Main electrocardiographic features in Early Repolarization - 2009

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Heart rate:
Predominant sinus bradycardia frequently associated with respiratory sinus arrhythmia.

PR interval:
First degree AV block is observed in 5% to 39% among professional athletes. In the non-athlete population it is observed in 0.65% of cases.

QRS axis:
Vertical electrical axis is the rule. The frontal plane QRS axis and ST segment axis and T wave axis are all in the same direction.
QRS duration: (90 ± 10 ms) subjects than in age-matched healthy controls (80 ± 10 ms).

QRS morphology:
Notching or slurring of the terminal QRS complex.
Prominent, relatively deep but narrow q waves may appear in the left precordial leads.
QRS voltage: Eventually, voltage criteria of LVH are observed in male competitive athletes: SV1+ RV5 > 35 mm (Positive Sokolow index). High QRS voltage is more frequent in male athletes, but its correlation with LVH is low. Voltage decreases after deconditioning is slow. The distinction between the physiological athlete's heart and pathological conditions has critical implications for professional athletes. An abrupt transition may occur from right-oriented complexes to left-oriented complexes in the precordial leads, secondary to counterclockwise rotation on precordial leads. About two-thirds of clockwise rotation and counterclockwise rotation could be attributed to the septal angle by anatomical rotation of the heart in one plane around the long axis, but other factors appear to be responsible for such ECG findings in the remaining one-third of cases. Relatively higher positions of the precordial ECG leads, as observed in the vertical heart, appeared to be responsible for clockwise rotation in some patients, and left septal fascicular block is suspected to be responsible for counterclockwise rotation in others patients.

J-point elevation: Notching, irregular or slurring contour of the terminal QRS complex (J point). Variant of Osborn wave is seen in ERP.

ST segment:

Widespread ST segment elevation; (precordial greater than limb leads) The characteristic ST segment is elevated, upward, concave, confined more frequently in precordial leads, with reciprocal depression only in aVR. The concavity is observed at the initial up-sloping portion of ST segment or upwardly concave ST segment morphology. Unfortunately, concave ST morphology cannot be used to rule out ST elevation from AMI with left anterior descending coronary occlusion because it is common in these circumstances. The ST elevation is most frequently evident in ECG lead V4. There is a distinct J wave and ST segment in the left precordial leads V4 through V6. The ST elevation in ERP is usually < 2 mm (but can rarely be > 5 mm) in the precordial leads and the greatest ST elevation is usually seen in the mid-to-left precordial leads.
The ST segment elevation is usually < 0.5 mm in the limb leads.

T wave characteristics:

Concordant T waves of large amplitude (prominent, matching T waves), typical pseudo-asymmetrical (‘symmetroid”) or slightly asymmetrical, matching T waves often of large amplitude, upright, tall and peaked, most conspicuously from V2 to V4 or V5, sometimes seen in leads DII, DIII and aVF as a rule. T waves may appear as of large amplitude, "peaked" or pointed, symmetric and matching. Vagotonic or high T wave voltages followed by U waves are frequent when sinus bradycardia is present. Tall, positive ad symmetric or symmetroid T waves are not only seen occasionally in the very early stages of MI, but also in hyperkalemia and in ERP sinus bradycardia.

QT intervals:
QT maximum: The maximum Q-onset-T-end interval. This parameter is higher in ERV subjects than in normal controls.

QTp maximum: maximum Q-onset-T-peak interval. This parameter is higher in ERV subjects than in age-matched healthy controls.

Rate-corrected QTc maximum: This parameter is lower in ERP subjects than in age-matched healthy controls.

QTpc maximum: This parameter is lower in ERV subjects than in age-matched healthy controls.

U wave:

because bradycardia U waves are frequent, in ERV they are best observed in the V3 lead. U waves are frequent when sinus bradycardia is present.

Other ECG characteristics of ERP:

Relative temporal stability of the ST segment and T wave pattern is observed.
Reciprocal changes are not seen in ERP. There are no evolutionary short-term changes in the ST segment and T waves; and Q waves do not appear.
ERP or Early Repolarization Variant (ERV) is an enigmatic electrocardiographic phenomenon, characterized by prominent J wave and ST-segment elevation in multiple leads.
Recently, there has been renewed interest in ERP because of similarities to the

arrhythmogenic Brugada syndrome (BrS). Not much is known about the epidemiology of ERP and several studies have reported that this condition is associated with a good prognosis.
Both ERP and BrS exhibit some similarities including the ionic underlying mechanism, the analogous responses to changes in heart rate and autonomic tone, sympathicomimetics (isoproterenol test) as well as in sodium channel and beta-blockers. These observations raise the hypothesis that ERP may be not as benign as traditionally believed. Additionally, there are documents showing that ST-segment height in the man is greatly influenced by central sympathetic nervous activity, both at baseline and during physiologic and pharmacological stress. Central sympathetic dysfunction regularly results in multilead ST-segment elevation or J wave that decreases or below isoelectric baseline during low dose isoproterenol infusion. An early-repolarization pattern in the inferior leads of a standard electrocardiogram is associated with an increased risk of death from cardiac causes in middle-aged subjects(1).

POSSIBLE SIMILARITIES BETWEEN ERV AND Brugada Syndrome (BrS)

• More frequent in males
• Both occur more frequently in young adults and in individuals without apparent structural heart disease
• Both may influence just the V1-V2 leads: Rarely (9%), can ST elevation be observed in ERP only in the right precordial leads: V1-V2, or in the inferior ones (2).
When ST elevation is normal, it can reach up to 3 mm in V2-V3, especially in young people. In those individuals over 40 years, it seldom exceeds 2 mm. Both can show incomplete RBBB pattern or right bundle branch conduction disorder: in BrS, it can present atypical features, RBBB-like and of the saddle type by exclusive elevation of the J point. S wave with delay in the left leads: DI, aVL, V5 and V6, could be absent as it is to be expected in a classic RBBB.
The elements considered as typical in BrS are: 1) elevation of the terminal part of QRS (prominent J wave): 2) elevated and descending ST, not related to lesion of ischemic (idiopathic) injury; 3) negative T wave in the right precordial leads; 4) normal QTc or near normal; 5) absence of final delay in left leads as it would be expected in a classic RBBB3.
In ERV, when associated to athlete's heart, QRS can present a moderate extension (100 ms to 110 ms) in 15% of the cases, which in nonathlete, normal population, in a 2.4% is called outflow tract hypertrophy. In this case r' does not exceed the 5 mm and is lower than S in the same lead: rSr';
Both may improve repolarization during the stress test with use of isoproterenol;
Both respond to a shortening of AP phase 2 in a part of ventricular thickness, and intensification of fast repolarization notch (phase 1) mediated by transmural dispersion of ventricular repolarization by a larger notch in the Ito channel4.
The alteration of the Ito and ICa2+-L channels in BrS and in ERP are the electrophysiologic substrate that explains the J point and ST segment elevation, because they cause the intensified notch in phase 1 and suppression in phase 2 duration in the epicardium and in the endocardium of ventricular wall thickness.

ELEMENTS FOR DIFFERENTIAL DIAGNOSIS BETWEEN ERP AND BrS

I) Family background
ERP: negative
BrS: frequently positive
II) Ethnic Group

ERP: predominantly in African descendents(5), or equally common in all races(6)
BrS: predominantly in Asian group (58%) and Caucasian people(7)
III) Gender
ERP: male gender predominance.
BrS: great predominance in the male gender (male/female ratio – 8:1 in non Asian and 10:1 in Asian people.
IV) Response to IC group antiarrhythmic agents
BrS: flecainide, used in a 10 mg/Kg dosage in 10 minutes, increases ST elevation and QRS duration in a more significant way in patients with BrS than in individuals without the entity, and only in those it triggers ventricular extrasystoles(8).
ERP: it can induce a pattern similar to BrS; however, the degree of ST elevation caused by the drug is much higher in patients with BrS than in patients without the disease.
BrS patients with Inferior and lateral ECG repolarization abnormalities have longer baseline PR intervals(9).
Both an S wave width ≥80ms in V1 and ST elevation ≥1.8mm in V2 are highly specific indicators of VF and criteria for high-risk BrS(10).
There are several references in literature to patients with elevation of the J point and ST segment convex to the top or straight descendent in inferior leads (Brugada sign) or concomitantly ST-segment elevation in the right precordial and inferior leads II, III, and aVF(3) in absence of hypothermia, ischemia or electrolytic disorders, which we call “atypical Brugada pattern”, atypical BrS, variant BrS, or BrS variant or idiopathic VF (a variant of the BrS with ST-segment elevation in inferior leads(11).
Pilsicainide may induce PVCs and PVT in atypical BrS and the infusion of isoproterenol suppress the arrhythmias and normalize the ST-segment elevation(12).
Potet et al.(13) identified a G752R mutation on SNC5A that produced ST segment elevation and prominent J wave in leads II, III, and aVF. The authors provide genetic demonstration that Brugada ECG anomalies related to a unique SCN5A mutation can be observed either in the inferior or the right precordial leads.
The early repolarization pattern in inferolateral leads is not an uncommon finding in BrS, and this pattern is not associated with a worse outcome in subjects with BrS(14).
The spontaneous ERP occurred more frequently among patients with BrS than in 283 family members not having BrS (11% versus 6%, P=0.03). Class I antiarrhythmic drug administration provoked inferior-lateral coved Brugada pattern in 13 patients with BrS. These patients had longer baseline PR intervals and Class I antiarrhythmic drug induced QRS interval prolongation (108 to 178 versus 102 ms to 131 ms, P<0.001). In 3 patients, the Class I antiarrhythmic drug provoked coved Brugada pattern only present in the inferior leads. Inferior-lateral ERP occurs spontaneously relatively frequently in BrS. These patients have a more severe phenotype. Class I antiarrhythmic drug administration provokes inferior-lateral coved Brugada pattern in 4.6% of patients. The Class I antiarrhythmic drug exceptionally provoked coved Brugada pattern only observed in the inferior leads(15).
Type 1 ECG Brugada pattern in the peripheral leads was observed in 4.2% of patients during ajmaline test (10.3% of positive tests) and was associated with longer QRS and greater QTc prolongation compared with the rest of the patients(16).
Atypical Brugada Syndrome or IVF with J waves in inferior, lateral or inferior lateral leads
Until to day two mutations in genes SCN5A and KCNJ8 had been identified

1) On SCN5A gene. (17)
2) On KCNJ8 gene(18;19): Missense variant in exon 3 (NC-000012) of the KCNJ8 gene, a subunit of the K(ATP) channel2;3. Genomic DNA sequencing of K(ATP) channel genes

showed missense variant in exon 3 (NC_000012) of the KCNJ8 gene, a subunit of the K(ATP) channel, conferring predisposition to dramatic repolarization changes and ventricular vulnerability.
From a multicenter cohort of 122 patients (90 male, age 37 +/- 12 years) with IVF and ERP in the inferolateral leads.
Haïssaguerre et al.(19) selected all patients with more than 3 episodes of VF (multiple) including those with electrical storms (≥3 VF in 24 h). Multiple recurrences of VF occurred in 27% of patients with ERP and may be life threatening. Isoproterenol in acute cases and quinidine in chronic cases are effective antyharrhithmic drugs. The last one is necessary associated to ICD.
The so-called atypical BrS is characterized by ECG abnormalities of the J wave, and ST-segment elevation appeared in the inferior and/or lateral leads. The ERP in inferolateral leads is not an uncommon finding in BrS(2). There is a high incidence of the ERP confined in inferolateral leads in patients with IVF. The ECGs have an elevation of the QRS-ST junction of at least 0.1 mV from baseline in the inferior or lateral lead, manifested as QRS slurring or notching. Among patients with a history of IVF, there is an increased prevalence of ERP.

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