The prognostic value of early repolarization with ST-segment elevation in African Americans

Marco V. Perez, MD,* Abhimanyu Uberoi, MD, MS,* Nikhil A. Jain, BS,* Euan Ashley, MRCP, Dphil,* Mintu P. Turakhia, MD, MAS,*† Victor Froelicher, MD, FACC*†

*From the *Division of Cardiovascular Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California; †Division of Cardiovascular Medicine, Department of Medicine, Veterans Affairs Palo Alto Health Care System, Palo Alto, California.*

BACKGROUND Increased prevalence of classic early repolarization, defined as ST-segment elevation (STE) in the absence of acute myocardial injury, in African Americans is well established. The prognostic value of this pattern in different ethnicities remains controversial.

OBJECTIVE Measure association between early repolarization and cardiovascular mortality in African Americans.

METHODS The resting electrocardiograms of 45,829 patients were evaluated at the Palo Alto Veterans Affairs Hospital. Subjects with inpatient status or electrocardiographic evidence of acute myocardial infarction were excluded, leaving 29,281 subjects. ST-segment elevation, defined as an elevation of >0.1 mV at the end of the QRS, was electronically flagged and visually adjudicated by 3 observers blinded to outcomes. An association between ethnic-
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= coronary artery disease; ECG = electro
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Introduction

Cardiovascular disease remains one of the leading causes of death in African Americans in the United States.[1,2] African Americans have worse outcomes from cardiovascular disease, when compared with the populations of European descent.[3–6] The reasons for these differences are not well understood, and the differences are likely due to a combination of socioeconomic,[7,8] environmental, and genetic differences.[9]

The 12-lead cardiac electrocardiogram (ECG) is the test most commonly used to evaluate patients with cardiovascular disease. Differences in ECG patterns between ethnic populations may represent variation in cardiac anatomy and physiology that could help explain racial differences in cardiovascular disease. It was established as early as 1976 that markers of early repolarization on the ECG were significantly more common in African Americans,[10] a finding that has been validated in numerous populations studies.[11–14] Early repolarization was initially defined half a century ago[15–17] as the presence of ST-segment elevation (STE) with or without other ECG characteristics such as J waves and was found to be common and benign in young, predominantly white, populations.[13,14]

Recent studies have defined early repolarization as the presence of terminal QRS slurring or J waves without a focus on the presence of STE,[18–21] and some have linked these characteristics to poor cardiovascular outcomes. The retrospective analyses that reported that patients with idiopathic ventricular fibrillation had a high prevalence of terminal QRS slurring[19] or J-point elevation[22–24] raised concern that early repolarization may not be as benign as was originally believed. Subsequent population studies using similarly modified definitions of early repolarization identified terminal QRS slurring as a predictor of cardiac death.[20,21,25,26]

Address reprint requests and correspondence: Dr Marco V. Perez, MD, Cardiac Electrophysiology and Arrhythmia Service, Stanford University,300 Pasteur Dr #H2146, Stanford, CA 94305-5233. E-mail address: mvperez@stanford.edu.

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Although QRS slurring has received more recent attention, it is the classic repolarization pattern that includes STE which is more prevalent in African Americans. The prognostic value of STE in this group may have ethnic-specific implications on the need for further cardiovascular evaluation. The prognostic value of early repolarization in African Americans has not been well studied. We sought to establish whether or not the classic repolarization pattern predicts cardiovascular death in the African American population.

Methods

Study design

The Palo Alto Veterans Affairs Health Care System uses a computerized ECG system (GE Healthcare, Wauwatosa, WI) to collect, store, and analyze ECGs. This system has been validated by both the US Food and Drug Administration and the European Community and is widely used across the world. The current study involved the retrospective analysis of 45,829 inpatient and outpatient ECGs obtained between March 1987 and December 1999 at the Palo Alto Veterans Affairs Health Care System. All patients were seen at the main Veterans Affairs facility or its satellite clinics, and ECGs were ordered by health-care providers for standard clinical indications, usually to screen for occult disease and to obtain a baseline when initiating care. For patients with multiple ECGs, only the first ECG was considered since serial ECGs were obtained only for clinical indications and not as part of the routine protocol. Since clinical diagnostic codes were not available, we excluded those with inpatient status (n = 12,319) to eliminate ECGs possibly associated with acute coronary syndromes and other acute processes. Furthermore, ECGs exhibiting atrial fibrillation or flutter (n = 1253), ventricular rates greater than 100 beats/min (n = 2,799), QRS durations greater than 120 ms (n = 3141), paced rhythms (n = 290), ventricular preexcitation (n = 42), and acute myocardial infarction (n = 29) were excluded, leaving 29,281 patients for analysis. Age, sex, weight, and height of each patient were recorded. The African American race was determined by self-report at the time of ECG acquisition.

ECG analysis

The recorded data on each ECG included the timing and voltages at each of the points of the PQRST complex of the basic 8 leads with derivation of the remaining 4 leads. From these measurements, the Romhilt–Estes criteria for left ventricular hypertrophy[27] and left axis were calculated. Standardized computerized ECG criteria as described by the GE 12-lead electrographic analysis program were used for the diagnosis of Q waves, left atrial enlargement, and bundle branch blocks. We defined early repolarization as the STE of 0.1 mV or more at the end of the QRS complex, extending throughout the ST segment. All ECGs exhibiting STE as determined by the computer measurements were reread by 3 observers (blinded to outcomes), corrected when necessary. The criterion requiring STE in 2 contiguous leads in the inferior (II, III, and AVF) and lateral (I, aVL, V4–V6) lead groups was applied. In this way, visual inaccuracy was accounted for without losing computer accuracy. The criteria for the diagnosis of coronary artery disease (CAD) corresponded to Minnesota codes 1.1 to 1.3, 4.1 to 4.3, 5.1 to 5.2, 7.1, and 7.4, which were automatically derived. The ST slope was automatically calculated as the slope of the ST segment compared with the baseline horizontal line and reported in degrees. The ECGs were also coded for ST depression and diagnostic Q waves.

Outcomes

The primary outcome variable was time to cardiovascular mortality. The California Health Department Service and Social Security Death Indices were used to ascertain the vital status of each patient as of December 31, 2002. An accuracy of causes of deaths was reviewed by 2 clinicians blinded to ECG results and confirmed by using the Veterans Affairs computerized medical records. Follow-up was complete.

Statistical analysis

Unpaired t tests were used for the comparisons of continuous variables, and χ^2 tests were used to compare dichotomous variables between patient groups. All variables were first tested for the normality of distribution. Statistical significance was defined by $P < .05$. An association between ethnicity and early repolarization was measured by using multivariate logistic regression models adjusted for age, sex, heart rate, and CAD by Minnesota criteria and reported as odds ratios with 95% confidence intervals (CIs). Cox proportional hazards regression analysis was performed to determine whether early repolarization patterns were predictive of subsequent cardiovascular death. Hazard ratios (HRs) with 95% CIs for early repolarization abnormalities were calculated by using a model adjusted for age and sex as well as a model adjusted for age, sex, heart rate, and CAD. Proportional hazard assumptions were met as verified by plotting the log-negative-log of within-group freedom from atrial fibrillation. The Kaplan–Meier method was used to estimate the rates of cardiovascular mortality in the subgroups of early repolarization patterns stratified by African American race. SAS version 9.2 (SAS Institute, Inc, Cary, NC) was used for all statistical analyses.

Results

Baseline demographics and ECG characteristics

After exclusion of inpatients and patients who met the exclusion criteria noted above, there remained 29,281 patients with ECGs available for analysis. The patients were on average aged 55 years; 13% were women; and there were a total of 3885(13.3%) African Americans. African American subjects were younger (49.3 vs 55.0 years; $P < .0001$), were less likely to be women (8.5 vs 13.4; $P < .0001$), and had a similar body mass index (27.4 vs 27.3; $P = .30$) compared with non-African American subjects (Table 1). African American subjects were more likely to have ECG-evident left ventricular hypertrophy and left atrial enlarge-

Table 1 Differences in baseline demographics and ECG characteristics between patients with and without early repolarization (lateral or inferior STE) by race

	African Americans			Non-African Americans			African Americans vs non-African Americans
Characteristic	No repol (n = 3644)	Repol (n = 241)	P*	No repol (n = 24,973)	Repol (n = 423)	P*	P†
Demographics							
Age (y)	49.8 ± 13	42.1 ± 12	<.0001	56.0 ± 15	47 ± 15	<.0001	<.0001
Sex (female)	328 (9.0)	3 (1.2)	<.0001	3385 (13.5)	21 (5.0)	<.0001	<.0001
Weight (kg)	85 ± 18	82 ± 15	.021	82 ± 18	80 ± 15	.006	<.0001
BMI	27.5 ± 5.5	26.2 ± 4.4	.0014	27.3 ± 5.5	25.8 ± 4.5	<.0001	.30
ECG characteristics							
Heart rate	71.6 ± 12	66.3 ± 12	<.0001	70.6 ± 13	64.3 ± 13	<.0001	.0003
LVH	98 (2.7)	13 (5.4)	.015	328 (1.3)	21 (5.0)	<.0001	<.0001
RVH	7 (0.2)	1 (0.41)	.46	49 (0.2)	0	.362	.86
LAE	155 (4.2)	3 (1.2)	.022	715 (2.9)	5 (1.2)	.039	<.0001
Q waves	266 (7.3)	8 (3.3)	.019	2666 (10.7)	42 (9.9)	.621	<.0001
QTc	416 ± 23	405 ± 17	<.0001	418 ± 22	412 ± 25	<.0001	<.0001
QTc > 450 ms	262 (7.2)	4 (1.7)	.001	1960 (7.8)	24 (5.7)	.098	.035
PR	162 ± 25	162 ± 25	.544	160 ± 32	158 ± 23	.121	<.0001
QRS	90.3 ± 10	89.5 ± 9.0	.228	92.3 ± 10	90.9 ± 10	.005	<.0001
Left-axis deviation	221 (6.1)	5 (2.1)	.010	1758 (7.0)	13 (3.1)	.0015	.008
Right-axis deviation	43 (1.2)	3 (1.2)	.93	472 (1.9)	8 (1.9)	.999	.002
CAD	929 (25.5)	28 (11.6)	<.0001	6755 (27.0)	84 (19.9)	.0009	.003

Values are presented as total number (percentage of subjects) or mean ± standard deviation.

BMI = body mass index; CAD = coronary artery disease by Minnesota criteria; ECG = electrocardiogram; LAE = left atrial enlargement; LVH = left ventricular hypertrophy; QTc = corrected QT interval; RVH = right ventricular hypertrophy; STE = ST-segment elevation, Repol = early repolarization.

*P value represents significance from the t test for continuous variables and χ^2 test for categorical variables between those with early repolarization (STE lateral or inferior) and those without repolarization for the corresponding race.

†P value for differences between all African Americans and non-African Americans.

ment but less likely to have pathologic Q waves, prolonged corrected QT interval, or CAD by Minnesota criteria (Table 1). These patients were followed for an average of 7.6 ± 3.8 years, resulting in a total of 6739 deaths (1995 cardiovascular deaths), with 675 deaths (205 [23.2%] cardiovascular deaths) occurring in African Americans and 6064 deaths (1790 [22.8%] cardiovascular deaths) in non-African Americans.

Early repolarization is more common in African Americans

There were 185 patients with inferior-only STE, 479 with lateral-only STE, and 664 with lateral or inferior STE. The age-adjusted prevalence of each repolarization pattern was higher in African Americans compared with non-African Americans (Figure 1) and was most pronounced in the lateral or inferior STE repolarization pattern (6.4% vs 1.7%; P <.001).

To assess whether or not African American race was independently associated with this early repolarization pattern, logistic regression analysis was performed. On univariate analysis, African Americans were almost 4 times as likely to manifest this early repolarization pattern. After correction for age, sex, heart rate, and CAD by Minnesota criteria, African Americans were still more likely to manifest the lateral or inferior STE pattern (odds ratio 3.1; 95% CI 2.7–3.7; P <.0001) (Table 2).

Prognostic value of early repolarization patterns in African Americans

African Americans with lateral or inferior STE were younger (42.1 vs 49.8 years; P <.0001), were less likely to

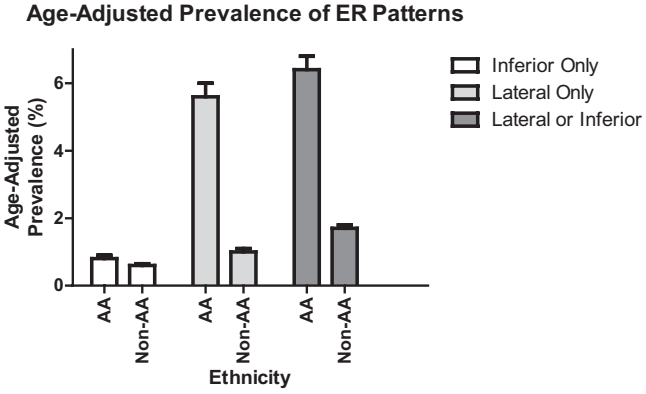

Figure 1 Age-adjusted prevalence of different early repolarization patterns by ethnicity. All differences were statistically significantly different with P <.0001, with the exception of the inferior-only ER pattern (P = .16). Error bars represent standard errors. AA = African Americans; ER = early repolarization.

Table 2 Multivariate analysis of correlations with early repolarization (lateral or inferior STE) adjusted for multiple covariates

Variable	Univariate model	*P*	CI	Age and sex adjusted	*P*	CI	Multivariate model	*P*	CI
African American	3.9	.0001	3.3–4.6	3.0	.0001	2.6–3.5	3.1	.0001	2.7–3.7
Age (per 1 y)	0.95	.0001	0.95–0.96	0.95	.0001	0.95–0.96	0.96	.0001	0.95–0.96
Sex (female)	0.25	.0001	0.16–0.38	0.24	.0001	0.16–0.40	0.25	.0001	0.16–0.37
CAD	0.55	.0001	0.45–0.68	0.87	.21	0.7–1.1	0.86	.16	0.69–1.06
HR (per beat)	0.96	.0001	0.956–0.969	0.96	.0001	0.96–0.97	0.96	.0001	0.96–0.97

Values are presented as odds ratios. The multivariate model was adjusted for age, sex, heart rate, African American race, and CAD.
CAD = coronary artery disease by Minnesota criteria; CI = 95% confidence interval; HR = heart rate.

be women (1.2% vs 9%; $P < .0001$), and had a slightly lower body mass index (26.2 vs 27.5; $P = .0014$) compared with African Americans without STE. African Americans with inferior STE also had slower heart rates and were more likely to have evidence of left ventricular hypertrophy (5.4% vs 2.7%; $P = .015$) but less likely to have left atrial enlargement, pathologic Q waves, a prolonged corrected QT interval, or CAD by Minnesota criteria (11.6% vs 25.5%; $P < .0001$) as compared with African Americans without STE.

To illustrate the univariate associations between the STE patterns and cardiovascular mortality in African Americans and non-African Americans, the Kaplan–Meier plots of freedom from cardiovascular death were generated (Figure 2). There were clear separations of the plots with the inferior or lateral STE pattern conferring lower rates of cardiovascular death for both African Americans and non-African Americans (log-rank statistic $P < .001$). However, rates of cardiovascular death were lower in the African Americans with the inferior STE pattern, while rates of cardiovascular death were higher in the non-African Americans with the inferior STE pattern (log-rank statistic $P < .001$).

To further assess the association between the different early repolarization patterns and cardiovascular death, multivariate Cox proportional hazards regression analysis was performed (Table 3). On univariate analysis, the lateral or inferior STE (HR 0.39; 95% CI 0.2–0.89; $P = .02$) and the lateral-only STE (HR 0.46; 95% CI 0.2–1.0; $P = .06$) patterns were protective of cardiovascular death in African Americans. However, after adjustment for age and sex, these differences were attenuated and no longer statistically significant. With adjustment for age, sex, heart rate, and CAD, there were no significant associations between cardiovascular death and the lateral or inferior STE pattern (HR 0.75; 95% CI 0.3–1.7; $P = .50$), the lateral STE pattern (HR 0.93; 95% CI 0.4–2.1 $P = 0.86$;), or the pattern with lateral and inferior STE in any lead (HR 0.73; 95% CI 0.1–5.2; $P = .76$). Additional adjustment with a sex–STE interaction term did not significantly affect these HRs or their statistical significance. The hazard of the inferior-only STE could not be estimated because there were no African American deaths in this group. A Cox proportional hazards regression analysis was also performed with the entire cohort, and it was found that after adjusting for lateral or inferior STE, age, sex, African American race, heart rate, and CAD, a race–STE interaction covariate was marginally associated with cardiovascular mortality (HR 0.45; 95% CI 0.2–1.1; $P = .08$).

This was in contrast to the non-African American cohort, where there was a modest but statistically significant association between cardiovascular death and the lateral or inferior STE pattern (HR 1.60; 95% CI 1.1–2.4; $P = .02$) and the inferior STE pattern (HR 2.13; 95% CI 1.3–3.6; $P = .005$) after adjusting for age, sex, heart rate, and CAD (Table 3). However, when subjects with CAD evident on the ECG by Minnesota criteria were excluded from the study, a significant association between early repolarization and cardiovascular death in non-African Americans was not present.

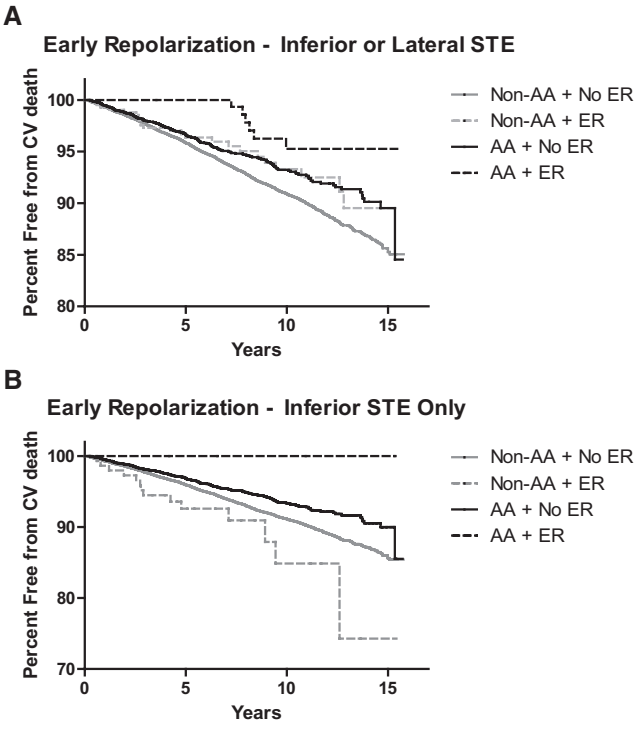

Figure 2 Kaplan–Meier plot of freedom from cardiovascular death by ethnicity and presence of early repolarization in the (A) inferior or lateral leads and (B) inferior leads only. Log-rank statistic for each plot $P < .001$. AA = African American; CV = cardiovascular; ER = early repolarization; STE = ST-segment elevation.

Table 3 Cox proportional hazard regression analysis testing the time-dependent association between different early repolarization patterns and cardiovascular death by race

Variable	Univariate HR	P	CI	Age- and sex-adjusted HR	P	CI	Multivariate HR	P	CI	Multivariate no CAD HR	P	CI
African Americans												
Lat or Inf STE	0.39	.02	0.2–0.89	0.616	.24	0.3–1.4	0.75	.50	0.3–1.7	0.93	.88	0.37–2.3
Lat STE	0.46	.06	0.2–1.0	0.73	.45	0.3–1.7	0.93	.86	0.4–2.1	1.19	.70	0.48–2.9
Inf STE	—	NA	NA	—	NA	NA	—	NA	NA	—	—	NA
Non-African Americans												
Lat or Inf STE	0.75	.16	0.5–1.1	1.4	.10	0.94–2.1	1.60	.02	1.1–2.4	1.15	.67	0.60–2.2
Lat STE	0.40	.01	0.2–0.8	0.92	.80	0.5–1.7	1.15	.67	0.6–2.2	0.80	.66	0.30–2.1
Inf STE	1.6	.07	0.9–2.7	2.1	.004	1.3–3.6	2.13	.005	1.3–3.6	1.8	.21	0.73–4.2

Values are presented as hazard ratios (HRs). In models where there were no deaths, the HRs were not reported. The multivariate model was adjusted for age, sex, heart rate, and coronary artery disease (CAD) by Minnesota criteria. The multivariate no CAD model excluded patients with CAD by Minnesota criteria and was adjusted for age, sex, and heart rate.

CI = 95% confidence interval; Elev = elevation; Inf = inferior; Lat = lateral; NA = nonapplicable; STE = ST-segment elevation.

Table 4 Morphologic differences in early repolarization patterns between African Americans and non-African Americans

ECG characteristic	African Americans (n = 241)	Non-African Americans (n = 423)	P*
Corresponding TWI	18 (7.5)	56 (13.2)	.023
Corresponding Q waves	1 (0.41)	22 (5.2)	.0012
ST slope (deg)	6.3 ± 21	−3.1 ± 28	<.0001
T-wave axis (deg)	35 ± 24	41 ± 30	.015
QTc (ms)	404 ± 17	411 ± 24	.0001
QTc > 450 ms	4 (1.6)	24 (5.7)	.0133
QRS (ms)	89.4 ± 9	90.9 ± 10	.0676
Left-axis deviation	5 (2.07)	13 (3.0)	.446
Right-axis deviation	3 (1.2)	8 (1.9)	.530
LVH pattern	13 (5.4)	21 (5.0)	.809
CAD by Minnesota criteria	28 (11.6)	84 (19.8)	.0064

Values are presented as total number (percentage of subjects) or mean ± standard deviation.

CAD = coronary artery disease; LVH = left ventricular hypertrophy, QTc = corrected QT interval; TWI = T-wave inversion. Corresponding TWI and Corresponding Q waves = T-wave inversions or Q waves, respectively, in the same distribution as the repolarization abnormalities.

**P* value represents significance from the *t* test for continuous variables and χ^2 test for categorical variables between African Americans and non-African Americans.

Differences in coexisting ECG characteristics

To better understand the morphologic variations between the STE patterns in African Americans and the STE patterns in non-African Americans, we studied differences in coexisting ECG characteristics between the 2 populations with inferior or lateral STE (Table 4). African Americans with the inferior or lateral STE pattern had a much lower prevalence of corresponding T-wave inversions (7.5% vs 13.2%; $P = .023$), corresponding Q waves (0.41% vs 5.2%; $P = .0012$), corrected QT-interval prolongation (1.6% vs 5.7%; $P = .0001$), or CAD (11.9 vs 19.8; $P = .0064$). In addition, the ST slope in African Americans with early repolarization was much higher than that in non-African Americans with early repolarization (6.3° vs −3.1°; $P < .0001$). When subjects with CAD evident on the ECG by Minnesota criteria were excluded, the ST slope in African Americans with early repolarization remained higher than that in non-African Americans with early repolarization (5.8° vs 1.3°; $P = .021$). To further study the effects of the ST slope on mortality in subjects without CAD, we performed a multivariate analysis in the combined African American and non-African American cohort, adjusting for age, sex, race, and heart rate. We found that the ST slope was inversely correlated with cardiovascular death with an HR of 0.99 for every 1° rise in the ST slope ($P < .0001$).

Discussion

Early repolarization is benign in African Americans

Although it was well established that classic early repolarization is more common in African Americans, we now report that this finding does not confer additional cardio-

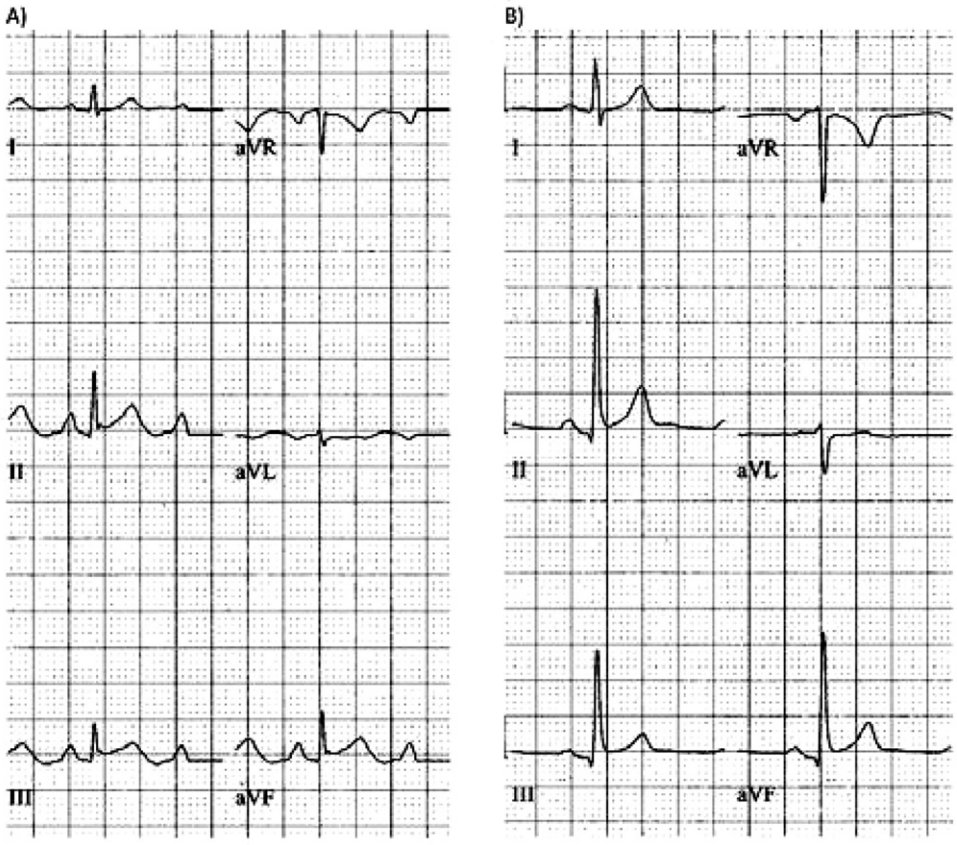

Figure 3 Examples of classic early repolarization patterns seen in African Americans. **A:** Sixty-year-old African American man with inferior ST-element elevation (STE) and J waves. **B:** Thirty-nine-year-old African American man with inferior STE and mild terminal QRS slurring.

vascular risk. ECGs are the most common tests performed during the evaluation for cardiovascular disease and there is growing interest in routine screening for cardiovascular disease in asymptomatic athletes,[28,29] many of whom are African Americans. Decisions regarding the need for further noninvasive imaging in asymptomatic African Americans with early repolarization abnormalities depend on the prognostic value of these characteristics.

The classic early repolarization pattern, which requires the presence of STE, was often referred to in the older literature as the "benign early repolarization" pattern,[30] primarily because of its frequency and benign nature observed in young asymptomatic populations.[13,14] The seminal finding by Haissaguerre et al[19] that patients with idiopathic ventricular fibrillation more frequently had evidence of "early repolarization" challenged the benign nature of this term. The definition of "early repolarization" has been evolving. The new definition includes patterns of terminal slurring of the QRS or the presence of J waves without requiring the presence of STE, and these have been lumped into the term *early repolarization*. While many have adopted the new definitions,[18,20,21] others point to the need to distinguish the different early repolarization patterns.[31] We chose to use the classic definition of early repolarization—the presence of STE with or without coexisting ECG features such as J waves (Figure 3)—since its higher prevalence in African Americans has been well established. We believe this analysis in African Americans helps answer a long-standing question regarding the benign nature of this finding in this cohort and complements the information that is known about the alternative forms of early repolarization whose nature is less benign.

Clinicians taking care of the approximately 6% of African Americans with STE are often concerned about the increased risk conferred by this pattern. However, we found in multivariate analysis that there is no correlation between any of the classic early repolarization patterns and cardiovascular death (Table 3). Of note, even in the non-African American population, where the cardiovascular death HR is approximately 2 for the inferior STE pattern in our study and others,[20] early repolarization alone is not sufficient to change management in an asymptomatic patient with a low prior probability of cardiovascular disease.

The meaning of early repolarization

An elevated ST segment possibly represents the presence of differential timing of repolarization in different regions of the myocardium.[32] Terminal QRS slurring and J waves, on the other hand, are more likely a manifestation of variations in a variety of currents,[33,34] which can be indicative of familial channelopathy syndromes.[35] The slurring of the terminal QRS and the presence of J waves without STE likely represent distinct electroanatomic processes with different prognostic implications than the classic STE patterns

and, in some cases, may be representative of remote myocardial infarction.[36]

Why African Americans have an increased prevalence of classical early repolarization remains a mystery. African American athletes also manifest different forms of early repolarization associated with conditioning,[37] suggesting that the electrocardiogram may also need to be interpreted differently in African American athletes.[38] It is possible that there are underlying genetic differences between ethnicities that result in different patterns of repolarization. The new repolarization patterns also appear to have a component of familial heritability,[18] implying an underlying genetic basis.

Differences in the prognostic value of early repolarization between ethnicities are a clue that there may be fundamental differences in the etiologies of the early repolarization patterns. We identified several morphologic features that helped distinguish the African American early repolarization pattern from the non-African American pattern (Table 4). Many of the coexisting characteristics found in the non-African Americans, such as Q waves and CAD by Minnesota criteria, have been associated with cardiovascular mortality. When subjects with CAD evident on the ECG by Minnesota criteria were excluded from the analysis, the hazard in the non-African Americans was eliminated, suggesting that underlying CAD may indeed be driving the modest association between early repolarization and cardiovascular mortality in non-African Americans (Table 3). Others have reported that subjects with early repolarization who had negative-sloping ST segments have a worse outcome than those with positive-sloping ST segments.[39] Nevertheless, when we excluded subjects with CAD evident on the ECG, we found that the slope of the ST segment in African Americans was still higher compared with that in non-African Americans, which suggests that the differences in the patterns between African Americans and non-African Americans are not fully explained by differences in underlying coronary disease. We also found that in the combined population of patients without ECG-evident CAD, the ST slope itself was inversely correlated with cardiovascular mortality, suggesting that the ST slope is either an independent marker of coronary heart disease or a marker of non-coronary etiologies of cardiovascular death.

Strengths and limitations

To our knowledge, this is the largest population study in African Americans of the classic early repolarization pattern. This is also one of the first and largest studies to report the prognostic value of early repolarization in African Americans, a population that is often underrepresented in clinical studies. The study of ethnic differences among the Veterans Affairs population has the advantage of reducing socioeconomic differences by providing more equal access to the health care system, which, in contrast to other studies,[3–6] may help explain why rates of ECG-evident coronary disease are higher in our non-African American cohort.

There are a few limitations worth noting. The reasons for referral for ECG and the clinical status of each patient at the time of the ECG were not thoroughly documented; however, these ECGs were ordered as per physician discretion, which is comparable to a real-word setting. Incorporating concurrent clinical data was unfortunately beyond the scope of this project since it would require reviewing manually nearly 30,000 records, coding for the clinical status at the time of the ECG measurement, and adding these covariates to our data set. We have taken care to exclude patients who might have had the ECG taken during an acute illness or with advanced cardiac disease by excluding inpatients, patients with wide QRS, in atrial fibrillation, or in sinus tachycardia. In addition, the ECGs were gathered from a predominantly male population.

Conclusions

In summary, we have reviewed the differences in ECG characteristics between African Americans and non-African Americans and confirmed that the adjusted prevalence of classic early repolarization patterns is approximately 3-fold higher in African Americans. We demonstrated, however, that early repolarization does not confer an increased hazard of cardiovascular mortality in African Americans. We also found that the early repolarization patterns in African Americans differ from those in non-African Americans. Further studies in genetics and electrophysiology will be necessary to help elucidate the reasons for these differences. Decisions regarding further diagnostic testing in asymptomatic black men should not depend on the presence of classic early repolarization patterns on ECG.

References

1. National Heart, Lung, and Blood Institute, ed. 2009 NHLBI Morbidity and Mortality Chart Book. Bethesda, MD: NHBLI; 2009.
2. Jones DW, Chambless LE, Folsom AR, et al. Risk factors for coronary heart disease in African Americans: the atherosclerosis risk in communities study, 1987–1997. Arch Intern Med 2002;162:2565–2571.
3. Liao Y, Cooper RS. Continued adverse trends in coronary heart disease mortality among blacks, 1980–91. Public Health Rep 1995;110:572–579; discussion 570–572.
4. Sempos CT, Bild DE, Manolio TA. Overview of the Jackson Heart Study: a study of cardiovascular diseases in African American men and women. Am J Med Sci 1999;317:142–146.
5. Dries DL, Exner DV, Gersh BJ, Cooper HA, Carson PE, Domanski MJ. Racial differences in the outcome of left ventricular dysfunction. N Engl J Med 1999;340:609–616.
6. Sempos C, Cooper R, Kovar MG, McMillen M. Divergence of the recent trends in coronary mortality for the four major race–sex groups in the United States. Am J Public Health 1988;78:1422–1427.
7. Fang J, Madhavan S, Alderman MH. The association between birthplace and mortality from cardiovascular causes among black and white residents of New York City. N Engl J Med 1996;335:1545–1551.
8. Popescu I, Nallamothu BK, Vaughan-Sarrazin MS, Cram P. Racial differences in admissions to high-quality hospitals for coronary heart disease. Arch Intern Med 2010;170:1209–1215.
9. Lettre G, Palmer CD, Young T, et al. Genome-wide association study of coronary heart disease and its risk factors in 8,090 African Americans: the NHLBI CARe Project. PLoS Genet 2011;7:e1001300.
10. Kambara H, Phillips J. Long-term evaluation of early repolarization syndrome (normal variant RS-T segment elevation). Am J Cardiol 1976;38:156–157.
11. Roukoz H, Wang K. ST elevation and inverted T wave as another normal variant mimicking acute myocardial infarction: the prevalence, age, gender, and racial distribution. Ann Noninvasive Electrocardiol 2011;16:64–69.
12. Crouse SF, Meade T, Hansen BE, Green JS, Martin SE. Electrocardiograms of collegiate football athletes. Clin Cardiol 2009;32:37–42.

13. Klatsky AL, Oehm R, Cooper RA, Udaltsova N, Armstrong MA. The early repolarization normal variant electrocardiogram: correlates and consequences. Am J Med 2003;115:171–177.
14. Thomas J, Harris E, Lassiter G. Observations on the T wave and S-T segment changes in the precordial electro-cardiogram of 320 young Negro adults. Am J Cardiol 1960;5:468–472.
15. Myers GB, Klein HA, Stofer BE, Hiratzaka T. Normal variations in multiple precordial leads. Am Heart J 1947;34:785–808.
16. Grant RP, Estes EH Jr, Doyle JT. Spatial vector electrocardiography: the clinical characteristics of S-T and T vectors. Circulation 1951;3:182–197.
17. Wasserburger RH, Alt WJ. The normal RS-T segment elevation variant. Am J Cardiol 1961;8:184–192.
18. Noseworthy PA, Tikkanen JT, Porthan K, et al. The early repolarization pattern in the general population: clinical correlates and heritability. J Am Coll Cardiol 2011;57:2284–2289.
19. Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. N Engl J Med 2008;358:2016–2023.
20. Sinner MF, Reinhard W, Muller M, et al. Association of early repolarization pattern on ECG with risk of cardiac and all-cause mortality: a population-based prospective cohort study (MONICA/KORA). PLoS Med 2010;7:e1000314.
21. Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. N Engl J Med 2009;361:2529–2537.
22. Rosso R, Kogan E, Belhassen B, et al. J-point elevation in survivors of primary ventricular fibrillation and matched control subjects: incidence and clinical significance. J Am Coll Cardiol 2008;52:1231–1238.
23. Abe A, Ikeda T, Tsukada T, et al. Circadian variation of late potentials in idiopathic ventricular fibrillation associated with J waves: insights into alternative pathophysiology and risk stratification. Heart Rhythm 2010;7:675–682.
24. Nam GB, Ko KH, Kim J, et al. Mode of onset of ventricular fibrillation in patients with early repolarization pattern vs. Brugada syndrome. Eur Heart J 2009;31:330–339.
25. Haruta D, Matsuo K, Tsuneto A, et al. Incidence and prognostic value of early repolarization pattern in the 12-lead electrocardiogram. Circulation 2011;123:2931–2937.
26. Olson KA, Viera AJ, Soliman EZ, Crow RS, Rosamond WD. Long-term prognosis associated with J-point elevation in a large middle-aged biracial cohort: the ARIC study. Eur Heart J 2011 (Epub ahead of print).
27. Romhilt DW, Estes EH Jr. A point-score system for the ECG diagnosis of left ventricular hypertrophy. Am Heart J 1968;75:752–758.
28. Perez M, Fonda H, Le VV, et al. Adding an electrocardiogram to the preparticipation examination in competitive athletes: a systematic review. Curr Probl Cardiol 2009;34:586–662.
29. Wheeler MT, Heidenreich PA, Froelicher VF, Hlatky MA, Ashley EA. Cost-effectiveness of preparticipation screening for prevention of sudden cardiac death in young athletes. Ann Intern Med 2010;152:276–286.
30. Brady WJ, Chan TC. Electrocardiographic manifestations: benign early repolarization. J Emerg Med 1999;17:473–478.
31. Surawicz B, Macfarlane PW. Inappropriate and confusing electrocardiographic terms: J-wave syndromes and early repolarization. J Am Coll Cardiol 2011;57:1584–1586.
32. Benito B, Guasch E, Rivard L, Nattel S. Clinical and mechanistic issues in early repolarization of normal variants and lethal arrhythmia syndromes. J Am Coll Cardiol 2010;56:1177–1186.
33. Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. Circulation 1996;93:372–379.
34. Janse MJ, van Capelle FJ, Morsink H, et al. Flow of "injury" current and patterns of excitation during early ventricular arrhythmias in acute regional myocardial ischemia in isolated porcine and canine hearts: evidence for two different arrhythmogenic mechanisms. Circ Res 1980;47:151–165.
35. Haissaguerre M, Chatel S, Sacher F, et al. Ventricular fibrillation with prominent early repolarization associated with a rare variant of KCNJ8/KATP channel. J Cardiovasc Electrophysiol 2009;20:93–98.
36. Michael MA, El Masry H, Khan BR, Das MK. Electrocardiographic signs of remote myocardial infarction. Prog Cardiovasc Dis 2007;50:198–208.
37. Rawlins J, Carre F, Kervio G, et al. Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. Circulation 2009;121:1078–1085.
38. Uberoi A, Stein R, Perez MV, et al. Interpretation of the electrocardiogram of young athletes. Circulation 2011;124:746–757.
39. Tikkanen JT, Junttila MJ, Anttonen O, et al. Early repolarization: electrocardiographic phenotypes associated with favorable long-term outcome. Circulation 2011;123:2666–2673.