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EPICARDIAL SUBSTRATE ABLATION FOR BRUGADA SYNDROME WITH FREQUENT ICD SHOCKS: SHORT AND MID-TERM OUTCOMES

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ABSTRACT

Background: While implantable cardioverter defibrillator (ICD) remains the cornerstone therapy for high-risk Brugada syndrome patients, recurrent ventricular arrhythmias and frequent ICD shocks can significantly impair their quality of life. Epicardial substrate ablation targeting abnormal electrograms has been reported as a potential therapeutic option for these patients. This study aims to evaluate the feasibility, safety and outcomes of epicardial substrate ablation in patients with Brugada syndrome experiencing recurrent ventricular arrhythmias and frequent ICD shocks.

Methods: We conducted a single-center retrospective study including patients with symptomatic type 1 Brugada syndrome who underwent ICD implantation at Hanoi Heart Hospital between 2016 and 2026. Among them, patients who experienced recurrent appropriate ICD shocks despite medical therapy and subsequently underwent epicardial catheter ablation were included. Electroanatomical mapping was performed using a three-dimensional mapping system to identify abnormal epicardial substrates. Radiofrequency ablation was delivered to eliminate these substrates. Procedural characteristics, complications, and follow-up outcomes were analyzed.

Results: 11 male patients (mean age 46.18 ± 14.43 years) underwent epicardial ablation. Successful epicardial access was achieved in all cases. The mean procedure time was 172.4 ± 12.8 minutes. The anterior RVOT was the primary ablation target in all patients, with additional lateral or inferolateral substrate identified in some cases. During a median follow-up of 39 (7–78) months, ventricular arrhythmia recurrence occurred in three patients (27.3%), and repeat ablation was required in two (18.2%). 8 patients (72.7%) remained free of ICD shocks. One patient developed pericarditis requiring pericardiocentesis, and one developed ICD infection during follow-up.

***Conclusion*:** Epicardial substrate ablation appears to be a feasible and safe strategy for reducing ventricular arrhythmia burden and ICD shocks in patients with Brugada syndrome. Larger studies are needed to confirm its long-term efficacy.

Keywords: *Brugada syndrome, recurrent ICD shock, radiofrequency ablation, epicardial access.*

1. INTRODUCTION

Brugada Syndrome (BrS) is an inherited arrhythmogenic disorder characterized by a typical ECG pattern and a high risk of sudden cardiac death (SCD) due to ventricular fibrillation (VF), primarily in young individuals with structurally normal hearts [1]. So far, guidelines have been indicating that the implantable cardioverter-defibrillator (ICD) is the mainstay of management of therapy to prevent death [1], [2]. However, ICDs do not prevent the occurrence of arrhythmias, furthermore, some patients may develop multiple ICD shock which will eventually drain out its battery, leading the patient a significant burden on re-implantation and reduced quality of life. Recently, it has been discovered that the arrhythmogenic substrate, predominantly located in the epicardium of the right ventricular outflow tract (RVOT) and right ventricle (RV), can be a target of ablation to reduce arrhythmia occurrence in BrS patients [3], [4]. The ablation of RVOT abnormal substrate from the epicardial approach was first described by Nademanee et al on 9 BrS patients with recurrent, frequent ICD shocks which showed an excellence outcome with no recurrence of VT/VF [3]. Since then, several authors have published case series and small trials regarding to this new technique [4], [5], [6] with positive results, raising a potential resolution for BrS patients. This complex technique for such a rare disease requires technically difficult approaches, advanced equipment, and a high-volume center with surgical backup available in case of complications. Given the limited data from Vietnam regarding this treatment procedure, we conducted this study to assess the feasibility, safety, and clinical outcomes of epicardial substrate ablation in Brugada syndrome with recurrent ICD shocks.

2. MATERIAL AND METHODS

2.1. Study design

This was a single-center retrospective study with longitudinal follow-up. All patients admitted to Hanoi Hospital between 2016 and 2026 with a diagnosis of high-risk Brugada syndrome requiring implantable cardioverter-defibrillator (ICD) implantation, defined by: (1) symptomatic presentation, including syncope or aborted sudden cardiac death (SCD); and (2) spontaneous type 1 Brugada pattern on admission electrocardiogram (ECG). The flow chart study was presented in Figure 3.

Among patients who underwent (ICD) implantation, we took into study those who experienced multiple appropriate ICD shocks requiring hospitalization and subsequently underwent catheter ablation. The study protocol was approved by the Institutional Ethics Committee of the hospital.

2.2. Diagnostic criteria

Brugada syndrome (BrS) is defined by (1) typical ECG: coved ST-segment elevation ≥ 2 mm (0.2 mV) followed by a negative T wave in >1 right precordial lead (V1-V3) at fourth, third or second intercostal space and (2) symptomatic presentation: ventricular fibrillation (VF), polymorphic ventricular tachycardia (VT), history of SCD <45 years old in family, coved-type ECGs in family members, inducibility of VT with programmed electrical stimulation, syncope, or nocturnal agonal respiration [1]. Since provocation drug is not available in our country, only spontaneous type 1 ECG fulfils the diagnosis of BrS.

The indication for ICD implantation in BrS

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was based on ESC 2023 guideline: BrS patient with aborted cardiac arrest or evidence of spontaneous sustained VT (class I), type 1 BrS patient with arrhythmic syncope (class IIa). ICD implantation in asymptomatic BrS with inducible VF during PES is considered as Class IIa [2].

Candidate for ablation of epicardial substrate required these conditions: (1) having received in ICD for management of BrS, (2) multiple appropriate ICD shocks, (3) failure with medical treatment (ie. Amiodarone, lidocaine, betablocker since Quinidine is not available in Vietnam) (4) patient consent for the procedure. Any VT/VFs secondary to toxic, electrolyte imbalance, myocardial infraction were excluded in our study.

2.3. Protocol for catheter ablation

2.3.1. Preparation of patient

All patients underwent general anesthesia with endotracheal intubation. A quadripolar catheter (SJM) was put in RV apex through femoral veins for the purpose of VF induction, one decapolar catheter (SJM) was inserted through the left subclavian vein for coronary sinus recording. The patient's arterial pressure is measured throughout the procedure via a 5-F catheter in the left femoral artery.

2.3.2. Endo/Epicardial access

Endocardial access was via femoral vein. To get to epicardial space, we followed the protocol of Sosa et al [7]: pericardial puncture was performed by an epidural introducer needle (Chiba needle, Blueneem®), under the guidance of fluoroscopy with injection of contrast to locate the position of needle tip. When the needle is confirmed in correct position, we introduced a floppy guidewire (Runthrough NS, Terumo®) to the pericardial space, the needle was then withdrawn, following several dilator insertions, then floppy guidewire was changed with a stiff 0.035-inch wire. A steerable sheath (Agilis EPI, Abbott®, MN, USA) was then introduced.

2.3.3. Mapping and identification of arrhythmogenic substrate

Mapping of the endocardial and epicardial RVOT were performed by 3D mapping system (CARTO 3, Biosense Webster®, USA), using high-density mapping catheter (Pentaray NAV, Biosense Webster®; 1mm electrodes with 2-6-2 interelectrode pacing). We initiated mapping of the endocardial RVOT prior to epicardial mapping to provide a reliable anatomical delimitation of the RV boundaries [8]. We identified the epicardial substrate based on these criteria [4]: (1) Low voltage of $\leq$ 1 mV, (2) split or fractionated signals with $\geq$ 2 components separated by > 20 ms isoelectric intervals, (3) long duration (> 80 ms) or late potentials extending beyond the end of QRS complex (Figure 1). The identification was made directly during the mapping phase by both bioengineer and electrophysiologist. Before ablation, coronary angiography was performed to map the location of the coronary artery system. Since Ajmaline is not available in Vietnam, we didn't perform the provocative testing during the mapping procedure.

2.3.4. Ablation delivery

After identification of abnormal substrate, we withdrew the mapping catheter and inserted a 7.5F open-irrigation radiofrequency ablation catheter with contact force (Thermocool Navistar, Biosense Webster®, USA), with the speed of irrigation 15 ml/min. By monitoring the arterial pressure waveform, aspiration of pericardial fluid is performed when 150ml of irrigation has been delivered or when MAP <65mmHg to prevent significant tamponade. Power of ablation was controlled at 35-45W, we started to ablate from the center of the substrate and progressively move outward until all delayed activity is eliminated. PVC was also the target of ablation if presented during epi/endocardial mapping.

2.3.5. Post-ablation remapping and criteria of completion

Based on the study of Pappone et al, we finish the procedure when these endpoints are achieved: (1) Normalization of the ST elevation in right precordial RVOT lead; (2) replacement the abnormal substrate with low voltage scar (<0,5mV); and (3) VT/VF non-inducibility is confirmed [8] (See Figure 2). After finishing the procedure, pericardial fluid is completely aspirated and the steerable catheter is withdrawn, the wound is then closed with one knot of simple suture. Patients receive 7 days of corticosteroid and antibiotic after the procedure.

2.3.6. Follow-up

Post-operative 12-lead ECG, 24-h ambulatory ECG, and echocardiography were done before discharge. All patients were followed up for symptoms, 12-lead ECG and ICD examination every 3 months for the first year and every year thereafter.

2.4. Statistical analysis

All the statistical analyses were performed using IBM SPSS statistical software version 26.0. Categorical variables are presented as frequencies and percentages. Normally distributed continuous variables are expressed as the mean ± standard deviation (X ± SD) and median (interquartile range 25 and 75) if the distribution is nonnormal. The butterfly chart was made using Python programming language (version 3.10).

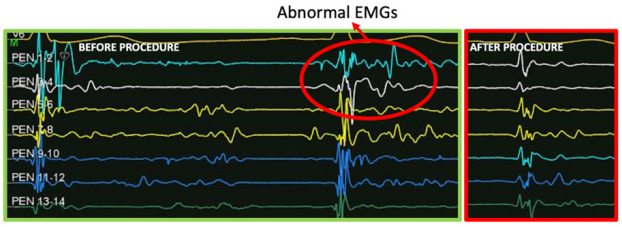

Figure 1. Illustration of abnormal electrograms identified by epicardial mapping (left side) and the result of ablation (right side)

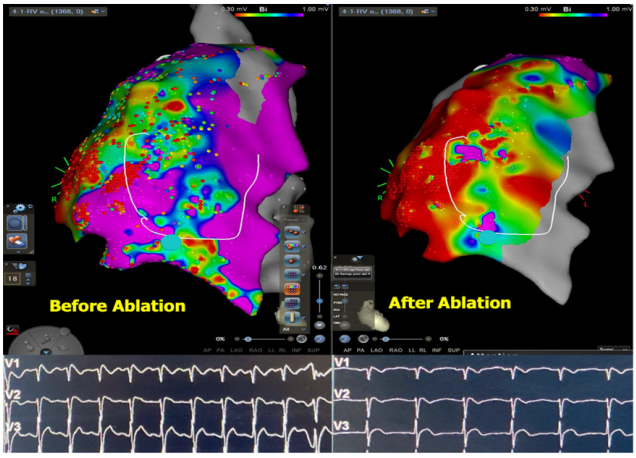

Figure 2. Epicardial abnormal substrate mapping before ablation (left side) and after ablation (right side)

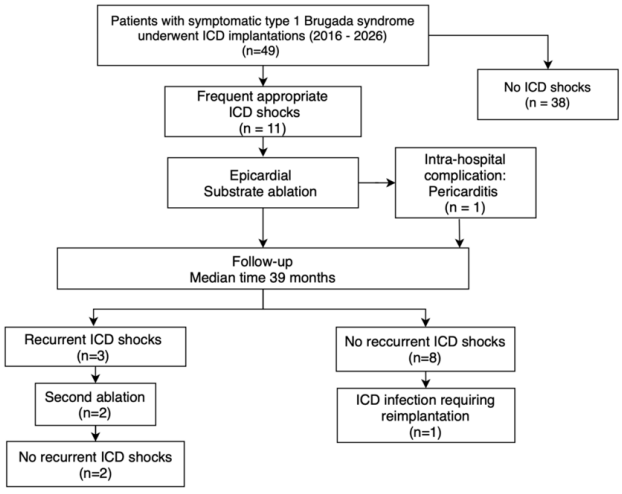

Figure 3. Flow chart of study

3. RESULTS

Between 2016 - 2026, there were 49 patients with symptomatic type 1 BrS who underwent ICD implantation. During follow-up, 11 patients experienced frequent VT/VF and multiple ICD shocks. We obtained consent from all of them for the ablation procedure.

Among the 11 patients who experienced frequent appropriate ICD shocks, the mean age was 46.18 ± 14.43 years and all were male (Table 1).

Initial presentation included syncope in 7 patients (63.6%) and aborted cardiac arrest in 4 patients (36.4%). Most patients had preserved mental status (90.9%), while cognitive impairment was observed in one patient (9.1%). A family history of sudden cardiac death was reported in one patient (9.1%). Spontaneous type 1 ECG pattern was present in all patients (100%), while none had drug-induced type 1 ECG. Concomitant arrhythmias included premature ventricular contractions in 3 patients (27.3%) and early repolarization syndrome in 1 patient (9.1%). Genetic testing for SCN5A mutation was not performed in any patient. ICD implantation was indicated as Class I in 10 patients (90.9%) and Class IIa in 1 patient (9.1%). The median ICD shock-free period was 32 months (IQR 12–61), and the median number of ICD shocks before ablation was 10 (IQR 7–50). The detailed individual data was presented in Supplementary Table S1.

Table 1. Patient characteristics before ablation

Variable		Ablation group (n=11)
Age, years (mean ± SD)		46.18 ± 14.43
Male sex, n (%)		11 (100%)
Initial presentation, n (%)	Syncope	7 (63.6%)
	Aborted cardiac arrest	4 (36.4%)
Mental status, n (%)	Preserved	10 (90.9%)
	Cognitive impairment	1 (9.1%)
	Family history of SCD, n (%)	1 (9.1%)
	Spontaneous Type 1 ECG, n (%)	11 (100%)
Concomitant arrhythmia, n (%)	PVC	3 (27.3%)
	Early repolarization syndrome	1 (9.1%)
ICD indication, n (%)	Class I	10 (90.9%)
	Class IIa	1 (9.1%)
Duration of ICD shock-free period, months (median, Q1-Q3)		32 (12 - 61)
Number of ICD shocks before ablation, time (median, Q1-Q3)		10 (7 - 50)

SCD: Sudden cardiac arrest,
ICD: implantable cardioverter-defibrillator

In the ablation group (n = 11), epicardial access was successfully achieved in all patients (100%). The substrate location is illustrated in Figure 4. The mean total procedure time was 172.36 ± 12.79 minutes. The mean total radiofrequency application time was 20.02 ± 8.16 minutes, with a mean fluoroscopy time of 22.27 ± 14.03 minutes. The mean number of ablation applications was 60.27 ± 22.07. These parameters were presented in Table 2.

Table 2. Procedural characteristics

Variable	Ablation group (n=11)
Successful epicardial access, n (%)	11 (100%)
Substrate location	See figure 4
Total procedure time, minutes (mean ± SD)	172.36 ± 12.79
Total RF delivery time, minutes (mean ± SD)	20.02 ± 8.16
Fluoroscopy time, minutes (mean ± SD)	22.27 ± 14.03
Number of RF applications, (mean ± SD)	60.27 ± 22.07

Ablation of epicardial substrate were all performed in the anterior RVOT (100%). One patient benefited from endocardial PVC ablation, however, no epicardial abnormal substrate was found in

these patients. There were 3 patients identified with lateral RVOT abnormal substrate and one with inferolateral substrate

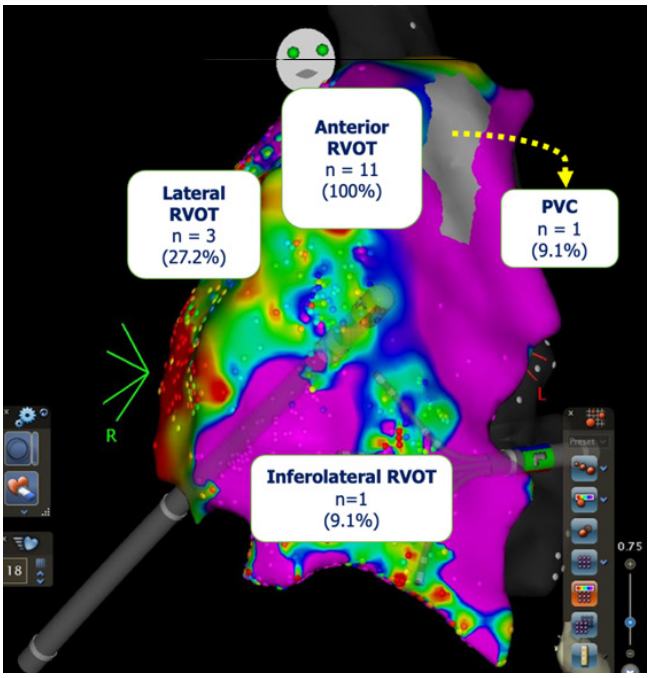

Figure 4. Substrate location identified and ablated

One in-hospital complication was observed, consisting of pericarditis requiring pericardiocentesis (9.1%). During a median follow-up of 39 (7–78) months, recurrence of ventricular arrhythmias occurred in 3 patients (27.3%). Repeat ablation was performed in 2 patients (18.2%) (Table 4). One patient (9.1%) had ICD infection requiring device removal and reimplantation on the contralateral side (see Table 3).

Table 3. Follow-up outcomes

Variable	Ablation group (n=11)
Follow-up duration, months (median, (Q1-Q3))	39 (7 - 78)
VT/VF recurrence, n (%)	3 (27.3%)
Repeat ablation performed, n (%)	2 (18.2%)
In-hospital complications, n (%)	
Pericarditis requiring pericardiocentesis	1 (9.1%)
Mid-term complications, n (%)	
ICD infections requiring reimplantation on the opposite side	1 (9.1%)

Table 4. Number of ICD shocks after ablations

Patient	Total number of ICD shocks		
	Before ablation	After 1st ablation	After 2nd ablation
1	7	5	0
2	500	0	-
3	150	0	-
4	50	1	0
5	35	0	-
6	15	0	-
7	5	0	-
8	10	5	N/A
9	5	0	-
10	7	0	-
11	7	0	-

N/A: Not available

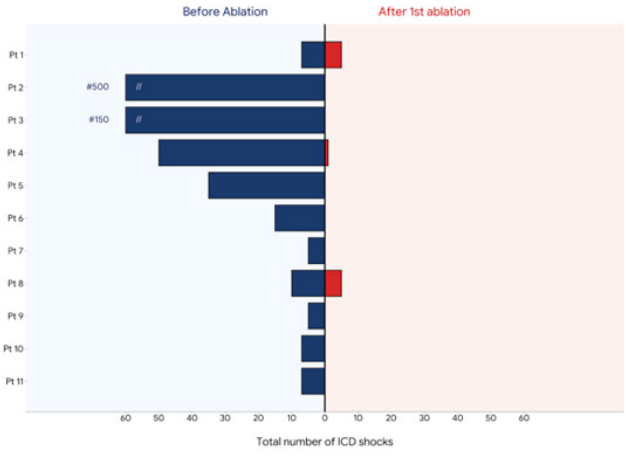

Figure 5. Reduction of ICD shocks before and after first ablation

4. DISCUSSION

To our best knowledge, this is the first report of epicardial radio-frequency ablation in Brugada syndrome with frequent ICD shocks in Vietnam. All of the patients in our study were male, which showed male predominance of BrS. Although Brugada syndrome is usually reported in healthy young men, we had performed ablation in 3 elderly patients (above 70 years old) with favorable outcomes. A study by Pappone C. et al in 135 patients showed that the mean age was approximately 39.6 years, with a range from 18 to 71 years [8]. In addition to ICD implantation, all patients were advised to avoid risky drugs, alcohol, cannabis... and promptly treat fever, according to ESC 2022 guideline [2]. This could be beneficial and could contribute to longer life expectancy of BrS patients. The median duration of ICD shock-free in our study was 32 months, which may reflect the progressive nature of abnormal substrate that facilitates VT/VF occurrence.

With regard to the epicardial approach, successful access to the pericardial space was achieved in all patients with no serious complication. Epicardial radiofrequency catheter ablation has been reported as a highly effective method and is considered safe, with low rates of complications when performed in experienced centers [9]. The risk of perforation as well as tamponade or coronary injuries are low but still exist, requiring experienced operators and available surgical back-up in case of emergency. Studies have shown that pericarditis is the most common complication: A meta-analysis in 2023 encompassing 15 case series and 347 patients, the pooled incidence of pericarditis or pericardial effusion was 9.3% [9]. The BRAVE trial showed that among 42 ablated patients, there was only one case of acute hemopericardium [4]. In our study, one patient happened to develop pericarditis post ablation that required anti-inflammatory treatment and pericardiocentesis. We develop a hypothesis that the parietal wall of pericardium can be affected by RF delivery, therefore, adequate RF irrigation and contact force option of the catheter showing the force direction is crucial to focus the RF energy only to the epicardial surface. Of note, irrigation fluid should be drained completely after the procedure and epicardial catheter should be withdrawn as soon as possible, ideally after the procedure to prevent potential infection.

The anterior RVOT is the target of ablation in all patients of our study, this is also the finding of other authors. Furthermore, high-density 3D mapping has revealed that the substrate can extend beyond the anterior region. Yasuhito et al showed in their meta-analysis that while 100% of epicardial cases involved the RVOT, the abnormal substrate extended beyond it to the RV inferior wall (17% of cases), the RV anterior wall (14%), and the RV lateral/free wall (6%) [9]. Therefore, a detailed, meticulous mapping pre-ablation is crucial in order to eliminate substrate and trigger of arrhythmia.

The mean procedure time in our study was 172.36 ± 12.79 minutes, this is identical with the study of Brugada P. et al (156 minutes) [6] and Pappone C. et al (169 minutes) [8]. The procedure time is longer in patients with additional ablation on inferolateral RVOT or lateral RVOT.

The procedures were technically succesfull in all 11 patients. During a median follow-up of 39 months, all patients experienced a significant reduction in the number of ICD shocks (see Table 4 and Figure 5). Notably, 8 of 11 patients remained free from ICD shocks (72.7%). As Nademanee concluded in his study, 83% remained VF free after a single procedure and 90% after a repeat ablation [4]. The recurrent ICD shocks occurred in 3 patients, however, the burden of shocks were markedly lower than before the ablation (Table 4). Concomitant arrhythmias may have a role in contributing to the recurrent rate. Nademanee et al demonstrated in his study that the "pure" Brugada ECG pattern had better outcomes. In constrast, patients having a combined Brugada pattern with an early repolarization pattern were at

a significantly higher risk for VF recurrence and were more likely to fail the initial ablation session [4]. One patient in our study developed ICD infection during follow-up, which was not linked to the procedure: this patient had experienced a total of 500 ICD shocks which required four ICD replacements before the ablation, this was already a strong risk factor for device infection.

Together, these findings had demonstrated the efficacy of epicardial substrate ablation in BrS patients, with excellent outcomes and significant improvement of patient's quality of life.

Finally, our study had several limitations: Firstly, since specific drugs (ajmaline, flecainide IV) are not available in Vietnam, we did not perform the pharmacological provocation test. This fact can affect the success rate because of missing the masked additional substrate [6]. Secondly, genetic testing for SCN5A mutation, which was recommended by current guidelines, was not performed in all patients. Thirdly, the sample size was small, which limits the ability to generalize our findings, larger studies about efficacy and outcome of epicardial ablation of BrS patient in Vietnam are needed in order to better evaluate this specific therapy.

5. CONCLUSION

Epicardial substrate ablation is a feasible and effective therapeutic strategy for patients with Brugada syndrome experiencing recurrent ventricular arrhythmias and frequent ICD shocks. Our single-center study showed that the procedure can be done safely with a high success rate via epicardial access and a substantial reduction in ICD shock burden during follow-up. Larger studies are needed to further validate this therapy for Brugada syndrome patients.

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