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Review

Brugada syndrome and early repolarization syndrome: Cellular basis and clinical features

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ABSTRACT

Brugada syndrome (BS) and early repolarization syndrome (ERS) are newly introduced electrical disorders responsible for ventricular fibrillation (VF) and sudden cardiac death in patients with structurally normal hearts. The electrocardiographic J wave, a hallmark of these two syndromes, plays a critical role in the pathophysiology of malignant ventricular tachyarrhythmias. BS and ERS share many clinical characteristics, including male preponderance, circadian distribution of VF episodes, prevalence of concomitant atrial tachyarrhythmias, dynamic behavior of J waves, and response to therapeutic managements. In this review, we compare the key clinical manifestations of BS and ERS with their underlying cellular electrophysiologic mechanisms.

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1. Introduction

Sudden cardiac death (SCD) in the absence of structural heart diseases accounts for 5–10% of all sudden cardiac deaths and is caused by primary electrical disorders or ion channel diseases [1,2]. Identification of the ion channels and their genetic mutations responsible for SCDs has opened a new area of translational research in cardiac electrophysiology [3–8].

Long QT syndrome has been recognized as an important cause of SCD [3]. The genetic mutation and the basic electrophysiologic mechanisms in SCD were elucidated recently, long after the recognition of its clinical entity [4]. In contrast, key cellular electrophysiologic features underlying the development of ventricular fibrillation (VF) associated with Brugada syndrome (BS) and early repolarization syndrome (ERS) were described well before the recognition of clinical entities [9–11]. Unlike other ion channel diseases, BS and ERS share many electrocardiographic and clinical features [5,12]. Both syndromes are represented by electrocardiographic J waves that demonstrate similar dynamic behavior such as a pause or bradycardia dependence and short-coupled extrasystole-induced polymorphic ventricular arrhythmia [13]. J waves can be suppressed in both ERS and BS with the administration of isoproterenol and quinidine and with pacing. ERS and BS have been reported to occur simultaneously in the same individual or in different members of the same family [14]. In this review, we describe similarities and differences in the cellular electrophysiology and clinical features of BS and ERS.

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2. Demographic and arrhythmia characteristics: gender, circadian pattern of VF, and atrial arrhythmias

The prevalence and arrhythmic risk of BS and ERS differ considerably. The BS ECG pattern occurs rarely in the general population, while the ER pattern is a common ECG phenomenon, especially in young men and athletes (Fig. 1). The BS pattern portends a high risk of developing arrhythmias, while the ER pattern portends a relatively low risk of sudden death. In a Japanese population study, the prevalence of the typical coved-type BS ECG is estimated to occur in approximately 0.12% of the general population [15]. The odds ratio of sudden unexpected death in this BS ECG group was 52.63, relative to that of control subjects [16].

The prevalence of the ER pattern depends on the definition of ER. When the traditional definition of ER (more emphasis on the ST segment elevation with or without the J wave) is used, the prevalence is approximately 2% [17,18]. When defined as J wave > 1 mm regardless of the ST segment elevation (a new definition), the prevalence is approximately 5–12% [19–23]. The suggestion that ER may be associated with fatal ventricular tachyarrhythmia (VTA) resulted in considerable confusion in clinics because of the high prevalence of ER in the general population. Over the past several years, numerous case-control and population studies have introduced a renewed concept on the prognosis of individuals with the ER pattern [17–23]. In brief, ER can be categorized into several types. The traditional definition of ER that emphasizes on the ST segment elevation is not associated with adverse outcome [17,18]. The new definition of ER includes J wave with or without ST segment changes. ER with "J wave and rapidly ascending ST segment" is considered a benign variant. However, "J waves with horizontal/descending ST segment" changes have been associated with an increased risk of arrhythmic death [22]. There is confusion because of the marginally increased risk of arrhythmic deaths. Although statistically significant, the absolute value of the risk of arrhythmic death in this group is still extremely low, with an odds ratio of 13.8 for developing idiopathic VF in a case-control study [24] and a relative risk of 1.43 for arrhythmic death in a population study [22]. Before the publication of these studies, ER pattern was regarded as "forme fruste" BS because of their similar electrocardiographic and electrophysiologic background in basic experimental studies [25,26]. Considering the low odds of malignant arrhythmia, it is yet too premature to assume that all the subjects with ECG ER pattern (even those with the malignant form of ER) require medical attention for a risk of SCD.

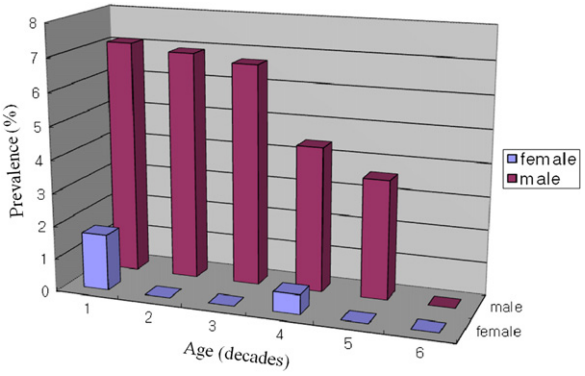

Fig. 1. Prevalence of early repolarization electrocardiograms in the general population. All 1,395 patients had their ECG recorded between 1 May 2007 and 15 May 2007 at the department of Health Medicine, Asan Medical Center (modified from reference [45] with permission).

Both ERS and BS show a strong male preponderance. In papers published on BS, men account for approximately 70–90% of patients. In the experimental model of canine wedge preparation, the spike-and-dome morphology of the action potential (AP) was more prominent in the male than in the female dog preparations [27]. The prominent epicardial notch was caused by higher I_{To} density in the male ventricular epicardial cells than in the female preparations. This provides the electrophysiologic background for male dog wedges to develop tachyarrhythmias (phase 2 reentry) in response to class IC antiarrhythmic agents, the combined blockade of Na^+ and Ca^{2+} currents induced by terfenadine or increased outward K^+ current induced by pinacidil [27]. This difference in AP morphology is thought to underlie the gender-associated differences in the prevalence of ER pattern in the general population.

The difference in ventricular AP morphology observed between male and female subjects may be related to the presence of different sex hormones. Experiments in ovariectomized rats show that estrogen may be involved in one of the mechanisms responsible for the reduction in Kv4.3 expression and function in the myometrium. Testosterone has been reported to shorten the AP duration by enhancing slowly activating delayed rectifier K^+ current (I_{Ks}) and suppressing the L-type Ca^{2+} current (I_{caL}) [28]. Shimizu et al. showed a strong positive association between BS and higher testosterone levels (hypertestosteronemia) and a strong inverse association between BS and body mass index [29]. The disappearance of the Brugada phenotype after surgical castration is a direct evidence of the role of sex hormones. Typical Brugada-type ECG patterns that had persisted over several decades were eliminated after surgical castration [30]. In addition, it was reported that electrocardiographic ST segment levels were significantly decreased after androgen-deprivation therapy, which suggests that testosterone may modulate the early phase of ventricular repolarization, as seen in patients with BS and ERS [31].

The circadian variation of VF shows a similar nocturnal pattern in patients with BS and ERS [32] (Fig. 2). This is in contrast to the

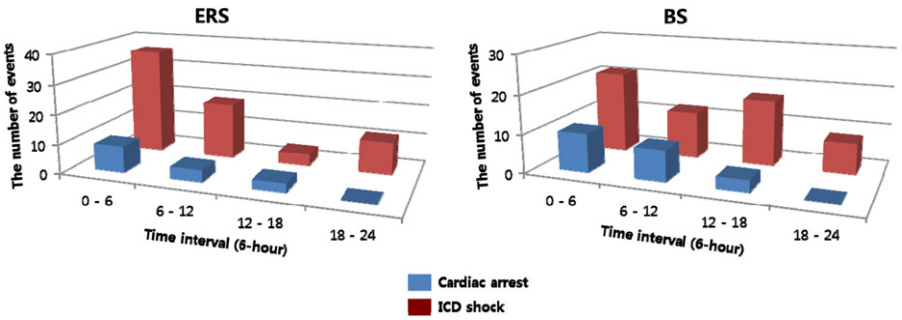

Fig. 2. Circadian pattern of ventricular tachyarrhythmias in patients with Brugada syndrome (BS) and early repolarization syndrome (ERS). Circadian patterns of cardiac arrest as the initial presentation (blue column) and appropriate implantable-cardioverter defibrillator shocks (red column) in patients with ERS and BS. Significant peaks in the number of ventricular tachyarrhythmias (cardiac arrest and appropriate shock) were observed between 12 AM and 6 AM in both the ERS and BS groups (modified from reference [32] with permission).

circadian pattern of VTAs in patients with ischemic heart diseases [33]. In a Korean cohort of patients with ERS and BS who underwent implantable cardioverter defibrillator (ICD) implantation, the timing of VTAs, including that of cardiac arrest and appropriate shocks, peaked between midnight and early morning (12 AM and 6 AM). A significant seasonal peak of appropriate shocks was observed between spring and summer in patients with ERS, whereas no such consistent seasonal pattern was observed in patients with BS [33].

VTAs in patients with structural heart diseases occur more commonly during the daytime and in winter when the ventricular myocardium is more vulnerable to ischemia. This is associated with neurohumoral activation (plasma catecholamine concentration) that results in increased cardiac workload, higher coronary resistance, higher blood pressure, and increased blood viscosity during the daytime and in the winter. Ventricular refractoriness shows a consistent variation, with the shortest refractory period observed during waking hours and the longest observed during sleep. This ventricular myocardial status may provide additional risk in the maintenance of VF under acute ischemia [34].

The similarity in the circadian patterns of ERS and BS may be due to their shared effect of vagal activity. Vagal activity is highest during the night when the incidence of cardiac arrest and appropriate shock peaks in ERS and BS patients, whereas sympathetic activity is highest in the morning and in winter when the incidence of VTAs peaks in patients with structural heart diseases [35]. The loss of the epicardial AP dome is the basis for an elevated J point and ST segment elevation, and phase 2 reentry serves as a trigger of circus movement reentry that are responsible for VF in patients with BS. The loss of the epicardial dome (BS) or the depression of epicardial plateau (ERS) is caused by an outward shift in the balance of currents at the end of phase 1 of the AP. Vagal stimulation or autonomic neurotransmitters such as acetylcholine facilitate loss of the epicardial AP dome by suppressing I_{Ca} and/or augmenting potassium current, whereas β-adrenergic agonists restore the dome by augmenting I_{Ca}. These experimental results are in line with the circadian distribution of VF in BS and ERS patients.

Atrial tachyarrhythmias have been documented in a significant proportion of patients with BS and are an important cause of inappropriate shock. The incidence of atrial tachyarrhythmias and the development of inappropriate shock is also similar in patients with BS and ERS [36]. In our Korean patient cohort of BS and ERS, during a mean follow-up of approximately 5 years, no significant differences were found in the prevalence of atrial tachyarrhythmias (mostly atrial fibrillation) and in the incidence of inappropriate shocks due to these atrial tachyarrhythmias. It is speculated that the arrhythmogenic substrate in both BS and ERS is not restricted to the ventricular level but may be extended to the atrium [37].

3. Cellular electrophysiologic basis of BS and ERS

Ventricular AP exhibits considerable variation or regional difference across the transmural direction of the ventricular myocardium. The J wave originates from the heterogeneous distribution of a transient outward current-mediated spike-and-dome morphology of the AP across the ventricular wall. The presence of a prominent AP notch in the epicardium but not in the endocardium provides a voltage gradient that manifests as a J wave or as an elevated J-point in the ECG [38,39]. This unique epicardial AP shape indicates that epicardial repolarization is more susceptible to changes in response to drive cycle lengths, extrastimulation, drugs, or ischemia [40–42]. The heterogeneous loss of the AP dome caused by ischemia, bradycardia, or pharmacologic interventions (sodium channel blocker flecainide or acetylcholine) results in the development of a large dispersion of repolarization within the epicardium by abbreviation and marked prolongation of AP durations [40–42]. A dispersion of repolarization also occurs between the epicardial and M cell APs. This exaggerated dispersion of repolarization is followed by local re-excitation (phase 2 reentry) because of the AP dome propagating from sites where it was maintained to sites where it was abolished. The ECG J wave, a clinical marker of the AP notch, represents the vulnerability of the epicardial AP to a sudden disappearance of the AP dome (known as all-or-none repolarization) and susceptibility to fatal VTAs (Fig. 3A).

Based on the close relationship of the canine wedge model to human ECGs, individuals with prominent J waves (ERS) or J/ST elevation (BS) are thought to have accentuated ventricular AP notch and the potential to lose their AP dome because of extrinsic factors such as vagal stimulation, sodium channel blocker, or ischemia. The known genetic mutations discovered in patients with BS are compatible with the above electrophysiologic abnormalities. Loss-of-function mutations in the genes responsible for inward sodium current (I_{Na}) and inward calcium current (I_{Ca}) cause a decrease in the inward current components of the AP and gain-of-function mutations in the transient outward potassium current (I_{To}), ATP-dependent potassium current ($I_{K\text{-}ATP}$) genes cause an increase in the outward current components. This results in a net outward shift in the balance of currents, rendering the AP dome more susceptible to collapse. The sudden disappearance of the AP dome markedly abbreviates the AP duration while the repolarization duration is maintained where the AP dome is preserved (Fig. 3A).

The basic electrophysiology underlying normal J/ST/T wave, ER, and BS ECGs is a continuous spectrum. In normal hearts, the J wave is not prominent, and the ST segment is isoelectric because there are no voltage gradients in the AP plateau phase. In some physiologic or pathologic conditions (genetic, hormonal, or drug induced) in which the AP notch is accentuated either by poor inward currents or increased outward currents, the voltage gradients manifest as J wave and ST segment elevation. Accentuation of the AP notch is more pronounced in the right ventricular epicardium, where the notch is intrinsically more prominent. Until these changes progress to a certain degree, the T wave remains positive because the epicardial repolarization is followed by endocardial and M cell repolarization. This explains the typical ECG features of ER pattern (Fig. 3B, left panel). As these electrophysiologic processes become more pronounced, further accentuation of the AP notch delays development of I_{Ca}, delaying the epicardial dome and repolarization even later than that of the M cell or endocardial regions. This reverses the final repolarization sequence through the transmural myocardial layers, inducing a coved-type ST segment elevation (Fig. 3B, right panel). In a profoundly abnormal condition, an extreme accentuation of the AP notch causes further shift in the balance of inward/outward currents, which leads to the loss of the AP dome and initiates phase 2 reentry, as described above (Fig. 3A). Therefore, the basic pathophysiology of malignant tachyarrhythmias in patients with BS and ERS seems identical and only differs in the severity of the background electrophysiologic milieu.

4. Electrocardiographic features: J wave dynamics and mode of onset of VF

BS is characterized by unique ECG features of coved-type J/ST/T waves (type I Brugada ECG pattern) and a high risk of developing VF. Suggestive but less confirmative ECG findings are saddleback type J/ST/T waves, or type II/III Brugada patterns. Prompted by the similarity in ECG features and the potential of converting this ER to Brugada ECG patterns, the benign nature of the ER

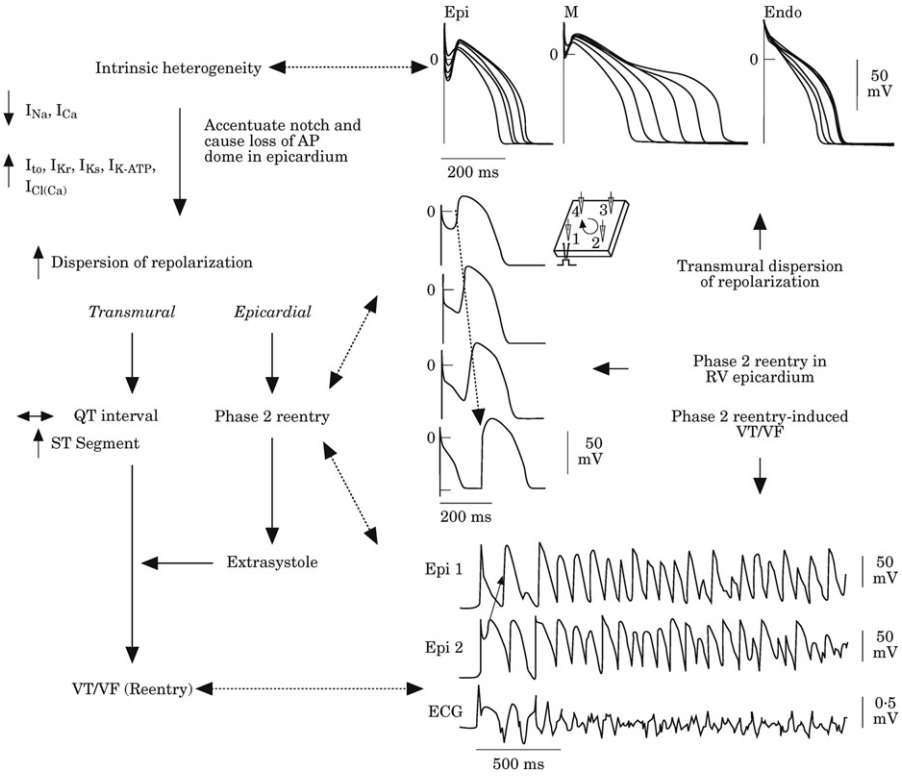

Fig. 3. The proposed mechanism of ventricular arrhythmias and ECG changes in BS and ERS. (A) Ventricular action potentials (APs) demonstrate a considerable variation across the transmural direction of the ventricular myocardium. The presence of a prominent AP notch in the epicardium but not in the endocardium provides a voltage gradient that manifests as a J (Osborn) wave or elevated J-point in the ECG (top). Heterogeneous loss of the AP dome by ischemia, bradycardia, or pharmacologic interventions (sodium channel blocker flecainide or acetylcholine) results in the development of a large dispersion of repolarization within the epicardium by abbreviation and marked prolongation of AP durations. A dispersion of repolarization also occurs between the epicardial and M cell APs. This exaggerated dispersion of repolarization is followed by local re-excitation (phase 2 reentry) caused by the AP dome propagating from sites where it was maintained to sites where it was abolished (middle and bottom). (B) In normal hearts, the J wave is not prominent, and the ST segment is isoelectric because there are no voltage gradients in the AP plateau phase. In some physiologic or pathologic conditions (genetic, hormonal, or drug induced) in which the AP notch is accentuated, the AP notch manifests as J wave and ST segment elevation. Until these changes progress to a certain degree, the T wave remains positive because the epicardial repolarization is followed by the endocardial and M cell repolarization. This explains the typical ECG features of ER pattern (left panel). As the above electrophysiologic process becomes more pronounced, further accentuation of the AP notch delays the development of an inward calcium current, delaying the epicardial dome and repolarization even later than that of the M cell or endocardial regions. This reverses the final repolarization sequence through the transmural myocardial layers, inducing a coved-type ST segment elevation (right panel). In a profoundly abnormal condition, an extreme accentuation of the notch causes further shift in the balance of inward/outward currents, which leads to the loss of the AP dome and initiation of phase 2 reentry, as explained above (modified from reference [43] with permission).

pattern was questioned based on a few clinical case reports and basic electrophysiologic studies by using canine wedge preparation [25,26].

The ECG features of these two syndromes are based on the presence of J waves, in addition, the dynamic behavior of the J waves in both syndromes shows similar cycle length-dependent pattern. The J wave and ST segment elevation in BS demonstrate a pause-dependent accentuation and acceleration-dependent attenuation [44]. The amplitudes of J waves in ERS accentuate after long cycle lengths or after long coupling intervals (Fig. 4).

Although the J/ST waves show similar dynamic patterns, the mode of onset and coupling intervals of premature ventricular contractions (PVCs) initiating VF episodes are slightly different [45]. In patients with ERS, most (42/58, 72.4%) VF episodes were precipitated by PVCs with a short–long–short sequence of activation, while this cycle length alternans was less frequently (13/86, 15.1%) observed in patients with BS (Fig. 5). Coupling intervals were significantly shorter in patients with ERS than in those with BS (Fig. 6). The reason for this distinction in the mode of onset of VF between BS and ERS is not clear. A plausible explanation is that, in BS, the electrophysiologic milieu for arrhythmogenesis is mature enough for a single VPC to initiate VF, whereas in ERS, only a critically timed PVC in the presence of maximum dispersion of refractoriness provided by long preceding coupling interval can precipitate VF [45]. This distinction does not negate the close association between ERS and BS. Rather, it supports the idea that ERS is a "forme fruste" or a clinical variant of BS, with both being part of the same broader category of "J wave syndrome".

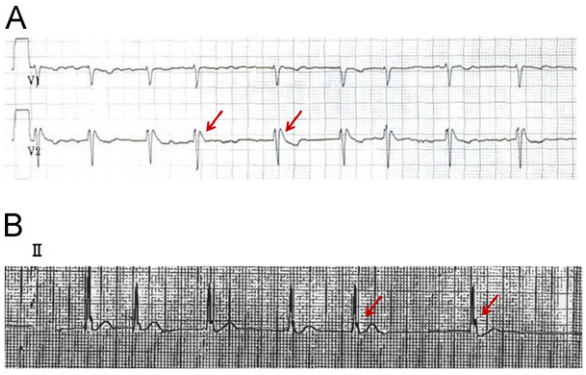

Fig. 4. Dynamic behaviors of J waves in patients with BS and ERS. (A) A 49-year-old male patient presented with aborted sudden cardiac death. ECG (V1 and V2) recorded 7 h after resuscitation revealed AF with variable R–R intervals. The J wave following the longer R–R interval (second arrow) is slightly augmented compared with that after the shorter interval (first arrow). A full-blown type I BS ECG pattern was induced by the intravenous administration of flecainide. (B) A 12-lead ECG from a 39-year-old male patient with ERS and atrial fibrillation. A dynamic change in the amplitudes of the J waves is noted. The J waves are augmented after a long R–R interval of a slow ventricular response.

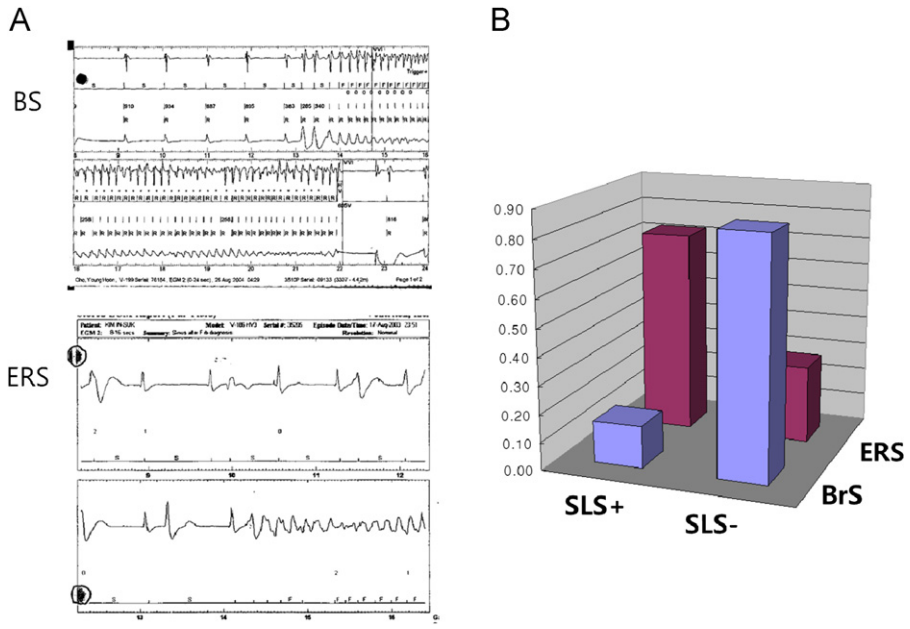

Fig. 5. Mode of onset of ventricular fibrillation (VF) in patients with BS and ERS. (A) Upper panel shows an intracardiac electrogram at the onset of VF in a patient with BS. VF was initiated by a single premature ventricular contraction without a short–long–short sequence. Lower panel shows an intracardiac electrogram at the onset of VF in a patient with ERS. VF was initiated after post-ectopic pause following bigemini ventricular premature beats with a short–long–short sequence of activation. (B) The number of VF episodes initiated by PVCs with (SLS+) and without (SLS−) a short–long–short (SLS) sequence of activation in patients with BS (lilac) and ERS (magenda). VF episodes in ERS patients were commonly initiated by PVCs with a SLS sequence of activation. A SLS sequence was observed in 42/58 (72.4%) VF episodes in the ERS patients, but in only 13/86 (15.1%) of VF episodes in patients with BS (modified from reference [45] with permission).

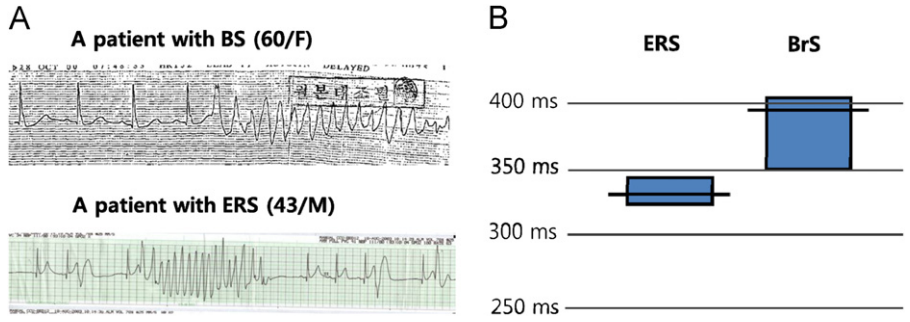

Fig. 6. Coupling intervals of premature beats at the onset of ventricular fibrillation (VF) in patients with BS and ERS. (A) Upper panel shows an electrocardiogram at the initiation of VF in a 60-year-old female patient with BS. VF was initiated by a single premature ventricular contraction with a coupling interval of 420 ms. Lower panel shows an ECG recorded at the onset of VF in a 43-year-old male patient with ERS. VF was initiated by a bigemini premature ventricular contraction (PVC) with a short–long–short sequence and a coupling interval of 320 ms. (B) The PVCs preceding the VF episodes in patients with ERS exhibited significantly shorter coupling intervals than the PVCs preceding the VF episodes in patients with BS (328 [320,340] ms vs. 395 [350,404] ms, $p < 0.01$) (modified from reference [45] with permission).

In contrast to the above similarities, the prevalence of positive late potentials [12,45–47] and the response to sodium channel blockade [48,49] differ between patients with BS and those with ERS. Roten et al. observed that the ER pattern in patients with ERS was attenuated by the administration of intravenous ajmaline. This novel finding, together with the low prevalence of late potentials, was proposed as evidence supporting the repolarization hypothesis of ERS. This is in contrast with the electrophysiologic findings (accentuation of J/ST wave changes, prevalent late potentials, and the presence of delayed potentials in the epicardium) in patients with BS, which supports the depolarization hypothesis. However, the pathogenetic mechanism in BS and ERS is not a simple dichotomy of depolarization and repolarization abnormalities. The early phase of ventricular repolarization is an overlap of late depolarization and early repolarization processes. In addition, these two processes affect each other. A change in the depolarization process causes a change in the repolarization process. This explains why a mutation or pharmacologic suppression of the sodium channel (and decrease in inward sodium current) is linked to an increased or accentuated phase 1 notch of repolarization process. Therefore, the response of BS patients to sodium channel antagonists may also be viewed as evidence supporting the repolarization hypothesis. Likewise, the response to ajmaline or attenuation of inferolateral ER pattern in patients with ERS may have been due to the conduction delay (and increased S wave amplitude) that masked or attenuated the J waves of ER pattern. The results and interpretation of the effects of sodium channel blocker in patients with BS or ERS need to be redefined.

5. Phenotype overlap in patients with BS and ERS

The typical type I BS ECG pattern shows spontaneous fluctuation and often manifests remote from VF events or in the absence of class IC antiarrhythmic drugs. By contrast, J waves and ER pattern in patients with ERS are stable over a long term and

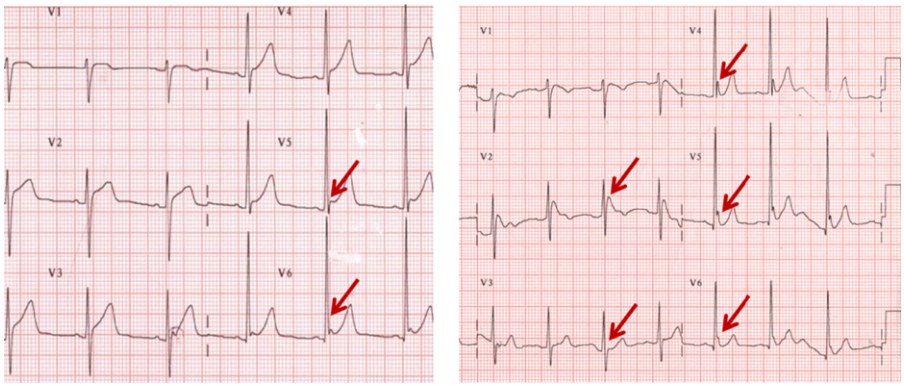

Fig. 7. Augmentation of J wave and ST segment elevation and phenotype transition in ERS. A 50-year-old male patient presented with recurrent seizure-like episodes and aborted sudden cardiac arrest. The initial ECG revealed small J waves present in the lateral precordial leads. The follow-up ECG taken 30 min before the onset of ventricular fibrillation (VF) revealed greatly augmented J waves (red arrows) in both the lateral precordial and right precordial leads. Change in the right precordial lead (V2) mimics ECG changes of BS.

transiently manifest only during the peri-event period. Except for minor changes in amplitudes, the distribution of J wave or ST segment elevation in each ERS patient seldom changes significantly during follow-up. Although uncommon, a considerable overlap or shift in shape or distribution of the J waves (phenotype transition) may occur in patients with BS and ERS. For example, some patients with BS have been reported to demonstrate a background ER pattern [14]. In contrast, some patients with inferolateral ERS showed prominent J wave augmentation in the right precordial leads during peri-event periods (Fig. 7). This is an important clue that suggests ERS shares a key electrophysiologic mechanism with BS, providing further evidence to support the concept of "J wave syndrome".

6. Risk stratification

The risk stratification of subjects who display a BS-type ECG pattern remains controversial. A history of syncope is the most important prognostic marker, but the predictive value of electrophysiologic study remains controversial. The prognostic importance of electrophysiologic study proposed in the early reports by Brugada et al. [50,51] has been challenged by subsequent investigations that failed to prove the efficacy of electrophysiology studies [52–55]. The annual cardiac event rate was reported as 7.7% in patients with aborted SCD, 1.9% in patients with syncope, and 0.5% in asymptomatic patients [54]. Because of this low risk and the uncertain predictive role of electrophysiologic study, a simpler approach is used, wherein the decision regarding ICD implantation is based largely on fatal ventricular arrhythmia or symptoms (syncope) [56]. An electrophysiologic study in asymptomatic subjects was designated a Class IIb indication. Other factors such as family history and SCN5A mutations were concluded to have little prognostic importance [54].

The risk stratification of patients with ERS is even more confusing and further studies are required. As mentioned in the demographics, the traditional definition of ER emphasizes the presence of ST segment elevation, and the subjects with ER with this traditional concept do not have adverse outcomes [17,18]. In contrast, patients with ER according to the new definition (the presence of the terminal QRS notch or slur, irrespective of the ST segment changes) [19–22], have prognostic implications. More specifically, individuals with J waves that were followed by ascending ST segment changes do not show an increased risk of arrhythmic death; however, those with J waves that were accompanied by horizontal/descending ST segment changes had an increased risk of arrhythmic death compared with those without the ER pattern [22]. Nevertheless, the hazard ratio of the arrhythmic death risk in the latter subgroup rises only slightly (hazard ratio, 1.43). Considering the low risk of arrhythmic death observed in the population study, even the high-risk marker of ER pattern (J wave and horizontal/descending ST) seems to reflect a modifying factor for specific arrhythmic risk in patients with acquired structural heart diseases, rather than an indicator of a primary arrhythmic syndrome, as discussed by the authors [22].

Although other risk markers such as high amplitude J waves in the inferior leads have been suggested, a better scheme for risk stratification is necessary. The presence of a type I BS ECG pattern indicates the necessity for ICD implantation in patients with syncope of unknown causes. Currently, electrocardiographic ER parameters are hardly useful for risk stratification in primary prevention purposes, and none of these parameters are used as indicators of ICD implantation [57]. Global appearance of J waves and ST segment elevation has been known to indicate a highly arrhythmogenic substrate [13]. However, patients with electrical storm manifest this phenotype only during a short time window of peri-event periods that last several minutes or hours. The "ambulatory" phase ECG in these patients with electrical storms shows an ER pattern that is practically indistinguishable from that of a benign ER pattern [58].

7. Treatment and prevention of VF in patients with BS or ERS

Pharmacologic management of BS and ERS is identical owing to the shared pathophysiologic mechanism. The suppression of electrical storm in patients with BS or ERS can be achieved by administering intravenous isoproterenol [45,59,60]. In patients with ERS, the occurrence of VF episodes is always accompanied by a prominent accentuation of the J wave and commonly preceded by bigeminy PVC in a short–long–short sequence [45]. These electrocardiographic indicators are extremely useful for guiding therapy and estimating the response to treatment in patients admitted for the management of the electrical storm. In patients with a pacemaker or ICD, atrial pacing at >90 beats/min abolished the ECG changes and prevented the recurrence of VF [45].

For long-term management, quinidine and cilostazol have been shown to be effective in both BS and ERS [45,59–62]. Catheter ablation of trigger PVCs targeting the earliest ventricular endocardial activation or targeting the Purkinje potential may be successfully performed in patients with BS and ERS [12,63]. In selected patients with BS, substrate ablation in the epicardial region of delayed potentials has also been proposed [64].

8. Conclusions

Patients with BS and ERS share common electrocardiographic and clinical features. The J waves observed in patients with both these syndromes are believed to play a key role in VF pathogenesis. Similarities in the clinical manifestations, ECG features (particularly J wave dynamics), and responses to autonomic or pharmacologic interventions suggest that BS and ERS are different variants of a common broader syndrome or "J wave syndrome". Identifying subjects with a high risk of SCD remains a matter of debate.

Conflict of interest

There are no conflicts of interest to disclose.

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