Original Article

Usage of Shanghai Scoring System for Predicting Ventricular Arrhythmic Events in Brugada Syndrome (BrS) Patients in Thailand

Kumpol Chintanavilas[1*], Nilubon Methachittiphan[2], Sirin Apiyasawat[2]

Abstract

Background: Many risk factors are associated with ventricular arrhythmic events in Brugada syndrome (BrS) patients. The Shanghai scoring system for diagnosis of BrS was initially published in 2015.[1] A single study also validated using this scoring system for risk stratification of arrhythmic events in BrS patients.[2] There has been no study to demonstrate the role of this scoring system in the risk stratification of BrS patients in the Thai population. This study aimed to evaluate the role of the Shanghai scoring system in predicting ventricular arrhythmic events in Thai BrS patients.

Methods: We studied a retrospective cohort of BrS patients who were diagnosed from 1999 to 2019 at Ramathibodi Hospital. The patients were classified according to the Shanghai scoring system. All patients were followed for arrhythmic events and clinical outcomes.

Results: 54 eligible Patients were found with BrS (14 with cardiac arrest, 30 with syncope, 3 agonal respirations and 7 asymptomatic) and were classified by the Shanghai score into group A (very high risk); score ≥ 5.5 (n = 34), group B (high risk); score 4-5 (n = 14) and group C (non-high risk); score ≤ 3.5 (n = 6). During the mean follow-up period of 114 months, 11 arrhythmic events occurred (1 sudden cardiac arrest, 9 appropriate ICD therapy, 1 documented VT/VF from surface ECG). Incidence of ventricular arrhythmic events was highest in Group A (26.5%), followed by Group B (14.3%) and no event in Group C. Shanghai scores of more than 3.5 tend to be associated with increased ventricular arrhythmic events (HR 4.85, CI 0.037-630.2, $p = 0.525$), compared to the lower risk group (Shanghai score ≤ 3.5). Five inappropriate ICD shocks occurred. Device-related complications occurred in 8 patients, with lead fracture being the most frequent complication (9.3%).

Conclusions: Risk stratification by the Shanghai scoring system may be useful in predicting ventricular arrhythmic events in Thai BrS patients. However, a larger cohort is needed for statistically significant results.

Keywords: Brugada syndrome, Shanghai scoring system, Risk stratification, Arrhythmic events

[1] Chulabhorn International Collage of Medicine, Thammasat University, Cooperative learning center, Piyachart 2, 99 Moo 18, Klongluang, Rangsit, Pathum Thani 12120 Thailand
[2] Ramathibodhi Hospital, 270 Rama VI Road, Rajataewe, Bangkok 10400 Thailand
[*] **Corresponding author:** Kumpol Chintanavilas, M.D., Chulabhorn International Collage of Medicine, Thammasat University, Cooperative learning center, Piyachart 2, 99 Moo 18, Klongluang, Rangsit, Pathum Thani 12120 Thailand
Email: kumpol07@staff.tu.ac.th

Introduction

Since 1992, Brugada syndrome (BrS) has been described and defined as a genetically determined channelopathy leading to ventricular arrhythmia, syncope and sudden death in young males.[3] Incidence of this syndrome in adults is approximately 0.05-0.6% with an average age of diagnosis around 41 years old.[4] Many studies have shown that clinical presentation is the strongest predictor of recurrent major arrhythmic events while other predictors such as spontaneous type 1 ECG, and family history of sudden cardiac death at age 45 years, also show considerable risks.[4-9] In 2015, the Shanghai scoring system for the diagnosis of Brugada syndrome was published (Table 1).[1] This scoring system includes clinical presentation, electrocardiography, family history of BrS or sudden cardiac arrest and pathogenic mutations in BrS susceptibility genes. Only one study demonstrated the role of diagnosis and risk stratification in this scoring system.[2] At present, validation of this scoring system for risk stratification in Thailand has not been carried out. This study aimed to validate this score for risk stratification of arrhythmic events in Thai Brugada syndrome patients.

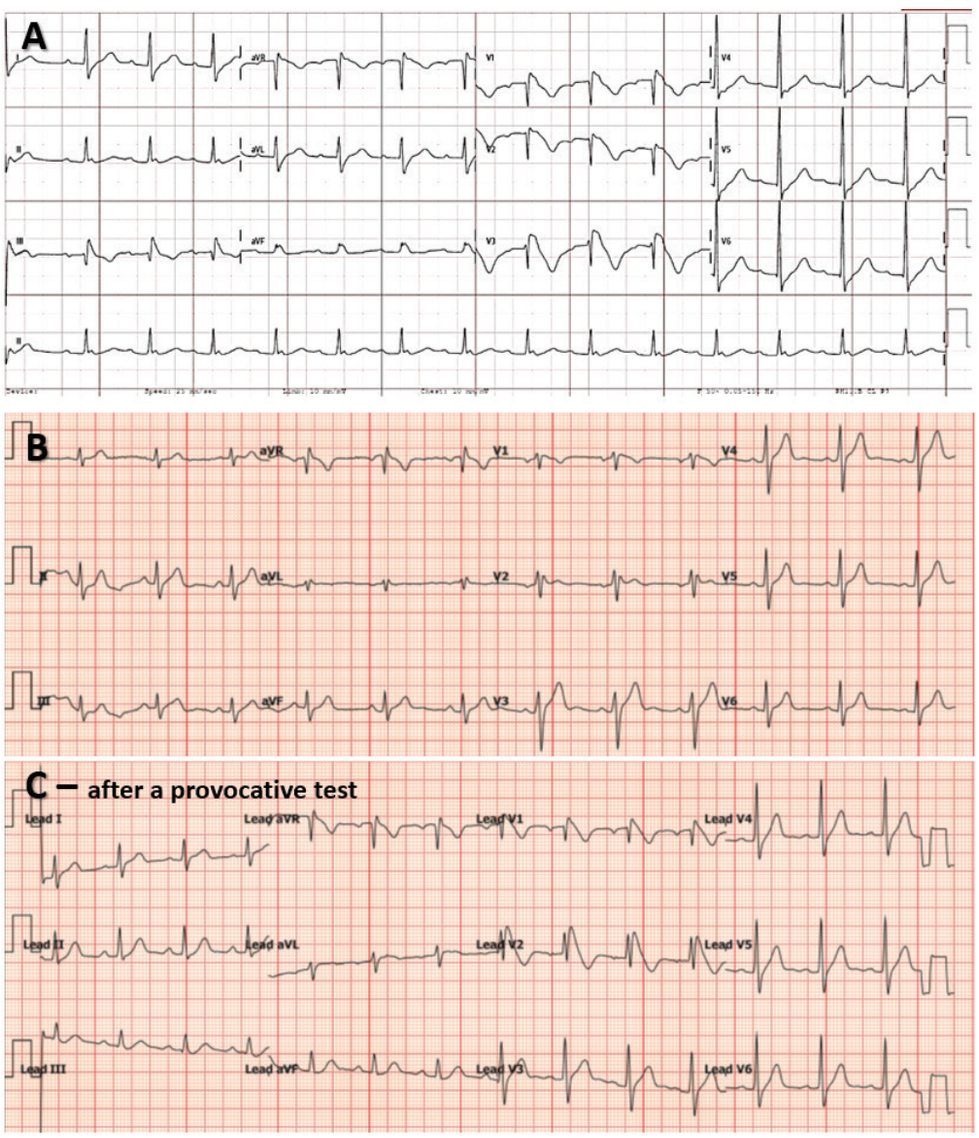

Figure 1 Type 1 Brugada pattern electrocardiogram, (A) Electrocardiogram of a 32-year-old man who survived ventricular fibrillation, (B) Baseline electrocardiogram of a 41-year-old man with a history of arrhythmic syncope and (C) electrocardiogram after provocative by flecainide and high intercostal lead

Table 1 Proposed Shanghai score system for diagnosis of Brugada syndrome[1*]

	Points
I. ECG (12-Lead/Ambulatory) *	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type1Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
**Only award points once for the highest score within this category. One item from this category must apply.*	
II. Clinical History*	
A. Unexplained cardiac arrest or documented VF/polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients ≤ 30 years without alternative etiology	0.5
**Only award points once for the highest score within this category*	
III. Family History	
A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD < 45years in first- or second-degree relatives with negative autopsy	0.5
**Only award points once for the highest score within this category.*	
IV. Genetic Test Result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5
Score (requires at least 1 ECG finding) ≥3.5 points: Probable/definite BrS 2-3 points: Possible BrS < 2 points: Nondiagnostic	

BrS = Brugada syndrome; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia

[*]C. Antzelevitch et al. / Journal of Arrhythmia 32 (2016) 315-339

Methodology

This is a retrospective cohort study of patients who were diagnosed with BrS between 1999 and 2019 at Ramathibodhi Hospital. After an electronic record review from 701 patients who were diagnosed with ICD10 code I49.0 (Ventricular fibrillation and flutter), I49.8 (Other specified cardiac arrhythmia e.g., Brugada syndrome, Long QT syndrome), and I49.9 (Cardiac arrhythmia, unspecified). Based on the presence of type 1 BrS pattern ECG with no other heart diseases, sixty-two BrS patients were identified 3 patients who had incomplete data for Shanghai score calculation at diagnosis and 5 patients who followed up less than 1 year were excluded. According to risk stratification from the study of Kawada (2018), 54 eligible patients (sudden cardiac arrest: n = 14, syncope: n = 30, nocturnal agonal respiration: n = 3, asymptomatic: n = 7) were classified into three groups based on their Shanghai score at diagnosis; Group A or very high risk (Score ≥5.5), Group B or high risk (Score 4-5) and group C or non-high-risk (Score ≤3.5). Arrhythmic events were defined as sudden cardiac death, appropriate shock or ATP delivery by an ICD, and/or documented VT/VF by conventional ECG. Device-related complications were defined as an inappropriate shock, device infection, leads and pocket-related complications. The study protocol was approved by the institutional Ethics committee of the Office of The Committee for Research Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

Continuous variables are expressed as mean ± SD. Categorical variables are expressed as numbers and percentages. An unpaired *t*-test was used to test for significant differences between continuous variables, while chi-square or Fisher's exact tests were used for categorical variables. Survival and cumulative hazards were calculated using the Kaplan-Meier method. Differences between survival curves were compared using the log-rank test. All statistical analyses were performed using SPSS 23 for Windows. A *p-value* of less than 0.05 was considered statistically significant.

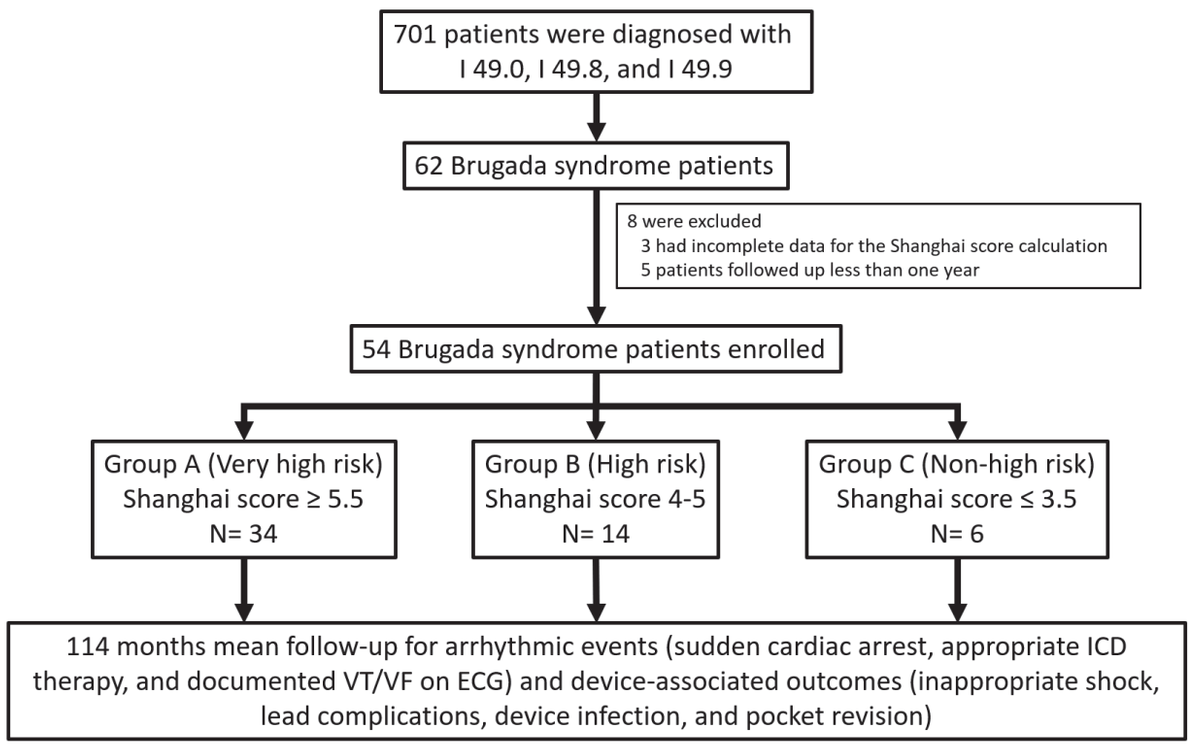

Figure 2 Flow chart of the patient population

Results

After an electronic record review of 701 patients with diagnosed ICD10 codes I49.0, I49.8, and I49.9, 62 BrS patients were identified. Three patients were excluded due to incomplete data for Shanghai score calculation at diagnosis and 5 patients were followed for less than 1 year. A total of 54 Patients (group A-score ≥ 5.5; n = 34, group B-score 4-5; n = 14, group C-score ≤ 3.5; n = 6) were followed up for 114.1 ± 63.2 months. Two Brugada patients with automated implantable cardioverter defibrillator (AICD) and Shanghai scores less than 3.5 were also included in group C. The mean age of diagnosis was 45.8 years and 98.1% of patients were male. Of all the patients who displayed type 1 ECGs that appeared spontaneously (n = 44), two were caused by febrile illness (n = 2) and seven were induced by sodium channel blockers (n = 7). Syncope and sudden cardiac arrest were common presenting symptoms and 31.5% of patients had a family history of sudden cardiac arrest or Brugada syndrome. Inducible ventricular fibrillation was demonstrated in 3 out of 8 asymptomatic patients in group A.

Table 2 Clinical characteristics of the study patients, according to Shanghai score group

Characteristics	All patients (N = 54)	Group A Very high risk (N = 34)	Group B High risk (N = 14)	Group C Non-high risk (N = 6)	P-value
Age, years	45.8 ± 13.2	45.35 ± 12.7	45.3 ± 16	49.3 ± 10.2	
Male	53 (98.1)	34 (100)	14 (100)	5 (83.3)	0.017
Shanghai score	5.4 ± 1.45	6.29 ± 0.91	4.42 ± 0.4	3.16 ± 0.6	
ECG 12 lead Spontaneous type 1 ECG	44 (81.5)	33 (97)	7 (50)	4 (66.7)	0.01
Fever-induced type 1 ECG	2 (3.7)	1 (2.9)	1 (7.1)	0 (0)	NS
Drug-induced type 1 ECG	8 (14.8)	0 (0)	6 (42.6)	2 (33.3)	0.001
Clinical history Cardiac arrest or VT/VF	14 (25.9)	14 (41.2)	0 (0)	0 (0)	0.004
Nocturnal agonal respiration	3 (5.6)	2 (5.9)	1 (7.1)	0 (0)	NS
Suspected arrhythmic syncope	22 (40.7)	18 (52.9)	4 (28.6)	0 (0)	0.029
Syncope of unclear mechanism	8 (14.8)	0 (0)	8 (57.1)	0 (0)	0
AF/AFL in patients < 30 yrs of age	1 (1.9)	0 (0)	1 (7.1)	0 (0)	NS
Family history in first- or second-degree relatives Definite Brs	4 (7.4)	4 (11.8)	0 (0)	0 (0)	NS
Suspicious SCD related to Brs	8 (14.8)	4 (11.8)	3 (21.4)	1 (16.7)	NS
Unexplained SCD at < 45 yrs of age	5 (9.3)	3 (8.8)	2 (14.2)	0 (0)	NS
Probable pathogenic mutation (SCN5A)	0 (0)	0 (0)	0 (0)	0 (0)	NS
LVEF (%)	64.7 ± 5.5	64.3 ± 5.2	63.4 ± 6.7	69 ± 3.67	NS
EPS	8 (14.8)	4 (11.8)	3 (21.4)	1 (16.7)	NS
Inducible VF	3 (5.6)	3 (8.8)	0 (0)	0 (0)	NS
AICD implantation	47 (87)	30 (88.2)	14 (100)	3 (50)	0.023
Follow-up, months	114.1 ± 63.2	124.18 ± 70.4	105.6 ± 42.3	77 ± 49	NS

Values are n (%) or mean ± SD

ECG = electrocardiogram; AF = atrial fibrillation; AFL = atrial flutter; BrS = Brugada syndrome; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia; LVEF = left ventricular ejection fraction; EPS = electrophysiologic study; AICD = automated implantable cardioverter defibrillator; NS = not significant

Overall, the mean Shanghai score was 5.4 ± 1.45. 63% of the patients were classified to group A or Shanghai score ≥ 5.5. AICD implantation was performed on 87% of patients, with higher prevalence in group A and group B (88.2% in group A, 100% in group B, and 50% in group C based on the patient's insistence to have the AICD implantation after discussion, $p = 0.023$).

Table 3 Outcomes of study patients, according to Shanghai score groups

Outcomes	All patients (N = 54)	Group A Very high risk (N = 34)	Group B High risk (N = 14)	Group C Non-high risk (N = 6)	P-value
Arrhythmic event	11 (20.4)	9 (26.5)	2 (14.3)	0 (0)	0.27
Sudden cardiac arrest	0 (0)	0 (0)	0 (0)	0 (0)	
Appropriate AICD therapy	10 (18.5)	9 (26.5)	1 (7.1)	0 (0)	0.13
Documented VT/VF	1 (1.9)	0 (0)	1 (7.1)	0 (0)	0.23
Inappropriate shock	5 (9.3)	2 (5.9)	3 (21.4)	0 (0)	0.17
Device-related complications	13 (24.1)	8 (23.5)	5 (35.7)	0 (0)	0.20
Lead fracture	5 (9.3)	3 (8.8)	2 (14.2)	0 (0)	0.59
CIED Infection	1 (1.9)	1 (2.9)	0 (0)	0 (0)	0.74
Pocket revision	2 (3.7)	2 (5.9)	0 (0)	0 (0)	0.53

Values are n (%)
AICD = automated implantable cardioverter defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia; CIED = cardiac implantable electronic device; NS = not significant

During the mean 114-month follow-up period, a total of 11 arrhythmic events occurred with one case of documented ventricular fibrillation by surface electrocardiogram. 10 patients had appropriate ICD therapy that led to radiofrequency ablations in three patients. Arrhythmic events were highest in group A (26.5%) followed by group B (14.3%) and none in group C. When comparing the very high-risk group (Shanghai score ≥5.5) to the cohort, the incidence of arrhythmic events was higher but did not reach statistical significance (26.5% vs 11.8%, $p = 0.147$, HR 2.44, CI 0.52-11.4, $p = 0.26$).

Non-high-risk patients with a Shanghai score ≤3.5 had no incidence of ventricular arrhythmic events, while those with a score >3.5 showed a trend towards an increase in arrhythmic events (22.2% vs 0%, HR = 4.85, CI 0.037-630.2, $p = 0.525$).

Device-related complications occurred in 13 patients, including 5 cases of lead fracture, 2 cases of pocket-related complications and one case of CIED infection. In addition, 5 patients experienced inappropriate shocks, with one associated with lead fracture, one resulting from electrocautery interference and one triggered by a supraventricular episode (1 case of atrial fibrillation, 1 case of supraventricular tachycardia and 1 case of sinus tachycardia).

Table 4 The annual incidence of ventricular arrhythmia stratified by Shanghai score and compared with another study[2]

Group	Shanghai score	Annual incidence of ventricular arrhythmia	
		Current study	S. Kawada (2018)[2]
Very high risk	≥5.5	2.8%	2.5%
High risk	4-5	1.5%	1.76%
Moderate risk	3.5	0%	0.68%
Low risk	<3.5		0%

Discussion

The present study demonstrated a difference in the frequency of ventricular arrhythmic events between different Shanghai score risk-predicting groups without genetic testing results. Compared to a previous study by S. Kawada in 2018, this study showed a comparable incidence of ventricular arrhythmia in the very high-risk group with a Shanghai score of ≥ 5.5 (26.5% vs 25%) and the high-risk group with a Shanghai score of 4-5 (14.3% vs 17.6%). Both studies confirm the usefulness of the Shanghai scoring system as a prognostic tool for managing BrS patients. Non-high-risk patients especially score less than 3.5 have very low incidence of ventricular arrhythmias.

Ventricular arrhythmia in our very high-risk group was lower compared to symptomatic BrS patients who presented with sudden cardiac arrest or syncope (26.5% vs 32.9%) in another study.[10] This may be due to the inclusion of asymptomatic patients with risk factors such as family history.

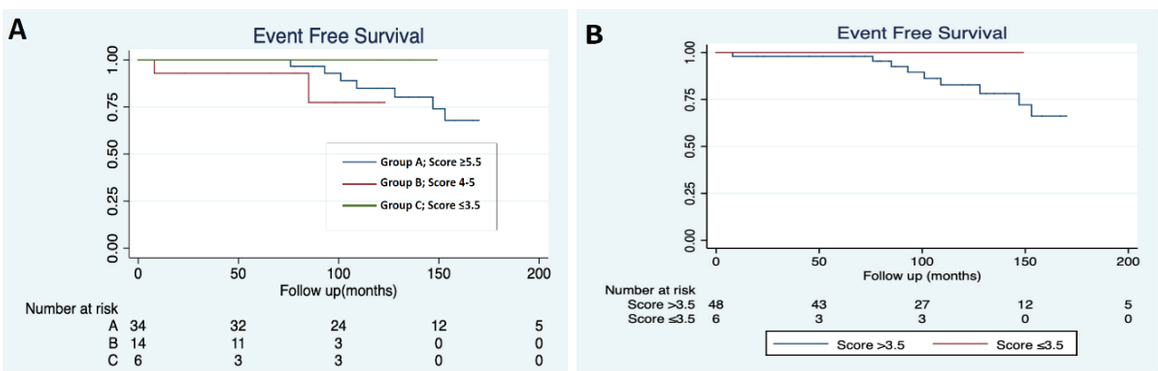

Figure 3 Cumulative event-free survival as a function of score, (A) Event-free survival of the entire cohort classified by the group, (B) Event-free survival is classified by intermediate-low risk (Shanghai score ≤ 3.5) compared to the higher risk group (Shanghai score > 3.5)

There were no ventricular arrhythmic events observed in non-high-risk patients. However, survival analysis demonstrated a trend towards an increased ventricular arrhythmic event in patients with a Shanghai score of more than 3.5 or higher risk (22.2% vs 0%, HR= 4.85, CI 0.037-630.2, $p = 0.525$). The validation of this cutoff could not be proved by this study due to the very small number of lower risk population, resulting in no ventricular arrhythmic events and a wide range of hazard ratios. Therefore, the generalization of these results is limited and requires further studies with larger populations in the intermediate and low-risk groups.

Moreover, this study rarely performed genetic tests (only 2 cases, with negative results). This may have made Shanghai scores in our cohort lower than in other studies. However, our study results may reflect the feasibility of using clinical-based, non-genetic testing Shanghai score for risk stratification, which may be applicable to countries with limited resources like Thailand. A further study with a larger cohort is needed to confirm the true accuracy of this method.

This study has certain limitations. Firstly, BrS had no specific diagnosis based on the ICD-10 code, which may have led to missed cases during enrollment. The majority of the patients in this study were very high risk with a very high Shanghai score, which limits the generalizability of this study to the true populations of BrS. Further studies with a larger number of intermediate and low-risk patients may provide more helpful data for using the Shanghai scoring system to identify patients who will benefit from ICD, and to reassure asymptomatic low-risk BrS patients.

Conclusion

Risk stratification by the Shanghai scoring system, without genetic testing, may be useful in predicting ventricular arrhythmic events in BrS patients in Thailand.

References

1. Antzelevitch C, Yan GX, Ackerman MJ, et al. J-wave syndromes expert consensus conference report: emerging concepts and gaps in knowledge. *Heart Rhythm.* 2016;13:e295-324.
2. Kawada S, Morita H, Antzelevitch C, et al. Shanghai Score System for Diagnosis of Brugada Syndrome: Validation of the Score System and System and Reclassification of the Patients. JACC: *Clinical Electrophysiology.* 2018;4(6):724-30.
3. Pranata R. Brugada syndrome: A brief review on diagnostic approach, risk stratification, and management. *Int J Cardiovasc Acad.* 2019;5:1-7.
4. Priori SG. Natural history of Brugada syndrome: insights for risk stratification and management. *Circulation.* 2002; 105: 1342-7.
5. Probst V, Veltmann C, Eckardt L, et al. Long-term prognosis of patients diagnosed with Brugada syndrome: results from the FINGER Brugada Syndrome Registry.*Circulation.* 2010;121:635-43.
6. Takagi M, Aonuma K, Sekiguchi Y, et al. The prognostic value of early repolarization (J wave) and ST-segment morphology after J wave in Brugada syndrome: multicenter study in Japan. *Heart Rhythm.* 2013; 10: 533-9.
7. Brugada J, Brugada P. Determinants of sudden cardiac death in individuals with the electrocardiographic pattern of Brugada syndrome. *Pacing Clin Electrophysiol.* 2003; 26: 957.
8. Huang Z, Patel C, Li W, et al. Role of signal-averaged electrocardiograms in arrhythmic risk stratification of patients with Brugada syndrome: a pro-spective study. *Heart Rhythm.* 2009; 6: 1156-62.
9. Brugada J, Brugada R, Brugada P. Determinants of sudden cardiac death in individuals with the electrocardiographic pattern of Brugada syndrome and no previous cardiac arrest. *Circulation.* 2003; 108: 3092-6.
10. Makarawate P, Chaosuwannakit N, Vannaprasaht S. Clinical characteristics and treatment outcomes of patients with Brugada syndrome in north eastern Thailand. *Singapore Med J.* 2014; 55(4): 217-220.