Early Repolarization: Innocent or Dangerous?

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Abstract: Electrocardiographic (ECG) findings of wide QRS complexes in right precordial leads with saddle ST elevation in patients with polyarthritis, palpitations and family history of syncope urged us to review early repolarization syndrome (ERS). ERS is commonly seen in young men. The main ECG features are as follows: wide spread concave ST-segment elevation, more in the precordial leads (usually V2–V4); notching or irregular contour of J point and prominent concordant T waves with large amplitude. ERS was historically considered as a benign ECG variant. In recent years, it has emerged as a marker for increased risk of sudden cardiac death. The purpose of this review was to describe the ECG manifestations of this syndrome and to review the literature concerning its arrhythmogenic potential. The authors found it important not only discussing the rate of ERS life threatening but also to reemphasize its differences from other syndromes. Some of the last are much more dangerous: acute myocardial infarction and Brugada syndrome. The tables will be helpful for physicians to distinguish ERS from other syndromes in patients with chest pain and ST elevation.

Key Indexing Terms: Early repolarization; Sudden death; Brugada syndrome; J wave; ST-segment elevation. **[Am J Med Sci 2013;346(3): 226–232.]**

Electrocardiographic (ECG) findings of wide QRS complexes in right precordial leads with saddle ST elevation in patients with polyarthritis, palpitations, personal and family history of syncope urged us to review early repolarization syndrome (ERS).

ERS was historically considered as a benign ECG variant. In the recent years, it has emerged as a marker for increased risk of sudden cardiac death (SCD).[1–7]

Early repolarization (ER) was first described in 1936 by Shipley and Hallaran. They analyzed the ECG of 200 normal persons, aged 20 to 35 years, and noted that a normal variant of ST elevation occurred quite frequently. They observed this in lead II in 25% of the men and 16% of the women.[8] With the advent of the 12-lead ECG, Myers et al[9] pointed out its location in the precordial leads. Grant[10] studied the clinical characteristics of the ST-T vectors and coined the term "early repolarization" for this ECG variant. Tomaszewski[11] described elevated J point in an accidentally frozen human. The point was also known as an Osborn wave after being highlighted by Osborn in hypothermic dogs.[12] ERS is seen in both extracardiac and cardiac disorders: brain injury, hypervagotonia, hypercalcemia, spinal cord injury and vasospastic angina.

Up to 48% of the patients come to emergency department with chest pain, and ECG is performed as the first instrumental investigation.[13] The ECG syndrome of ER is found in 1% to 5% of the population.[2] It is common in young individuals (27.5%) and shows preponderance to men (77%).[14] Sixty thousand ECGs were analyzed for 5 years. Six hundred (1%) revealed ER. Features of ER were compared with race-, age- and sex-matched controls. They found that among patients with ER, 93.5% were Caucasian, 77% were men, 78.3% were younger than 50 years and only 3.5% were older than 70 years.[15] The ERS is often observed in athletes, cocaine users, patients with hypertrophic obstructive cardiomyopathy and in patients with defects and/or hypertrophy of the interventricular septum.[16]

ERS is one of several syndromes producing ECG ST-segment elevation (STE). For decades, the clinical significance of this syndrome has been largely limited to its contribution to the differential diagnosis of ST-elevation myocardial infarction (STEMI), pericarditis and of the highly arrhythmogenic Brugada syndrome (BrS). There are more and more studies suggesting that ERS may be related to electrophysiological instability and even may be associated with vulnerability to ventricular fibrillation (VF).[1–7]

Here, we describe the ECG manifestations of this syndrome. We review the latest literature to understand whether ERS is benign ECG changes or is it really one of the causes of VF and sudden death. We also reemphasize its differences from other common syndromes, some of which are life threatening such as acute myocardial infarction (AMI) and the BrS.

ERS DEFINITION

A common ECG variant characterized by J-point elevation manifested either as terminal QRS slurring (the transition from the QRS segment to the ST segment) or notching (a positive deflection inscribed on terminal QRS complex) associated with concave upward STE and prominent T waves in at least 2 contiguous leads.[17]

ERS ECG SIGNS

ST-Segment Elevation

The ST-segment elevation that begins at the "J point" (the junction between the end of the QRS complex and the beginning of the ST segment). The degree of STE encountered in ERS is usually less than 2 mm (80%–90%) but may approach 5 mm in certain individuals. Only 2% of the cases of ERS manifest STE greater than 5 mm.[13]

ST-Segment Morphology

It appears as if it has been lifted upward evenly from the isoelectric baseline at the J point, preserving the normal concavity of the initial upsloping portion of the ST segment-T wave complex. This STE morphology distinguishes ERS-related STE from that associated with STEMI, which is usually a convex STE (Figure 1).

ST-Segment Distribution

The degree of STE in ERS is usually greatest in leads V2–V5 and less often found in the limb leads. Isolated ERS in the limb leads is a very rare finding. Such isolated STE in the inferior or lateral leads should prompt consideration of another explanation for STE.[13]

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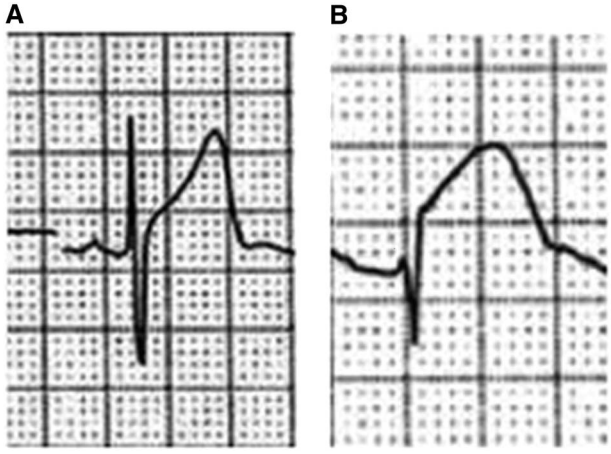

FIGURE 1. (A) Nonacute myocardial infarction cause of ST-segment elevation because of benign early repolarization. (B) ST-elevation myocardial infarction with nonconcave ST-segment morphology.

J-Point Features

There are 2 main types of J waves. The first is a distinct well-defined notch on the down stroke of the QRS complex. The second is slurred down stroke of R wave when the R wave was gradually transformed to the ST segment with upright concavity (Figure 2). An analysis of the ECG of 65 patients with the ERS revealed more than 1 pattern of the J point in the same individual.[18]

QRS Features

1. Rapid QRS transition in the precordial leads with counter clockwise rotation.
2. "Pseudo-R" pattern in lead V1 or V2 that is similar to the pattern of incomplete/complete right bundle branch block (RBBB) but without right axis deviation of the QRS vector (that is seen in RBBB).

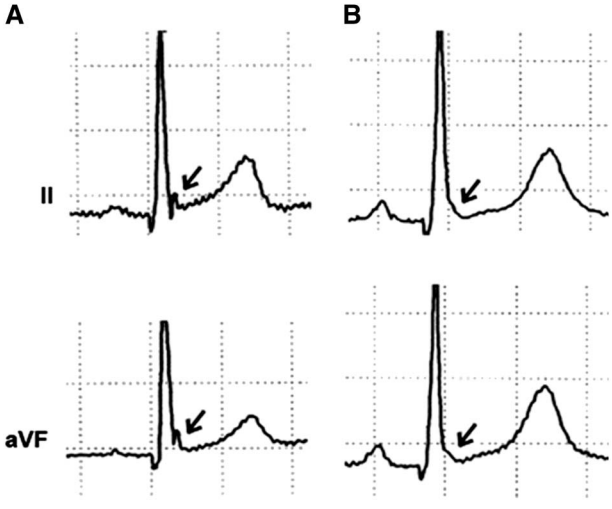

FIGURE 2. Patterns of the J point: (A) a distinct well-defined notch on the down stroke of R wave (B) when the R wave was gradually transformed to the ST segment with upright concavity.

T-Wave Features

Prominent T waves of large amplitude and slightly asymmetric morphology are encountered. The T wave may appear "peaked," suggestive of hyperacute T wave encountered in AMI. The prominent T waves are concordant with the QRS complex and are usually found in precordial leads. The height of the T waves in ERS ranges from ~6.5 mm on the precordial distribution to 5 mm in the limb leads.[13]

Temporal Stability

Long-term follow-up of ECGs (of the same individuals) reveals relatively constant pattern. However, the magnitude of ERS may lessen over time as the patient ages. In 25% to 30% of the patients with ERS previously documented on ECG, a repeat ECG will reveal complete disappearance of the pattern many years later.[14,16] There is also a normalization of the STE with rapid pacing or during exercise.[19] A study that followed athletes during marathon showed that the STE disappeared after exertion in 14 of 20 marathon runners.[20] Table 1 summarizes the ECG manifestations of ERS.

ERS AND ARRHYTHMIA

ER is a common ECG finding that for many decades was considered to be benign. Its potential to cause cardiac arrhythmias has been hypothesized from experimental studies. One study reviewed data from 206 case subjects who were resuscitated after cardiac arrest because of idiopathic VF and assessed the prevalence of ERS. The ERS was found to be more frequent in subjects with idiopathic VF than in control subjects (31% versus 5%, $P < 0.001$). Those subjects with ERS were more likely to have a history of syncope or sudden cardiac arrest during sleep than those without ERS. During a mean follow-up of 61 ± 50 months, defibrillator monitoring showed a higher incidence of recurrent VF in case subjects with a repolarization abnormality than in those without such an abnormality ($P = 0.008$).[1] Another study assessed the prevalence and prognostic significance of ER on 12-lead electrocardiography in a community-based general population of middle-aged subjects —during a mean follow-up of 30 ± 11 years. They found that J-point elevation of at least 0.1 mV in the inferior leads was associated with an increased risk of death from cardiac causes ($P = 0.03$); subjects with J-point elevation of more than 0.2 mV in the inferior leads had a markedly elevated risk of death from cardiac causes ($P < 0.001$) and from arrhythmia ($P = 0.01$). They concluded that an early-repolarization pattern in the inferior leads of a standard ECG is associated with an increased risk of death from cardiac causes in middle-aged subjects.[2]

TABLE 1. ECG characteristics of early repolarization

ECG component	Characteristics
STE	Wide spread STE more in the chest leads (usually V2–V4) than in the limb leads
ST-segment morphology	Concavity of initial upsloping portion of ST segment
J point	Elevation and notching or irregular contour of J point
T waves	Prominent concordant with large amplitude
Influence on ST segment	Reduction in STE with sympathoadrenal factors or with rapid pacing
	Normalizing during exercise and with aging

ECG, electrocardiographic; STE, ST-segment elevation.

The prognostic modulation of ER-associated risk by ST-segment variations was also assessed on the basis of observations from 2 independent samples of young healthy athletes from Finland and the United States. Most of the athletes had an ascending/upsloping ST variant after ER. Subsequently, ECGs from a general population of middle-aged subjects were analyzed to assess the prognostic modulation of ER-associated risk by ST-segment variations. In subjects with ER $>$ 0.2 mV in the inferior leads and horizontal/descending ST-segment variant, the hazard ratio of arrhythmic death increased to 3.14. However, in subjects with ascending ST variant, the relative risk of arrhythmic death was not increased (hazard ratio of 0.89; 95% confidence interval, 0.52–1.55).[3] Similar results were found in another study in which they reviewed all the ECG records of the 5,976 atomic-bomb survivors, who were examined at least once between July 1958 and December 2004. There were 1,429 ER pattern cases, and the patients with ERS pattern had an elevated risk of unexpected death. In addition, both slurring and notching were related to higher risk of unexpected death (hazard ratio, 2.09; $P = 0.03$), as was ER pattern manifestation in both the inferior and lateral leads (hazard ratio, 2.50; $P < 0.01$).[4]

Recently, the presence of ER with "horizontal ST segment" was found to predict arrhythmic death during long-term follow-up in a large population study.[5] The study showed that the presence of J waves strongly correlates with a history of idiopathic VF among patients with this disorder. When they focused only on those patients with J waves and graded their ST-segment morphology as either "horizontal" or "ascending" according to predefined criteria, they found that the presence of J waves was associated with a history of idiopathic VF with an odds ratio (OR) of 4.0 (95% confidence interval, 2.0–7.9), but having both J waves and horizontal/descending ST segment yielded an OR of 13.8 for having idiopathic VF.[5,6]

In summary, ERS is usually benign variant, but in rare specific circumstances, it may be malignant form. It is important to recognize these ECG variants and point to the patients who are at risk to develop malignant ventricular arrhythmia. According to the above-mentioned studies, patients with ER and the following ECG criteria may have an increased risk to develop ventricular arrhythmia:

- ER pattern manifestation in both the inferior and lateral leads.
- J-point elevation of at least 0.1 mV in the inferior leads was associated with an increased risk of death from cardiac causes.[1]
- Slurred and notched J points were related to higher risk of unexpected death.[3]
- Horizontal/descending ST variant had an increased risk of arrhythmic death.[4,5]
- Patients with both J waves and horizontal/descending ST segment indicated an increased OR for idiopathic VF.[4,5]

Despite the above studies so far, it is not clear weather asymptomatic patients who are at risk of ventricular arrhythmia according to the ECG, without prior ventricular tachycardia/VF should undergo a preventive implantable cardioverter-defibrillator implantation. Many more studies are needed to evaluate the cost/effectiveness of preventive implantable cardioverter-defibrillator implantation in asymptomatic patients with ERS and unfavorable ECG criteria.

DIFFERENTIAL DIAGNOSIS

Acute STEMI and ERS

The initial ECG is crucial in accurately selecting patients with chest pain for early revascularization. The ECG remains the most immediately accessible and widely used diagnostic tool for guiding emergency treatment strategies. Treatment with thrombolysis or primary percutaneous coronary interventions reduces the mortality rate of patients with STEMI presenting within 12 hours. Patients presenting $>$12 hours are generally considered to be ineligible for reperfusion therapy but eligible for percutaneous coronary interventions.[21] Since time is myocardium and time is outcome,[22] it is important to make the diagnosis of myocardial infarction as quickly as possible. It is also important not to confuse other causes of STE with AMI as reperfusion therapy is an invasive treatment with well-known complications.

Another study checked the impact of the ECG on the delivery of thrombolysis for patients with AMI. Patients with suspected AMI received thrombolytic therapy if they fulfill the suitable criteria, and 93 patients received thrombolytic therapy. In 10 patients (11%), AMI did not occur, and ER was responsible for ST elevation in 3 patients (the other ST elevation were because of left ventricular hypertrophy and old myocardial infarction).[23] To prevent mistaken diagnosis and unjustified treatment, physicians must be aware of the different entities and become familiar with its ECG features.

The ECG differences between STEMI and ERS include the following: (1) In AMI, the evolving ECG changes (Q waves, ST-T changes) are confined to the leads reflecting the area of myocardium involved with reciprocal changes in the opposite leads. As it was mentioned before, the precordial leads are mostly involved. (2) The ST elevation of STEMI usually has a convex pattern, whereas in ERS, there is a concave ST elevation. (3) One study assessed the diagnostic accuracy of various ECG STE criteria for the prehospital ECG diagnosis of AMI. STE alone lacks the positive predictive value necessary for reliable prehospital myocardial infarction diagnosis. Inclusion of reciprocal changes in prehospital ECG myocardial infarction criteria improved the positive predictive value to more than 90%.[24] (4) The ECG manifestations of ischemia evolve in a matter of hours or days, whereas ECG changes in ERS remain stable over extended period.

Pericarditis and ERS

Acute pericarditis is a common cause of chest pain and abnormal ECGs, especially in young adults. It can be difficult to distinguish between acute pericarditis and ERS because of similar morphologic features at the initial ECGs. Some investigators concluded that it is not possible to differentiate between these 2 conditions according to the initial ECGs and that serial ECGs, and the existence of clinical criteria are needed.[25] Other investigators examined different quantitative ECG differentiation of acute pericarditis from ERS. They found that an ST/T ratio in lead V6 of 0.25 or greater distinguished all patients with pericarditis from those with ERS. This ECG criterion was also found to be highly predictive for pericarditis in other studies.[26] Another difference is that the ECG changes of acute pericarditis usually undergo a typical evolution over days and weeks, whereas the changes seen in ERS tend to be stable over a period of years. Depression of the pTa segment (between p and q) during pericarditis may be helpful in differentiating from ERS.

As was mentioned above, exercise testing in people with ERS was found to make ST elevation return to isoelectric baseline. It was believed that ECG exercise responses distinguish pericarditis from repolarization. Yet a case report from 1986 has shown also a decline of the ST elevation in the ECG of the patient with acute pericarditis.[27] Moreover, exercise testing is contraindicated during active pericarditis because of the possibility of myocarditis. In experimental

myocarditis, exercise augments intramyocardial virus replication with greater cardiac hypertrophy, more extensive inflammation and more necrosis and death than in nonexercised control subjects.

BrS and ERS

Brugada and Brugada[28] described 8 cases of a very arrhythmogenic state with similar ECG manifestations during sinus rhythm. All patients had a tendency to develop SCD, usually because of ventricular tachycardia/VF. Typically, there is no evidence of structural heart disease. BrS has been linked to a mutation of the gene SCN5A (20%), which encodes for the fast cardiac sodium channel.[29] Defected gene induces transient outward current Ito causing epicardial reentry and myocardial vulnerable "window." Quinidine was found to inhibit Ito and reduces VF episodes.[30] The diagnosis BrS states that ECG changes might be revealed after a challenge with sodium current blockers (flecainide, ajmaline, etc.) or fever.

The ECG manifestation of this syndrome includes ST elevation but unlike ERS:

1. High take-off STE (higher 0.2 mV) of coved (type 1, Figure 3) or saddleback type (type 2, Figure 4).
2. The ST elevations are, usually, seen in leads V1 to V3 and are accompanied by negative T waves. In patients with BrS, the appearance of prominent J waves is limited to the leads facing the right ventricular outflow tract where Ito is most prominent. The more prominent Ito in the right ventricular epicardium provides for a greater outward shift in the balance of current, which promotes the appearance of the J wave in this region of the ventricular myocardium. In the case of ERS, the appearance of prominent J waves may be limited to other regions of the ventricular myocardium because of the presence of heterogeneities in the distribution of other currents such as Ik-ATP.[29]
3. Sometimes the QRS has a pattern of RBBB (Figure 3).[31]
4. Type 3 of BrS has either a coved (type 1 like, T-negative) or a saddleback (type 2 like, T-positive) pattern but with less than 0.2 mV J-point elevation and less than 1 mm ST elevation and therefore is not uncommon in healthy subjects[29] (Figure 5).

Vagal stimulation or adrenergic blockade may cause transformation of type 3 to type 1 and may carry risk of sudden death.

Bianco et al[32] suggested that measurements of 2 mm for the maximum right precordial STE with QRS duration > 0.11 seconds ensures 100% positive and 80% negative predictive values for the presence of the BrS. These manifestations also distinguish this arrhythmogenic state from the ERS. Like in the ERS, the STE in patients with BrS was augmented after infusion of beta-blockers and was reduced after beta-adrenoceptor stimulation by intravenous isoproterenol.[33–35]

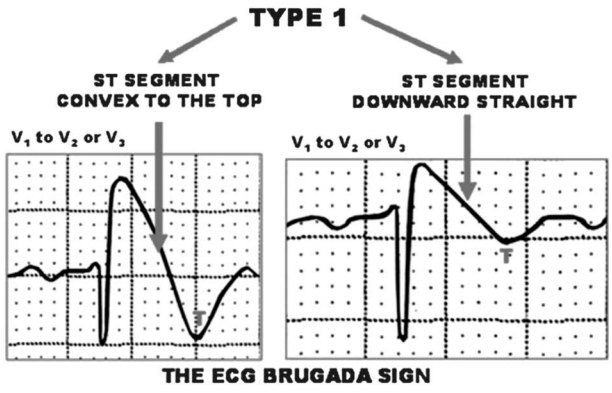

FIGURE 3. Brugada syndrome.

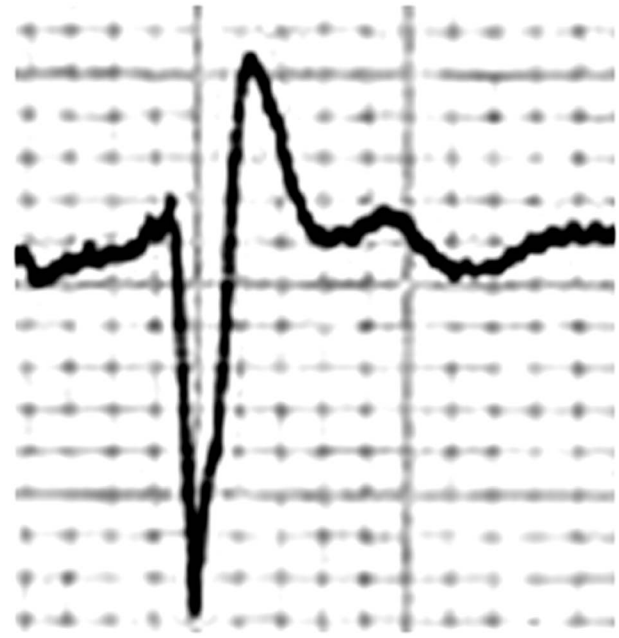

FIGURE 4. Type 2 Brugada syndrome.

Differentiating J Waves Caused by Conduction Versus Repolarization

J waves can arise from either repolarization or depolarization abnormalities. When caused by the latter, the apparent J wave is expected to appear as a notch interrupting the terminal part of the QRS, with little or no STE. Another way of distinguishing is the response to increased rate or atrial premature response. When caused by delayed conduction, the notched appearance should become accentuated with acceleration of rate or prematurity. When caused by repolarization

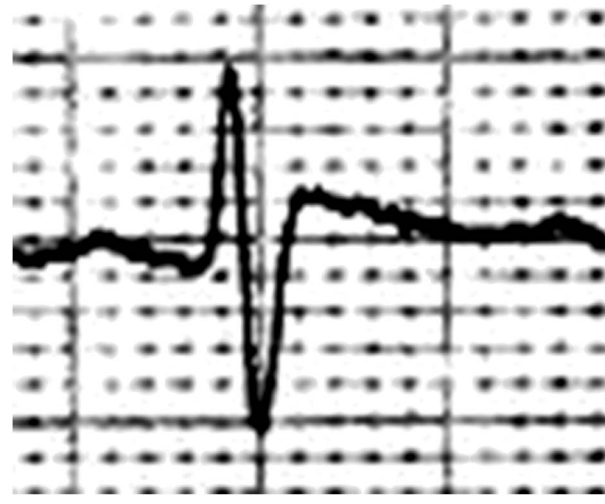

FIGURE 5. Type 3 Brugada syndrome.

problems, the amplitude of the J wave should diminish because of insufficient time for the Ito to reactivate.[29]

We summarized the clinical and the ECG manifestations of each one of the above-mentioned syndromes (Table 2). That can help to evaluate the patients with chest pain and ST elevation in the emergency room.

DISCUSSION

ER, involving STE and, sometimes, prominent J waves at the QRS-ST junction, has been considered as a normal ECG variant for over 60 years. A growing number of case reports and case-control studies indicate that in some instances, ER patterns are associated with increased risk of idiopathic VF.

But the highly arrhythmogenic BrS is in fact (in Europe at least) not so arrhythmogenic as suggested by the seminal Brugada paper. In the large series of BrS events, rates in asymptomatic patients were low (5%–7.7%). Symptoms and spontaneous type 1 ECG were predictors of arrhythmic events, whereas gender, familial history of SCD, inducibility of ventricular tachyarrhythmias during electrophysiological study and the presence of an SCN5a mutation were not predictive of arrhythmic events.[36] Another trial with evaluation of 29,281 resting ambulatory ECGs found no significant association between any components of ER and cardiac mortality.[37] ST elevation was present in 2.3% and was present in both the inferior and lateral territories in only 0.1%. J wave (notch/slur) was present in 14%. Adjusted hazard ratio demonstrated no association among J wave, ST elevation and cardiovascular mortality.[37] Controversy exists what should be used as criteria for ERS: J wave or ST elevation?[17] ACC/AHA/HRS recommendations include a statement that the term "early repolarization" is used frequently to characterize a normal QRS-T variant with J-point elevation.[38] ERS is most

TABLE 2. The clinical and ECG manifestations of ERS, acute myocardial infarction, pericarditis and BrS

Variables	ERS	Myocardial infarction	Pericarditis	BrS
Clinical characteristics	Usually asymptomatic	Heavy, squeezing or crushing retrosternal pain, accompanied by weakness, nausea, sweating, vomiting	Retrosternal pain, aggravated by deep inspiration, coughing—relieved by leaning forward	Palpitation
				Syncope
				Sudden cardiac death
Predisposing or risk factors	Familial occurrence	Hypertension, diabetes mellitus, smoking, hypercholesterolemia	Viral, chest trauma, metastatic neoplasm, autoimmune	Genetic
Age	Young	Usually adults >50	Any age	Young
Sex	Men > women	Men, but incidence equals after menopause in women	No differentiation	Men > women
Physical examination	Usually normal	Pallor, tachycardia, S3, S4, apical systolic murmur because of mitral regurgitation	High fever, pericardial friction rub	Usually normal
ECG				
ST segments	Concave elevated ST segments	Convex ST elevation	Concave elevated ST segments	ST-segment elevation of either coved or saddleback
Affected leads	V2–V4	According to the involved coronary artery	Limb and precordial leads	V1–V3
Follow-up	Constant but normalizing with aging	Evolve in a matter of hours or days	ST elevation become normal after a few days	Usually persistent ST elevation
T waves	Prominent, concordant with large amplitude	Normal/hyperacute and then inverted	Inverted only after ST normalized ST/T ratio >0.25	Negative T waves
QRS	Notch/slur at the J point	Q waves, New LBBB	May show low voltage	A pattern of right bundle branch block
Arrhythmias	Sinus bradycardia, VT/VF	Atrial: AF. Ventricular: VPBs, VT/VF	Sinus tachycardia, atrial fibrillation	VT/VF
Influence of drugs/ exercise	Exercise testing makes ST elevation return to isoelectric baseline	Exercise testing with ST-T changes (ST depression) indicates residual ischemia	Exercise testing is contraindicated during active pericarditis	ST segment was augmented after infusion of β-blockers and reduced after an exercise
Laboratory findings	Usually normal	Troponin—↑, leukocytosis	Leukocytosis, ESR—↑	Usually normal
Echocardiogram	Usually normal	Segmental dyskinesis	Pericardial fluid	Usually normal
Coronary angiogram	Usually normal	Abnormal	Usually normal	Usually normal

BrS, Brugada syndrome; ECG, electrocardiogram; ERS, early repolarization syndrome; LBBB, left bundle branch block; VF, ventricular fibrillation; VT, ventricular tachycardia.

frequently found in the inferolateral leads but not in the V2 to V5 (although ST elevation, if any, might be more pronounced in those leads).

Specific ER pattern morphologies and location are associated with an adverse prognosis. According to the above-mentioned studies, there is elevated risk of death from cardiac causes/arrhythmia in persons with ERS if:

1. ERS is associated with unexplained syncope or unexplained family history of SCD,
2. J point or STE $\geq$ 0.2 mV occurs in the inferior and inferior-lateral or global leads,
3. transient J-wave augmentation (a high risk for VF) or slurred and notched J point are registered,
4. appearance of distinct and prominent J waves occurs,
5. association of ERS with abbreviated QT intervals is disclosed,
6. association with horizontal or descending ST segment is found and
7. appearance of closely coupled premature beats is recorded.[5,6,28]

In opposite, rapidly ascending ST segments after the J point, the dominant ST pattern in healthy athletes, seems to be a benign variant of ER.[3]

Recent data showed that the ER pattern in inferolateral leads is not an uncommon finding in BrS.[39] That study did not witness a worse outcome in subjects with BrS.

However, ERP and BrS share many remarkable cellular, ionic and ECG similarities and behave comparably in terms of their response to heart rate, pharmacologic agents and neuromodulation. The extent to which ERP and BrS may overlap remains unclear. Recently, symptomatic patient was described, whose ECG signature evolved spontaneously from ERP alone to ERP with a concomitant BrS type 1 ECG pattern over a short number of days.[40] This case lends further strength to the notion that these 2 ECG patterns may be more closely related than had been initially thought.

Familial occurrence of the syndrome has been suggested. Indeed, a study comprised 1,877 individuals from 505 Caucasian nuclear families found that individuals with at least one affected parent had a 2.5-fold increased risk of presenting with ER on ECG (OR, 2.54, $P = 0.005$). Familial transmission was more frequent when the mother was affected (OR, 3.84; $P = 0.008$) than when the father was affected, and they concluded that ERS is a heritable phenotype.[16]

Should we undergo electrophysiological study for patients with asymptomatic ERS similar to the strategy often applied in patients with symptomatic Br? What about cardiodefibrillator implantation in symptomatic patients with unfavorable ECG and ERS?

The answers to these questions are needed to be further investigated. As seems today, a part from the unfavorable ECG variants, most subjects exhibiting an ERS are at minimal risk to develop idiopathic VF with no need for electrophysiological study.

ERS has also importance in the ST elevation work-up in patients presenting with chest pain. Physicians must be aware with ECG characteristics of each entity to avoid unnecessary invasive procedures and therapies.

REFERENCES

1. **Haïssaguerre M, Derval N, Sacher F, et al.** Sudden cardiac arrest associated with early repolarization. N Engl J Med 2008;358:2016–23.
2. **Tikkanen JT, Anttonen O, Junttila MJ, et al.** Long-term outcome associated with early repolarization on electrocardiography. N Engl J Med 2009;361:2529–37.
3. **Tikkanen JT, Junttila MJ, Anttonen O, et al.** Early repolarization: electrocardiographic phenotypes associated with favorable long-term outcome. Circulation 2011;123:2666–73.
4. **Haruta D, Matsuo K, Tsuneto A, et al.** Incidence and prognostic value of early repolarization pattern in the 12-lead electrocardiogram. Circulation 2011;123:2931–7.
5. **Rosso R, Glikson E, Belhassen B, et al.** Distinguishing "benign" from "malignant early repolarization": the value of the ST-segment morphology. Heart Rhythm 2012;9:225–9.
6. **Rosso R, Adler A, Halkin A, et al.** Risk of sudden death among young individuals with J waves and early repolarization: putting the evidence into perspective. Heart Rhythm 2011;8:923–9.
7. **Mehta M, Jain AC, Mehta A.** Early repolarization. Clin Cardiol 1999; 22:59–65.
8. **Shipley RA, Hallaran WR.** The four-lead electrocardiogram in two hundred normal men and women. Am Heart J 1936;11:325.
9. **Myers GB, Klein HA, Stofer BE, et al.** Normal variations in multiple precordial leads. Am Heart J 1947;34:785–808.
10. **Grant RP, Estes EH, Doyle JT.** Special vector electrocardiography. The clinical characteristic of S-T and T vectors. Circulation 1951;3: 182–97.
11. **Tomaszewski W.** Changement elctrocardiographiques observes chez un home mort de froid. Arch Mal Coeur Vaiss 1938;31:525–8 (in French).
12. **Osborn JJ.** Experimental hypothermia: respiratory and blood pH changes in relation to cardiac function. Am J Physiol 1953;175:389–98.
13. **Brady WJ, Chan TC.** Electrocardiographic manifestations: benign early repolarization. J Emerg Med 1999;17:473–8.
14. **Gussak I, Antzelevitch C.** Early repolarization syndrome: clinical characteristics and possible cellular and ionic mechanisms. J Electrocardiol 2000;33:299–309.
15. **Mehta MC, Jain AC** Early repolarization on scalar electrocardiogram. Am J Med Sci 1995;309:305–11.
16. **Reinhard W, Kaess BM, Debiec R, et al.** Heritability of early repolarization: a population-based study. Circ Cardiovasc Genet 2011;4: 134–8.
17. **Derval N, Shah A, Jais P.** Definition of early repolarization: a tug of war. Circulation 2011;124:2185–6.
18. **Kambara H, Phillips J.** Long-term evaluation of early repolarization syndrome (normal variant RS-T segment elevation). Am J Cardiol 1976; 38:157–6.
19. **Huston TP, Puffer JC, Rodney WM.** The athletic heart syndrome. N Engl J Med 1985;313:24–31.
20. **Gibbons LW, Cooper KH, Martin RP, et al.** Medical examination and electrocardiographic analysis of elite distance runners. Ann N Y Acad Sci 1977;301:283–96.
21. **Schiele F, Hochadel M, Tubaro M, et al.** Reperfusion strategy in Europe: temporal trends in performance measures for reperfusion therapy in ST-elevation myocardial infarction. Eur Heart J 2010;31:2614–24.
22. **Gibson CM.** Time is myocardium and is outcomes. Circulation 2001; 104:2632–4.
23. **Sharkey SW, Berger CR, Brunette DD, et al.** Impact of the electrocardiogram on the delivery of thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1994;73:550–3.
24. **Otto LA, Aufderheide TP.** Evaluation of ST segment elevation criteria for the prehospital electrocardiographic diagnosis for acute myocardial infarction. Ann Emerg Med 1994;23:17–24.
25. **Wanner WR, Schaal SF, Bashore TM, et al.** Repolarization variant vs acute pericarditis. A prospective electrocardiographic and echocardiographic evaluation. Chest 1983;83:180–4.

26. **Ginzton LE, Laks MM.** The differential diagnosis of acute pericarditis from the normal variant: new electrocardiographic criteria. Circulation 1982;65:1004–9.

27. **Saviolo R, Spodick DH.** Electrocardiographic responses to maximal exercise during acute pericarditis and early repolarization. Chest 1986;90:460–2.

28. **Brugada P, Brugada J.** Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol 1992;20:1391–6.

29. **Antzelevitch C.** Genetic, molecular and cellular mechanisms underlying the J wave syndromes. Circ J 2012;76:1054–65.

30. **Belhassen B, Glick A, Viskin S.** Efficacy of quinidine in high-risk patients with Brugada syndrome. Circulation 2004;110:1731–7.

31. **Benito B, Guasch E, Rivard L, et al.** Clinical and mechanistic issues in early repolarization of normal variants and lethal arrhythmia syndromes. J Am Coll Cardiol 2010;56:1177–86.

32. **Bianco M, Bria S, Gianfelici A, et al.** Does early repolarization in the athlete have analogies with the Brugada syndrome? Eur Heart J 2001; 22:504–10.

33. **Rennyson SL, Littmann L.** Brugada-pattern electrocardiogram in propranolol intoxication. Am J Emerg Med 2010;28:256.e7–8.

34. **Aouate P, Clerc J, Viard P, et al.** Propranolol intoxication revealing a Brugada syndrome. J Cardiovasc Electrophysiol 2005;16: 348–51.

35. **Miyazaki T, Mitamura H, Miyoshi S, et al.** Autonomic and antiarrhythmic drug modulation of ST segment elevation in patients with Brugada syndrome. J Am Coll Cardiol 1996;27:1061–70.

36. **Probst V, Veltman C, Eckardt L, et al.** Long-term prognosis of patients diagnostic with Brugada syndrome: results from the Finger Brugada Syndrome registry. Circulation 2010;121:635–43.

37. **Uberoi A, Jain NA, Perez M, et al.** Early repolarization in an ambulatory clinical population. Circulation 2011;124:2208–14.

38. **Rautaharju PM, Suravicz B, Gettes LS, et al.** American Heart Association Electrocardiography and Arrhythmias Committee. Recommendations for the standardization. Circulation 2009;119: e241–50.

39. **Letsas KP, Sacher F, Probst V, et al.** Prevalence of early repolarization pattern in inferolateral leads in patients with Brugada syndrome. Heart Rhythm 2008;5:1685–9.

40. **McIntyre WF, Pérez-Riera AR, Femenía F, et al.** Coexisting early repolarization pattern and Brugada syndrome: recognition of potentially overlapping entities. J Electrocardiol 2012;45:195–8.