CONTEMPORARY REVIEW

J wave syndromes

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The J wave, also referred to as an Osborn wave, is a deflection immediately following the QRS complex of the surface ECG. When partially buried in the R wave, the J wave appears as J-point elevation or ST-segment elevation. Several lines of evidence have suggested that arrhythmias associated with an early repolarization pattern in the inferior or mid to lateral precordial leads, Brugada syndrome, or arrhythmias associated with hypothermia and the acute phase of ST-segment elevation myocardial infarction are mechanistically linked to abnormalities in the manifestation of the transient outward current (I_{to})-mediated J wave. Although Brugada syndrome and early repolarization syndrome differ with respect to the magnitude and lead location of abnormal J-wave manifestation, they can be considered to represent a continuous spectrum of phenotypic expression that we propose be termed *J-wave syndromes*. This review summarizes our current state of knowledge concerning J-wave syndromes, bridging basic and clinical aspects. We propose to divide early repolarization syndrome into three subtypes: *type 1,* which displays an early repolarization pattern predominantly in the lateral precordial leads, is prevalent among healthy male athletes and is rarely seen in ventricular fibrillation survivors; *type 2,* which displays an early repolarization pattern predominantly in the inferior or inferolateral leads, is associated with a higher level of risk; and *type 3,* which displays an early repolarization pattern globally in the inferior, lateral, and right precordial leads, is associated with the highest level of risk for development of malignant arrhythmias and is often associated with ventricular fibrillation storms.

KEYWORDS Brugada syndrome; Cardiac arrhythmia; Early repolarization syndrome; Hypothermia; Idiopathic ventricular fibrillation; J-point elevation; ST-segment elevation myocardial infarction; Sudden cardiac arrest; Sudden cardiac death; Transient outward current

ABBREVIATIONS **VF** = ventricular fibrillation; **VT** = ventricular tachycardia

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Introduction

The J point denotes the junction of the QRS complex and the ST segment on the ECG, marking the end of depolarization and the beginning of repolarization. The J wave, also referred to as the Osborn wave, in recognition of Osborn's landmark description in the early 1950s,[1] is a deflection with a dome or hump morphology in the same direction as the R wave, immediately following the QRS complex of the surface ECG. The clinical and arrhythmogenic significance of J-wave abnormalities were largely ignored until a report in 1996 elucidated the ionic and cellular bases of the J wave and pointed out its potential role in life-threatening tachyarrhythmias.[2] Several lines of evidence suggest that arrhythmias associated with an early repolarization pattern in the inferior or mid to lateral precordial leads (i.e., classically defined early repolarization pattern), Brugada syndrome, some cases of idiopathic ventricular fibrillation (VF) with an early repolarization pattern in the inferior, inferolateral, or global leads, as well as arrhythmias associated with hypothermia and the acute phase of ST-segment elevation myocardial infarction are mechanistically linked to abnormalities in the manifestation of the transient outward current (I_{to})-mediated J wave.

Although Brugada syndrome and early repolarization syndrome differ with respect to the magnitude and lead location of abnormal J-wave manifestation, they can be considered to represent a continuous spectrum of phenotypic expression that we propose to be termed *J-wave syndromes.*[3–7] This review summarizes our current state of knowledge concerning J-wave syndromes, bridging basic and clinical aspects.

Historical perspective of J wave and J wave–related clinical phenomena

In 1938, Tomaszewski[8] provided the first description of hypothermic J wave in an accidentally frozen man. He described the J wave as a very slowly inscribed deflection between the QRS complex and the ST segment of the ECG.

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In 1953, Osborn[1] described in acidotic and hypothermic dogs what he called a "current of injury" that fibrillated at rectal temperatures less than 25°C. This so-called "current of injury" was later named the *Osborn wave*.[9]

An early repolarization pattern on the ECG was first described in 1936 by Shipley and Hallaran,[10] who evaluated the four-lead ECG of 200 healthy young men and women. They described J deflection as slurring or notching of the terminal part of QRS complex and considered it to be a normal variant. This ECG phenomenon was ascribed to accelerated ventricular repolarization with 2% prevalence in healthy adults. In 1961, Wasserburger and Alt[11] further defined early repolarization as an elevated takeoff of the ST segment at the J junction of the QRS complex varying from 1 to 4 mm from the isoelectric line accompanied by downward concavity of the ST segment and symmetrically limbed T wave often of large amplitude in the mid to left precordial leads. In subsequent years, several investigators sought to characterize the clinical importance of the ECG early repolarization pattern but failed to find any immediate- or long-term consequences.[12]

A shift away from a benign view of the J wave began in 1984 when Otto et al[13] presented three cases of VF that occurred during sleep in young male southeast Asian refugees who had structurally normal hearts. The only prominent ECG abnormality in these patients was a prominent J wave accompanied by ST segment elevation. In the Philippine capital city of Manila, from 1948 to 1982 a total of 722 apparently healthy young males died during sleep from a disease then called "bangungut" (to rise and moan during sleep) in their native language.[14] In the 1980s, the United States Center for Disease Control received approximately 120 case reports of sudden cardiac death among southeast Asian refugees living in the United States who apparently had been healthy.[15] Aizawa et al[16,17] reported similar cases of idiopathic VF in which the ECGs exhibited prominent J waves in the inferior leads.

In 1992, Pedro and Josep Brugada[18] published a landmark study describing eight sudden cardiac death patients in whom the ECG revealed "right bundle branch block" and ST-segment elevation in precordial leads V_1 to V_3, without obvious structural heart diseases. In 1996, we and others named this entity "Brugada syndrome."[2,19] In many cases of Brugada syndrome, the "right bundle branch block" appears without an S wave in the left precordial leads, suggesting that, in these cases, the right bundle branch block is apparent and that R′ represents an accentuation of the J wave. A consensus report published in 2002 delineated diagnostic criteria for the syndrome. A second consensus conference report, published in 2005, focused on risk stratification schemes and approaches to therapy.[20]

In 1999, Gussak and Antzelevitch[3] suggested that early repolarization may be malignant in some cases, based on observations that an early repolarization pattern in arterially perfused wedge preparations can easily convert to one in which phase 2 reentry gives rise to polymorphic ventricular tachycardia (VT)/VF. Evidence supporting this hypothesis was provided by Kalla et al[21] and Takagi et al[22] in 2000. They reported VF in patients with prominent J wave and ST-segment elevation in inferior leads without structural heart diseases and postulated that idiopathic VF with an early repolarization pattern in inferior leads may represent a variant of the Brugada syndrome. In 2008, Haissaguerre et al[23] and Nam et al[7] demonstrated a definitive association between J waves with an early repolarization pattern and VF. All of these clinical observations suggested a critical role for the J wave in the pathogenesis of many different forms of idiopathic VF.[5,21,24–27]

Ionic and cellular mechanisms for the J wave and associated arrhythmogenesis

Since the 1980s, work from our group first proposed that transmural differences in early phases of the action potential (phases 1 and 2) are responsible for inscription of the ECG J wave.[28,29] The ventricular epicardium commonly displays action potentials with a prominent I_{to}-mediated notch or spike and dome. A prominent I_{to}-mediated action potential notch in ventricular epicardium but not endocardium produces a transmural voltage gradient during early ventricular repolarization that registers as a J wave or J-point elevation on the ECG. Direct evidence supporting this hypothesis was obtained in arterially perfused canine ventricular wedge preparations in 1996 (Figure 1).[2]

Factors that influence I_{to} kinetics or ventricular activation sequence can modify the manifestation of the J wave on the ECG. For example, because of its slow recovery from inactivation, I_{to} is reduced following an acceleration of heart rate, resulting in a decrease in the magnitude of the J wave.[30,31]

An increase in net repolarizing current, due to either a decrease of inward currents or augmentation of outward currents, accentuates the notch leading to augmentation of the J wave or the appearance of ST-segment elevation. A further increase in net repolarizing current can result in partial or complete loss of the action potential dome, leading to a transmural voltage gradient that manifests as greater ST-segment elevation.[30–32] This was the first compelling evidence that ST-segment elevation can occur in the absence of myocardial ischemia. In regions of the myocardium exhibiting a prominent I_{to}, such as the epicardium of right ventricle, marked accentuation of the action potential notch results in a transmural voltage gradient that leads to coved ST-segment elevation, which is the only form of ST-segment elevation diagnostic of Brugada syndrome (Figure 2B). A further outward shift of the currents active during the early phase of the action potential can lead to loss of the action potential dome, thus creating a dispersion of repolarization between epicardium and endocardium as well as within epicardium, between the region where the dome is lost and regions at which it is maintained (Figure 2C).

Because accentuation of the action potential notch and loss of the dome are due to an outward shift of currents secondary to either a decrease in inward currents (I_{Na} and I_{Ca}) or an