Early Repolarization in an Ambulatory Clinical Population

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***Background*—**The significance of early repolarization, particularly regarding the morphology of the R-wave downslope, has come under question.

***Methods and Results*—**We evaluated 29 281 resting ambulatory ECGs from the VA Palo Alto Health Care System. With PR interval as the isoelectric line and amplitude criteria $\geq$0.1 mV, ST-segment elevation is defined at the end of the QRS, J wave as an upward deflection, and slur as a conduction delay on the QRS downstroke. Associations of ST-segment elevation patterns, J waves, and slurs with cardiovascular mortality were analyzed with Cox analysis. With a median follow-up of 7.6 years, there were 1995 cardiac deaths. Of 29 281 subjects, 87% were male (55$\pm$14 years) and 13% were female (56$\pm$17 years); 13% were black, 6% were Hispanic, and 81% were white or other. Six hundred sixty-four (2.3%) had inferior or lateral ST-segment elevation: 185 (0.6%) in inferior leads and 479 (1.6%) in lateral leads, 163 (0.6%) in both, and 0.4% had global elevation. A total of 4041 ECGs were analyzed with enhanced display, and 583 (14%) had J waves or slurring, which were more prevalent in those with than in those without ST-segment elevation (61% versus 13%; $P<0.001$). ST-segment elevation occurred more in those with than in those without J waves or slurs (12% versus 1.3%; $P<0.001$). Except when involving only inferior leads, all components of early repolarization were more common in young individuals, male subjects, blacks, and those with bradycardia. All patterns and components of early repolarization were associated with decreased cardiovascular mortality, but this was not significant after adjustment for age.

***Conclusions*—**We found no significant association between any components of early repolarization and cardiac mortality. **(*Circulation*. 2011;124:00-00.)**

Key Words: electrocardiography ■ death ■ follow-up studies

ST-segment elevation in the absence of acute infarction was first reported in the ECGs of healthy individuals in 1947[1] and called early repolarization in 1951.[2] This "normal RS-T segment elevation variant" was characterized as ST-segment elevation at the end of the QRS complex with a distinct notch (J wave) or slur on the downslope of the R wave by Wasserburger and Alt in 1961.[3] In 1976, Kambara and Phillips[4] reported that early repolarization was more common in young male individuals and blacks, and appeared typically in lateral leads and less frequently in inferior leads. Whereas the key feature of early repolarization has been ST-segment elevation because of its critical association with myocardial infarction or ischemia and pericarditis, morphology of the downslope of the R wave has long been noted and thought to be benign.

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Recent studies that suggested an association between early repolarization and cardiovascular death did not use the traditionally characteristic ST-segment elevation in their definition; rather, they focused on the morphology of the downslope of the R wave. The seminal article by Haissaguerre and colleagues[5] was based on a retrospective analysis of 206 individuals with idiopathic ventricular fibrillation (VF) with structurally normal hearts. The subjects were found to have a higher prevalence of J waves or slurring of the QRS downstroke compared with age-matched control subjects. Subsequently, a community epidemiological study reported that only J waves or slurring in the inferior leads had an adjusted hazard of 2 for association with cardiac death.[6] Together, these studies were contrary to the previously held notion that early repolarization in healthy athletes and a general clinical population[7] was a benign finding. On the basis of these 2 studies, cellular physiologists hypothesized that early repolarization should be included in the pathological categories of J-wave syndromes[8] and ST-segment elevation channelopathies.[9]

If these new observations and hypotheses were confirmed, they could have a profound impact on the preparticipation examination and on ECG screening in general, because athletes, blacks, and young male individuals often exhibit a

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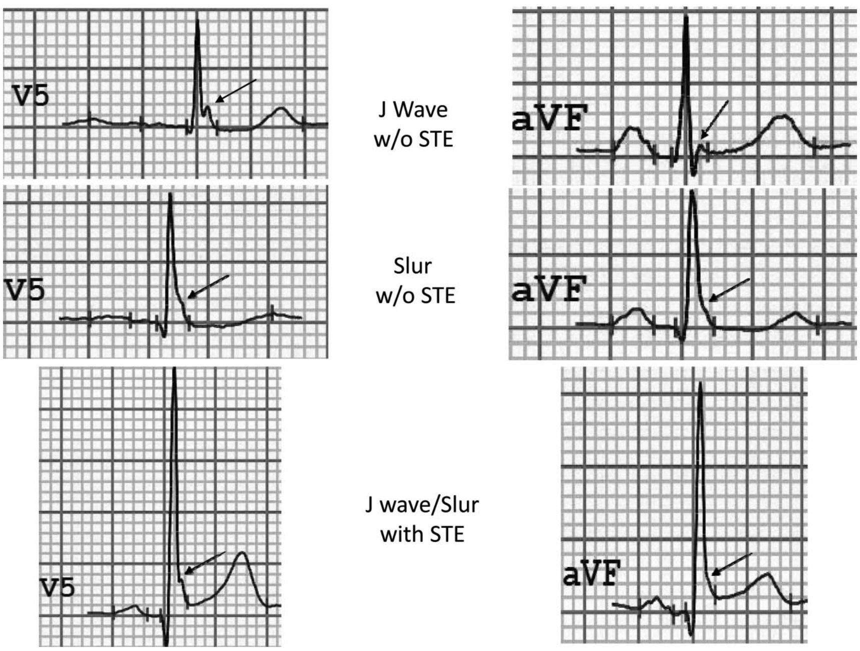

Figure 1. Examples of slurs and J waves with and without ST-segment elevation (STE; [0.1 mm]). Arrow points to amplitude measurement point for the slur and J wave; blue hash line at the end of QRS is the computerized ST measurement point.

higher prevalence of early repolarization than the general population.[4,10] The burden of requiring further testing of this potentially large cohort with early repolarization would be prohibitive.

In an attempt to clarify this controversy, we evaluated the prevalence and prognosis of early repolarization, defined by ST-segment elevation and the morphology of the downslope of the R wave, in a large outpatient population.

Methods

Clinical Population

We performed a retrospective study of 45 829 inpatient and outpatient ECGs from March 1987 to December 1999 at the VA Palo Alto Health Care System. Since 1987, the VA Palo Alto Health Care System has used a centralized, computerized ECG system for the collection, storage, and analysis of ECGs (GE Healthcare, Wauwatosa, WI). This system has been approved by the US Food and Drug Administration and the European Union and is widely used around the world. All patients were seen at the main VA facility or its satellite clinics, and ECGs were ordered by healthcare providers for standard clinical indications, usually to screen for occult disease and to obtain a baseline when care is initiated. For patients with multiple ECGs, only the first ECG was considered because serial ECGs were obtained only for clinical indications, not as part of routine protocol. Because 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 a trial fibrillation or flutter (n=1253), ventricular rates >100 bpm (n=2799), QRS durations >120 milliseconds (n=3141), paced rhythms (n=290), ventricular preexcitation (n=42), and acute myocardial infarction (n=29) were excluded, leaving 29 281 patients for analysis. Race was determined by self-report at the time of ECG acquisition. Unfortunately, incorporating the concurrent clinical data was beyond the scope of this project because that would have required manually reviewing all records, coding the clinical variables, and adding them to the database. Furthermore, the inclusion of additional variables would be inconsistent because a protocol was not in place for gathering the data.

ECG Interpretation

With the PR interval as the isoelectric line and the amplitude criteria as ≥0.1 mV, J waves were defined as an upward deflection, slurs as a conduction delay beginning on the QRS downstroke, and ST-segment elevation at the end of the QRS complex. All ECGs exhibiting ST-segment elevation as determined by the computer measurements were reread by 3 observers (blinded to outcomes) and corrected when necessary (4.5%). In general, the criterion requiring ST-segment elevation in 2 contiguous leads in any lead group (inferior: II, III, and AVF; lateral: I, aVL, and V_4–V_6; anterior: V_1–V_3) was applied. However, if an ST-segment elevation classification resulted in a group size <1% of the total population, then only 1 lead with ST-segment elevation in the territory was considered sufficient for classification. This way, visual inaccuracy was accounted for without losing computer accuracy. As in prior studies,[5,6] anterior lead elevation was not considered separately but was included in the global ST-segment elevation pattern. The ECGs were also coded for left ventricular hypertrophy, ST-segment depression, diagnostic Q waves, and Minnesota Codes consistent with coronary artery disease. Figure 1 provides examples of slurs and J waves with and without ST-segment elevation.

A subset of the population (n=4041) were in a data structure in which the ECGs could be displayed on a 24-in computer screen in multiple formats, enabling careful classification of slurring on the downslope of the R and J waves. These patients were visually coded for ≥0.1-mV slurs on the downslope of the R and J waves by an experienced interpreter. A random sample of 100 (half with and half without J waves or slurring) were reread, and the agreement was 95% owing to slight differences in amplitude measurements.

To determine the natural history of early repolarization, 250 patients with ECGs exhibiting the greatest amplitude of early repolarization were reviewed to see if they had another ECG >1 year later. Their serial ECGs, obtained for clinical indications and not by protocol, were then reviewed and manually coded.

Outcomes

The primary outcome variable was time to cardiovascular mortality. The California Health Department Service and Social Security Death Indexes were used to ascertain the vital status of each patient as of December 31, 2002, for the total population and, as of December 31, 2010, for the digital data subset. Accuracy of causes of deaths was reviewed by 2 clinicians blinded to ECG results and confirmed with the Veterans Affairs computerized medical records. Sufficient data

Table 1. Population Characteristics of the Total Population for Comparison Between the Patterns of ST-Segment Elevation

Characteristic	All Subjects	No ST-Segment Elevation in Lateral or Inferior Leads	ST Elevation Inferior Leads Only	*P*	ST-Segment Elevation Lateral Leads Only	*P*	ST-Segment Elevation Inferior or Lateral	*P*	ST-Segment Elevation Both Inferior and Lateral (Any)	*P*	ST-Segment Elevation Global (Any)	*P*
n (%)	29 281	28 617 (97.7)	185 (0.6)		479 (1.6)		664 (2.3)		163 (0.6)		119 (0.4)	
Age, y	55±15	55±15	52±16	0.005	42±13	<0.001	45±15	<0.001	42±14	<0.001	40±13	<0.001
Male, n (%)	25 544 (87.2)	24 904 (87.0)	168 (90.8)	0.14	472 (98.5)	<0.001	640 (96.4)	<0.001	158 (96.9)	<0.001	116 (97.5)	<0.001
Black, n (%)	3885 (13.3)	3644 (12.7)	31 (16.8)	0.1	210 (43.8)	<0.001	231 (34.8)	<0.001	62 (38.0)	<0.001	49 (41.2)	<0.001
Body mass index, kg/m^2	27.3±5.5	27.3±5.5	25.8±5.4	0.002	26.0±4.1	<0.001	26.0±4.5	<0.001	24.5±3.4	<0.001	24.6±3.4	<0.001
Heart rate, bpm	70.6±12.6	70.7±12.6	69.6±13.1	0.3	63.2±12.3	<0.001	65.0±12.9	<0.001	66.0±12.4	<0.001	66.1±12.2	<0.001
QTc duration, ms	418±22	418±22	413±30	0.005	408±19	<0.001	409±23	<0.001	407±22	<0.001	405±22	<0.001
QRS duration, ms	92±10	92±10	90±11	0.002	91±9	0.004	90±10	<0.001	90±9	0.008	90±9	0.05
Coronary artery disease on ECG, n (%)	7796 (26.6)	7684 (26.9)	51 (27.6)	0.77	61 (12.7)	<0.001	112 (16.9)	<0.001	12 (7.4)	<0.001	5 (4.2)	<0.001
Romhilt-Estes LVH score >3, n (%)	1241 (4.2)	1155 (4.0)	6 (3.2)	0.5	80 (16.7)	<0.001	86 (13.0)	<0.001	21 (12.9)	<0.001	17 (14.3)	<0.001
ST-segment depression (V_5 <−0.5 mV), n (%)	1974 (6.7)	1963 (6.9)	10 (5.4)	0.47	1 (0.2)	<0.001	11 (1.7)	<0.001	1 (2.3)	0.002	0 (0)	0.003
Inferior Q waves, n (%)	2079 (7.1)	2044 (7.1)	25 (13.5)	<0.001	10 (2.1)	<0.001	35 (5.3)	0.06	4 (9.3)	0.021	2 (1.7)	0.02
Anterior Q waves, n (%)	593 (2.0)	588 (2.1)	3 (1.6)	0.7	2 (0.4)	0.012	5 (0.8)	0.019	4 (9.3)	0.7	2 (1.7)	0.8
CV deaths, n (%)	1995 (6.8)	1966 (6.9)	14 (7.6)	0.68	15 (3.1)	<0.001	29 (4.4)	0.011	4 (2.5)	0.027	2 (1.7)	0.03
Annual CV mortality, %	0.86	0.87	0.92		0.33		0.49		0.16		0.11	

LVH indicates left ventricular hypertrophy; CV, cardiovascular.

were not available to classify arrhythmic deaths. Follow-up was complete.

Statistical Analysis

NCSS software 2007 (Kayesville, UT) and SAS version 9.1 were used for all statistical analyses. Unpaired *t* tests were used for comparisons of continuous variables, and χ^2 tests were used to compare dichotomous variables between patient groups. Survival analysis was performed with the Kaplan-Meier method. The Kaplan-Meier method also was used to estimate the survival rates. The log-rank test was used to compare the estimated survival rates of the patient groups. The hazard ratio estimated from the Cox proportional hazards model was used to determine the associations between ST-segment elevation patterns and outcome. This hazard ratio was adjusted for age, sex, and ethnicity.

Results

Of the 29 281 patients, 25 544 (87.2%) were male and were on average 55±14 years of age. The remaining 3737 patients (12.8%) were female and on average 56±17 years of age. The ethnic distribution was as follows: black, 13%; Hispanic, 6%; and white (and other), 81%. There were 6739 deaths (1995 cardiovascular, 30%) over a mean follow-up of 7.6±3.8 years.

The cohort was stratified into subgroups based on presence and location of ST-segment elevation: no ST-segment elevation, inferior lead only, lateral lead only, inferior or lateral lead, inferior and lateral leads, and global elevation (inferior, lateral, and anterior elevation). There were no significant differences in the baseline characteristics between those without ST-segment elevation and patients with ST-segment elevation except for those with isolated inferior lead elevation. The isolated inferior lead elevation group was older, had a higher heart rate, were less likely to be male, and exhibited more ECG abnormalities, particularly inferior Q waves (13.5%), than the other groups.

Table 1 provides the demographics, ECG findings, and annual cardiovascular mortality of the total population and its subgroups according to patterns of ST-segment elevation. Patients with lateral ST-segment elevation, isolated or as part of a more global pattern, were significantly younger and had a lower heart rate, a lower prevalence of any ECG abnormality other than left ventricular hypertrophy, and a higher prevalence of black race.

The early repolarization pattern in ≥2 contiguous leads was present in 664 subjects (2.3%): 185 (0.6%) in inferior leads and 479 (1.6%) in lateral leads, with elevation in both territories in 43 subjects (0.1%). Because of the small number of patients with contiguous lead elevation in inferior and lateral leads (n=43), we instead considered those with elevation in 1 lead per territory (n=163 patients, 0.6%). The same was done for global elevation (n=30 when requiring contiguous elevation but 119 [0.4%] when using 1 lead per territory). No patients exhibited ST-segment elevation >0.2 mV in either the inferior or lateral lead. Figures 2 through 5 exhibit the Kaplan-Meier curves of freedom from cardiovascular death in the different ST-segment elevation patterns. The hazard ratio estimated from the Cox proportional hazards model was used to determine the associations between ST-segment elevation patterns and outcome. This hazard ratio was adjusted for age, sex, and ethnicity. They showed that ST-segment elevations ≥0.1 mm in lateral leads (Figure 2), in inferior or lateral leads with J waves or slurs (Figure 4), or with global ST-segment elevation (Figure 5) were associated with a trend to decreased mortality, although not statistically significantly. ST-segment elevations of ≥1 mm in inferior leads (Figure 3) did not demonstrate such trends. They appeared to be of no consequence in terms of mortality.

Table 2 presents the demographics of the subset of 4041 that were available for enhanced visualization, enabling

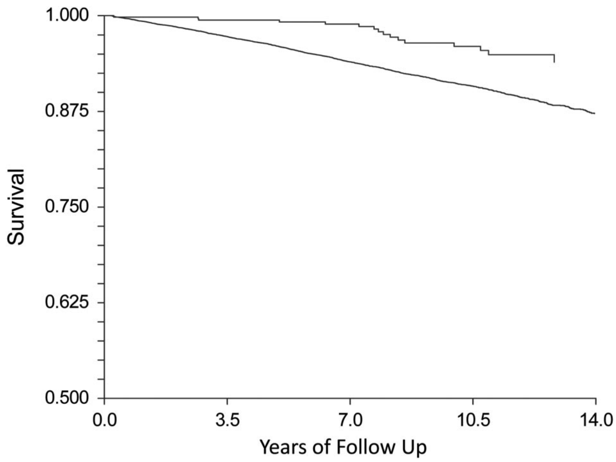

Figure 2. The red line represents the group with ST-segment elevations in lateral leads >1 mm (0.1 mV); the blue line below is the survival curve for all others.

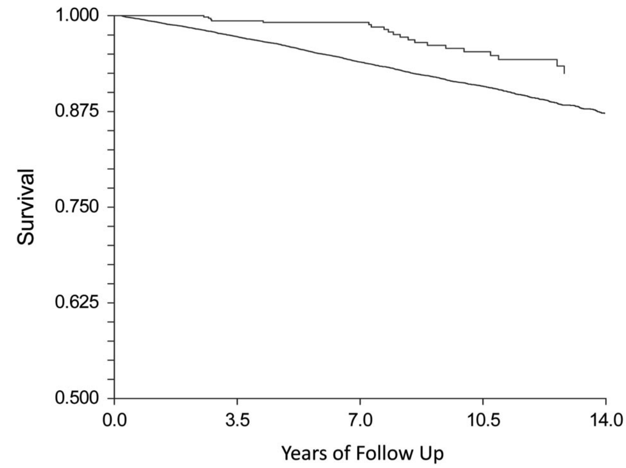

Figure 4. The red line represents the group with ST-segment elevation >1 mm (0.1 mV) in inferior or lateral leads with a J wave or slur; the blue line below is the survival curve for all others.

coding for J waves and slurring on the downslope of the R wave in addition to the ST level measurements. Only minor differences were found between them and the entire population. There were 1082 deaths (245 cardiovascular, 23%) over a mean follow-up of 9.1±3 years. J waves or slurring occurred in 583 (14%), more commonly in those with ST-segment elevation than those without ST-segment elevation (61% versus 13%; $P<0.001$). ST-segment elevation occurred more frequently in those with than in those without J waves or slurs (12% versus 1.3%; $P<0.001$). J waves or slurring was more common than ST-segment elevation (14% versus 2.9%; $P<0.001$), with 1.8% having both ST-segment elevation and a J wave or a slur. Patients with lateral lead early repolarization were significantly younger and had a lower heart rate, a lower prevalence of any ECG abnormality, and a higher prevalence of black race.

Table 3 provides unadjusted and adjusted hazard ratios for the subgroups according to patterns of ST-segment elevation for cardiovascular mortality. The most striking finding is the decreased risk associated with ST-segment elevation, either isolated or as part of any other more global pattern. Although the significance disappears with covariate adjustment, these trends remain. This was also found in the group with global elevation. No significant adjusted or unadjusted hazard associated with inferior lead elevation was found in the overall group. Multivariate models were created to adjust for age, sex, and black ethnicity; a second model also adjusted for resting heart rate, body mass index, and other ECG abnormalities. When included in the multivariate models, all of the covariates were associated with cardiovascular mortality except race and body mass index.

Table 4 provides unadjusted and adjusted hazard ratios for the association between J waves, slurs, ST-segment elevation, and cardiovascular mortality in the 4041 coded for the R-wave downslope patterns. All of the patterns except those with a small sample size were significantly associated with a lowered risk for cardiovascular death. The significance for protection disappeared with adjustment, but the trend remained, and no pattern was associated with an increased risk.

Of the 250 patients with the greatest amplitude of early repolarization, 122 were found to have a repeat ECG >1 year

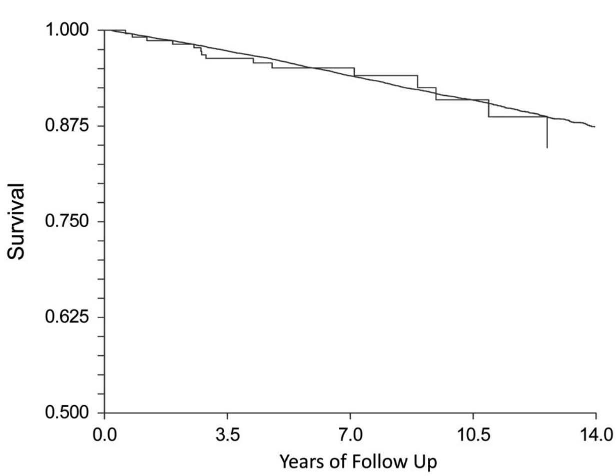

Figure 3. The red line represents the group with ST-segment elevations in inferior leads >1 mm (0.1 mV); the blue line below is the survival curve for all others.

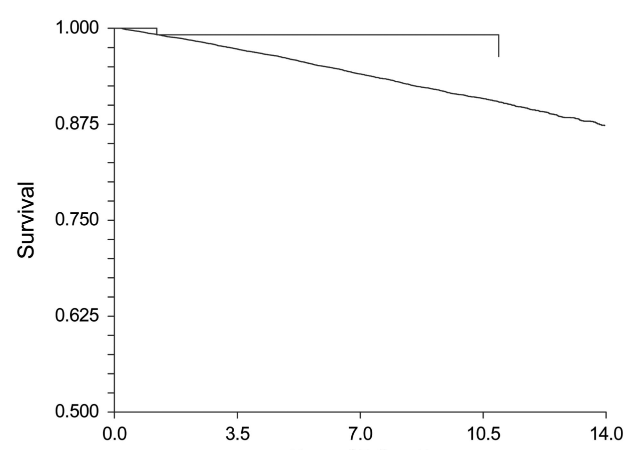

Figure 5. The red line represents the group with global ST-segment elevations, in all lead distributions, >1 mm; the blue line below is the survival curve for all others.

Table 2. Population Characteristics of the Subset of the Population That Could Be Coded for Patterns of R-Wave Morphology for Comparison With the Total Population

Characteristic	All Subjects (n=29 281)	R-Wave Morphology Subset (n=4041)	*P*	Any Lateral Slur/J Wave (n=256 [6.3%])	*P*	Any Inferior Slur/J Wave (n=386 [9.6%])	*P*	Any Slur/J Wave and ST-Segment Elevation (n=72 [1.8%])	*P*
Age, y	55±15	57±14	0.01	51±13	<0.001	55±13	0.001	48±12	<0.001
Body mass index, kg/m^2	27.3±5.5	28.5±6.2	0.02	27±5	0.05	27.9±5	0.08	26±4	0.02
Male, n (%)	25 544 (87)	3634 (90)	0.03	245 (96)	0.001	347 (90)	NS	69 (96)	0.001
Black, n (%)	3,885 (13.3)	506 (12.5)	0.1	78 (30)	<0.001	50 (13)	NS	26 (36)	<0.001
Heart rate, bpm	70.6±12.6	73±16.6	<0.01	67±14	0.01	73±16	NS	64±11	<0.001
QTc duration, ms	418±22	416±26	0.2	407±17	0.008	413±19	0.09	404±17	0.06
QRS duration, ms	92±10	91±12	0.3	88±8	0.008	90.5±9	0.05	88±8	0.02
Coronary artery disease on ECG, n (%)	7796 (26.6)	1012 (25)	0.09	31 (12)	<0.001	77 (20)	<0.01	8 (11)	<0.001
Romhilt-Estes LVH score >3, n (%)	1241 (4.2)	116 (2.9)	<0.01	2 (1)	0.005	14 (3.6)	0.06	9 (12)	<0.001
ST depression (V_5 <−0.5 mV) , n (%)	1974 (6.7)	342 (8.5)	<0.01	0 (0)	<0.001	15 (4)	0.008	0 (0)	0.05
ST-segment elevation, inferior or lateral, n (%)	664 (2.3)	118 (3)	0.06	58 (23)	<0.001	29 (8)	0.005	72 (100)	By definition
Inferior Q waves	2079 (7.1)	351 (8.7)	<0.01	11 (4)	<0.001	16 (4)	0.005	5 (7)	0.07
Anterior Q waves	593 (2.0)	90 (2.2)	0.07	3 (1)	0.02	6 (1.6)	0.03	1 (1)	0.06

LVH indicates left ventricular hypertrophy.

later. After an average of 7 years, 35 still reached the amplitude criteria for early repolarization, but most no longer exhibited early repolarization, and in another 29, no sign of a slur or J wave was present. Thus, the majority did not exhibit early repolarization on the second ECG. Chart review revealed that 5 patients developed heart disease between ECGs, but all of the second ECGs were obtained as part of routine follow-up.

Discussion

To the best of our knowledge, this is the largest multiethnic, long-term population study of the association between ST-segment elevation and cardiovascular death. The subset is equivalent in size to the 2 previous population studies of J waves and slurs and the only such study to consider ST-segment elevation also. We found no statistically significant associations between the components of early repolarization (ie, ST-segment elevation, J waves, or slurs) and cardiovascular death in this ambulatory clinical population.

In an apparently asymptomatic, healthy population, early repolarization has been considered to be a benign finding. However, ST-segment elevation patterns, with or without J waves, can also be found in hypothermia, ischemia, and the Brugada syndrome.[11–17] The J waves of hypothermia, also called Osborn waves, are usually more marked than those seen routinely. The ST-segment elevation seen in Brugada syndrome is isolated to the right precordial leads, often with right ventricular conduction delays, which result in an R′ with the same timing of a J wave. Elegant cellular physiology studies have associated both ECG patterns with channelopathies, which has led to concerns that their presence, even in apparently healthy individuals, could be markers of cardiac events.[12,18–22] Several recent clinical articles have supported this hypothesis.[5–8,13,23] The results of our study challenge this hypothesis, supporting the long-held clinical belief that early repolarization is primarily a benign phenomenon.

The seminal paper by Haissaguerre and colleagues[5] was based on a unique, high-risk population of 202 individuals with ventricular tachycardia or fibrillation and no other evidence for heart disease. Two surprising observations were made in this important study: In 18 subjects with ECG tracings at the time before VF or tachycardia, dynamic ST-segment elevation similar to that seen with coronary spasm was noted, and there was a higher prevalence of

Table 3. Cox Hazard Analysis of the Total Population of 29 281 Ambulatory Clinic Patients With Cardiovascular Death as Outcome

Characteristic	Unadjusted Relative Risk (95% CI)	*P*	Age-Adjusted Relative Risk (95% CI)	*P*	Adjusted Relative Risk (95% CI)	*P*
ST-segment elevation in inferior leads only	1.29 (0.76–2.18)	0.34	1.77 (1.05–2.99)	0.03	1.73 (0.93–3.3)	0.08
ST-segment elevation in lateral leads only	0.39 (0.23–0.64)	<0.001	0.84 (0.50–1.4)	0.5	0.83 (0.50–1.50)	0.52
Global elevation	0.23 (0.06–0.90)	0.04	0.97 (0.62–1.5)	0.9	0.98 (0.6–1.5)	0.9
ST-segment in inferior and lateral leads	0.34 (0.13–0.90)	0.03	0.89 (0.34–2.39)	0.82	0.69 (0.17–2.76)	0.76

CI indicates confidence interval. Multivariate-adjusted analysis includes age, sex, black race, body mass index, heart rate, and ECG abnormalities.

Table 4. Cox Proportional Hazard Analysis of Population Subset (n=4041) That Could Be Coded for Morphology of the R-Wave Downslope With Cardiovascular Death as the Outcome

Characteristic	n (%)	Unadjusted Relative Risk (95% CI)	*P*	Age-Adjusted Relative Risk (95% CI)	*P*	Adjusted Relative Risk (95% CI)	*P*
Inferior slurs	234 (5.8)	0.5 (0.3–1.1)	0.08	0.7 (0.4–1.5)	0.4	0.8 (0.4–1.7)	0.6
Lateral slurs	104 (2.6)	0.6 (0.2–1.6)	0.3	0.7 (0.3–1.8)	0.4	0.8 (0.3–2.2)	0.7
Inferior J waves	152 (3.8)	0.5 (0.2–1.2)	0.1	0.5 (0.2–1.3)	0.2	0.6 (0.3–1.6)	0.3
Lateral J waves	152 (3.8)	0.2 (0.05–0.8)	0.02	0.4 (0.1–1.8)	0.2	0.5 (0.1–2.1)	0.3
Any slur or J wave	583 (14.4)	0.5 (0.3–0.8)	0.002	0.6 (0.4–1.0)	0.05	0.7 (0.5–1.2)	0.2
Any J wave	292 (7.2)	0.3 (0.2–0.7)	0.006	0.5 (0.2–1.1)	0.08	0.6 (0.3–1.3)	0.2
Any slur	319 (7.9)	0.6 (0.3–1.0)	0.06	0.7 (0.4–1.3)	0.3	0.9 (0.5–1.5)	0.6
Any lateral slur/J wave	256 (6.3)	0.3 (0.2–0.8)	0.009	0.6 (0.2–1.2)	0.2	0.7 (0.3–1.5)	0.4
Any inferior slur/J wave	386 (9.6)	0.5 (0.3–0.9)	0.02	0.6 (0.4–1.1)	0.1	0.7 (0.4–1.3)	0.3
Any slur/ J wave and lateral/inferior elevation	72 (1.8)	0.4 (0.1–1.6)	0.2	0.9 (0.2–3.8)	0.9	1.2 (0.3–4.7)	0.8

CI indicates confidence interval. Slur or J wave indicates R-wave downslope J wave or slur ≥0.1 mV adjusted for age, sex, and abnormal ECG.

slurring and notching, or J waves, on their resting ECGs than in control subjects (31% versus 5%). Rosso et al[23] reported contradicting results in 45 patients with idiopathic ventricular fibrillation, 124 matched control subjects, and 121 athletes; they found that the prevalence of ST-segment elevation and QRS slurring was similar in all 3 groups. Merchant et al[24] compared 39 patients with idiopathic ventricular tachycardia/VF, 23% of whom had 1-mm ST-segment elevation, with 200 normal patients with ST-segment elevation. They found notching (J wave) to be more prevalent in idiopathic VF (44% versus 5%). In these 2 articles, notching on the R-wave downslope, or a J wave, was considered early repolarization in the absence of ST-segment elevation.

These studies, concentrating on patients with idiopathic ventricular tachycardia/VF, were followed by a community-based epidemiological study that factored baseline characteristics and used visually interpreted ECGs, which included manual measurements of ST-segment elevation, notching, and slurring in the inferior and lateral leads, with cardiovascular death as the outcome.[6] This study found no hazards associated with these patterns in the lateral leads but an adjusted hazard of roughly 2 for inferior lead ST-segment elevation. The subjects with inferior ST-segment elevation had a higher prevalence of Minnesota Code ECG findings, which are associated with coronary artery disease. The example this study provides for this group exhibited ST-segment elevation occurring over inferior Q waves, which is a pattern that has been associated with wall motion abnormalities of aneurysms after a myocardial infarction. In an earlier clinical population undergoing voluntary health screening, Klatsky and colleagues[7] analyzed 2000 ECGs for ST-segment elevation and reported that 15% had 0.5-mm and 33% had 1.0-mm ST-segment elevation. Those with ST-segment elevation were more likely to be male, <40 years old, bradycardic, black, or physically active. No deaths were reported, and their hypothesis that ST-segment elevation would lead to hospitalizations or cardiac diagnoses was not supported. In a case-cohort study, Sinner et al[25] considered notching on the QRS downslope, or a J wave, early repolarization in the absence of ST-segment elevation. They found these R-wave downslope patterns to be associated with a 2- to 4-fold increased risk of cardiac mortality in those between 35 and 54 years of age, particularly when located inferiorly.

On the basis of their cellular physiology experiments and the 2 recent key studies,[5,6] Antzelevitch and Yan[8] have proposed dividing early repolarization into 3 subtypes: type 1, which displays an ST-segment elevation pattern predominantly in the lateral precordial leads; type 2, which displays an ST-segment elevation pattern predominantly in the inferior or inferolateral leads and is associated with a higher level of risk; and type 3, which displays an ST-segment elevation pattern in the inferior, lateral, and right precordial leads and is associated with the highest level of risk for development of malignant arrhythmias. They included the above types in a category of J-wave syndromes consisting of early repolarization, ischemia, Osborn waves, and Brugada patterns. Our results do not support a clinical utility for this typing or classification.

There are limitations to our study, including a predominantly male population and the use of computerized ECG technology. Whereas we focused on the traditional definition of early repolarization, only a 10% subset considered the independent prognostic value of terminal QRS slurring and J waves. Variation between studies regarding the prevalence of early repolarization may be explained by the wide variation in criteria and population selection. Although our results are more similar to the results of Tikkanen et al,[6] who also showed no risk of death for lateral lead patterns, the differing results of Sinner et al[25] could be due to the limitations of the case-cohort design. Our application of computerized measurements and display with visual confirmation are more consistent with current clinical practice. Development of algorithms to identify and quantify R-wave slurring and J waves should be a priority for future studies. Sufficient data were not available to classify arrhythmic deaths.

Conclusions

We have demonstrated that common patterns of ST-segment elevation, global ST-segment elevation, or J waves and slurring are not associated with cardiovascular death in an asymptomatic outpatient population. Decisions such as whether to perform additional diagnostic tests should be based on symptoms, family history, and all available clinical information and not the benign classic ECG patterns of early repolarization.

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Disclosures

None.

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CLINICAL PERSPECTIVE

A common interpretative statement from modern ECG machines, particularly when testing healthy, young male subjects, is early repolarization. Although these statements are based on the level of the ST segment, recent studies have created concern about variations on the downslope of the R wave, specifically J waves and slurs. Using a large ambulatory clinical population and computerized techniques, we were unable to demonstrate an association of any of these components of early repolarization and cardiovascular death. Although perhaps more prevalent in certain high-risk groups, early repolarization is a benign ECG pattern in apparently healthy individuals with no significant predictive value.