarino V, Howard VJ, Howard G, Soliman EZ. Usefulness of atrial premature complexes on routine electrocardiogram to determine the risk of atrial fibrillation (From the REGARDS Study). *Am J Cardiol*. 2017;120:782–785. doi: 10.1016/j.amjcard.2017.06.007
16. Anaissie J, Monlezun D, Seelochan A, Siegler JE, Chavez-Keatts M, Tiu J, Pineda D, George A, Shaban A, Abi Rafeh N, et al. Left atrial enlargement on transthoracic echocardiography predicts left atrial thrombus on transesophageal echocardiography in ischemic stroke patients. *Biomed Res Int*. 2016;2016:7194676. doi: 10.1155/2016/7194676
17. Sardana M, Lessard D, Tsao CW, Parikh NI, Barton BA, Nah G, Thomas RC, Cheng S, Schiller NB, Aragam JR, et al. Association of left atrial function index with atrial fibrillation and cardiovascular disease: the Framingham offspring study. *J Am Heart Assoc*. 2018;7:e008435. doi: 10.1161/JAHA.117.008435
18. Habibi M, Samiei S, Venkatesh BA, Opdahl A, Helle-Valle TM, Zareian M, Almeida ALC, Choi E-Y, Wu C, Alonso A, et al. CMR-Measured left atrial volume and function and incident atrial fibrillation: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circ Cardiovasc Imaging*. 2016;9:e004299. doi: 10.1161/CIRCIMAGING.115.004299
19. Abhayaratna WP, Fatema K, Barnes ME, Seward JB, Gersh BJ, Bailey KR, Casaclang-Verzosa G, Tsang TSM. Left atrial reservoir function as a potent marker for first atrial fibrillation or flutter in persons > or = 65 years of age. *Am J Cardiol*. 2008;101:1626–1629.
20. Tsang TSM, Barnes ME, Bailey KR, Leibson CL, Montgomery SC, Takemoto Y, Diamond PM, Marra MA, Gersh BJ, Wiebers DO, et al. Left atrial volume: important risk marker of incident atrial fibrillation in 1655 older men and women. *Mayo Clin Proc*. 2001;76:467–475. doi: 10.4065/76.5.467
21. Gupta DK, Shah AM, Giugliano RP, Ruff CT, Antman EM, Grip LT, Deenadayalu N, Hoffman E, Patel I, Shi M, et al. Left atrial structure and function in atrial fibrillation: ENGAGE AF-TIMI 48. *Eur Heart J*. 2014;35:1457–1465. doi: 10.1093/eurheartj/eht500
22. Inciardi RM, Giugliano RP, Claggett B, Gupta DK, Chandra A, Ruff CT, Antman EM, Mercuri MF, Grosso MA, Braunwald E, et al. Left atrial structure and function and the risk of death or heart failure in atrial fibrillation. *Eur J Heart Fail*. 2019;21:1571–1579. doi: 10.1002/ejhf.1606
23. Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, Encinas J, Fought AJ, Topol EJ. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. *Am J Med*. 2014;127:e11–e17. doi: 10.1016/j.amjmed.2013.10.003
24. Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. *Pacing Clin Electrophysiol*. 2013;36:328–333. doi: 10.1111/pace.12053
25. The ARIC investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. *Am J Epidemiol*. 1989;129:687–702.
26. Jackson R, Chambless LE, Yang K, Byrne T, Watson R, Folsom A, Shahar E, Kalsbeek W. Differences between respondents and nonrespondents in a multicenter community-based study vary by gender and ethnicity. *J Clin Epidemiol*. 1996;49:1441–1446. doi: 10.1016/0895-4356(95)00047-X
27. Shah AM, Cheng S, Skali H, Wu J, Mangion JR, Kitzman D, Matsushita K, Konety S, Butler KR, Fox ER, et al. Rationale and design of a multicenter echocardiographic study to assess the relationship between cardiac structure and function and heart failure risk in a biracial cohort of community-dwelling elderly persons: the Atherosclerosis Risk in Communities study. *Circ Cardiovasc Imaging*. 2014;7:173–181. doi: 10.1161/CIRCIMAGING.113.000736
28. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). *Am J Cardiol*. 2008;101:1016–1022. doi: 10.1016/j.amjcard.2007.11.061
29. White AD, Folsom AR, Chambless LE, Sharret AR, Yang K, Conwill D, Higgins M, Williams O, Tyroler HA, The ARIC Investigators. Community surveillance of coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) Study: methods and initial two years' experience. *J Clin Epidemiol*. 1996;49:223–233. doi: 10.1016/0895-4356(95)00041-0
30. Eriksson H, Caidahl K, Larsson B, Ohlson LO, Welin L, Wilhelmsen L, Svärdsudd K. Cardiac and pulmonary causes of dyspnoea–validation of a scoring test for clinical-epidemiological use: the Study of Men Born in 1913. *Eur Heart J*. 1987;8:1007–1014. doi: 10.1093/oxfordjournals.eurheartj.a062365
31. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, Copper LS, Shahar E. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke*. 1999;30:736–743. doi: 10.1161/01.STR.30.4.736
32. Weuve J, Tchetgen Tchetgen EJ, Glymour MM, Beck TL, Aggarwal NT, Wilson RS, Evans DA, Mendes de Leon CF. Accounting for bias due to selective attrition: the example of smoking and cognitive decline. *Epidemiology*. 2012;23:119–128. doi: 10.1097/EDE.0b013e318230e861
33. Chiang JK, Kao HH, Kao YH. Association of paroxysmal supraventricular tachycardia with ischemic stroke: a National Case-Control study. *J Stroke Cerebrovasc Dis*. 2017;26:1493–1499. doi: 10.1016/j.jstrokecerebrovasdis.2017.03.005
34. Kamel H, Elkind MSV, Bhave PD, Navi BB, Okin PM, Iadecola C, Devereux RB, Fink ME. Paroxysmal supraventricular tachycardia and the risk of ischemic stroke. *Stroke*. 2013;44:1550–1554. doi: 10.1161/STROKEAHA.113.001118
35. Heckbert SR, Jensen PN, Austin TR, Chen LY, Post WS, Ambale Venkatesh B, Soliman EZ, Floyd JS, Sotoodehnia N, Kronmal RA, et al. Associations of left atrial function and structure with supraventricular ectopy: the Multi-Ethnic Study of Atherosclerosis. *J Am Heart Assoc*. 2021;10:e018093. doi: 10.1161/JAHA.120.018093
36. Go AS, Hlatky MA, Liu TI, Fan D, Garcia EA, Sung SH, Solomon MD. Contemporary burden and correlates of symptomatic paroxysmal supraventricular tachycardia. *J Am Heart Assoc*. 2018;7:e008759. doi: 10.1161/JAHA.118.008759
37. Kojima T, Kawasaki M, Tanaka R, Ono K, Hirose T, Iwama M, Watanabe T, Noda T, Watanabe S, Takemura G, et al. Left atrial global and regional function in patients with paroxysmal atrial fibrillation has already been impaired before enlargement of left atrium: velocity vector imaging echocardiography study. *Eur J Echocardiogr*. 2012;13:227–234. doi: 10.1093/ejechocard/jer281
38. Dewland TA, Vittinghoff E, Harris TB, Magnani JW, Liu Y, Hsu F-C, Satterfield S, Wassel C, Marcus GM. Inflammation as a Mediator of the association between race and atrial fibrillation: results from the health, aging, and body composition study. *JACC Clin Electrophysiol*. 2015;1:248–255. doi: 10.1016/j.jacep.2015.04.014
39. Whitman IR, Vittinghoff E, DeFilippi CR, Gottdiener JS, Alonso A, Psaty BM, Heckbert SR, Hoogeveen RC, Arking DE, Selvin E, et al. NT-pro BNP as a mediator of the racial difference in incident atrial fibrillation and heart failure. *J Am Heart Assoc*. 2019;8:e010868. doi: 10.1161/JAHA.118.010868
40. Gupta DK, Claggett B, Wells Q, Cheng S, Li M, Maruthur N, Selvin E, Coresh J, Konety S, Butler KR, et al. Racial differences in circulating natriuretic peptide levels: the atherosclerosis risk in communities study. *J Am Heart Assoc*. 2015;4:e001831. doi: 10.1161/JAHA.115.001831
41. Wiltshire J, Cronin K, Sarto GE, Brown R. Self-advocacy during the medical encounter: use of health information and racial/ethnic differences. *Med Care*. 2006;44:100–109. doi: 10.1097/01.mlr.0000196975.52557.b7
42. Eneanya ND, Winter M, Cabral H, Waite K, Henault L, Bickmore T, Hanchate A, Wolf M, Paasche-Orlow MK. Health literacy and education as mediators of racial disparities in patient activation within an elderly patient cohort. *J Health Care Poor Underserved*. 2016;27:1427–1440. doi: 10.1353/hpu.2016.0133
43. Hoit BD. Left atrial size and function: role in prognosis. *J Am Coll Cardiol*. 2014;63:493–505. doi: 10.1016/j.jacc.2013.10.055
44. Simpson RJ, Cascio WE, Schreiner PJ, Crow RS, Rautaharju PM, Heiss G. Prevalence of premature ventricular contractions in a population of African American and white men and women: the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J*. 2002;143:535–540. doi: 10.1067/mhj.2002.120298
45. Norby FL, Alonso A, Rooney MR, Maheshwari A, Koene RJ, Zhang M, Soliman EZ, Loehr LR, Mosley T, Gottesman RF, et al. Association of ventricular arrhythmias with dementia: the atherosclerosis risk in communities (ARIC) study. *Neurology*. 2021;96:e926–e936. doi: 10.1212/WNL.0000000000011122
46. Rooney MR, Soliman EZ, Lutsey PL, Norby FL, Loehr LR, Mosley TH, Zhang M, Gottesman RF, Coresh J, Folsom AR, et al. Prevalence and characteristics of subclinical atrial fibrillation in a community-dwelling elderly population: the ARIC study. *Circ Arrhythm Electrophysiol*. 2019;12:e007390. doi: 10.1161/CIRCEP.119.007390