JACC: CLINICAL ELECTROPHYSIOLOGY VOL. ■, NO. ■, 2018

PUBLISHED BY ELSEVIER

# Shanghai Score System for Diagnosis of Brugada Syndrome

## Validation of the Score System and System and Reclassification of the Patients

Satoshi Kawada, MD,[a] Hiroshi Morita, MD, PHD,[b] Charles Antzelevitch, PHD,[c] Yoshimasa Morimoto, MD,[a] Koji Nakagawa, MD, PHD,[a] Atsuyuki Watanabe, MD, PHD,[a] Nobuhiro Nishii, MD, PHD,[b] Kazufumi Nakamura, MD, PHD,[a] Hiroshi Ito, MD, PHD[a]

## ABSTRACT

**OBJECTIVES** The principal objective was to perform an initial test of the Shanghai Brugada Scoring System. Diagnosis of probable and/or definite Brugada syndrome (BrS), possible BrS, and nondiagnostic outcomes were assigned scores of ≥3.5, 2 to 3, and <2 points, respectively. The proposed score system was based on the available published reports and on weighted coefficients derived from limited datasets, with the understanding that these recommendations would need to undergo continuing validation.

**BACKGROUND** The 2016 HRS/EHRA/APHRS/SOLAECE J-Wave Syndrome Consensus Report proposed a scoring system for diagnosis of BrS that takes into account electrocardiographic recordings, genetic results, clinical characteristics, and family history.

**METHODS** The patient population consisted of 393 patients evaluated at our hospital for BrS (271 asymptomatic, 99 with syncope, and 23 with ventricular fibrillation [VF]) between 1996 and 2016. Subjects were classified into 4 groups: group A with a score of ≤3.0 points (n = 45); group B with a score of 3.5 points (n = 186); group C with a score of 4.0 to 5.0 points (n = 81); and group D with a score of ≥5.5 points (n = 81).

**RESULTS** Three hundred forty-eight (88%) patients had probable and/or definite BrS, and 81 (20%) had a score ≥5.5. During a follow-up of 97.3 months (range: 39.7 to 142.1 months), 43 patients experienced VF. Significant differences were seen among the 4 groups (p = 0.01). A malignant arrhythmic event did not occur in any patient with possible or nondiagnostic BrS.

**CONCLUSIONS** This study provided validation for the use of the Shanghai Score System for the diagnosis and risk stratification of patients with BrS. (J Am Coll Cardiol EP 2018;■:■–■) © 2018 by the American College of Cardiology Foundation.

Brugada syndrome (BrS) was first described in 1992 as a syndrome characterized by right bundle branch block with ST-segment elevation in the right precordial leads and development of ventricular tachyarrhythmias (ventricular tachycardia/ventricular fibrillation [VT/VF]) despite no evident underlying heart disease (1). Criteria for BrS in the first Consensus Report published in 2002

From the [a]Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan; [b]Department of Cardiovascular Therapeutics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan; and the [c]Lankenau Institute for Medical Research, Wynnewood, Pennsylvania. Conflicts of interest: Dr Hiroshi Morita and Dr Nobuhiro Nishii are affiliated with the endowed department by Japan Medtronic Inc. Dr. Morita was supported by JSPS KAKENHI (15K09082), the Tailor-made Medical Treatment Program with the BioBank Japan Project from the Japan Agency for Medical Research and Development, AMED (JP17km0405109), and a grant from the Suzuken Memorial Foundation (M22-031-4). Dr. Nishii was supported by JSPS KAKENHI (16K09437). Dr. Antzelevitch was supported by the National Institutes of Health (HL47678) and a grant from Pharmacyclics. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

Manuscript received December 4, 2017; revised manuscript received January 29, 2018, accepted February 1, 2018.

ISSN 2405-500X/$36.00 https://doi.org/10.1016/j.jacep.2018.02.009

**ABBREVIATIONS AND ACRONYMS**

**AF** = atrial fibrillation

**BrS** = Brugada syndrome

**CI** = confidence interval

**ECG** = electrocardiography

**HR** = hazard ratio

**ICD** = implantable cardioverter-defibrillator

**VF** = ventricular fibrillation

**VT** = ventricular tachycardia

focused on diagnostic criteria for BrS (2). According to the first Consensus Report, diagnosis of BrS was based on a spontaneous or drug-induced type 1 electrocardiogram (ECG) in conjunction with clinical symptoms. The Second Consensus Report in 2005 provided more details on the diagnosis of BrS, as well as risk stratification methods and therapeutic recommendations (3). In the 2013 Consensus Statement and 2015 Guidelines, it was proposed that BrS be diagnosed only by the existence of a type 1 ECG (4,5).

The recent J-Wave Syndrome Consensus Report proposed diagnosis of BrS by calculating a score based on ECG recordings, genetic results, family history, and clinical characteristics (6). The proposed Diagnostic Score System, referred to as the Shanghai BrS Score, was based on the available published reports and on weighted coefficients derived from limited datasets, with the understanding that these recommendations would need to undergo continuing validation as new data became available.

In the score system, the existence of a spontaneous type 1 ECG is important, but the score system also includes fever- or drug-induced type 1 ECG, history of arrhythmia or arrhythmic syncope, family history, and the results of a genetic test.

The aim of this study is to validate new diagnostic criteria and reclassify a typical BrS cohort using the Shanghai Score System. This study was designed to perform a test of practicality of the scoring system for diagnosis of BrS in patients evaluated for BrS at our hospital over a period of 20 years.

## METHODS

**PATIENT POPULATION.** All study protocols were approved by the Ethics Committee on Human Research and Epidemiology of Okayama University and Human Genome Studies of the Ethics Committee of Okayama University.

The patient population consisted of 393 patients who visited our hospital for a medical examination with suspicion of BrS between 1996 and 2016. Of these 393 patients, 271 were asymptomatic and 122 were symptomatic (syncope: n = 99, VF: n = 23) at the first visit to the hospital. We only included patients with the BrS pattern, which displayed type 1 ECGs that either appeared spontaneously (n = 311), were caused by febrile illness (n = 7), or were induced by the sodium channel blocker (n = 75). We did not include patients with nonspontaneous type 1 ECGs who did not convert to the type 1 ECG by the sodium channel blocker. Structural heart disease was excluded by routine examinations, including chest x-ray, laboratory tests, exercise stress test, and echocardiography. We used intravenous pilsicainide (1 mg/kg per 10 min), a pure sodium channel blocker, to unmask a type 1 BrS ECG in 82 patients (75 patients with drug-induced type 1 BrS ECG and 7 patients with fever-induced type 1 ECG) (7–9). Genetic analysis limited to *SCN5A* variants was performed in 167 patients. We regarded *SCN5A* gene mutation, which was detected during follow-up, as the score at the initial visit.

**FOLLOW-UP AND ARRHYTHMIC EVENTS.** Patients were followed every 6 months in the outpatient clinic, and the median duration of follow-up was 97.3 months (range: 39.7 to 142.1 months). Patient treatment, including implantable cardioverter defibrillators (ICDs), was based on the clinical judgment of the physician. Patients with an ICD were seen every 6 months for clinical review and device interrogation, whereas those without an ICD were followed at least once a year. Arrhythmic events were defined as sudden cardiac death, appropriate shock delivery by an ICD, and/or documented VT/VF by conventional ECG.

**APPLICATION OF THE SHANGHAI SCORE SYSTEM.** Table 1 shows the proposed Shanghai Score System (9). Diagnosis of probable and/or definite BrS, possible BrS, or a nondiagnostic score were assigned scores of ≥3.5, 2 to 3, and <2 points, respectively. We examined each item of the Shanghai Score System in 393 patients and calculated the point score at the first visit to our hospital.

**STATISTICAL ANALYSIS.** Continuous variables are expressed as mean ± SD or median (range). Categorical variables are expressed as numbers and proportions. We calculated the hazard ratio (HR) with 95% confidence interval (CI) for each variable that was significantly associated with the occurrence of a major arrhythmic event (VTs or sudden cardiac death, appropriate therapy by ICD) using Cox proportional analysis. 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 JMP 13.0 for Windows (SAS Institute, Cary, North Carolina). A p value <0.05 was considered statistically significant.

## RESULTS

**BASELINE CHARACTERISTICS OF THE PATIENTS.** Table 2 shows the characteristics of the 393 patients. The median age of the patients at enrollment was 45 years, and most were men (95.2%). All patients