Brugada electrocardiograms and Brugada Syndrome in Brunei Darussalam

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ABSTRACT

Introduction: Patients with Brugada syndrome have structurally normal hearts but are susceptible to ventricular tachyarrhythmia and sudden cardiac death. Brugada syndrome is divided into three types based on the electrocardiograms (ECGs) changes and clinical symptoms. This study reviews the clinical profile of patients with Brugada ECGs and Brugada syndrome seen in a tertiary referral centre. **Materials and Methods:** All patients who attended the Cardiology Unit of RIPAS hospital between March 2006 and February 2011, and found to have Brugada electrocardiograms (ECGs) were included in the study. The clinical and follow-up data of these patients were obtained through detailed medical records review. Asymptomatic patients with intermittent Brugada Type I ECG and Brugada Type II or III ECG underwent provocative testing with oral flecainide, a class 1c antiarrhythmic. Symptomatic patients referred to patients with aborted sudden death or syncope at time of diagnosis and underwent electrophysiological study (EPS). **Results:** There were 24 patients (mean age of 42.2 ± 11.1 years, range 29 to 59 years) were identified during the study period with majority male (n=19, 79%) and Malay (n=17, 70.8%) population. Seven (19.2%) patients had Brugada Type I, eight (33.3%) Type II and nine (37.5%) Type III changes. Seven patients presented with symptoms but four (16.7%) fulfilled the criteria for Brugada Syndrome, giving an estimated prevalence of 1 per 100,000 population. Symptoms were common in those with Type I changes and none in those with Type II changes. Fleccainide were done in 21 patients and was positive in 10 (47.6%), again mostly in those with Type I changes. EPS were done in eight patients (Type I changes, n=6 and Type II, n=2). Two patients had induced VF and VT respectively, all with Type I changes. The remaining four had no inducible changes. ICD were implanted in four patients all, with positive EPS studies. There were no death recorded during the study period. **Conclusions:** Brugada ECGs and Brugada Syndrome are seen in approximately 1 per 100,000 population affecting the different racial and ethnic groups. However, it is likely to be under-recognised and underestimated given that most are patients asymptomatic and detected incidentally.

Keywords: Arrhythmia, Brugada syndrome, sudden cardiac death, tachyarrhythmia

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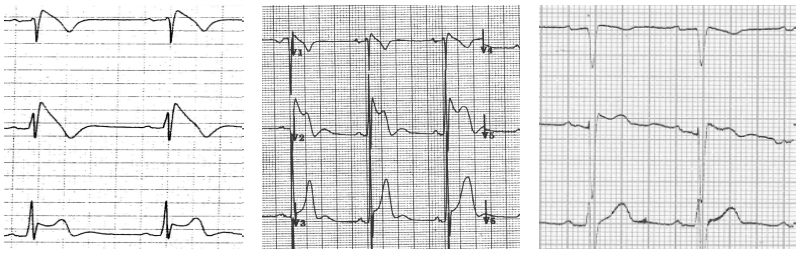
INTRODUCTION

Brugada syndrome is a cardiac disorder that is characterised by elevation of the ST-segment in the right precordial leads (V1 to V3) of the electrocardiogram (ECG). These patients have

Table 1: Types of Brugada and the electrocardiogram changes.

	Type I	**Type II**	**Type III**
J-wave amplitude	≥ 2 mm	≥ 2 mm	≥ 2 mm
T-wave	Negative	Positive or biphasic	Positive
ST-T configurations	Coved type	Saddle back	Saddle back
ST segment (terminal portion)	Gradual descending	Elevated ≥ 1 mm	Elevated ≤ 1 mm

Figs. 1: Type I, Type II and Type III Brugada ECG changes.



Type I **Type II** **Type III**

have structurally normal hearts but are susceptible to ventricular tachyarrhythmia and sudden cardiac death (SCD). The ECG changes of Brugada Syndrome were known among survivors of sudden cardiac arrests for a long time but were only first described in 1989. However, it was only in 1992 that it was recognised as a distinct entity by the Brugada brothers and as an important cause of SCD. Brugada syndrome is divided into three types based on the ECG changes and clinical symptoms (Table 1 and Figure 1).

Brugada Syndrome is familial and occurs via an autosomal mode of transmission. It has been linked to mutations in the SCN5A (sodium channel) gene which account for 18% to 30% of Brugada Syndrome cases. SCN5A gene encodes the alpha subunit of the cardiac sodium channel.

The incidence of Brugada Syndrome ranges between five and 66 per 10,000, and it is endemic in Southeast Asia. It is the most important cause of SCD in young men in Thailand and Laos. There is a male predominance (8:1 ratio of male: female), and arrhythmic events typically occur at about 40 years. Ventricular fibrillation and SCD usually occur at rest and at night. ECG changes constitute the signature of Brugada Syndrome with Type I being the most diagnostic. ECG changes are often dynamic or concealed, and can be unmasked by fever, sodium channel blockers, vagotonic agents, alpha-adrenergic agonists, beta-adrenergic blockers, tricyclic or tetracyclic antidepressants, glucose and insulin, hyperkalaemia, hypokalaemia, alcohol and cocaine toxicity. [1, 2]

The clinical data of patients with Brugada ECG and Brugada syndrome are available from many parts of the world. However, there is no data available on our patients. This study reports the clinical profile of patients with Brugada ECGs and Brugada syndrome seen in the Brunei Darussalam, a developing southeast Asian nation.

MATERIALS and METHODS

All patients who attended the Division of Cardiology, Department of Medicine of RIPAS Hospital, a tertiary referral centre either as inpatient or outpatient between March 2006 and February 2011, and found to have Brugada-like ECGs were included in this study.

All patients with suspected ECG changes of Brugada Syndrome underwent detailed cardiac evaluation that included: detailed history (clinical symptoms, family history of Brugada Syndrome and SCD, prior cardiac history and risk factors), physical examinations, laboratory investigations that included cardiac enzymes, chest radiograph and echocardiograms. Provocation tests and electrophysiological studies (EPS) were carried out for selected patients. Prior to provocation tests, all the patients underwent echocardiograms, exercise stress tests, and 24-hour ambulatory Holter monitoring.

Asymptomatic patients with intermittent Brugada Type I ECG and Brugada Type II or III ECG underwent provocative testing with oral flecainide, a class 1c anti-arrhythmic agent under continuous haemodynamic and ECG monitoring in the Coronary Care Unit. The test was considered positive when there was conversion of Brugada Type II or III ECG changes to Brugada Type 1 ECG. Symptomatic patients referred with aborted SCD or syncope at time of diagnosis underwent EPS.

Data on clinical and follow-up were obtained through review of medical records and telephone interviews.

RESULTS

There was a male predominance (19 males, 79%) and the ethnic breakdown were 17 (70.8%) Malay, one (4.2%) Chinese, three (12.5%) Ibans, two (8.3%) Dusuns, and one Filipino.

There were seven patients with Brugada Type I (29.2%), eight Type II (33.3%) and nine Type III (37.5%) ECG changes respectively.

Seven patients presented with symptoms; palpitations in three, chest pain in three, syncope in two and cardiac arrest in one. Two asymptomatic patients had fever during their initial presentations possibly triggering the Brugada changes. Symptoms were common in those with Type I changes and none in those with Type II changes.

Fleccainide were done in 21 patients and was positive in 10 (47.6%), again mostly in those with Type I changes.

EPS were done in eight patients (Type I changes, n=6 and Type II, n=2). Two patients had induced VF and VT respectively, all with Type I changes. The remaining four had no inducible changes. ICD were implanted in four patients all, with positive EPS studies.

Overall, four patients (16.7%, mean age: 33.5 ± 10.8 years, 2 men) fulfilled the criteria for Brugada Syndrome, giving an estimated prevalence of 1 per 100,000 population. The remaining 20 patients with Brugada ECG changes (83.3%) were slightly younger with a mean age of 44 ± 10.5 years with a male preponderance.

The summary of all studied patients is shown in Table 2.

Table 2: Summary of all the patients with Brugada Like ECG and Brugada Syndrome.

Case	Age (yr)	Gender	Race	FHx SCD	Symptoms	Brugada type	Flecainide Challenge	EPS	ICD
1	29	M	Malay	No	Palpitations	Type I (Intermittent)	Positive	Yes/VF	Yes
2	24	F	Malay	Yes	Palpitations/ Syncope	Type I (Intermittent)	Not done	Yes/VF	Yes
3	32	M	Chinese	No	Palpitations/ Syncope	Type I (Fixed)	Not done	Yes/VT	Yes
4	37	M	Malay	No	Asymptomatic	Type I (Fever)	Positive	Yes/ non-inducible	No
5	26	F	Malay	No	Asymptomatic	Type I (Fever)	Positive	Yes/ non-inducible	No
6	49	F	Dusun	No	Survivor of cardiac arrest	Type I (Fever)	Positive	Yes/VF	Yes
7	59	F	Malay	No	Asymptomatic	Type I	Positive	No	No
8	37	M	Malay	No	Asymptomatic	Type II	Negative	No	No
9	42	M	Malay	No	Asymptomatic	Type II	Negative	No	No
10	35	M	Iban	No	Asymptomatic	Type II	Negative	No	No
11	46	M	Filipino	Yes	Asymptomatic	Type II	Negative	Unknown	Unknown
12	49	M	Malay	No	Asymptomatic	Type II	Refused	No	No
13	49	M	Malay	No	Asymptomatic	Type II	Positive	No	No
14	52	M	Dusun	No	Asymptomatic	Type II	Positive	No	No
15	58	M	Malay	No	Asymptomatic	Type II	Positive	No	No
16	36	M	Malay	No	Chest pain	Type III	Negative	No	No
17	64	M	Malay	No	Chest pain	Type III	Negative	No	No
18	41	M	Malay	No	Chest pain	Type III	Positive	Yes/ non-inducible	No
19	46	M	Malay	No	Asymptomatic	Type III	Negative	No	No
20	33	M	Malay	No	Asymptomatic	Type III	Negative	No	No
21	37	M	Iban	No	Asymptomatic	Type III	Negative	No	No
22	39	F	Malay	No	Asymptomatic	Type III	Negative	No	No
23	60	M	Malay	No	Asymptomatic	Type III	Positive	Yes/ non-inducible	No
24	33	M	Iban	No	Asymptomatic	Type III	Positive	No	No

Note: SCD; Sudden cardiac death, EPS; Electrophysiological study, ICD, Implantable defibrillator device, VT, Ventricular tachycardia, VF; Ventricular fibrillation

DISCUSSION

In our study, we showed that Brugada ECG changes and Brugada Syndrome is not rare in Brunei Darussalam. It affects both genders and all racial groups. The majority were asymptomatic and were detected incidentally after ECG were done for other reasons. However, the true estimate of the number of patients with Brugada-like ECGs and Brugada Syndrome in Brunei Darussalam is unknown and is likely to be under estimated given that most are asymptomatic.

In keeping with findings of previous studies from other countries, Brugada-like ECGs were more prevalent in males than in females. However the mean age (44 years) of diagnosis in our present study appeared to be slightly older than previously reported. [3, 4] The reported mean age of patients with Brugada are around fifty to sixty years.

The higher prevalence of Brugada Type II or III ECGs was similar to those found

by other studies. [5]

Brugada syndrome are patient who has clinical manifestation that had resulted in presentations. In our studies, there were four (16.7%) fulfilled the criteria for Brugada Syndrome out of the total seven patients who had symptoms. This gave an estimated prevalence of 1 per 100,000 population. The mean age of diagnosis of Brugada Syndrome was 33.5 years and this is similar to results of previous studies. In our patients, there was equal sex ratio which differed from results of other studies. This is probably due to small study sample. [4, 6]

The unmasking of a typical Brugada Type I ECG was seen in three patients during febrile state. This feature of Brugada Syndrome has been reported in several case studies. The underlying mechanism is related to the temperature dependency of the sodium channel. [7, 8]

Although provocation with oral flecainide was performed in five out of the seven patients with spontaneous Brugada Type I ECG, it is noteworthy to mention that in patients with Brugada Type I ECG, provocative drug testing is not of additional diagnostic value. The test is recommended to clarify the diagnosis in patients with Type II or III ECG. [2]

Out of the six patients who were asymptomatic and developed Brugada Type I after provocation with oral flecainide, two patients had EPS that were non-inducible for VF/VT. These patients will probably have a benign prognosis. It has been shown that asymptomatic patients with an abnormal ECG only on drug challenge have a benign clinical course. [1]

All our four symptomatic patients with Brugada Syndrome at high risk of sudden death received ICD implants as per current recommendation. [2] The Finger BS Registry showed that symptoms and spontaneous Type I ECG were predictors of arrhythmic events. The four patients who had inducible VF/VT on EPS also had spontaneous Brugada Type I ECG, and they were symptomatic in the form of syncope, palpitations and aborted sudden cardiac death implicating the development of spontaneous ventricular arrhythmias. [9]

It has been reported that inducibility of VF during EPS was an independent predictor of VF. [10] One of our Brugada Syndrome patient who had inducible VF during EPS developed an episode of VF after ICD implantation, and received an appropriate shock for VF. On the other hand, it has been reported that ICD therapy is not entirely benign [11] and this was demonstrated by one patient in the present study who received inappropriate shocks due to SVT.

In conclusion, Brugada-like ECGs and Brugada Syndrome is present in the Bruneian population involving the various racial and ethnic groups. Our number of patients is probably under-estimated of the actual number as some asymptomatic patients are yet to be diagnosed. Further studies are needed to evaluate the true prevalence and also to study in detail the characteristics and differences of Brugada Syndrome among the various racial groups and genders and also to assess the long term follow up of treated and untreated patients.

REFERENCES

1: Wilde AA, Antzelevitch C, Borggrefe M, et al. Proposed diagnostic criteria for the Brugada syndrome: consensus report. Circulation 2002; 106:2514-9.

2: Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. Circulation 2005; 111:659-70.

3: 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.

4: Priori SG, Napolitano C, Gasparini M, et al. Natural history of Brugada syndrome: insights for risk stratification and management. Circulation 2002; 105:1342-7.

5: Furuhashi M, Uno K, Tsuchihashi K, et al. Prevalence of asymptomatic St segment elevation in right precordial leads with right bundle branch block (Brugada-type ST shift) among general Japanese population. Heart 2001; 86:161-6.

6: Eckardt L, Probst V, Smiths JP, et al. Long-term prognosis of individuals with right precordial ST-segment elevation Brugada syndrome. Circulation 2005; 111:257-63.

7: Antzelevitch C, Brugada R. Fever and the Brugada syndrome. Pacing Clin Electrophysiol 2002; 25:1537-9.

8: Dumaine R, Towbin JA, Brugada P, et al. Ionic mechanisms responsible for the electrocardiographic phenotype of the Brugada syndrome are temperature dependent. Circ Res 1999; 85:803-9.

9: Ouali S, Boughzela E, et al. Clinical and Electrophysiological Profile of Brugada syndrome in the Tunisian population. PACE; 34;47-53

10: Brugada P, Brugada R, Brugada J. Patients with an asymptomatic electrophysiological testing. Circulation 2005; 112:279-85.

11: Sidik NP, Quay CN, Loh CN, Chen LY. Prevalence of Brugada sign and syndrome in patients presenting with arrhythmic symptoms at a Heart Rhythm Clinic in Singapore. Europace 2009; 11:650-6.