Primary Cardiac Electrical Diseases: Baseline and Retrospective Outcomes of a Multicenter Registry from Thailand

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ABSTRACT

Objective: Primary cardiac electrical diseases are the leading cause of sudden cardiac arrest in patients with apparently normal structured heart. The purpose of this study was to assess the distribution of primary cardiac electrical diseases, as well as to assess the prognosis and predictive factors for future ventricular arrhythmia in Thai patients.

Materials and Methods: Patients with primary cardiac electrical diseases who came for clinic visit at Siriraj Hospital, Buddhachinarat hospital, and Chonburi hospital were enrolled. History was acquired from interview and medical record.

Results: There were 120 patients in the study. The most prevalent primary cardiac electrical disease was Brugada syndrome. Sixty nine patients experienced prior sudden cardiac death episode and all of the patient in this group had ICD implanted. None of the patient with ICD died after a median follow up of 8.59+5.01 years. Recurrent ventricular arrythmia rate was 47.8%. Among patients who had ICD implanted for primary prevention, none had sudden cardiac arrest/ new ventricular arrythmia episode detected. The only predictor of future lethal arrythmia is history of prior sudden cardiac arrest.

Conclusion: Brugada syndrome is the most common etiologic cause of primary cardiac electrical disease in Thailand. ICD is extremely effective for secondary prevention of sudden cardiac arrest.

Keywords: Primary cardiac electrical disease; Brugada syndrome (Siriraj Med J 2023; 75: 316-320)

INTRODUCTION

Primary cardiac electrical diseases are the leading cause of sudden cardiac arrest in patients with apparently normal structured heart.[1] Several reports have been published since 1981 regarding the incidence of sudden unexplained deaths in Southeast Asian refugees, immigrant workers, immigrants, and other subpopulations in Thailand.[2-5] Brugada syndrome, early repolarization syndrome, and long QT syndrome are among the most common cause of sudden cardiac death in Thailand.[6] Based on global publications, prognosis of Brugada syndrome varies.[7-10] *Makarawate et al* reported a very high recurrence of lethal arrhythmia in the northeastern Thai population, or 32% in 12 months.[11] There are no reports regarding prognosis of asymptomatic patients with this disease in the Thai population. The purpose of this study was to assess the distribution of primary cardiac electrical diseases, as well as to assess the prognosis and predictive factors for future ventricular arrhythmia in Thai patients.

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https://doi.org/10.33192/smj.v75i4.261703

MATERIALS AND METHODS

Study population

Patients diagnosed with primary cardiac electrical disease who had a follow-up at Siriraj Buddhachinaraj, and Chonburi Hospitals were enrolled.

The inclusion criteria were:

1. Patients who survived cardiac arrest with normal structural heart or
2. Patients diagnosed with primary cardiac electrical disease, including Brugada syndrome, long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, pulseless monomorphic ventricular tachycardia, and primary ventricular fibrillation

The exclusion criteria were:

1. Patients with structural heart diseases identified as the etiology of cardiac arrest such as acute coronary syndrome, hypertrophic cardiomyopathy, and dilated cardiomyopathy
2. Patients with severe comorbidities with an expected survival time of less than three years
3. Patients who refused to participate in the study

Baseline characteristics of patients were recorded in an electronic database. Recorded variables included age at diagnosis, sex, hometown, diagnosis, history of sudden cardiac arrest, history of syncope, family history of sudden cardiac arrest, coronary artery disease, baseline hypertension, baseline diabetes mellitus, left ventricular ejection fraction, and current medication. Hometown was classified as northeastern Thailand or not northeastern Thailand. History of sudden cardiac arrest was defined as cardiac arrest from ventricular arrhythmia with successful cardiopulmonary resuscitation. History of syncope was defined as syncopal episodes from cardiac/ presumed cardiac arrhythmia. The etiologic diseases were diagnosed either during initial clinic visit, by retrospective chart review, or during follow up.

Patients had follow-up visits at arrhythmia clinic every six months. Both retrospective and prospective data was collected from electronic databases at a hospital. Implantable cardioverter defibrillator (ICD) programming depended on the implant physician. In ICD patients, an episode of sustained ventricular arrhythmia was collected from device interrogation. Data of patients who had their follow-up visit outside the study sites was collected from telephone interviews. Here, we reported baseline characteristics, including etiologic diseases of sudden cardiac arrest, as well as follow-up data acquired from the electronic database.

Statistical analysis

Continuous variables are presented as mean±S.D or median±SD. Categorical variables are presented as frequency and percentage of the population. Comparisons of characteristic variables were done using the Chi-square test or t-test for continuous variables. All statistical tests were two-tailed, with a p-value <0.05 considered statistically significant. Variables with a p-value of ≤0.1 were included in multivariate analysis. Logistic regression analysis was used for multivariate analysis. Effect of significant variables was reported by the odds ratio and 95% confidence interval. All statistical analyses were performed using SPSS version 18.

RESULTS

Between October 2017 and October 2020, a total of 120 patients were enrolled. The majority (83, 69.2%) of patients were male. The mean age was 47.8±14.1. Hypertension, and diabetes, were diagnosed in 16 (13.3%), and six (5.0%) patients, respectively. Four (0.3%) patients had a history of coronary artery disease. Brugada syndrome was the most common cause of primary cardiac electrical disease in this study, as 84 (70.0%) patients were diagnosed with this disease. Long QT syndrome, monomorphic ventricular tachycardia, and primary ventricular fibrillation was diagnosed in 10 (8.3%), 14 (11.7%), and 11 (9.1%) patients, respectively. One patient with ventricular fibrillation had pre-excitation syndrome. The patient underwent successful radiofrequency ablation without any recurrent ventricular arrhythmia; hence, ICD was not implanted in this patient. Twenty-four (20.0%) patients had a family history of unexplained sudden cardiac arrest. Sixty-nine (57.5%) patients experienced prior sudden cardiac arrest episodes. Regarding current medication, 54 (45.0%) patients were prescribed beta-blockers. Amiodarone was the only antiarrhythmic agent used, and was prescribed to 16 (19.2%) patients. Ninety-nine (96.0%) patients underwent ICD implantation. From this group, 27 (28.1%), had ICD implanted for primary prevention. All patients with primary prevention were diagnosed with Brugada syndrome. The baseline characteristics of patient are presented in Table 1.

After a median follow-up time of 8.59±5.01 years, 119 (99.2%) patients survived. One patient denied treatment and died from recurrent ventricular fibrillation. Recurrent ventricular arrhythmia was found in 33 (47.8%) patients who experienced prior cardiac arrest. For patients who did not have prior cardiac arrest, 27 (52.9%) had ICD implanted, and there was no new ventricular arrhythmia detected by the device. Six (22.2%) patients who had ICD

TABLE 1. Baseline characteristics of patients.

Baseline characteristics	Total N=120
Age (years)	47.8±14.1
Sex (male)	83 (69.2%)
Home town (Northeastern Thailand)	36 (29.0%)
Diagnosis	
Brugada syndrome	85 (70.8%)
Long QT syndrome	10 (8.3%)
Monomorphic ventricular tachycardia	14 (11.7%)
Ventricular fibrillation	11 (9.1%)
History of sudden cardiac arrest	69 (57.5%)
History of presumed cardiac syncope	38 (31.7%)
Family history of sudden cardiac arrest	24 (20%)
History of diabetes mellitus	6 (5.0%)
History of hypertension	16 (13.3%)
Coronary artery disease	4 (0.3%)
Left ventricular ejection fraction (%)	66.4±6.6
Cardiac electrophysiologic study	19 (15.8%)
Inducible ventricular arrhythmia	15 (78.9%)
Medication	
Beta-blocker	54 (45%)
Amiodarone	16 (19.2%)
ICD implanted	95 (79.1%)
Primary prevention	27 (28.1%)

Data presented as mean±S.D. or total number (%). All patients had structurally normal heart proven from echocardiogram. Other cardiac investigations including coronary angiogram, cardiac magnetic resonance imaging, exercise test, and genetic test were done according to clinical indication.

implanted for primary prevention suffered inappropriate ICD therapy. From univariate analysis, age, amiodarone usage, and previous cardiac arrest were identified as predictors for future ventricular arrhythmia. However, previous cardiac arrest was the only predictor identified from multivariate analysis. Table 2 describes detailed information regarding univariate analysis of predictors for recurrent event.

DISCUSSION

Among primary cardiac electrical disease in the Thai population, Brugada syndrome is the most common etiologic disease in both symptomatic and asymptomatic patients. This finding gives additional information as a previous study only included survivors of sudden cardiac arrest.[6] Furthermore, Brugada syndrome is not only common in Northeastern Thailand, but also in other parts of the country. The prevalence may possibly be higher, as we included only patients with spontaneous type 1 ECG and no challenge test was performed. There was not any early repolarization syndrome in this study. In fact, all patients with an initial diagnosis of early repolarization syndrome had spontaneous type 1 Brugada ECG during long term follow-up. For long QT syndrome, the prevalence was low. This could be explained by the relatively high age of patients in this study. Most patients with abnormally long QT intervals were excluded from the study due to identifiable causes, such as QT prolonging medication. It is still uncertain if genetic testing can increase the prevalence of long QT syndrome. Pulseless monomorphic ventricular tachycardia is the third most common cause. All patients in this study had idiopathic ventricular tachycardia from the outflow tract. In general, patients with idiopathic ventricular tachycardia have a good prognosis. However, the disease could be fatal, and there were several reports of cardiac arrest.[12,13] Idiopathic ventricular fibrillation is a rare cause of cardiac arrest and 11 (9.1%) patients from

TABLE 2. Baseline characteristics of patients.

Patient characteristics	No recurrent/ new event	Recurrent/ new event	O.R. (95% CI) Univariate analysis	P value	O.R. (95% CI) Multivariate analysis	P value
Age (years)	51.0±14.6	43.9±13.5	0.95 (0.93-0.99)	0.02*	0.96 (0.91-1.01)	0.13
Sex (male)	36 (43.4%)	47 (56.6%)	0.90 (0.34-2.36)	0.83		
Hometown in northeastern Thailand	18 (50%)	18 (50%)	1.12 (0.41-3.02)	0.82		
Diagnosis (Brugada syndrome)	51 (60.7%)	33 (39.3%)	0.88 (0.45-1.86)	0.31		
History of sudden cardiac arrest	19 (26.1%)	50 (73.9%)	20.15 (5.65-71.84)	0.00*	12.16 (2.22-66.75)	0.00*
History of presumed cardiac syncope	19 (50%)	19 (50%)	1.54 (0.66-3.59)	0.31		
Family history of sudden cardiac arrest	11 (45.8%)	13 (54.2%)	1.06 (0.37-2.99)	0.91		
Beta-blocker used	22 (40.7%)	32 (59.2%)	0.95 (0.42-2.20)	0.91		
Amiodarone used	5 (31.2%)	11 (68.7%)	4.00 (1.51-13.90)	0.03*	2.36 (0.42-13.29)	0.33

Data presented as mean±S.D. or n: O.R. = Odds ratio
*Statistically significant

this study fit into this category. Some of these patients may have been diagnosed with Brugada syndrome had the challenge test been done. Another possibility is that patients with ST segment elevation myocardial infarction had spontaneous reperfusion.

Regarding medication, 45% of patients were treated with beta-blockers. This concurs with guidelines for long QT syndrome and ventricular arrhythmia. However, 26% of Brugada syndrome patients were also prescribed beta-blockers. The rational for using beta-blockers for Brugada syndrome was based on findings from a study of sudden cardiac death patients which did not only include Brugada syndrome, but also patients with other causes of ventricular arrhythmia.[14] Whether beta-blockers are effective for Brugada syndrome is questionable. Nineteen percent of patients were prescribed amiodarone for suppression of recurrent ventricular arrhythmia. None of the patients underwent catheter ablation. The procedure might be more effective with less complication in the long term.

We found that 47.8% of patients with previous cardiac arrest from ventricular arrhythmia had a recurrent event. Implantable cardioverter defibrillators (ICD) are extremely effective as only one patient who refused treatment died after a median follow-up of 8.59±5.01 years. This could be explained by the age group of the patients, which was rather young with low co-morbidity. The finding concurs with several reports which have shown that unsuccessful defibrillation in a structurally normal heart is rare.[15,16] We could not identify other predictors for lethal ventricular arrhythmia in Brugada syndrome patients who did not experience prior sudden cardiac arrest. Patients who did not have prior cardiac arrest, who had strong family history of sudden cardiac arrest/ unexplained syncope, or inducible ventricular arrhythmia, did not experience any appropriate ICD therapy. The data is reliable as 52.9% of patients in this group had an ICD implanted (All patients in this group were diagnosed with Brugada syndrome). Moreover, besides the lack of benefit, 10 (37%) patients suffered inappropriate ICD shock. The finding implies that ICD implantation for primary prophylaxis is not cost-effective. This is different from the current recommendation for Brugada syndrome. Previous guidelines recommended ICD implantation for patients with presumed arrhythmic syncope without documented ventricular arrhythmia.[17,18] Recently, guidelines have recommended implantable loop recorder (ILR) for arrhythmia detection in this group of patients.[19] Regarding the risk stratification method, genetic testing might be helpful. However, only 20-30% of Brugada syndrome patients have known genetic mutations.[20,21] For Long QT syndrome, monomorphic ventricular tachycardia, and ventricular fibrillation, ICD implants are for secondary prophylaxis only and the rate of recurrent ventricular arrhythmia is comparable to Brugada syndrome.

CONCLUSION

Brugada syndrome is the most prevalent primary cardiac electrical disease in Thailand. Recurrent ventricular arrhythmia rate is high. ICD therapy is very effective for this group of patients.

Study limitations

There are several limitations of this study. First, it only includes patients who had a follow-up at the study center. There was potential selection bias as not all patients came to the hospital, especially patients who did not have prior cardiac arrest. Second, the number of patients in the study was low and enrolment of more patients, especially asymptomatic patients, would allow us to identify other risk factors for future events. Third there was missing/ erroneous data, as some was taken from incomplete medical records or interviews about symptoms in the past, for which the patients may not be able to remember the details after several years.

REFERENCES

1. Wever E, Medina E. Sudden death in patients without structural heart disease. J Am Coll Cardiol. 2004;43:1137-44.
2. Blackwell CC, Busuttil A, Weir DM, Saadi AT, Essery SD. Sudden unexpected nocturnal deaths among Thai immigrant workers in Singapore. The possible role of toxigenic bacteria. Int J Leg Med. 1994;106:205-8.
3. Baron RC, Thacker SB, Gorelkin L, Vernon AA, Taylor WR, Choi K. Sudden death among Southeast Asian refugees. An unexplained nocturnal phenomenon. J Am Med Assoc. 1983;250:2947-51.
4. Gilbert J, Gold RL, Haffejee CI, Alpert JS. Sudden cardiac death in a southeast Asian immigrant: clinical, electrophysiologic and biopsy characteristics. Pacing Clin Electrophysiol. 1986;9: 912-4.
5. Nademanee K, Veerakul G, Nimmannit S, Chaowakul V, Bhuripanyo K, Likittanasombat K, et al. Arrhythmogenic marker for the sudden unexplained death syndrome in Thai men. Circulation. 1997;96:2595-600.
6. Thamaree S, Sunsaneewitayakul B. Clinical characteristic and clinical course of aborted sudden cardiac death patients with structurally normal heart in King Chulalongkorn Memorial Hospital. J Med Assoc Thai. 2013;96:272-9.
7. Brugada J, Brugada R, Antzelevitch C, Towbin J, Nademanee K, Brugada P. Long-term follow up of individuals with the electrocardiographic pattern of right bundle branch block and ST-segment elevation in precordial leads V1 to V3. Circulation. 2002;105:73-8.
8. Eckardt L, Probst V, Smits JPP, Bahr ES, Wolpert C, Schimpf R. Long-term prognosis of individuals with right precordial ST-segment-elevation Brugada syndrome. Circulation. 2005; 111:257-63.
9. Priori SG, Napolitano C, Gasparini M, Pappone C, Della bella P, Giordano U. Natural history of Brugada syndrome. Insights for risk stratification and management. Circulation. 2002;105: 1342-7.
10. Priori SG, Gasparini M, Napolitano C, Della Bella P, Ottonelli AG, Sassone B. Risk stratification in Brugada syndrome: results of the PRELUDE registry. J Am Coll Cardiol. 2012;59:37-45.
11. Makarawate P, Tianchetsada C, Sahasthas D, Wongvipaporn C. Clinical outcomes of post cardiac arrest survival patients receiving automatic implantable cardioverter defibrillator implantation at Srinagarind hospital and Queen Sirikit heart center of the northeast Khon Kaen university. Srinagarind Med J. 2013;28:214-9
12. Bottoni N, Quartieri F, Lolli G, Lori M, Manari A, Menozzi C. Sudden death in a patient with idiopathic right ventricular outflow tract arrhythmia. J Cardiovasc Med. 2009;10:801-3.
13. Noda T, Shimizu W, Taguchi A, Aiba T, Satomi K, Suyama K, et al. Malignant entity of idiopathic ventricular fibrillation and polymorphic ventricular tachycardia initiated by premature extrasystoles originating from the right ventricular outflow tract. J Am Coll Cardiol. 2005;46:1288-94.
14. Nademanee K, Veerakul G, Mower M, Likittanasombat K, Krittayapong R, Bhuripanyo K, et al. Defibrillator versus B-blockers for unexplained death in Thailand (DEBUT). Circulation. 2003;107:2221-6.
15. Greene H, DiMarco J, Kudenchuk P, Scheinman M, Tang A, Reiter M, et al. Comparison of monophasic and biphasic defibrillation pulse waveforms for transthoracic cardioversion. Am J Cardiol. 1995;75:1135-9.
16. Dalzell G, Cunningham S, Anderson J, Adgey A. Electrode pad size, transthoracic impedance and success of external ventricular defibrillation. Am J Cardiol. 1989;64:741-4.
17. Priori S, Wilde A, Horie M, Cho Y, Behr E, Berul C, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Heart Rhythm. 2013;10:1932-63.
18. Al-Khatib S, Stevenson W, Ackerman M, Bryant W, Callans D, Curtis A, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Circulation. 2018;138:e272-391.
19. Zeppenfeld K, Hansen J, Riva M, Winkel B, Behr E, Blom N, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022;43:3997-4126.
20. Juang J, Horie M. Genetics of Brugada syndrome. J Arrhythm 2016;32:418-25.
21. Alings M, Wilde A. Brugada syndrome: clinical data and suggested pathophysiological mechanism. Circulation. 1999;99: 666-73.