Attendance-related Healthcare Resource Utilisation and Costs in Patients With Brugada Syndrome in Hong Kong: A Retrospective Cohort Study

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Abstract: Understanding health care resource utilisation and its associated costs are important for identifying areas of improvement regarding resource allocations. However, there is limited research exploring this issue in the setting of Brugada syndrome (BrS).This was a retrospective territory-wide study of BrS patients from Hong Kong. Healthcare resource utilisation for accident and emergency (A&E), inpatient and specialist outpatient attendances were

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analyzed over a 19-year period, with their associated costs presented in US dollars. A total of 507 BrS patients with a mean presentation age of 49.9 ± 16.3 years old were included. Of these, 384 patients displayed spontaneous type 1 electrocardiographic (ECG) Brugada pattern and 77 patients had presented with ventricular tachycardia/ventricular fibrillation (VT/VF). At the individual patient level, the median annualized costs were $110 (52-224) at the (A&E) setting, $6812 (1982-32414) at the inpatient setting and $557 (326-1001) for specialist outpatient attendances. Patients with initial VT/VF presentation had overall greater costs in inpatient ($20161 [9147-189215] vs $5290 [1613-24937],P < 0.0001) and specialist outpatient setting ($776 [438-1076] vs $542 [293-972], P = 0.015) compared to those who did not present VT. In addition, patients without Type 1 ECG pattern had greater median costs in the specialist outpatient setting ($7036 [3136-14378] vs $4895 [2409-10554],p=0.019). There is a greater health care demand in the inpatient and specialist outpatient settings for BrS patients. The most expensive attendance type was inpatient setting stay at $6812 per year. The total median annualized cost of BrS patients without VT/VF presentation was 78% lower compared to patients with VT/VF presentation. (Curr Probl Cardiol 2023;48:101513.)

Introduction

Cardiac channelopathies refer to a heterogeneous group of disorders caused by a malfunction of ion channels in the structurally normal heart, leading to increased risks of ventricular tachycardia (VT), fibrillation (VF) and thus sudden cardiac death (SCD).[1,2] In recent years, there has been an increased exploration of a relatively rarer type of cardiac channelopathy known as Brugada syndrome (BrS), which is particularly prevalent in Asia.[3,4] The diagnosis of BrS requires the presence of a spontaneous or drug-induced electrocardiographic pattern characterised by coved-shaped ST-segment elevation in the right precordial leads,[5] which are due to a combination of depolarisation and repolarisation abnormalities.[6] Common clinical manifestations of BrS include syncope, aborted SCD and palpitations.[7] Its main treatment is the use of

an implantable cardioverter defibrillator (ICD),[8] which delivers electrical shocks to abort arrhythmic events.[9] Alternatively, pharmacological agents such as quinidine, disopyramide and β-adrenergic agents have shown effective in the prevention or suppression of arrhythmic events.[10]

Despite recent scientific advances, there has been limited exploration of the worldwide prevalence and economic burden of BrS patients, which may also differ between ethnicities and geographical regions.[11] Due to inadequate data to perform the analysis as well as few proactive measures to target unnecessary attendances or utilisation, this poses a major obstacle to maximizing the system's potential in delivering cost-effective medical care. Specifically on BrS, only two studies have been published on the cost-effectiveness of ICD interventions,[12,13] but no further analyses on the overall health care resource utilisation and burden for the wider BrS cohorts. Moreover, health care resource utilisation and related costs differ significantly even within the BrS population, as the affected patients are at different levels of arrhythmic risk. Not only is the diagnosis process challenging as the majority of patients with BrS are asymptomatic,[14] but active surveillance, diagnostic testing, arrhythmia risk prediction and subsequent management can be costly. Accurate diagnosis and careful resource utilisation are vital not only for prompt treatment, but it allows physicians to eliminate redundancy in the health care organisation. Hence, this entails the need for an integrated, in-depth investigation of the health care resource utilisation of BrS patients. Therefore, the present paper aims to investigate the attendance-related health care utilization and its costs for BrS patients from Hong Kong, China.

Methods

Study Population

This retrospective study was approved by The Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee. The cohort consists of patients diagnosed with BrS between January 1st, 1997 to December 31st, 2020 in public hospitals or private clinics managed by the Hong Kong Hospital Authority. This cohort has been used previously by our team for identifying the different risk factors of arrhythmic events[15] as well as the development of predictive models for risk stratification.[16] The identification of patients and attendance information were obtained from Clinical Data Analysis and Reporting System (CDARS), a territory-wide database that centralizes patient information from 43 local hospitals and their associated outpatient and

ambulatory care facilities. This system has been utilized previously by our team for conducting clinical and epidemiological studies for the other ion channelopathies of long QT syndrome[17] and catecholaminergic polymorphic ventricular tachycardia (CPVT).[18]

The diagnosis of BrS was made initially by case physicians. However, this was further confirmed by G.T. and N.S.M. through an assessment of documented electrocardiograms (ECGs), case notes, genetic reports and diagnostic test results in accordance with the 2017 Expert Consensus Statement.[19] Diagnosis of BrS was established based on electrocardiographic criteria, family history, clinical symptoms and genetic tests by the participating institution at the time of entry.[20]

Clinical and Electrocardiographic Data Collection

The following baseline clinical data were extracted from the electronic health records:[1] sex;[2] age of first characteristic ECG presentation and last follow-up;.[3] follow-up duration;[4] syncope manifestation and its frequency;[5] family history of SCD and the specific ion channelopathy;[6] performance of electrophysiological study (EPS), 24-hours Holter study, ion channelopathy-specific genetic testing, and the respective results;[7] presentation of sustained VT and its frequency;[8] presence of other arrhythmias;[9] ECG performance;[10] implantation of ICD;[11] period between the initial presentation of characteristic ECG and the first post-diagnosis VT/VF episode;[12] initial disease manifestation (asymptomatic, syncope, VT/VF);[13] occurrence, cause and age of death. Other arrhythmias include sick sinus syndrome, atrial tachyarrhythmias, bradycardia, atrioventricular block and supraventricular tachyarrhythmias. The baseline ECG is the documented ECG recorded at or the earliest after the initial characteristic ECG presentation.

Health Care Utilisation and Cost Analyses

Health care resource utilization for accident and emergency (A&E), inpatient and outpatient attendances were analyzed over 19 years (2001 to2019). The attendance costs were calculated using unit costs published by the local government. These costs were annualized in Hong Kong Dollars and later converted to US Dollars.

Statistical Analysis

Fisher's exact test was used to compare categorical variables and was represented as a total number and percentage. For baseline

characteristics, continuous and discrete variables were expressed as a mean and standard deviation (SD) value, which was compared by using the t-test. For utilization and costs, values were presented as median (interquartile range-IQR) and compared using. Mann-Whitney-Wilcoxon Test was performed to verify the statistical significance of subgroup analysis. Statistical significance was defined as $P < 0.05$. All statistical analysis was performed using R Studio (Version: 1.3.1073).

Results

Baseline Characteristics and Demographics

A total of 507 BrS patients (468 [92.3%] males and 39 ([7.7%] females) were included. The mean presentation age of this cohort was 49.9 ± 16.3 years old. 384 (75.7%) patients displayed the spontaneous type 1 ECG BrS pattern. A family history of BrS and SCD was found in 15 (3.0%) patients and 41 (8.1%) patients, respectively. Of the 50 (9.9%) patients who received a genetic test, 16 (3.2%) patients returned positive. The cohort was further stratified based on the occurrence of VT/VF as the initial disease presentation, which was present in 77 BrS patients. No statistical significance was identified when the two groups were compared based on sex, type 1 BrS pattern, family history of BrS, family history of SCD, the performance of sodium channel blocker challenge and its positive findings, Holter study and the arrhythmia found, positive genetic test, treadmill test, baseline ECG markers and the presentation of syncope initially. Regarding the baseline ECG characteristics, patients with presentation of VT/VF demonstrated greater QRS interval (112.3 ± 25.5 vs 105.2 ± 22.0), QTc (429.5 ± 42.9 vs 414.2 ± 30.5) and QT interval (375.9 ± 48.0 vs 367.8 ± 41.2) but lower T axis (48.2 ± 28.2 vs 55.5 ± 25.5) compared to patients without VT/VF presentation. The baseline characteristics of this cohort, including a comparison of BrS patients with and without VT/VF presentation, are summarized in Table 1.

Health Care Resource Utilization and Costs

The total number of attendances for A&E, inpatient and specialist outpatient settings in the cohort were 5094, 4074 and 28,493 respectively. At the single patient level, the median number of attendances for A&E, inpatient, inpatient length of stay and special outpatient settings were 6 (3-12), 5 (2-10), 90 days(25-378) and 38 (18-76), respectively. These corresponded to median costs of $949 (474-1818)

TABLE 1. Baseline characteristics of the cohort

Variables	BrS patients (n = 507)	BrS patients with VT/VF presentation (n = 77)	BrS patients without VT/VF presentation (n = 430)	P-*value*
Clinical characteristics				
Female	39 (7.7)	2 (2.6)	37 (8.6)	0.0999
Presentation age (years)	49.9 ± 16.3	47.3 ± 17.2	50.4 ± 16.1	<**0.0001**
Current age	57.1 ± 16.3	55.5 ± 17.4	57.4 ± 16.1	<**0.0001**
Initial type 1 BrS ECG pattern	315 (62.1)	48 (62.3)	267 (62.1)	**0.0233**
Type 1 BrS ECG pattern	384 (75.7)	53 (68.8)	331 (77.0)	0.148
Family history of BrS	15 (3.0)	2 (2.6)	13 (3.0)	1
Family history of sudden cardiac death	41 (8.1)	6 (7.8)	35 (8.1)	1
Syncope	220 (43.4)	55 (71.4)	165 (38.4)	<**0.0001**
VT/VF	77 (15.2)	77 (100)	0 (0)	<**0.0001**
Symptomatic	242 (47.7)	77 (100)	165 (38.4)	<**0.0001**
Sodium channel blocker challenge	218 (43.0)	38 (49.4)	180 (41.9)	0.261
Positive sodium channel blocker challenge	192 (37.9)	30 (39.0)	162 (37.7)	0.899
EPS	110 (21.7)	27 (35.1)	83 (19.3)	**0.00393**
Arrhythmia-induced in EPS	75 (14.8)	23 (29.9)	52 (12.1)	**0.000183**
Implantable cardioverter defibrillator	134 (26.4)	62 (80.5)	72 (16.7)	<**0.0001**
Holter study	137 (27.0)	19 (24.7)	118 (27.4)	0.677
Arrhythmia on Holter study	61 (12.0)	11 (14.3)	50 (11.6)	0.567
Atrial arrhythmia	79 (15.6)	22 (28.6)	57 (13.3)	**0.00175**
Genetic test	50 (9.9)	13 (16.9)	37 (8.6)	**0.0359**
Positive genetic test	16 (3.2)	4 (5.2)	12 (2.8)	0.283
Performance of treadmill test	60 (11.8)	6 (7.8)	54 (12.6)	0.337
Echocardiogram	233 (46.0)	43 (55.8)	190 (44.2)	0.0633
EEG	57 (11.2)	21 (27.3)	36 (8.4)	<**0.0001**
Abnormalities on EEG	16 (3.2)	11 (14.3)	5 (1.2)	<**0.0001**
Initial asymptomatic	306 (60.4)	11 (14.3)	295 (68.6)	<**0.0001**
Initial syncope	159 (31.4)	24 (31.2)	135 (31.4)	1
Initial VT/VF	42 (8.3)	42 (54.5)	0 (0)	<**0.0001**
Baseline ECG characteristics				
Heart rate	80.9 ± 20.0	84.6 ± 24.0	80.2 ± 19.1	<**0.0001**
P-wave duration	114.7 ± 18.2	119.5 ± 14.7	113.8 ± 18.7	<**0.0001**
PR interval	169.4 ± 29.0	170.1 ± 29.3	169.3 ± 29.0	<**0.0001**
QRS interval	106.4 ± 22.7	112.3 ± 25.5	105.2 ± 22.0	<**0.0001**
QTc interval	416.6 ± 33.2	429.5 ± 42.9	414.2 ± 30.5	<**0.0001**
QT interval	369.0 ± 42.4	375.9 ± 48.0	367.8 ± 41.2	<**0.0001**
P-wave axis	61.2 ± 22.3	59.2 ± 22.8	61.5 ± 22.2	<**0.0001**
QRS axis	58.5 ± 39.3	65.7 ± 53.4	57.1 ± 36.1	<**0.0001**
T axis	54.4 ± 26.0	48.2 ± 28.2	55.5 ± 25.5	<**0.0001**
R wave in lead V5	1.5 ± 0.6	1.3 ± 0.6	1.6 ± 0.6	<**0.0001**
S wave in lead V1	0.6 ± 0.3	0.5 ± 0.3	0.6 ± 0.4	<**0.0001**
1st degree atrioventricular block	54 (10.7)	11 (14.3)	43[10]	0.314
Interventricular delay	146 (28.8)	34 (44.2)	112 (26.0)	**0.00241**

Abbreviations: BrS: Brugada syndrome; VT/VF: ventricular tachycardia/ fibrillation; EPS: electrophysiological study; EEG: electroencephalogram; QTc: corrected QT.
*P< 0.001 significant
Bold values indicate P<0.05.

TABLE 2. All cause BrS health care utilisation and costs. Median and IQR values are presented. Costs are shown in US dollars.

Attendance type	Attendances	Costs ($)	Annualised costs ($/yr)
Accident & Emergency	6 (3-12)	949 (474-1818)	110 (52-224)
Inpatient	5 (2-10), 90 (25-378) days	58724 (16279-247625)	6812 (1982-32414)
Special Outpatient	38 (18-76)	5353 (2524-11089)	557 (326-1001)

for A&E, $58724 (16279-247625) for inpatient setting and $5353 (2524-11089) for special outpatient setting. To corroborate, the median annualized costs were $110 (52-224) for A&E, $6812 (1982-32414) for inpatient setting and $557 (326-1001) for special outpatient setting (Table 2).

Patients with initial VT/VF presentation had significantly higher inpatient (8 [5-15] vs 4 [2-9], $P < 0.0001$) and specialist outpatient attendances (52 [26-98] vs 34 [17-71], $P = 0.003$), as well as longer inpatient-stay duration (391 days [157-1231] vs 71 days [19-280], $P < 0.0001$) compared to patients without VT/VF presentation. While there was almost no difference in costs in A&E setting for both groups, the annualized costs for patients who presented with VT/VF were significantly higher in the inpatient ($20161 [9147-189215] vs $5290 [1613-24937], $P < 0.0001$) and specialist outpatient setting ($776 [438-1076] vs $542 [293-972], $P=0.015$). The attendance and cost comparison between patients with and without VT/VF presentation is shown in Supplementary Table 1. To corroborate, patients who displayed non-type 1 BrS ECG pattern demonstrated higher number of total attendances (58 [27-119] vs 44 [22-92], $P = 0.052$) and higher annualized costs in the inpatient ($7646 [1375-27356] vs $6659 [2131-33877], $P = 0.549$) and specialist outpatient setting ($691 [373-1132] vs $542 [307-940], $P = 0.023$) in comparison to patients who displayed type 1 BrS ECG pattern (Supplementary Table 2).

Discussion

This is the first territory-wide cohort study examining the health care utilization and its related costs in BrS. Several major findings were identified in this study.[1] BrS patients require more services from inpatient and specialist outpatient settings.[2] The most expensive attendance type was inpatient stay at $6812 per year, followed by outpatient clinics at $557

per year and A&E at $110 per year;[3] The total median annualized cost of BrS patients without presentation of VT/VF was 78% less compared to their counterparts. In addition, this study also provided supportive evidence for specific ECG parameters and clinical characteristics that are associated with a higher risk for VT/VF amongst BrS patients.

There is well-established evidence proposing the association between BrS and increased risks of VT/VF and SCD.[21,22] However, the optimal management of BrS patients remains a challenge in the health care setting with difficulties in accurate risk stratification.[23,24] The use of an ICD has shown to be effective in averting the occurrence of SCD for BrS patients.[25] Nonetheless, not only does this technology bear short and long-term medical risks, but it is also a high-maintenance, costly intervention.[26] BrS patients with recovered SCD and severe VT/VF history are classified as high risk and require an ICD implantation as secondary prevention.[27,28] For these patients, it is estimated that the recurrence rate of arrhythmic events is approximately 48% across 10 years without timely intervention.[29] While some patients at high risk are eligible for ICD implantation, the clinical guidelines surrounding the recommendation of ICDs for asymptomatic BrS patients remain ambiguous.[13] Furthermore, other forms of therapy catheter ablation though effective for BrS patients with recurrent VT/VF episodes,[30] were found to be a cost-ineffective option compared to anti-arrhythmic drug therapies for other cardiac diseases.[31] These options are less likely to be prioritised for patients without a history of VT/VF or other symptoms. Hence, this may explain why the economic burden of patients who displayed pre-existing VT/VF was significantly higher compared to those without pre-existing VT/VF.

The paucity of cost analysis evidence is further exacerbated by the rarity of BrS in Asian countries, therefore posing an issue of practicality for obtaining clinical trial data. Current research on BrS originates primarily from community-based studies of young people in Japan.[32] Nakano *et al.* found that Asian patients are susceptible to a higher mortality rate from sudden lethal arrhythmias and BrS remains one of the leading causes of SCD.[33]. Compared to research studies conducted in other Asian countries, the prevalence of BrS in Hong Kong is relatively low. Tse *et al.* found P-wave duration, PR interval and QT interval to be significant predictors of atrial fibrillation in a cohort of 275 BrS patients from Hong Kong.[34] Lee *et al.* further verified the predictive value of ECG markers and clinical characteristics for BrS risk stratification in a study consisting of 516 patients from Hong Kong.[35] From other geographical regions, there have been published studies on the cost-effectiveness of ICDs,[12] and the comparative effectiveness of ICDs for asymptomatic BrS

patients.[13] In the future, the findings of this study may extrapolate towards the development of a most cost-effective, patient-centred resource utilization model. Resultantly, proper resource utilization can ensure the patient achieves the optimum health outcome while reducing the financial burden on the patient.

Conclusion

The health care resource utilization and costs of BrS patients in Hong Kong were studied. The findings of this study can provide crucial insight into improving the management and health care resource allocation surrounding BrS.

Author Contributions

SL, CTC—data acquisition, statistical analysis, cost analysis, manuscript drafting, manuscript revision OHIC, TTLL, DR, KJ, WTW, SHC, NSM, TL, GT—study conception, manuscript drafting, manuscript revision

Data availability

The dataset generated from this study is available upon request to the corresponding author.

The anonymized dataset for this study is available from the corresponding author upon request.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cpcardiol.2022.101513.

REFERENCES

1. Fernández-Falgueras A, Sarquella-Brugada G, Brugada J, et al. Cardiac Channelopathies and sudden death: ecent Clinical and Genetic Advances. *Biology (Basel)* 2017:6.
2. Napolitano C, Bloise R, Monteforte N, et al. Sudden Cardiac death and Genetic Ion Channelopathies. *Circulation* 2012;125:20272034.
3. Vutthikraivit W, Rattanawong P, Putthapiban P, et al. Worldwide prevalence of Brugada Syndrome: A systematic review and Meta-Analysis. *Acta Cardiol Sin* 2018;34:267277.
4. Rattanawong P, Ngarmukos T, Chung Eugene H, et al. Prevalence of Brugada ECG pattern in Thailand from a population-based cohort study. *J Am Coll Cardiol* 2017;69:1355–6.
5. Sarquella-Brugada G, Campuzano O, Arbelo E, et al. Brugada syndrome: clinical and genetic findings. *Genet Med* 2016;18:3–12.
6. Brugada R, Campuzano O, Sarquella-Brugada G, et al. Brugada syndrome. *Methodist Debakey Cardiovasc J* 2014;10:25–8.
7. Krahn AD, Behr ER, Hamilton R, et al. Brugada Syndrome. *JACC Clin Electrophysiol* 2022;8:386–405.
8. Lee S, Li KHC, Zhou J, et al. Outcomes in Brugada Syndrome patients with implantable Cardioverter-Defibrillators: insights from the SGLT2 Registry. *Front Physiol* 2020;11:204.
9. Conte G, Sieira J, Ciconte G, et al. Implantable cardioverter-defibrillator therapy in Brugada syndrome: a 20-year single-center experience. *J Am Coll Cardiol* 2015;65:879–88.
10. Argenziano M, Antzelevitch C. Recent advances in the treatment of Brugada syndrome. *Expert Rev Cardiovasc Ther* 2018;16:387–404.
11. Chahine M, Fontaine JM, Boutjdir M. Racial disparities in Ion Channelopathies and inherited Cardiovascular Diseases associated with sudden Cardiac Death. *J Am Heart Assoc* 2022;11:e023446.
12. Wang K, Yamauchi K, Li P, et al. Cost-effectiveness of implantable cardioverter-defibrillators in Brugada syndrome treatment. *J Med Syst* 2008;32:51–7.
13. Khurshid S, Chen W, Bode WD, et al. Comparative Effectiveness of Implantable Defibrillators for Asymptomatic Brugada Syndrome: a decision-Analytic Model. *J Am Heart Assoc* 2021;10:e021144.
14. Letsas KP, Asvestas D, Baranchuk A, et al. Prognosis, risk stratification, and management of asymptomatic individuals with Brugada syndrome: a systematic review. *Pacing Clin Electrophysiol* 2017;40:1332–45.
15. Lee S, Wong WT, Wong ICK, et al. Ventricular Tachyarrhythmiarisk in paediatric/young vs adult Brugada Syndrome patients: a Territory-Wide study. *Front Cardiovasc Med* 2021;8:671666.
16. Lee S, Zhou J, Chung CT, et al. Comparing the performance of published risk scores in Brugada syndrome: a multi-center cohort study. *Curr Probl Cardiol* 2022:101381.
17. Lee S, Zhou J, Jeevaratnam K, et al. Paediatric/young vs adult patients with long QT syndrome. *Open Heart* 2021;8.

18. Chung CT, Lee S, Zhou J, et al. Clinical characteristics, Genetic basis and Healthcare Resource utilisation and costs in patients with Catecholaminergic Polymorphic Ventricular Tachycardia: a Retrospective cohort study. *RCM* 2022:23.
19. Antzelevitch C, Yan GX, Ackerman MJ, et al. J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge. *Europace* 2017;19:665–94.
20. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. *Heart Rhythm* 2013;10:1932–63.
21. Malik BR, Ali Rudwan AM, Abdelghani MS, et al. Brugada Syndrome:cClinical features, risk stratification, and management. *Heart Views* 2020;21:88–96.
22. Aziz HM, Zarzecki MP, Garcia-Zamora S, et al. Pathogenesis and Management of Brugada Syndrome: recent advances and protocol for Umbrella Reviews of Meta-Analyses in major Arrhythmic events risk stratification. *J Clin Med* 2022:11.
23. Chung CT, Bazoukis G, Radford D, et al. Predictive risk models for forecasting arrhythmic outcomes in Brugada syndrome: a focused review. *J Electrocardiol* 2022;72:28–34.
24. Letsas KP, Vlachos K, Conte G, et al. Right ventricular outflow tract electroanatomical abnormalities in asymptomatic and high-risk symptomatic patients with Brugada syndrome: Evidence for a new risk stratification tool? *J Cardiovasc Electrophysiol* 2021;32:2997–3007.
25. El-Battrawy I, Roterberg G, Liebe V, et al. Implantable cardioverter-defibrillator in Brugada syndrome: long-term follow-up. *Clin Cardiol* 2019;42:958–65.
26. Sears SF, Rosman L, Sasaki S, et al. Defibrillator shocks and their effect on objective and subjective patient outcomes: results of the PainFree SST clinical trial. *Heart Rhythm* 2018;15:734–40.
27. Sacher F, Probst V, Maury P, et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study-part 2. *Circulation* 2013;128:1739–47.
28. Li KHC, Lee S, Yin C, et al. Brugada syndrome: a comprehensive review of pathophysiological mechanisms and risk stratification strategies. *Int J Cardiol Heart Vasc* 2020;26:100468.
29. Darar C, Mohammed EA, Mohammed B, et al. Risk stratification of sudden cardiac death in Brugada syndrome: an updated review of literature. *Egypt Heart J* 2022;74:25.
30. Chokesuwattanaskul R, Nademanee K. Role of Catheter Ablation for Ventricular Arrhythmias in Brugada Syndrome. *Curr Cardiol Rep* 2021;23:54.
31. Chen Y, Gomes M, Garcia JV, et al. Cost-effectiveness of ablation of ventricular tachycardia in ischaemic cardiomyopathy: limitations in the trial evidence base. *Open Heart* 2020;7:e001155.
32. Juang J-MJ, Chen C-YJ, Chen Y-H, et al. Prevalence and prognosis of Brugada electrocardiogram patterns in an elderly Han Chinese population: a nation-wide community-based study (HALST cohort). *Ep Europace* 2016;17:ii54–62.

33. Nakano Y, Shimizu W. Brugada Syndrome as a major cause of sudden Cardiac death in Asians. *JACC: Asia* 2022;2:412–21.
34. Tse G, Lee S, Mok NS, et al. Incidence and predictors of atrial fibrillation in a Chinese cohort of Brugada syndrome. *Int J Cardiol* 2020;314:54–7.
35. Lee S, Zhou J, Li KHC, et al. Territory-wide cohort study of Brugada syndrome in Hong Kong: predictors of long-term outcomes using random survival forests and non-negative matrix factorisation. *Open Heart* 2021;8.