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J Wave Syndrome: Clinical Diagnosis, Risk Stratification And Treatment

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Abstract

J wave syndrome has emerged from a benign electrocardiographic abnormality to a proarrythmic state and a significant cause of idiopathic ventricular fibrillation responsible for sudden cardiac death. Electrical genesis, genetics and ionic mechanisms of J wave syndromes are active areas of research. Typically two of these viz., Early repolarization syndrome (ER) and Brugada syndrome (BrS) are fairly well characterized enabling correct diagnosis in most patients. In early repolarization syndrome, J waves are seen in inferior (2,3, avF) or lateral leads (V4, V5, V6), while in Brugada syndrome they are best seen in right precordial leads (V1-V3). The first part of repolarization of ventricular myocardium is governed by Ito current i.e., rapid outward potassium current. The proposed mechanism of ventricular fibrillation (VF) and ventricular tachycardia (VT) storms is faster Ito current in the epicardium than in the endocardium resulting in electrical gradient that forms the substrate for phase 2 re-entry. Prevention of Ito current with quinidine supports this mechanism. Morphological features of benign variety of J wave syndrome and malignant/ proarrythmic variety have now been fairly well characterized. J waves are very common in young, athletes and blacks; risk stratification for VF/sudden cardiac death (SCD) is not easy. Association of both ER syndrome and Brugada syndrome with other disease states like coronary artery disease is being reported frequently. Those with ECG abnormality as the only manifestation are difficult to manage. Certain ECG patterns are more proarrythmic. Individuals resuscitated from VF definitely need an implantable cardiac defibrillator (ICD) but in others there is no consensus regarding therapy. Role of electrophysiology study to provoke ventricular tachycardia or fibrillation is not yet well defined. Radiofrequency ablation of epicardial substrate in right ventricle in Brugada syndrome is reported and is also under critical evaluation. In this review we shall discuss some interesting historical features, epidemiology, electrocardiographic features, and ionic mechanisms on pathogenesis, clinical features, risk stratification and treatment issues in J wave syndromes. Brugada syndrome is not discussed in this review.

Preamble

J wave /Early Repolarization (ER) wave names after junction point of QRS with ST segment on ECG and reflects junction point (J Point) of end of depolarization with initiation of repolarization on action potential curve. This J point is characterized by transient outward current called `Ito K` current which may not be homogenous in epicardium and endocardium in various parts of the heart/ ventricles. This gradient may result in a hump on action potential curve and on ECG. The initial description of a prominent J wave was in a case of hypothermia described by Osborne.[1] Some prevalence studies with reasonably long follow up in community set up concluded that J waves were an innocuous /benign condition. Interestingly, in 2008, Haissaguerre et al[2] published data of 206 patients, less than 60 years of age, who had sudden cardiac death due to idiopathic ventricular fibrillation (VF). They assessed the prevalence of ER and compared it with a control group who were matched for age, sex, race and level of physical activity from 22 international tertiary care arrhythmia centers. The prevalence of ER in sudden death group was higher than in control group (31% vs. 5%, p< 0.001).It was more in males who had history of syncope or sudden cardiac death (SCD) during sleep. In eight patients the origin of PVC that initiated VF was localizable to inferolateral left ventricle. On mean follow up of 61± 50 months ICD monitoring showed higher incidence of VF in case group with ER than without ER (Hazard ratio 2.1; 95% confidence interval 1.2 to 3,5; p=0.008). This seminal and landmark study defacto changed the whole concept of J wave from being a benign ECG abnormality to a proarrythmic state and a marker for VF/SCD. None of these cases had features of Brugada syndrome.

J wave hump is a common incidental finding in normal individuals, especially in blacks and athletes. A unique feature of J wave is that it may not be present all the times and actually has been seen to emerge just before onset of VF and also to disappear in survivors of VF. Hence we need to first look for J wave, identify its malignant nature, risk stratify the patient and if needed treat for VF. In this article we shall describe some historical events, physiological versus pathological J waves, benign Vs malignant J waves, transient vs. persistent J waves, identification of proarrythmic J waves, risk stratification of patients

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Disclosures:
None.

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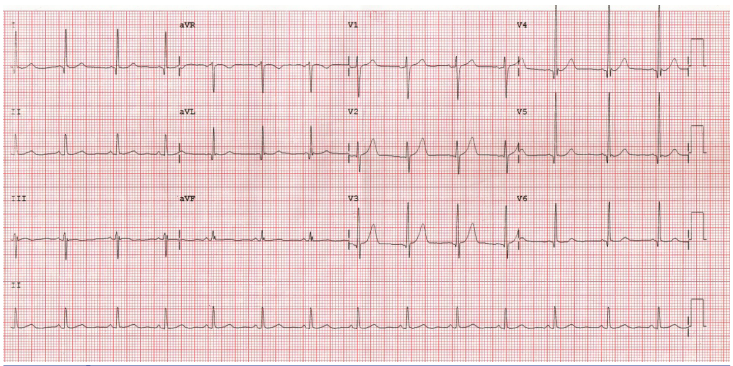

Figure 1: **Benign type ER**

and currently available treatment.

J Wave In Athletes

Abundant data demonstrate that early repolarization is very common among young athletes. Quattrini et al.[3] reported the prevalence and clinical significance of J wave/QRS slurring in a large population of competitive athletes. Seven hundred and four athletes (436 males [62%], age 25 ± 5 years) free of cardiovascular (CV) disease who had engaged in 30 different sports were examined. Serial clinical, ECG, and echocardiographic evaluations were available over 1 to 18 years of follow-up (mean 6 ± 4 years).Interestingly, J wave was found in 102 subjects (14%) and was associated with QRS slurring in 32 (4%). It was found most commonly in anterior, lateral, and inferior leads (n = 73 [72%]), occasionally in lateral leads (n = 26 [25%]), and rarely in inferior leads (n = 3 [3%]). Most of 102 athletes (n = 86 [84%]) also showed ST-segment elevation. During follow-up, no athlete with J wave experienced cardiac event or ventricular tachyarrhythmia, or developed structural CV disease. It was concluded that in athletes, early repolarization pattern was associated with other ECG changes, such as increased QRS voltages and ST-segment elevation, as well as LV remodeling, suggesting that it likely represented another benign expression of the physiologic athlete's heart. J wave/ER is common in highly trained athletes and does not convey risk for adverse cardiac events, including sudden death or tachyarrhythmia.

Proarrythmic J Wave

Tikkanen et al.[4] were the first to focus on the contour of the ST-segment in ER. To define a benign form, they initially studied two populations of healthy athletes, knowing that ER is particularly frequent in this group. The vast majority of healthy athletes with ER (85% in 1 series and 96% in the other) had a "rapidly ascending" ST-segment blending with the T-wave. They naturally assumed this rapidly ascending form to be benign. The remaining minority of athletes with ER featured an ST-segment that remained flat, horizontal, or even descended toward the T-wave. This "horizontal/descending" pattern drew suspicion to a "potentially malignant" variant of ER.

Morphological Classification of J Waves

Clearly, J waves can be physiological (benign) or pathological (malignant). Morphological features considered important are (i) J point elevation, (ii) height of J wave, (iii) slope of ST segment i.e., up- sloping, horizontal or downsloping and (iv) number of ECG leads showing these changes. So far no scoring method has evolved. Table 1 shows differences between physiological and pathological J waves.

Types of Early Repolarization (ER)

Antzelevitch et al described early repolarization syndrome into three subtypes[5]:

Type 1: Early repolarization pattern predominantly in the lateral precordial leads. This form is very prevalent among healthy male athletes and is rarely seen in VF survivors. (Fig.1)

Type 2: Early repolarization pattern predominantly in the inferior or infero-lateral leads. Numerous cases of otherwise idiopathic VF have this ECG pattern; this is also prevalent in healthy young males (Fig.2).

Type 3: Early repolarization pattern globally in the inferior, lateral, and right precordial leads. This is associated with the highest level of risk for development of malignant arrhythmia. It is often associated with VT/VF storms.

Tikkanen's Classification

They described ER as J-point and ST segment elevation >1mm in 2 or more contiguous leads.[4] Two types of J point elevation are described:

1. J point with rapidly ascending ST segment, considered a Benign form (Fig. 1,2)

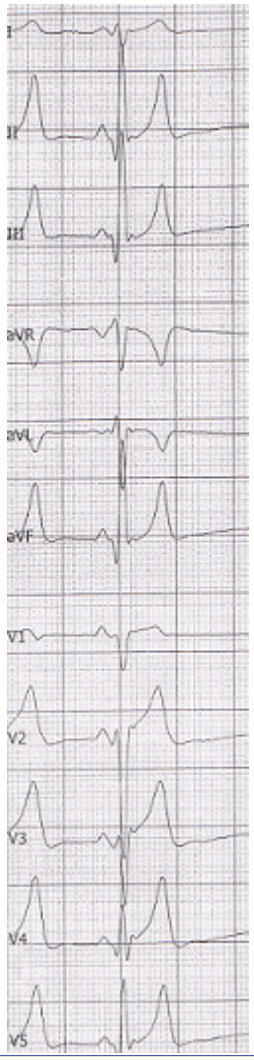

Figure 2: **ER with J point elevation in Inferior and lateral leads <1mV**

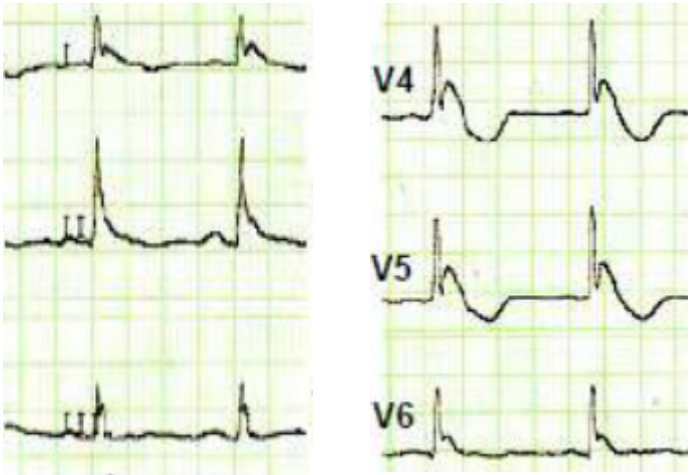

Figure 3: Malignant variety of ER with J point elevation >2mV in inferolateral leads with downsloping ST segment.

2. J point with horizontal or descending ST segment, considered a Malignant form (Fig. 3,4)

ER in Infero-lateral leads is more associated with ventricular fibrillation.[6] ER ECG pattern (> 1 mm) in the inferior/lateral leads occurs in 1-13% of the general population and in 15-70% of Idiopathic VF cases. In the pediatric age group it is even more prevalent. Male sex is strongly associated with ER ECG pattern; over 70% of subjects with ER are males. Its prevalence declines in males from early adulthood until middle-age which suggests a hormonal influence on the presence of ER. The ER pattern is more common in young physically active individuals, athletes, and African-Americans. There is an increased prevalence of ER in South-East Asians. The ER pattern is associated with high vagal tone, as well as hypothermia and hypocalcaemia.[7]

Genetic Basis And Variants

The genetic basis for early repolarization is not well defined. Genetic contributions to ER are suggested by anecdotal observations of a common familial history of SCD in subjects with ER and idiopathic VF. Familial ER has been reported to have an autosomal dominant inheritance pattern with incomplete penetrance. Two independent population-based studies also have suggested some degree of inheritance of the ER patterns in the general population, but the familial inheritance of malignant ER patterns has not been clearly demonstrated. A candidate gene approach in idiopathic VF patients with ER has identified a mutation in KCNJ8, which encodes a pore-forming subunit of the ATP-sensitive potassium channel.

Mutations in the L-type calcium channel genes, including CACNA1C, CACNB2B, and CACNA2D1 as well as loss-of-function mutations in SCN5A have also been associated with idiopathic VF with ER. Given the high prevalence of ER in the general population, ER likely has a polygenic basis that also is influenced by non-genetic factors.[8-10]

Clinical Diagnosis

Following clinical patterns are now known[11-14]:

1. Asymptomatic and incidentally detected J waves are very common in athletes. The prevalence and magnitude of ER increase as their training intensifies.

2. Malignant variety with Idiopathic VF and Sudden Cardiac Death (SCD). Idiopathic VF is reported with horizontal or down-sloping ST following J point elevation.

3. J waves with Coronary artery disease (CAD) with increased risk of ischemic VF. ER pattern recorded during ischemic event is strongest predictor of VF occurrence. Such pronounced J waves mostly appear prior to onset of VF. (11).(Fig.5)

4. J waves/ER has been linked to high cardiac death and arrhythmic death rates in vasospastic angina.

Laboratory Diagnosis

There are no validated techniques to provoke the ER pattern, although 12-lead Holter monitoring to detect transient ER pattern during bradycardia is warranted. In survivors of VF and in patients with polymorphic VT, clinical evaluation to rule out structural heart disease including echocardiogram, coronary angiography, magnetic resonance imaging (MRI), and selected endocardial biopsies should be performed to exclude other causes of VF.[15]

Risk stratification

The magnitude of the J-point elevation may have prognostic significance. Either slurred or notched J-point elevation ≥0.2 mV is relatively rare in the general population, but appears to be associated with an increased risk. Furthermore, J point elevation in idiopathic VF patients is of greater amplitude and ECG lead distribution compared to those with an established cause of cardiac arrest. The available data also suggest that transient changes in the presence and amplitude of J-point elevation portends a higher risk for VF. A horizontal or descending ST-segment following J-point elevation is associated with a worse outcome in the general population. Often,

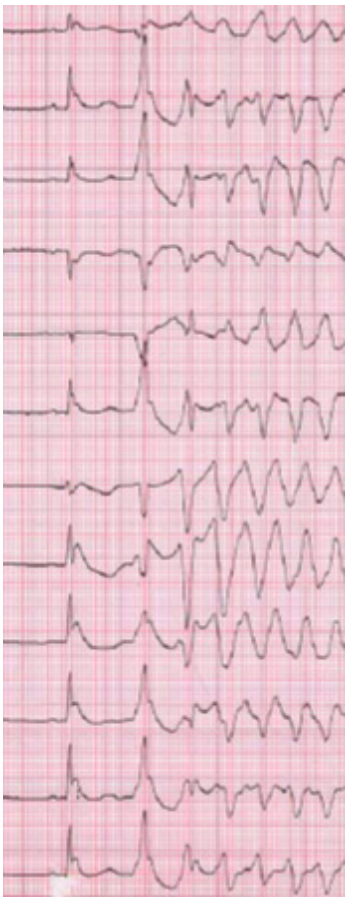

Figure 4: Ventricular tachycardia in same patient as in fig 3.

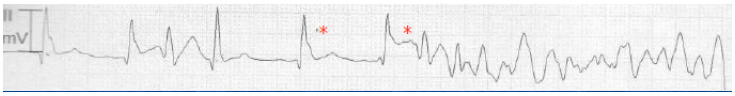

Figure 5: J point elevation prior to ventricular fibrillation

increase in amplitude of J wave is observed just before occurrence of PVCs initiating VF. This observation has been very helpful in distinguishing idiopathic VF.[14-16]

Management

The clinical implications of the observation of Type 1 and 2 ER pattern/J waves in the ECG of an asymptomatic subject are not clear at this stage. The presence of Type 3 ER/J waves is associated with three times the risk of developing VF. Because the presence of ER may increase the vulnerability to sudden death during an acute ischemic event, a plausible implication coming from the population studies is that middle-aged subjects with the ER pattern in the ECG, especially those with a high amplitude of J-point elevation (>2 mm) and horizontal or downsloping ST segment, should target a reduction in their long-term risk for acute coronary events in accordance with current practice guidelines. Electrical storm is relatively common after ICD implantation in patients with the ER syndrome. Case series evidence supports the acute use of Isoproterenol for suppression of recurrent VF, and Quinidine for long-term suppression. Isoproterenol is typically initiated at 1.0 μg/minute, targeting a 20% increase in heart rate or an absolute heart rate > 90 bpm, titrated to hemodynamic response and suppression of recurrent ventricular arrhythmia.[17]

Screening Of Family Members

No recommendations can be given to do ECG screening of the families of individuals with asymptomatic ER pattern or individuals with strong family history of ER/J wave or ER with VF. There are no established provocative tests to diagnose concealed ER in family members of J wave/ ER syndrome patients, although preliminary observations suggest that the Valsalva maneuver may assist in identifying concealed ER cases.[16]

At this time there are no clear recommendations regarding driving, competitive sports or genetic testing in patients with J wave/ER syndrome.[17]

Treatment

Following are recommendations from latest Consensus document of 2011 HRS/ACC/ESC.[17]

Class I

1. ICD implantation is recommended in patients with a diagnosis of J wave/ ER syndrome who have survived a VF/cardiac arrest

Class II a

1. Isoproterenol infusion can be useful in suppressing electrical/ VT storms in patients with diagnosis of J wave/ER syndrome

2. Quinidine in addition to an ICD can be useful for secondary prevention and suppression of VT/VF in patients with a diagnosis of J wave/ER syndrome

Class II b

1. ICD implantation may be considered in symptomatic family members of J wave/ER syndrome, with history of syncope in the presence of ST segment elevation >1mm in 2 or more inferior or lateral leads

Table 1: Differences between Benign and Malignant variety of J wave syndromes

Characters	Physiological J Wave	Pathological J wave
J point Elevation	<0.1 mV	>0.2 mV
Height of J wave	1-2 mm	>2mm
Descent of J wave	Up-sloping	Horizontal or Downsloping)
ECG Leads	Only V4-6 or II,III,aVf	Both, V4-6 plus II,III,aVf

2. ICD implantation may be considered in asymptomatic individuals who demonstrate a

High-risk ER ECG pattern (high J-wave amplitude, horizontal/ descending ST) in

Infero-lateral leads in the presence of a strong family history of juvenile unexplained sudden death with or without a pathogenic mutation

Class III

ICD implantation is not recommended in asymptomatic patients with an isolated J wave/ER pattern on ECG

Conclusion:

Idiopathic ventricular fibrillation (VF) accounts for significant cause of sudden cardiac death and is a challenge to electrophysiology physicians. Though coronary artery disease with ischemia and structural heart diseases are significant causes yet primary electrical disorders like long QT, Short QT, Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia are emerging as notable causes and transient or new onset significant J waves are being reported as proarrythmic for VF.

Understanding of J wave syndrome/ER syndrome has improved considerably, yet many questions in management of patients suffering from this condition remain unanswered. J wave is an ECG finding and not a clinical sign or symptom. The only known manifestation symptom is sudden cardiac death (SCD) or VF. Benign versus malignant morphological features of J wave are described yet sometimes dynamic variability of J wave shape especially in setting of CAD is intriguing.[18] Benign J waves are prominent among young, athletes and blacks. Risk stratification is only through ECG pattern; no clinical investigation like EP studies, microvolt T wave alternans etc are useful. If index event is VF and patient is successfully resuscitated, ICD implantation is recommended. Electrical storm should be managed with intravenous isoproterenol and then oral Quinidine. The latter by suppressing Ito current is highly useful. Role of Genetic testing is unclear. Vocational guidelines, participation in competitive exercises and driving guidelines are in stage of evolution.

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