

Electrocardiographic Early Repolarization Characteristics And Clinical Presentations in the Young:
A Benign Finding or Worrisome Marker for Arrhythmias?

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Abstract

Background: The early ECG repolarization QRS pattern (ERp), with J-point elevation of 0.1mV in two contiguous inferior and / or lateral leads, can be associated with ventricular arrhythmias among adults. The significance of an ERp in the young is unknown.

Objective: The purpose of this study was to assess the prevalence of ERp among young patients (pts), describe and correlate the characteristics with clinical presentations and any arrhythmias.

Methods: This was a 1year retrospective review of ECGs obtained from patients referred specifically for documented arrhythmias, possible arrhythmia-related symptoms or sports clearance. ECGs were analyzed for ERp (J point, ascending / horizontal patterns, location) and correlated with presenting complaints.

Results: Of 301 patient ECGs, an ERp was found in 177 (59%), (pts age 11.7 +/- 4.3 years); 54% male; 23% Caucasian. Of these, 6 pts had a family history of sudden cardiac death. Arrhythmias (72% atrial) occurred in 22 pts. Only 3 pts had ventricular arrhythmias (1 successfully ablated). The ascending ST segment and elevated J- point occurred in 77% and 51% of pts with and without arrhythmias respectively. In 73% of all pts, the ERp location was in inferior / lateral leads. Neither gender, ethnicity, large J- point, lead location, nor the combination of a horizontal ST segment with large J-point correlated with any arrhythmias.

Conclusions: ERp, especially the diffuse ascending pattern, is common among the young, in those of European ethnicity, found equally in both genders, and with no apparent correlation with atrial nor ventricular arrhythmias.

Introduction

The early repolarization ECG pattern (ERp), characterized by a J-point elevation of at least 0.1mV at the terminal part of the QRS in two contiguous inferior and/or lateral leads, may be a marker for arrhythmias and sudden cardiac death. The prevalence of an ERp is highly prevalent among the adult population, ranging between 5-13%. It is most commonly seen in young males of African ethnicity. Although, for decades, it was considered somewhat of a normal ECG variant especially among athletes and patients with bradycardia, studies performed in the early 1980's have raised concern that it may not always be a benign ECG finding [1-2]. Several initial cases reports in adults described that an ERp may be a marker of ventricular arrhythmias in the setting of idiopathic ventricular fibrillation. In the presence of myocardial ischemia, the risk for arrhythmias is increased.

Although there have been multiple definitions describing the different ERp characteristics, recommendations for ECG interpretation, established by the American Heart Association/ American college of Cardiology/ Heart Rhythm Society in 2009 defined the ERp as a J-point elevation with a rapidly up sloping or normal ST segment [3]. Most recently, the American Heart Association proposed definitions to help standardize the terminology used to determine ERp and suggested that ERp with ST- segment elevation should be differentiated from ERp with a terminal QRS slur/notch [4].

There are two described early repolarization morphology patterns: ascending and horizontal. The ascending pattern is considered to be present when there is 0.1 mV elevation of the ST segment within 100 ms after the J point and the ST segment merges gradually with the T wave. (Figure 1). This is in comparison to the horizontal pattern in which the ST segment elevation of 0.1 mV occurs within 100 ms after the J point and continues as flat until the onset of the T wave. (Figure 2). Terms, such as "benign" and "malignant" have been used to describe the ascending and horizontal patterns respectively [5,6].

Although older pts who exhibit life-threatening arrhythmias may express an abnormal ERp, the efficacy of using this ECG finding as a prognostic indicator for risk of or marker for ventricular arrhythmias among younger patients remains unanswered. Since an ERp has been reported to occur more frequently in relatives of patients who have had an idiopathic sudden cardiac arrest, a genetic association has been proposed [7]. Framington and British studies suggest that there is a two-fold increased risk of heritability in relatives of patients who exhibit the inferior-

lateral ERp [8-9]. This is of concern when evaluating younger patients and evaluating risk factors for sports participation. Overall, the significance of any of the early repolarization patterns among the young, with / without symptoms potentially attributable to abnormal heart rhythms, and with / without a family history of sudden cardiac death has not been reported and is largely unknown.

Methods

The electrocardiogram (ECG) database of the Cardiology Section of the Children's Hospital of Michigan, Wayne State University School of Medicine, was searched for all patients who were specifically referred to the Pediatric Cardiac Electrophysiology service for evaluation of known arrhythmias, suspected arrhythmias due to clinical complaints or sport clearance/drug administration screening between February 2014 and February 2015. Patients less than 18 years old with the diagnosis of having an early repolarization pattern (ERp), with or without documented arrhythmias, and with or without a family history of sudden cardiac death were included. Patients with repaired or non-repaired structural congenital heart disease, any cardiomyopathy, metabolic condition or coronary artery disease, or on medications which could affect the ECG, were excluded. All identified electrocardiograms were individually reviewed in a blinded fashion by a Pediatric Electrophysiologist to confirm the diagnosis of an ERp. Using established criteria as noted above, the ERp was defined by the presence of a J point-elevation of at least 0.1mV in at least two inferior and/or lateral leads. The location was described as being inferior if the ERp was localized in leads (II, III, aVF), lateral when in leads (V5-V6), and infero-lateral when in leads (II, III, aVF, V5, V6). In addition, the ECG patterns were classified into ascending and horizontal/descending per definition: ascending when the ST segment elevation merged gradually with the T wave and the horizontal/descending pattern, when the ST segment elevation following the J point continued flat until the onset of the T wave as seen in Figures 1 and 2.

The reviewed clinical patient data included the age, ethnicity, gender and family history of sudden cardiac death. Patient medical records were reviewed to document the clinical presentation for which the ECG was performed. Each patient's clinical presentation was reviewed for presence or absence of any documented atrial (narrow QRS tachycardia with/without pre-excitation, flutter, fibrillation) or ventricular (tachycardia, fibrillation) arrhythmias, presence or absence of possible cardiac arrhythmia-related symptoms including chest pain, palpitations, syncope, and dizziness. Patients referred for sports or pre-medication (e.g.: ADHD) clearance were reviewed for any associated symptoms. The respective ERp characteristics were compared between those patients with and without

documented arrhythmias in conjunction with the presence or absence of symptoms. The Children's Hospital of Michigan and Wayne State University Institutional Review Boards approved this descriptive retrospective study.

Statistics

The continuous and categorical variables were expressed by frequencies and means. The Fisher Exact test or Pearson's Chi-square test of proportional differences was employed to examine the possible associations between the asymptomatic patients and those with arrhythmias. The comparisons conducted on continuously scaled variables between the study groups were performed using a parametric independent sample t-test. Statistically significant associations were considered achieved at a p-value of <0.05 , two tailed. All statistical procedures were conducted using SPSS Version 22.0, IBM Inc.

Results

Patient Demographics

Of the 301 patients seen in the cardiac arrhythmia clinic during the study interval, 177 (59%) exhibited one of the two described ERp on their resting ECG. Of these, 97 patients (54%) were male and 80 (46%) were female. When separated into self-described ethnicity, 104 (59%) indicated African American, 41 (23%) European/Caucasian, 5 (3%) Hispanic and 27 (15%) non-listed. The mean age was 11.7 ± 4.3 years. A positive family history of sudden cardiac death was found in 6 (3.4%) patients.

Clinical Presentation

Non-specific cardiac symptoms with no documented arrhythmias were found in 97 patients (55%). Of these, 15 (15%) had syncope, 19 (20%) subjective palpitations, and 3 (3%) with seizure episodes. Since subjective chest discomfort may be a complaint associated with tachycardia in children, 51 patients (53%) with the complaint of chest pain were also included. A functional heart murmur was found in 9 (9%) pts. Documented arrhythmias (on clinic/ER ECGs, ambulatory event monitors or Holter recordings) were found in 21 (12%) patients. ECG screening before medication initiation, for sport clearance, or for a family history of cardiac disease/sudden death occurred in 59 (33%) patients, all of whom were asymptomatic from any known arrhythmias.

Arrhythmias

In total, only 21 of the 177 patients (12%) exhibited clinical arrhythmias. The ambulatory event and Holter monitors documented the arrhythmias in 11 patients, while among the remaining 10 patients the arrhythmias were documented on ECGs from clinic/ER visits. The arrhythmias were typical of a younger population and most (72%) of atrial or atrioventricular origin. There was no ventricular fibrillation or sudden death. Only 3 patients had stable monomorphic ventricular tachycardia that did not degenerate to a polymorphic form nor fibrillation. None of the 3 patients had family history for sudden cardiac death. One of these patients underwent an electrophysiology study, which demonstrated an inducible monomorphic ventricular tachycardia localized to the left ventricle, which was successfully ablated (Figure 3). He remained without further arrhythmias two years later. His resting ECG still showed the ascending ERp. The two remaining patients were effectively treated with beta-blockers. Overall, electrophysiology studies were performed in 13 of 21 patients. Specific arrhythmias and findings are presented in Table 1.

Specific ERp findings

Specific ECG patterns were variable: 137 of the 177 patients (77%) were noted to have the ascending pattern, while 40 patients (23%) exhibited the horizontal/descending pattern. Lead location for the ERp was also variable: 128 of the 177 patients (73%) had the ERp in the inferior and lateral ECGs leads (II, III, aVF, V5, V6), 31 patients (17%) in the inferior leads (II, III, AVF) and 18 patients (10%) in the lateral leads (V5, V6). J-point amplitude was almost comparable among all patients: 86 (49%) of the 177 patients exhibited a J-point amplitude measured at 0.1mV while among 91 (51%) patients, it was larger than 0.1mV.

The 3 patients with ventricular tachycardia exhibited an ascending ST segment pattern. None showed the horizontal/descending pattern. Of these 3 patients, 2 had large J amplitude $>0.1\text{mV}$, while in 1 of the 3 patients, the ERp was localized to the inferior leads. All patients with atrial arrhythmias showed both ascending and horizontal/descending ST segments, small and large J- points, and both localized and diffuse lead locations.

The demographic variables and the ERp characteristics were compared between patients with documented arrhythmia and those who were asymptomatic. There were no differences between female gender, European ethnicity, a large J- point, inferior lead locations, or a horizontal/descending ST segment pattern. In addition, the

combined horizontal/descending ST morphology with large J-point did not correlate with any of the two patient groups ($p = \text{NS}$) (Table 2). The same ERp characteristics were also compared between patients with documented arrhythmias and those with only non-specific cardiac symptoms (e.g.: subjective palpitations, syncope) but with no documented arrhythmias. None of the ERp characteristics correlated with any of the patient groups ($p = \text{NS}$) (Table 3).

Discussion

The early repolarization ECG pattern is common in the general population (5 to 13%) to which it has been identified as a possible marker for ventricular arrhythmias. The term, Early Repolarization Syndrome, has been applied to pts with an ERp and a history of ventricular arrhythmias or aborted cardiac death after excluding other causes of cardiac arrest. The 2013 Asia Pacific Heart Rhythm (APHRS) and European Heart Rhythm Association (EHRS) Societies defined the ERp as $> 1\text{-mm}$ J-point elevation in > 2 contiguous inferior or lateral leads and recommended an ICD implantation for patients who survived a cardiac arrest as class I therapeutic intervention [10]. However, the incidence of idiopathic ventricular fibrillation associated with an ERp is low (10 cases per 100,000 population) compared to the simple prevalence of any one patient exhibiting an ERp on a resting ECG. This raises the question of its reliability as a marker to detect patients at risk [11,12]. Among the young patients reviewed in our study population, ERp patterns were very common with over half (59%) exhibiting either of the two patterns. And although 21 (12%) patients exhibited documented arrhythmias, a ventricular origin was found in only 3 patients and none experienced ventricular fibrillation. This would argue for the unreliability of a ERp found on a resting ECG among the young as having any real predictive value or association with life-threatening arrhythmias.

Although the first case report of idiopathic ventricular fibrillation with an ERp on the surface ECG was published in 1984, the first definitive report describing an association between the ERp and ventricular arrhythmias was conducted later by Haissaguerre in 2008 [13]. In that study, an ERp was more frequently found among patients with idiopathic ventricular fibrillation than among control subjects (31% vs 5%, $P < 0.001$) [12]. The following year, Tikkanen reported on 630 of 10,864 patients who had an ERp associated with a J-point elevation of at least 0.1mV in the inferior leads. His findings concluded that the elevation was associated with an increased risk of death with the relative risk of 1.43 with 95% CI of 1.06-1.94 ($p = 0.03$). In that study, a even higher J-point of at least of 0.2mV

in the inferior leads was found to be associated with an increased risk of sudden death, with a relative risk of 2.92 and a 95% CI of 1.45-5.89 ($p = 0.01$) [14].

The pathophysiology of the ERp remains unclear and several explanations have been proposed. One theory is that the J-point elevation represents an earlier phase 1 of the cardiac action potential at the epicardial compared with endo- and midmyocardial cells, causing a disparity in ion exchange. This is related to increased transient outward potassium current or to a decreased inward sodium or calcium currents of the epicardial cells, resulting in a transmural voltage gradient with early repolarization currents within the ventricles. The resultant epi- endocardial electrical gradient could subsequently trigger phase 2 re-entry in adjacent and non-refractory myocardium allowing premature ventricular contractions to trigger ventricular fibrillation [15-16].

The clinical implications of the early repolarization patterns remain an enigma. There are multiple prognostic characteristics that have been described in the literature that predict ERp as a primary arrhythmic disorder. These characteristics include the location of the ERp, J- amplitude, morphology of the ST segment, and patient gender and ethnicity. However, these findings have not been universally replicated. Antzelevitch described an ECG classification based on the association of arrhythmic risk with spatial distribution [12-17]. Type 1 was described as having an ERp localized in the lateral precordial leads (V5, V6) and was considered to be benign among healthy male athletes. In type 2, the ERp occurs in the inferior (II, III, aVF) or infero-lateral leads and associated with a moderate level of risk. Type 3 was considered to have the highest relative risk and associated with an early repolarization pattern diffusely localized in the inferior, lateral and right-sided leads. Although originally thought that all of the three types may have a common pathophysiology, more recently this concept has been challenged [18-19]. The inferior location of the ERp, in addition to a large J-point amplitude ($> 0.1\text{mV}$), has been described as being associated with an increased risk for arrhythmias. As mentioned above, a J-point elevation of at least of 0.1mV in the inferior leads was reported to be associated with an increased risk of death [14]. In another study of 40 patients with idiopathic ventricular fibrillation, the J- point was higher above the baseline compared with patients without ventricular fibrillation [11]. In a case-cohort study of 6213 patients (1945 with ECGs) and with a mean follow up of 19 years, an the inferior ERp location was reported to associated with an increased risk of cardiovascular death (hazard ration of 3.15, 95% CI 1.58-6.28, $p=0.001$) for both sexes and to 4.27 (95% CI 1.90-9.61, $p< 0.001$) for men between 35-54 y [19]. However, this was not replicated in a later study on a much larger cohort of 20,661 patients with a median age of 17.5 years [21].

Our study substantiated this latter report. The inferior location ERp was found in 17% and large J- point amplitude >0.1 mV was found in 51% of our pediatric population with an ERp. The presence of the inferior location and the large J-point amplitude did not correlate with any of our patients who presented with arrhythmias, with non-specific cardiovascular symptoms or in those who were completely asymptomatic. The diffuse ERp, both inferior and lateral, was more frequently found as 73 % of our study population exhibited this pattern, when compared to the more localized pattern in the inferior or the lateral leads. The morphology of the ST segment was also described in several adult studies as an increased risk factor for arrhythmias in both the general population and in patients with idiopathic ventricular fibrillation. The horizontal or descending ST segment was described as associated with a higher risk of sudden death [6,14,23]. The horizontal/descending pattern was found in 23% of our patients and it did not correlate with any arrhythmias. In a comparable fashion, patients exhibiting the combination of the horizontal ST segment morphology associated with a large J-amplitude ($J > 0.1$ mV) were only found in 8 patients and also did not correlate with the presence of any arrhythmias.

Early repolarization ECG patterns are observed frequently in younger populations, males, athletes and especially in those of African descent [1,2,24]. Haissaguerre et al reported that the male gender with ERp in the inferior leads may be a greater risk of cardiac mortality than females [13]. An ERp was found almost equally in both genders of our study population and there was no difference in symptoms nor any documented arrhythmias. Although an ERp may be common among patients of reported African descent, it was found not to be over-represented among patients with idiopathic ventricular fibrillation [25]. In our present study, 23% of patients reported as having a European ethnicity and this did not correlate with the presence of any arrhythmias, raising the question if there is any clear attributable risk associated with ethnicity. The significance of a family history of sudden cardiac death in subjects with ERp is also not known. There is conflicting data in the literature and there are no clear recommendations regarding risk assessment that can be made [7]. In the largest case series among adults, only 16% of patients with a cardiac arrest and an ERp had a family history of sudden death [8]. In our study 6 (3.4%) patients with an ERp had a positive family history of sudden cardiac death yet none exhibited any arrhythmias.

The ER Syndrome describes patients with the ECG findings of repolarization associated with symptomatic arrhythmias. Only 21 of 177 patients in our study had symptomatic arrhythmias (mostly supraventricular) with only 3 of these with monomorphic ventricular tachycardia; none exhibited polymorphic tachycardia or ventricular

fibrillation. Of interest, and in deference to what has been reported in adult patients with an ERp, supraventricular arrhythmias were found in 18 patients while 1 patient presented with complete heart block as shown in Table 1. The limited number of patients with symptomatic arrhythmias in our study makes any assessment of the association of the different ECG findings inconclusive. The remainder of the patients with an ERp and non-specific cardiac-related symptoms (syncope, palpitations, etc) had no documented arrhythmias.

Study Limitations

The present study was a single center retrospective, descriptive evaluation and has limitations. There is a selection bias in that only the patients who were referred to our electrophysiology/arrhythmia clinic for documented or suspected heart rhythm or ECG issue were evaluated for the presence of the ERp. Since the incidence of idiopathic ventricular fibrillation is very rare in adults (10 cases per 100,000 population), the potential risk of sudden cardiac death and the occurrence of idiopathic ventricular arrhythmias is very minimal in children. This makes the assessment of the risk of the ERp as a primary arrhythmic disorder very challenging. There were a small number of patients with an ERp and symptomatic arrhythmias which limits the statistical power to analyze the associated risk factors. A larger cohort study is needed to assess the ERp as a screening prognostic factor and it remains the primary challenge in pediatric studies. Lastly, a prospective study of children with ERp followed clinically into adulthood for possible association with arrhythmia occurrence and persistence of the ERp is more challenging but is definitely needed before any definitive associated can be made of the benign or worrisome nature of a child exhibiting an early repolarization pattern on a resting ECG.

Conclusions

An ERp was found almost equally in both genders in our study pediatric population. Although, as expected, it was common among children of African, it was also seen frequently among those of European/Caucasian heritage (23%). The diffuse ascending ST segment pattern in both inferior and lateral leads was the most frequent finding in our population. Neither pattern (ascending or horizontal/descending) was associated with any arrhythmias. The "malignant" horizontal/descending pattern with a large J-point was also not common and did not correlate with any arrhythmias. As a result of this study, an ERp, when found in younger patients, even those with clinical arrhythmias

and a positive family for sudden death, is a very non-specific ECG finding and does not appear to be a marker for any potentially fatal arrhythmias.

Figure 1- Early Repolarization J-Point with the ascending ST segment pattern.

The Arrow demarcates the typical finding of an ascending pattern. There is ST segment slurring and it merges gradually with the T wave.

Figure 2- Early Repolarization J- point with the horizontal ST segment pattern

In comparison with the ascending pattern, the horizontal ERp shows that the ST segment continues as flat until the onset of the T wave.

Figure 3:

Top: Resting ECG in a patient with clinical ventricular tachycardia showing the ascending ERp

Bottom: Inducible monomorphic ventricular tachycardia following ventricular pacing plus two extrastimuli (arrow) during an EP study. This arrhythmia was mapped to the left ventricle and effectively ablated.

Table 1- Types of documented arrhythmias of patients with ERp

Table 2- Comparison of the gender, ethnicity and ERp characteristics between asymptomatic patients and patients with arrhythmias.

Table 3- Comparison of the gender, ethnicity and ERp characteristics between patients with cardiac related complaints with and without documented arrhythmias.

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Figure 1- Early Repolarization J-Point with the ascending ST segment pattern. The arrow demarcates the typical finding of an ascending pattern. There is ST segment slurring and it merges gradually with the T wave.

105x31mm (72 x 72 DPI)

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Figure 2- Early Repolarization J- point with the horizontal ST segment pattern. In comparison with the ascending pattern, the horizontal ERp shows that the ST segment continues as flat until the onset of the T wave.

105x34mm (72 x 72 DPI)

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Figure 3-
Top: Resting ECG in a patient with clinical ventricular tachycardia showing the ascending ERp
Bottom: Inducible monomorphic ventricular tachycardia following ventricular pacing plus two extrastimuli (arrow) during an EP study. This arrhythmia was mapped to the left ventricle and effectively ablated.

165x123mm (72 x 72 DPI)

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Types	Arrhythmias N = 21 (12%)
Ectopic Atrial Tachycardia	5
Atrial Flutter	1
Sinus node reentry tachycardia	1
AVRT	4
AVNRT	4
Complete Heart Block	1
Ventricular tachycardia	3
Narrow QRS complex tachycardia	2

	Arrhythmias (N = 21)	Asymptomatic (N = 59)	P-value
Female (n = 34)	59.1%	35%	0.057
Caucasian (n = 21)	39%	28%	0.391
J > 0.1 mV (n = 38)	50%	47.5%	0.839
Inferior location (n = 16)	32%	15%	0.214
Horizontal / Descending (n = 18)	27.3%	20.3%	0.504
Horizontal / Descending and J >0.1 mV (n = 8)	33.3%	46.2%	0.599

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	Arrhythmias (N = 21)	Cardiac symptoms with no Arrhythmias (N = 97)	P-value
Female (n = 59)	59.1%	47.4%	0.323
Caucasian (n = 27)	31.8%	20.8%	0.083
J >0.1 mV (n = 38)	50%	47.5%	0.839
Inferior location (n = 22)	32%	15.5%	0.162
Horizontal / Descending (n = 28)	27.3%	23%	0.210
Horizontal / Descending and J >0.1 mV (n = 8)	9.1%	6.2%	0.967

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