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Brugada Syndrome: A Review

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Abstract

The Brugada syndrome is a form of cardiac arrhythmia, characterized by electrocardiographic ST-Segment elevation in right precordial leads that affect young male patient, predisposing to malignant ventricular arrhythmia and sudden cardiac deaths. The majority of the patients with Brugada syndrome remain asymptomatic, however, patient can present with symptom like syncope, palpitation and aborted sudden cardiac death. Several pathogenic genes have been identified as associated with the disease but SCN5A is most prevalent one. The Brugada syndrome is diagnosed by typically cove shaped ST-segment elevation of >2 mm in greater than one precordial lead V1 and V2, occurring spontaneously or after provocative drugs test with IV administration of class 1 antiarrhythmic drug such flecainide or Ajmaline. Risk stratification and the need for treatment depend on the patient symptom, electrocardiography, family history and electrophysiological study. The treatment by implantable cardioverter defibrillators, the only effective treatment to date is appropriate. Other treatment options included pharmacological therapy (Quinidine) and Radiofrequency ablation of ventricular ectopies. This brief review focuses on epidemiology of Brugada syndrome, Genetic basis, mechanism, clinical presentation, ECG changes, risk stratification, Diagnostic criteria and management.

Keywords

Sudden Cardiac Death, Cardiac Arrhythmia, Ventricular Fibrillation, Risk Stratification, Implantable Cardioverter Defibrillator

1. Introduction

Brugada syndrome was initially described by Pedro and Joseph Brugada in 1992 [1]. Brugada syndrome is a rare cardiac arrhythmia characterized by electrocar-

diographic right bundle branch block and persistent ST-Segment elevation in right precordial lead. Brugada syndrome is defined electrocardiographically by a characteristic patter including J-Point and ST-segment elevation of 2 mm or greater, followed by a negative T wave in the right precordial leads [1]. It is closely linked to SCN5A gene mutation affecting the sodium channel function [1]. The typical arrhythmia of Brugada syndrome is polymorphic ventricular tachycardia which can potentially degenerate to ventricular fibrillation and high risk of sudden cardiac death, predominantly in younger male patient with structural normal heart [1]. Repetitive monomorphic ventricular tachycardia including ventricular flutter occurring in Brugada syndrome is potentially lethal events. Most patients with Brugada syndrome are diagnosed only after cardiac arrest [2]. The symptom usually appears around 40 years of age and males are more often symptomatic than females probably from the influence of hormones and gender distribution of ion channels across the heart. Currently, the only proven effective strategy for preventing sudden cardiac death (SCD) in Brugada syndrome patient is the use of implantable cardioverter defibrillators.

2. Epidemiology

Brugada syndrome has been estimated to account for 20% of sudden cardiac death in the absence of structural heart disease and may be responsible for between 4% and 12% of all patients with sudden cardiac death [3]. The prevalence of Brugada syndrome also varies greatly according to location, being higher in east and south-east Asian population (in Thailand, Japan and Philippines) than of European descent [4] [5] [6]. Current prevalence rates estimates of 5/10,000. In North America and Western Europe the prevalence of the syndrome is relatively lower [7]. A Japanese study reported the prevalence of a type-1 ECG pattern to be 12/10,000 [4]. In the endemic areas the Brugada syndrome may represent, after excluding accidents, the leading cause of death in individual younger than 40 years [8].

3. Genetics

Brugada syndrome is hereditary disease with an autosomal dominant patter of transmission and variable penetrance [9]. However, up to 60% may be sporadic that is absent in other relatives [10]. In 1998, the first pathogenic mutation in the SCN5A gene was identified, which encodes for the alpha-subunit of the cardiac sodium channel [11]. Since them, more than 350 pathogenic mutations in several genes have been published (SCN5A, GPD1L, SCN1B, SCN2B, SCN3B, RANGRF, SLMAP, KCNE3, KCNJ8, HCN4, KCNE5, KCND3, CACNA1C, CACNB2B, CACNA2D1 and TRPM4) [12]. These genes encode subunit of cardiac sodium, potassium, and calcium channel as well as genes involved in regulation of channels. Besides SCN5A genes, many BS related genes play role in regulating sodium channel function. It has been suggested that the gain of function caused by a mutation in the genes encoding channels that conduct outward

potassium currents (KCND3, KCNE3, KCNE5, and KCNJ8) predispose affected individuals to develop Brugada syndrome phenotype [13]. Brugada syndrome susceptibility genes were also found among calcium channels (CACNA1C, CACNB2b and CACNA2D1). The loss of function mutations involving the L-type calcium channel subunits, encoded by the CACNA1C, CACNB2B and CACNA2D1 genes respectively, in probands with Brugada syndromes. These genes only account for small percentage of Brugada syndrome [14]. Despite the high number of gene mutation, only about 35% of Brugada syndrome patient have been determined to have a genetic causes. Of them, nearly 30% carry pathogenic mutation in the SCN5A gene [15]. All other genes together are responsible for about 5% of all Brugada syndrome cases. Therefore 65% of cases do not have genetic origin. Several factors could explain the high number of Brugada syndrome patient without genetic alteration after genetic screening. The pathogenic mutation associated with Brugada syndrome could be localized in unknown genes or disease could be related to epigenetic factors, mainly DNA methylation, post translational modification and RNA Mechanism [16] [17].

4. Mechanism

Brugada syndrome was initially thought of as a channelopathy, an exclusively electrophysiological disorder produced by dysfunction of a cardiac ion channel involved in generation of the action potential in structural normal heart [1] [18] [19] [20]. More study reported patient with the Brugada ECG patterns showing structural abnormalities of right ventricle [21] [22]. This supports the theory that the pathophysiological mechanism of Brugada syndrome may be due to slowing of conduction in the right ventricle, accompanied by mild structural abnormalities [23]. Currently no single causal factor link all patient and thus the pathophysiological mechanism remain elusive [23]. Two hypotheses have been proposed-depolarisation theory and repolarisation theory, to explain the pathophysiology of type-1 ECG pattern and susceptibility to ventricular arrhythmia [20] [23] [24].

4.1. Repolarisation Hypothesis

According to this hypothesis, rebalancing of current at the end of phase 1 of the action potential (AP) leads to accentuation of the AP notch in the epicardium of the right ventricle. Such accentuation was believed responsible for the characteristic ST-Segment elevation [1] [18] [19] which is shown in **Figure 1**.

In the presence of pathophysiological condition such as a SCN5A mutation (leading to loss of function of sodium channel), outward current overwhelm inward current and the epicardium may then exhibit all-or-none repolarisation at the point where the phase-1 action potential reaches -30mv. The resulting loss of action potential dome at some but not all, epicardial sites could create marked epicardial dispersion of repolarisation. This gives rise to a transmural voltage gradient leading to transmural dispersion of repolarisation between the

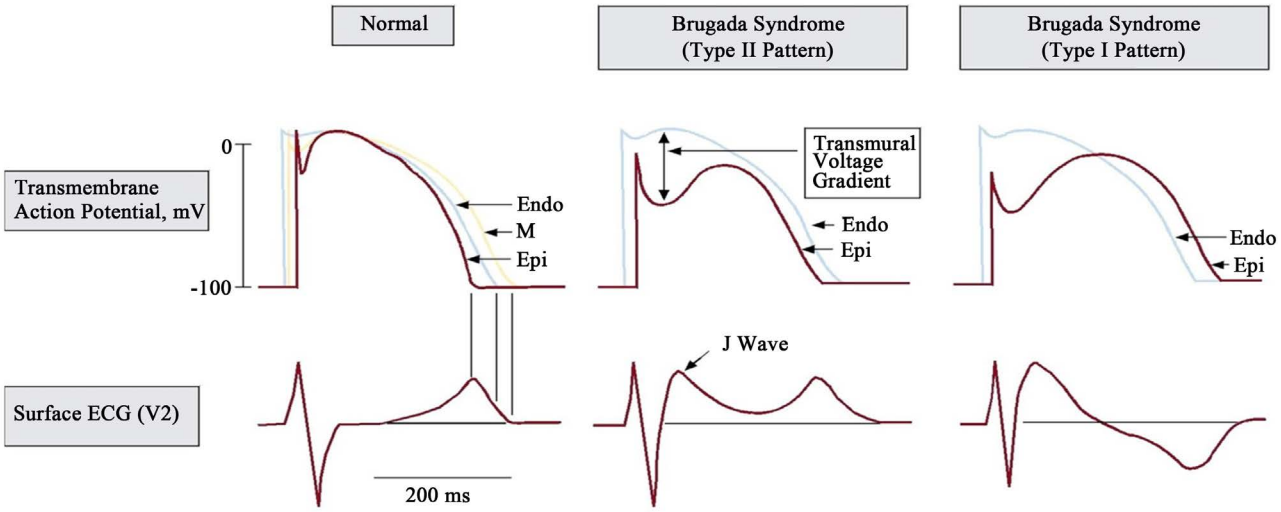

Figure 1. Schematic representation of the repolarisation disorder hypothesis [25]. (Reproduced with permission). Endo-Endocardium, M-Myocardium, EPI-Epicardium.

epicardium and endocardium which manifests as the characteristic ST-Segment elevation of the ECG [20] [21]. The T-wave remains positive when epicardial repolarisation precedes that of myocardial and endocardial regions resulting in characteristic type-2 ECG [25]. When sites in the epicardial region exhibit prolongation of action potential, reversed direction of repolarisation across the right ventricle wall may ensue, producing the inverted T-wave and resulting in the type-3 coved type ECG [25]. The repolarisation hypothesis could also explain the mechanism of ventricular arrhythmia initiation. When epicardial dispersion of repolarisation and transmural dispersion of repolarisation occur via-or-none repolarisation at some epicardial site, an arrhythmogenic substrate is formed. This creates a vulnerable window when an action potential can propagate from sites with normal repolarisation to sites with early repolarisation. The conduction of an action potential dome lead to local re-excitation via a phase-2 re-entry mechanism at the sites of early repolarisation and facilitates the development of extrasystoles beats from these sites [20] [25] [26]. This extrasystoles beats have been shown to initiates circus movement re-entry [26] and thus give rise to malignant ventricular arrhythmia [20].

4.2. Depolarisation Hypothesis

The depolarisation hypothesis is for the Brugada ECG and susceptibility to ventricular arrhythmia propose a conduction delay in the right ventricular outflow tract [23] [27]. The action potential is not fundamentally altered; rather conduction delay in the right ventricular outflow tract slows action potential development in right ventricle. This pathophysiological mechanism was believed to result in Brugada ECG pattern and provide an arrhythmogenic substrate via a re-entry circuit.

A third hypothesis involves a combination of both depolarization and repolarization abnormalities, as our groups has found using Frank vectorcardiograms

to compare patient with Brugada syndrome vs. patient with complete and incomplete right bundle branch block [28].

The Brugada syndrome is recognized as disorders with no structural defects [9], there is some evidence for involvement of mild structural abnormalities [29], which were not previously detectable by conventional cardiac imaging [1] [30]. Structural abnormalities found in the Brugada syndrome patient include focal fibrosis, myocarditis, apoptosis and fibrofatty replacement of the right ventricle free wall with right ventricle enlargement, dilation and right ventricle outflow tract enlargement [29] [30] [31]. It is suggested that such structural abnormalities play role in Brugada syndrome [29] [31] by contributing to slower conduction [32] [33].

5. Clinical Presentation of Brugada Syndrome

The clinical presentation can range from no symptom that is asymptomatic to sudden cardiac death. Initial presenting symptoms include palpitation, syncope, seizure and nocturnal agonal respiration [34]. About 25% of patients suffering from sudden cardiac death had already experienced a syncope episode due to arrhythmic complications such as polymorphic ventricular tachycardia or ventricular fibrillation [35]. In up to 20% of cases Supraventricular arrhythmia may exist, mainly atrial fibrillation [36]. Although Atrioventricular nodal reentry tachycardia and Wolff-Parkinson white syndrome has also been reported [37] [38]. Additionally an association with sinus dysfunction has been described [39]. Symptom occur more frequently during rest or during sleep (especially between 12 am and 6 am and rarely occurs during day time), febrile episodes or under predominance of vagal activity [40] [41] [42]. It is rare that they occur during exercise. The variation of the sympathetic-parasympathetic balance, hormonal and other metabolic factors are likely to contribute to this pattern. Increased vagal tone decrease acetylcholine mediated calcium current, which could lead to arrhythmogenesis by phase-2 reentry [43]. The causes of death in Brugada syndrome is ventricular fibrillation.

6. Electrocardiogram (ECG) Changes in Brugada Syndrome

The diagnosis of Brugada syndrome is based on both clinical finding and characteristic ECG pattern that occurs spontaneously or are induced by the use of sodium channel blocking agents. There are three known ECG subtype that can be detected in more than one of the right precordial leads (V1-V3) and have a diagnostic values [44].

6.1. Type-1 ECG Pattern

The type-1 ECG pattern is characterized by a Coved shape ST-Segment elevation greater than 2 mm (0.2 mv) followed by an inverted T-Wave in one or more of the right precordial lead, which occurs with or without provocation by sodium channel blocking agent [9] as shown in **Figure 2**.

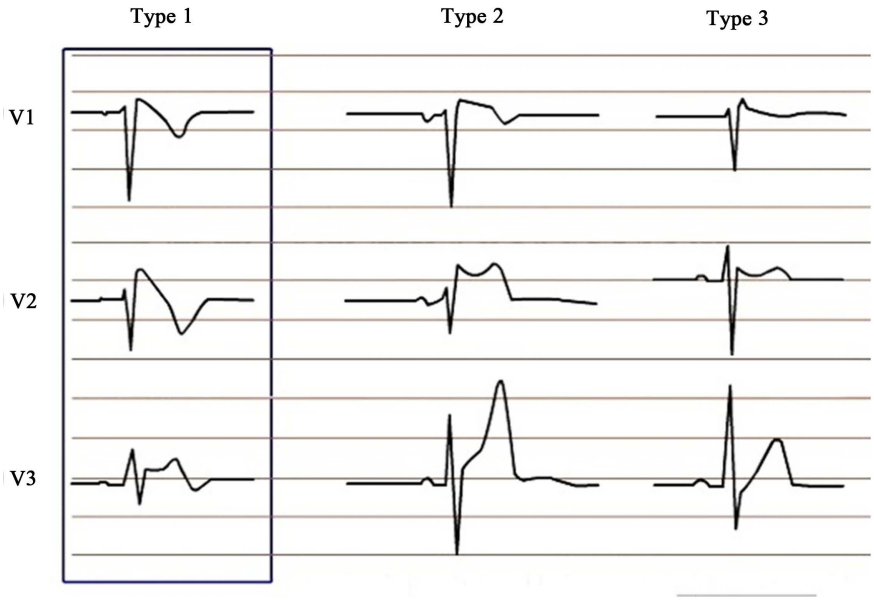

Figure 2. Figure showing pattern of ECG in Brugada Syndrome. Type-1 ECG pattern shows Coved ST-Segment elevation > 2 mm is followed by a negative T-Wave, with little or no isoelectric line separation that feature is present in from V1 to V2 in right precordial leads. Type-2 ECG patterns also characterized by ST-Segment Elevation followed by positive or biphasic T-wave that result in saddle back configuration. Type-3 ECG patterns show right precordial ST-Segment elevation< 1mm with saddle morphology [9].

This pattern must ensue alongside one of the following history of ventricular fibrillation, polymorphic ventricular tachycardia, and family history of unexplained sudden cardiac death in person older than 45 years, family history of coved-type ECG, inducibility of ventricular tachycardia with programmed electrical stimulation, syncope episodes or nocturnal agonal Respiration [9].

6.2. Type-2 ECG Pattern

In the type-2 ECG pattern, the ST-Segment resembles a saddleback, with an ST-Segment elevation at least 2 mm (0.2 mv), a trough of the ST-Segment elevation of at least 1 mm and then either a positive or biphasic T-Wave [9], shown in **Figure 2**.

6.3. Type-3 ECG Pattern

In the type-3 ECG pattern consists of either a Coved (type-1 like) or saddleback (type-2 like) ST-Segment elevation between 1 and 2 mm. Both type-2 and type-3 ECG finding occurs spontaneously without use of sodium channel blocking agent but they themselves they are not considered diagnostic, as shown in **Figure 2**.

If the type-2 or type-3 ECG pattern converted to type-1 ECG pattern after provocation by sodium channel blocking agents and at least one of the above mentioned characteristic finding is present, a diagnosis of Brugada syndrome is considered.

6.4. Other ECG Finding in Brugada Syndromes

The PR interval is often increased > 200 ms. There is a P-wave abnormality that is biphasic P wave and QRS complex is widening and fragmented QRS [45]. The prolongation of QT intervals in right precordial leads is also seen in Brugada syndrome [46].

7. Risk Stratification

Risk stratification of Brugada syndrome is aimed to identifying individuals most liable to sudden cardiac death, so that they can receive appropriate management. It is well accepted that etiology of Brugada syndrome is multifactorial, involving genetic, environmental and hormonal components that contribute to phenotype manifestation. Symptomatic presentations included aborted sudden cardiac death, syncope, seizure and nocturnal agonal respiration. Asymptomatic individuals should be assessed for relevant family history of sudden cardiac death. Individual with diagnosis of Brugada syndrome based on spontaneous or induced type-1 ECG pattern may present with or without symptom.

The Brugada syndrome typically manifests in adulthood, with mean age of 41 ± 15 years [9]. However the Brugada syndrome may manifest in children and the elderly, patients have been diagnosed at 2 days of life to 80 years [9]. It is 8 - 10 times more prevalent in men than in women [9] [35] [47] [48] [49]. This could be due to constitutional differences in transmembrane ionic current between two sexes [50]. The evidences suggests hormonal influence on the phenotypic gender differences, such as type-1 ECG regression after castration in men with prostate neoplasia [51] and presence of high concentration of testosterone in men with Brugada syndrome than control [52]. The family history is present in about 20% - 30% of the patients [53]. The prognosis also differ with gender, with a 4.5 - 5.5 times higher risk of SCD in men than women [48] [54].

The international Registry of Brugada syndrome reported that 25% of this population experienced sudden cardiac death or ventricular fibrillation during life time at mean age of 42 years [54]. Recently, in a large series of patients, aborted sudden cardiac death frequency was estimated to be 7.7%, 1.9% in patient with syncope only and 0.5% in entirely asymptomatic [55]. Other factors denoting increased risk of an adverse cardiac event included aborted sudden cardiac death, syncope spontaneous or unmask type-1 ECG pattern, family history of sudden cardiac death and inducibility of ventricular tachycardia or ventricular fibrillation during an electrophysiological study. Among patients presenting with aborted sudden cardiac death, the risk of its recurrence or ventricular fibrillation was 62% with a mean follow up time of 54 month. These patients have highest risk of future cardiac event so these patients have the most compelling indication for treatment with an implantable cardioverter defibrillator (ICD), the only treatment option demonstrated to be effective to data. Even if there is no history of cardiac arrest, Brugada syndrome is reported to carry an 8.2% risk of sudden cardiac death or ventricular fibrillation over 25 month [48]. In patient

with Brugada syndrome, inducibility of ventricular arrhythmia by electrophysiological means is predictors of poorer prognostic outcome. Inducible ventricular tachycardia or ventricular fibrillation by electrophysiological study warrants ICD treatment even for asymptomatic patient if they show a spontaneous type-1 ECG pattern or family history of sudden cardiac death [54]. All other patient warrant close follows up.

8. Diagnostic Criteria of Brugada Syndrome

Consensus statement regarding making diagnosis of Brugada syndrome:

The first consensus report of 2002 Proposed using ECG criteria alone and three Subtypes (type-1 pattern, type-2 pattern and type-3) of ECG feature have been recognized [56].

The second consensus published in 2005 for the diagnosis of Brugada syndrome the following are the necessary [9].

1) Presence of type-1 ECG pattern-descends ST-Segment elevation ≥ 2 mm in more than one right precordial lead, spontaneously or after exposure to sodium channel blocking drugs.

2) The presence of one of the following clinical manifestation:

- Documented ventricular fibrillation, polymorphic ventricular tachycardia.
- Family history of sudden cardiac death at <45 years of age without acute coronary syndrome.
- Coved shaped ECG in family members.
- Inducibility of ventricular tachycardia with programmed stimulation.
- Clinical history of non-vasovagal syncope or nocturnal agonal respiration.

In 2005, there have several clinical studies on sensitivity and specificity of ECG diagnosis of Brugada syndrome. Therefore proposed amendments to the diagnostic criteria [57], the Brugada syndrome is diagnosed when type-1 ECG pattern ST-Segment elevation is observed either spontaneously or after intravenous administration of sodium channel blockers in at least one right precordial lead (V1 and V2), placed in a standard or superior position.

The latest consensus statement of 2013 does not mentioned these additional clinical feature and only mentions the ECG features [50].

The Expert consensus statement, diagnosis and management of patients with inherited primary arrhythmic syndrome 2013 [58]:

1) Brugada syndrome is diagnosed in patient with ST-Segment elevation with type-1 morphology ≥ 2 mm in more than more lead among the right precordial lead V1, V2 positioned in second, third or fourth intercostals space occurring spontaneously or after provocative drugs test with intravenous administration of class 1 antiarrhythmic drugs.

2) Brugada syndrome is diagnosed in patients with type-2 or type-3 ST-Segment elevation in more than one lead among the right precordial lead V1, V2 positioned in the second, third or fourth intercostals space when provocation drug test with intravenous administration of class 1 antiarrhythmic drugs in-

duces type-1 ECG morphology.

Pharmacological test: Electrocardiogram unmasking.

When there is a clinical suspicion of Brugada syndrome without presenting an ECG with spontaneous type-1 ECG pattern, patient should undergo a pharmacological challenges test with sodium channel blocking drugs (Ajmaline, Flecainide, Procainamide, or Pilsicainide) [59], **Table 1** shows the drug used, dose and routes of administration. Other pharmacological agent also induce Brugada like ECG pattern include calcium channel blockers, beta blockers, antianginal drugs, psychotic drugs, alcohol, cocaine and bupivacaine [59].

The test is performed under continuous Electrocardiographic monitoring. At the beginning and end of the drugs test leads V1 and V2 should placed in the 2nd and 3rd intercostals space , as it increase the sensitivity of the ECG for detecting the diagnostic patterns [60] [61]. The test is considered positive only if a type-1 ECG pattern is obtained, shown in **Figure 3** and should be discontinued in the early onset of frequent ventricular premature beat or others ventricular arrhythmia [9]. Data available to date suggest that Ajmaline is the most effective in the diagnosis of Brugada syndromes [62].

9. Modulating Factors and Differential Diagnosis

Exposure to certain drugs or ionic change can produce ST-Segment elevation suggestive of Brugada syndrome, which may represent a certain genetic predisposition. Fever also modulates the phenotype and the risk of arrhythmias by

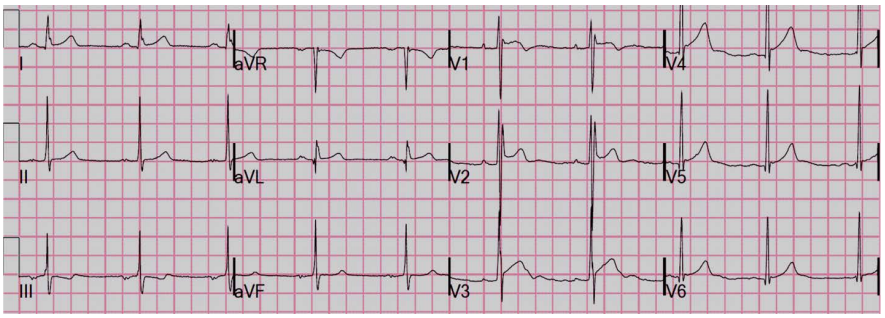

Figure 3. 12 leads Electrocardiogram (ECG) showing Brugada syndrome type-1 ECG pattern showed coved ST-Segment elevation > 2 mm is followed by negative T-Wave with little or no isoelectric separation in right precordial leads from V1 to V3 [9].

Table 1. Sodium channel blocking agents that can be used in provocation test to unmask the ECG in Brugada Syndrome [59].

	Drugs	Doses	Routes of Drugs Administration
•	Ajmaline	1 mg/kg over 5 minute	Intravenous
•	Flecainide	2 mg/kg over 10 minute	Intravenous
•	Procainamide	10 mg/kg over 10 minute	Intravenous
•	Pilsicainide	1 mg/kg over 10 minute	Intravenous
•	Flecainide	400 mg	Oral

accentuating the sodium channel inactivating, unmasking the type 1 pattern and triggering ventricular arrhythmias [63] [64] [65]. If any of these factors is present, it must be corrected. It is also important to exclude other causes of ST-Segment elevation before making the diagnosis. Some other causes of ST-Segment elevation are shown in Table 2.

10. Management of Brugada Syndrome

The treatment options for Brugada syndrome have been related to device related and. Pharmacological therapies. However education and prevention of arrhythmias via lifestyle awareness should also be considered.

10.1. Lifestyle Measures

The following life style measures are recommended in patients with diagnosis of Brugada syndrome:

1) Avoidance of drugs that aggravates or induces ST-Segment elevation in right precordial leads [68].

2) Avoidance of excessive alcohol intake.

3) Immediate treatment of fevers with antipyretic drugs.

Management of acute malignant arrhythmias or electrical storms included early defibrillators and resuscitation of patient followed by admission to specialized cardiac care unit. Any provocative factors such as fever should be treated with antipyretics and cold sponging. Any intake of arrhythmogenic drugs should be discontinued. Pharmacological treatment with isoprenaline 1 - 2 μg bolus intravenously followed by continuous infusion of 0.15 - 0.2 μg/minutes or Quinidine 300 - 1500 mg/day has been used for electrical stroma.

10.2. Device Management

The currently, the only proven effective strategy for preventing sudden cardiac death in Brugada syndrome patients is the use of an implantable cardioverter defibrillators (ICD) [54]. The most recently consensus published in 2013, report that implantable cardioverter defibrillators is the only established form of effective treatment to all symptomatic patients presenting with Brugada syndrome [57]. All asymptomatic patients should undergo further risk stratification and

Table 2. Differential diagnosis of Brugada syndrome [66] [67].

Following are the differential diagnosis of Brugada syndrome:
• Atypical right bundle branch block
• Left ventricular hypertrophy
• Acute pericarditis/myocarditis
• Acute myocardial ischemia or infarct (right Ventricle)
• Acute pulmonary thromboembolism
• Aortic dissecant aneurysm
• Arrhythmogenic right ventricular dysplasia

electrophysiological study to accesses their indication for an ICD [57]. ICD is indicated in patient with a spontaneous diagnostic type-1 ECG patter, who have a history of syncope juged to be likely caused by ventricular arrhythmias and also considered in patients with a diagnosis of Brugada syndrome who develop ventricular fibrillation during programmed electrical stimulation.

In asymptomatic patients whose type-1 ECG patterns is documented only after administration of sodium channel blockers, it is not recommended to performs regular monitoring without electrophysiological study for risk stratification nor ICD implantation [57]. Drugs that can causes Brugada like change in ECG are avoided and included: class 1 antiarrhythmic drug like flecainide, beta blockers, and Tricyclic antidepressant drugs, phenothiazines, Fluoxetine, anesthetics agent such as bupivacaine, procaine and alcohol [68] [69].

Complication of implantable Cardioverter defibrillator (ICD):

Although ICD are very effective in treating ventricular fibrillation and implantation procedure may lead to some surgical complication like bleeding, pneumothorax, perforation of vascular structures, cardiac tamponade and infection. Post implantation issues included displacement or fracture of leads and need to replace the device because of battery depletion.

10.3. Pharmacological Therapy

It has been shown that Quinidine, antiarrhythmic with blocking activity in the Ito and Ikr currents, reduces the incidence of arrhythmias induced in patient with Brugada syndrome [70] and has been used successfully in certain clinical conditions, such as the treatment of arrhythmia storm [71], multiple shock [72] [73] or alternative to ICD in children at risk of arrhythmia [74]. However Quinidine often causes side effect like diarrhoea, thrombocytopenia and hepatitis that resolve after drug discontinuation. The main concern relates to the potential pro-arrhythmic activity of Quinidine, there is risk of torsades de point, so there is a close monitoring is required during the first few days of therapy.

Quinidine therapy may be alternative to ICD, who are ineligible or person who refused such an intervention.

10.4. Catheter Ablation

After finding that ventricular fibrillation events in Brugada syndrome patient is caused by ventricular premature beats, catheter ablation of ventricular ectopies, was proposed as a therapeutic measure [75]. Thus, in 2011, Nademanee *et al.* published the first study showing preventions of ventricular fibrillation in Brugada syndrome patients by catheter ablation over the anterior right ventricular outflow tract epicardium [76].

11. Conclusion

The Brugada syndrome is an inherited syndrome characterized by typically ST-segment elevation in right precordial lead that affects young individual,

mostly male, predisposing to ventricular arrhythmia and sudden cardiac death. It is diagnosed by typically cove shaped ST-Segment elevation of >2 mm and negative T-wave with little or no isoelectric separation in more than one in right precordial leads. Several genetic mutations of the sodium, calcium and potassium channel have been involved. The majority of the patients with BS remain asymptomatic, however, the most frequent symptom is syncope or SCD secondary to PVT or VF. Risk stratification is mainly based on symptom and surface electrocardiogram. Implantable cardioverter defibrillator is the only proven effective strategy for preventing SCD in BS patients. However, there are still dought and controversies regarding the underlying mechanism, the influences of different modulating factors and how to stratify the risk and treatment asymptomatic patients. The patient diagnosed with Brugada syndrome is counseled, such that they and their relatives are informed.

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Conflicts of Interest

There authors have no Conflicts of interest to declare.

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Abbreviations

ECG: Electrocardiogram.
SCD: Sudden Cardiac Death.
BS: Brugada Syndrome.
PVT: Polymorphic Ventricular Tachycardia.
VF: Ventricular Fibrillations.