



Original Article

Outcomes of symptomatic Brugada syndrome patients with implanted cardioverter defibrillators: A report from an endemic area



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ABSTRACT

Background: In Thailand and Southeast Asia, Brugada syndrome (BS) is a common inheritable cause of sudden cardiac arrest (SCA) due to polymorphic ventricular tachycardia (VT) and ventricular fibrillation (VF). Currently, an implantable cardioverter defibrillator (ICD) is the recommended therapy for high-risk patients. This study aimed to report the outcomes of symptomatic BS patients with implanted ICD in an area in which BS is endemic.

Methods and results: We enrolled symptomatic BS patients who underwent ICD implantation between 2007 and 2010. In total, 62 patients met the study inclusion criteria. Among these patients, ICD was indicated for survivors of SCA (50 patients, 80%) and syncope patients (12 patients, 20%). During the mean follow-up period of 17 months, no patient died, and 20 patients (32%) received appropriate shock therapy. Inappropriate shock occurred in 6 patients (9.5%). The reasons for inappropriate shock were ICD lead fracture (3%) and supraventricular arrhythmia (6.5%). An infected ICD was found in 1 patient (1.5%).

Conclusions: The recurrent VT/VF rate in symptomatic BS patients was 32%. All events were successfully treated with ICDs, and there was no mortality in our setting.

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1. Introduction

Brugada syndrome (BS) is characterized by ST segment elevation (coved type) in the right precordial electrocardiographic (ECG) leads and sudden cardiac arrest (SCA) or death in patients with normal cardiac structure. The syndrome typically manifests during adulthood, with a mean onset age of 41 years [1,2]. The causes of SCA in BS are polymorphic ventricular tachycardia (VT) and ventricular fibrillation (VF) [1,2].

In Thailand and Southeast Asia, the incidence of Brugada ECG type 1 in patients with previous cardiac arrest is higher than that in the general population in Europe and the United States [3,4]. BS accounts for 47.2% of all sudden deaths in Northeastern Thailand and only 4–12% in the rest of the world [3,4]. SCA from VT and VF in BS patients occurs mainly at rest, predominantly during sleep [5]. The

typical ECG pattern changes over time and is mediated by post-exercise or pharmacologic interventions that interact with the autonomic nervous system (ANS) [6]. ST segment elevation in leads V1–V3 could be augmented by administration of sodium channel blockers and high intercostal ECG lead placement in patients with suspected BS who are at risk for VT/VF [7].

The implantable cardioverter defibrillator (ICD) is more effective than antiarrhythmic drugs for symptomatic BS patients, including those with aborted SCA and syncope [8,9]. The average mortality rate of BS from recurrent VT/VF may be high as 25% [10]; therefore, BS is considered the main public health problem in Northeastern Thailand and the Southeast Asian countries. By 2015, the Association of Southeast Asian Nations (ASEAN) Economic Community (AEC) project will be implemented by all governments in Southeast Asia. This project will allow Southeast Asians to work freely in any country in the region. Increased travel, particularly among workers in ASEAN countries, will occur. SCA was reported in a group of Thai workers in Singapore in the 1990s [11]. Therefore, healthcare personnel in the ASEAN community and Asia should be aware of this fatal condition in the years after 2015. More scientific reports of

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BS in Asian populations also need to be shared. Herein, we report the clinical outcomes of symptomatic BS patients treated with ICDs.

2. Material and methods

2.1. Study population

All patients diagnosed with BS who underwent ICD implantation at Queen Sirikit Heart Center of The Northeast (QSHC) and Srinagarind Hospital, Khon Kaen University, Thailand between 2007 and 2010 were included.

2.2. Diagnosis and clinical data

BS is clinically diagnosed in patients presenting with SCA or syncope on the basis of one of the following criteria: documented VT or VF, family history of sudden cardiac death at <45 years of age, similar type of Brugada ECG among family members, unexplained syncope, history of nocturnal agonal respiration with spontaneous type 1 Brugada ECG, or type 1 Brugada ECG after provocation using high intercostal ECG lead detection or after sodium channel blocker administration. A type 1 ECG was defined as a prominent coved ST segment elevation >2 mm followed by a negative T wave [10,12].

The following clinical data were collected: age at diagnosis, sex, family history of SCA, type of Brugada ECG at diagnosis, results of pharmacological testing or high intercostal lead detection for unmasking the coved type ECG pattern, presenting symptoms (survivor of SCA or syncope), and indication for ICD implantation. In addition, the following criteria were considered: device effectiveness assessed by the numbers of patients who received appropriate shock after ICD implantation (only the first appropriate shock was considered for analysis) and complications, including inappropriate shock and uneventful events after ICD implantation. All patients attended follow-up visits every 3–6 months for clinical review and device evaluation.

2.3. Statistical analysis

Clinical characteristics of the BS patients were categorized by presenting symptoms (SCA or unexplained syncope). Data are expressed as mean (standard deviation [SD]) or percentage. The unpaired *t*-test was used for comparisons of group mean values expressed as continuous variables, while the chi-square or Fisher's exact test was used to test differences in proportion. A *p* value <0.05 was considered statistically significant.

3. Results

3.1. Clinical characteristics

The demographic and clinical characteristics of the study population are summarized in Table 1. A total of 62 patients were

studied. Of these patients, 50 (80.6%) presented with SCA and 12 (19.4%) presented with syncope. Almost all patients were men (61 patients, 98.4%) and were born and living in Northeastern Thailand (60 patients, 96.8%). The mean (SD) age at diagnosis was 45 (9) years. A family history of SCA was noted in 26 patients (42%). A spontaneous coved-type Brugada ECG pattern was found in most patients (47 patients, 75.8%). The average follow-up period for all patients was 17 months.

3.2. Clinical comparison according to presenting symptom

There was no significant difference between BS patients presenting with SCA or syncope in terms of age, sex, family history of SCA, or ECG type (Table 1).

3.3. Clinical outcomes and complications of ICD

The clinical outcomes and complications of the patients with implanted ICDs are shown in Table 2. A single-chamber ICD was implanted in all patients. Twenty patients (32.3%) had recurrent VT/VF and were successfully treated with ICD or appropriate shock. Of these patients, 16 (80.0%) were in the SCA group. Eight patients (40%) received ICD shock when they were awake, and the shock occurred during the night for the other 12 patients (60%). Inappropriate shock by ICD occurred in 6 patients (9.7%), 3 in each group. Patients received amiodarone if there was evidence of recurrent VT/VF due to appropriate shocks. Reasons for inappropriate shock were ICD lead fracture (2 patients, 3%) and supraventricular arrhythmia (4 patients, 6.5%). Supraventricular arrhythmias consisted of sinus tachycardia (2 patients), supraventricular tachycardia (1 patient), and atrial fibrillation (1 patient). One patient (1.5%) in the syncope group had an infected ICD, which was removed and reimplanted after successful treatment of the infection.

4. Discussion

This study showed the rate of recurrent of VT/VF in symptomatic Thai BS patients who received ICD implantation as a secondary prevention. After approximately 1.5 years of follow-up, the recurrence of VT/VF in symptomatic BS patients in our series was 32%. All events were successfully treated by ICDs. The event rate in Thai patients was comparable with from the rate in other countries. After 3 years of follow-up of symptomatic Japanese BS patients, the rate of recurrent cardiac events after ICD implantation or secondary prevention was 25.7% [13]. Similarly, the VT/VF rate in European BS patients treated with ICD was somewhat higher, at 34% [13]. A report from France showed that most BS patients received ICD shock at random times, whereas in the present study, most patients (60%) experienced cardiac events during the night, similar to the findings of a previous report [3,9]. Thus, symptomatic BS patients in our region had cardiac events more frequently while they were sleeping.

Table 1
Clinical characteristics of 62 Brugada syndrome patients grouped according to presenting symptoms.

Characteristic	Sudden cardiac arrest (n=50)	Syncope (n=12)	<i>p</i> value
Mean age ± standard deviation (years)	46 ± 12	44 ± 9	0.058
Men (%)	50 (100%)	11 (92%)	0.194
Family history of sudden death (%)	22 (44%)	4 (33.3%)	0.531
Spontaneous type 1 ECG	38 (70%)	9 (75%)	0.942
Type 1 ECG after high intercostal lead	8 (16%)	2 (16.7%)	0.955
Type 1 ECG after sodium channel blocker administration	4 (8%)	1 (4.3%)	0.970
Residency region in Thailand –Northeastern	48 (96%)	12 (100%)	1.000

ECG: electrocardiogram.

Table 2
Outcome of 62 Brugada syndrome patients grouped according to presenting symptoms.

Characteristic	Sudden cardiac arrest (n=50)	Syncope (n=12)	p value
Mean follow-up time \pm standard deviation (months)	16 \pm 4	18 \pm 6	0.067
Patients with appropriate shock, n (%)	16 (32%)	4 (33.3%)	0.929
Patients with inappropriate shock, n (%)	3 (6.0%)	3 (25.0%)	0.081
Infected ICD, n (%)	0 (0%)	1 (8.3%)	0.193

ICD: implantable cardioverter defibrillator.

Although ICD therapy is the only proven effective treatment for symptomatic BS, some complications may occur after ICD implantation. In our study, inappropriate ICD shock occurred substantially less frequently compared to appropriate shock (9.7% vs. 32.3%). The inappropriate shock rate was lower than that of a previous report (20%) [14]. Depression or fear of shock therapy may occur in BS patients who receive inappropriate shocks [15]. In our study, the appropriate ICD shock rate was higher than that in the report by Sacher et al. (32.3% vs. 8%) [14]. This finding may be explained by differences in the study populations. In the present study, 50 of 62 patients (80.64%) were symptomatic and had SCA. However, SCA patients accounted for only 8% of all patients in the previous study [14]. To avoid inappropriate shock, adjustment of the ICD to only 1 VF zone with a detection rate above 180–200 bpm in young, active patients is recommended [16]. Another serious complication of infected ICD occurred in only 1 patient (1.6%). Because of the high rate of recurrent VT/VF and low rate of ICD complications, ICD treatment is recommended for all symptomatic BS patients [8–10].

Several clinical parameters have been demonstrated to predict a worse outcome in BS patients, including severe symptoms at diagnosis (SCA), spontaneous type 1 Brugada ECG at diagnosis, male sex, and family history of SCA [10]. The results of this study confirmed that symptomatic BS patients in our setting, particularly those presenting with SCA, should receive ICD therapy because of a high probability of recurrent VT/VF events. Subsequent device programming and regular follow-up are required to minimize the occurrence of inappropriate shock.

5. Conclusions

The recurrent VT/VF rate in symptomatic Thai BS patients was high, and these events were successfully treated with ICDs in our setting.

Conflicts of interests

none declared.

References

- [1] Brugada J, Brugada P, Brugada R. The syndrome of right bundle branch block ST segment elevation in V1 to V3 and sudden death—the Brugada syndrome. *Europace* 1999;1:156–66.
- [2] Ihor G, Antzelevitch C, Preben B, et al. The Brugada syndrome: clinical, electrophysiologic and genetic aspects. *J Am Coll Cardiol* 1999;33:5–15.
- [3] Tatsanavivat P, Chirawatkul A, Klungboonkrong V, et al. Sudden and unexplained deaths in sleep (Lai Tai) of young men in rural northeastern Thailand. *Int J Epidemiol* 1992;21:904–10.
- [4] Antzelevitch C, Brugada P, Brugada J, et al. Brugada syndrome: a decade of progress. *Circ Res* 2002;91:1114–8.
- [5] Himmunngan P, Sangwatanaroj S, Petmitr S, et al. HLA-class II (DRB & DQB1) in Thai sudden unexplained death syndrome (Thai SUDS) families (Lai-Tai families). *Southeast Asian J Trop Med Public Health* 2006;37:357–65.
- [6] Makimoto H, Nakagawa E, Takaki H, et al. Augmented ST-segment elevation during recovery from exercise predicts cardiac events in patients with Brugada syndrome. *J Am Coll Cardiol* 2010;56:1576–84.
- [7] Sangwatanaroj S, Prechawat S, Sunsaneewitayakul B, et al. New electrocardiographic leads and the procainamide test for the detection of the Brugada sign in sudden unexplained death syndrome survivors and their relatives. *Eur Heart J* 2001;22:2290–6.
- [8] Brugada J, Brugada R, Brugada P. Pharmacological and device approach to therapy of inherited cardiac disease associated with cardiac arrhythmias and sudden death. *J Electrocardiol* 2000;33(suppl):41–7.
- [9] Nademanee K, Veerakul G, Mower M, et al. Defibrillator versus beta blockers for unexplained death in Thailand (DEBUT): a randomized clinical trial. *Circulation* 2003;107:2221–6.
- [10] Brugada P, Benito B, Brugada R, et al. Brugada syndrome: update 2009. *Hellenic J Cardiol* 2009;50:352–72.
- [11] Goh KT, Chao TC, Heng BH, et al. Epidemiology of sudden unexpected death syndrome among Thai migrant workers in Singapore. *Int J Epidemiol* 1993;22:88–95.
- [12] Antzelevitch C. Brugada syndrome. *Pacing Clin Electrophysiol* 2006;29:1130–59.
- [13] Atarashi H, Ogawa S, Harumi K, et al. Three-year follow-up of patients with right bundle branch block and ST segment elevation in right precordial leads. *J Am Coll Cardiol* 2001;37:1916–20.
- [14] Sacher F, Probst V, Iesaka Y, et al. Outcomes after implantation of cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study. *Circulation* 2006;114:2317–24.
- [15] Sarkozy A, Boussy T, Kourgiannides G, et al. Long-term follow-up of primary prophylactic implantable cardioverter-defibrillator in patients with Brugada syndrome. *Eur Heart J* 2007;28:334–44.
- [16] Veltmann C, Kuschyk J, Schimpf R, et al. Prevention of inappropriate ICD shocks in patients with Brugada syndrome. *Clin Res Cardiol* 2010;99:37–44.