POLISH HEART JOURNAL

Kardiologia Polska
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957

Online first
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ISSN 0022–9032 e-ISSN 1897–4279

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Article type: Review

Received: June 2, 2025

Accepted: June 20, 2025

Early publication date: June 20, 2025

Challenges in the treatment of patients with Brugada syndrome: The current role of ablation

Short title: The current role of ablation in Brugada syndrome

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ABSTRACT

Brugada syndrome is an inherited ion channelopathy associated with an increased risk for ventricular arrhythmia and sudden death. Current management strategies to reduce arrhythmic risk are limited, with few pharmacological options that may be ineffective or cause side-effects leading to suboptimal dosing or cessation of treatment. There is substantial interest therefore in determining the long-term efficacy and safety profile of catheter ablation, to targeting triggers and electrophysiological substrates for ventricular arrhythmia. With the recent publication of small, randomized trials including the BRAVE study, the level of evidence is improving. However, the balance of risk verses benefit across the arrhythmic risk spectrum remains unclear and procedural technical challenges remain, particularly given most patients will require an epicardial approach for catheter ablation. This review outlines the current evidence in the published literature and highlights gaps in knowledge that should be prioritised in future studies.

Key words: ablation, Brugada syndrome, ventricular tachycardia

INTRODUCTION

Brugada syndrome is an inherited cardiac ion channelopathy associated with ventricular arrhythmia and sudden cardiac death [1]. It is characterized by the presence of J-point and coved ST segment elevation (type 1) at least 0.2 mV in leads V1 or V2 on the electrocardiogram (ECG) [2] (Figure 1). The sensitivity for detection of a Brugada phenotype may be increased by positioning electrodes in the high lead position (2^{nd} or 3^{rd} intercostal space) that overlies the right ventricular outflow tract (RVOT) [3]. For individuals with non-diagnostic patterns (type 2; saddleback, type 3; <2 mm elevation) with a relevant family history, a diagnostic Brugada pattern may be unmasked by administration of sodium channel blockers (e.g., ajmaline) [4]. However, in the absence of symptoms, a positive pharmacological challenge alone is not sufficient for a Brugada syndrome diagnosis, and a scoring system such as the Shanghai criteria can be used that incorporates clinical risk factors and genetic testing [5].

The worldwide pooled prevalence of Brugada syndrome is approximately 0.5 per 1000 individuals with the highest rates reported in Southeast Asians [7]. Unlike other channelopathies, patients with Brugada syndrome typically experience their first arrhythmic event during adulthood peaking between 38 and 48 years of age [8]. A meta-analysis including 18 studies and 4099 patients has reported an annual incidence of major arrhythmic events of 23.8 per 1000 person-years and the risk is greater for individuals with a history of cardiogenic syncope, cardiac arrest, male sex and inducible ventricular tachycardia (VT) or fibrillation (VF) during electrophysiology study [9–11]. The genetic architecture of Brugada syndrome is complex. In 20%–30% of individuals a loss-of function variant in the voltage-gated cardiac sodium ion channel alpha subunit (*SCN5A*) may be identified [12], however calcium and potassium channels have also been implicated [13]. More recently, in a longitudinal cohort of 2182 patients, Kukavica et al. [14] identified both loss-of-function SCN5A variants and a higher common variant polygenic risk score to be independently associated with arrhythmic events. This finding suggests there is potential to incorporate more complex genetic models to refine risk stratification and polygenic inheritance may also account for positive sodium channel blocker provocation tests in non-carriers of a SCN5A variant where a pathogenic variant has been identified in other family members [12, 15].

Experimental and computational studies have shown that phase 2 re-entry may be the mechanism of VF initiation in Brugada syndrome due to action potential heterogeneity in the right ventricular epicardium and endocardial conduction delay [16, 17]. Resulting closely

coupled premature ventricular complexes may trigger VF [16]. In addition, diffuse RVOT epicardial fibrosis and reduced gap junctional expression lead to functional conduction block and an arrhythmogenic substrate for VT circuits or wavebreak degenerating into VF [18].

THERAPEUTIC OPTIONS IN BRUGADA

All patients should avoid medication that cause adverse effects on channel function as listed on www.brugadadrugs.org [19, 20]. They should also treat fevers aggressively as they increase the risk type 1 patterns and ventricular arrhythmia [21]. For patients with arrhythmogenic syncope, insertion of an implantable cardioverter defibrillator (ICD) is recommended to prevent sudden death (class IIa) [22]. Unlike long QT syndrome where beta-blockers have good evidence for primary prevention, medical therapy with beneficial I_{to} channel blocking effects (e.g., class 1A antiarrhythmics; quinidine) in Brugada syndrome is typically reserved for individuals with recurrent symptomatic VT/VF [22]. Quinidine and hydroquinidine (similar pharmacokinetic properties to quinidine gluconate), appear to be effective at reducing arrhythmic burden in some studies and may prevent induction of VF during electrophysiology study in up to 88% of patients [23–25]. However, events still occur in up to 15% of patients on treatment [26]. Quinidine is also poorly tolerated at high doses due to its side effect profile and can have proarrhythmic affects [27]. In a nationwide survey by Anguera et al. [28], temporary discontinuation of quinidine due to side effects was a significant predictor of recurrent ICD shocks (HR, 4.6; 95% CI, 1.28–16.6) and for some patients this may also limit the maximum tolerated dose. These issues are further compounded internationally by the limited availability of quinidine, and hydroquinidine is the only preparation that can be accessed in many counties [27].

These challenges (availability, intolerance and failure to consistently suppress ventricular arrhythmia in some studies), are key elements that may lead to consideration of catheter ablation (currently ESC Guidelines 2022 class IIb indication) with the aim of targeting triggering PVCs and/or RVOT epicardial substrate modification [22]. This review focuses on the practical application of catheter ablation in Brugada syndrome and the gaps in knowledge that need to be addressed to improve management strategies in these patients.

CATHETER ABLATION TO MODIFY VENTRICULAR FIBRILLATION INDUCIBILITY

A role for catheter ablation in Brugada syndrome to supress recurrent ventricular tachycardia or fibrillation is not a new concept. At the turn of this century, multiple studies reported

initiation of VF preceded by premature ventricular beats of the same morphology to the triggering beat, typically arising from either the RVOT or Purkinje conducting system [29–31]. In 2004, Haïssaguerre et al. [32] reported successful modification of VF inducibility by targeting these sites with endocardial radiofrequency (RF) ablation in 3 Brugada patients. While this study was transformative in developing a new therapeutic strategy, experimental Brugada syndrome dog models (using pinacidil and pilsicainide in adult mongrel hearts) identified that epicardial targets may be more effective than endocardial [33]. This is borne out in clinical studies outlined below.

PREMATURE VENTRICULAR BEAT TRIGGER GUIDED ABLATION

Targeting of VF-triggering premature beats has been shown to have excellent long-term outcomes. 85% of premature beats may originate from the RVOT with the remainder from the RV body. However, patients with a QRS notch in lead V1 had more VF episodes and may not respond as well to endocardial ablation requiring an epicardial approach [34]. Targeting focal triggers can lead to normalisation of elevated ST segments, however some reports suggest that this effect may be transient and the relationship with modification of risk for sudden cardiac death remains unclear [35]. It is now established that a combined trigger and substrate-based approach can have excellent outcomes.

SUBSTRATE-BASED ABLATION

Nadamanee was the first to recognise the efficacy and favourable safety profile of epicardial substrate ablation in Brugada syndrome in 9 symptomatic patients with recurrent VF episodes [31]. Initially ajmaline was not employed to delineate the area of abnormal electrograms to target. This was extended by Pappone's group in 135 patients who utilized ajmaline to demonstrate these fractionated electrograms expanded over a wider area (2×) after sodium channel blockade [36]. Elimination of these fragmented ventricular potentials normalized the ECG and prevented VT/VF events [36]. Group 1 patients (n = 63) had documented VT/VF and Brugada syndrome-related symptoms while group 2 (n = 72) had inducible VT/VF without ECG documentation at the time of symptoms. About 27 patients of group 1 had experienced multiple implantable cardiac defibrillator shocks for recurrent VT/VF episodes. Radiofrequency ablation eliminated abnormal electrograms leading to ECG normalization and VT/VF non-inducibility in all patients. During a median follow-up of 10 months, the ECG remained normal even after ajmaline in all except 2 patients who underwent a repeated effective procedure for recurrent VF. Some questions were raised regarding the indication for ablation in

the patients with syncope or presyncope especially with drug-induced patterns where it is well recognized vasovagal events often occur in Brugada patients. The targeted area for ablation tagged by the abnormal low-voltage fractionated signals comprised of multiple distinct components separated by over 20 milliseconds (ms) of isoelectric segments, and long duration (≥70 ms) or late potentials that were beyond the end of the QRS complex. Nadamanee utilises an irrigated-tip catheter with contact force measurements ≥5 grams before radiofrequency energy is delivered. The power is titrated from 20 to 50 watts to achieve ≥10 ohms impedance reduction from baseline. This force and power should provide sufficient acute elimination effect on the target area. Effective lesions are confirmed by rapid disappearance of late/fractionated components and a decline in recorded signal amplitude (Figure 2). The endpoint is a complete elimination of substrate identified after ajmaline infusion over the RVOT and its vicinity. Non-inducible VT/VF and disappearance of the Brugada ECG pattern is used as an adjunct endpoint of ablation.

Multiple potential sites for substrate-based ablation have been reported; most frequently the epicardial RVOT (anterior or posterior) and less commonly RV anterior, inferior or free wall locations [37]. Predicting location is challenging and reliant on the identification of low voltage zones and fractionated late potentials (Figure 2) [31, 37, 38]. These sites of late potentials and fractionated electrograms are delineated utilising epicardial mapping ideally with a multipolar high density mapping catheter such as a high density grid (Abbott) or current Optrell catheters (Biosense). These catheters have small electrodes and close spaced bipoles with algorithms to enable omnipolar mapping which overcomes the issue of "bipolar blindness" of wavefront activation causing electrodes in one plane of activation not to develop a potential difference and hence not detect the wavefront. Elimination of long fractionated electrograms in sinus rhythm if a type 1 Brugada is present or after ajmaline/flecainide provocation to generate a type 1 Brugada ECG, is required as an endpoint. The BRAVO study reported substrate-based ablation primarily targeting these RVOT epicardium abnormal electrograms led to an impressive 96% VF-free survival rate for the 159 Brugada patients included, with an average follow up period of 48 months [39]. This cohort was high risk requiring recurrent VF or arrhythmogenic syncope to be included, along with either spontaneous or drug-provoked type 1 Brugada patterns [39]. To achieve this impressive outcome, repeat ablation was necessary in some cases with only 81% free of VF after a single procedure. One third of patients in the study had substrate sites outside of the epicardial RVOT (e.g., inferior RV epicardium) and therefore operators need to consider these to increase the likelihood of success but doing so will prolong the procedural time which is a recognized marker for increasing risk of complications [39, 40].

Drug provocation (e.g., ajmaline or flecainide) is used to identify abnormal substrates by promoting conduction delay and extending low voltage areas and regions with abnormal electrograms [37]. This approach has previously been demonstrated to correlate with RV electrical and mechanical abnormalities [41]. However, the optimal strategy for provocation is unknown and alternative agents have been suggested including propafenone, procainamide and warmed saline [42]. The optimal ECG markers of success in a substrate-guided approach are also yet to be established. Nademanee et al. [39] has reported normalisation of the type 1 Brugada ECG pattern (whether with or without sodium channel blockade) was the only predictor of a VF free outcome. While recurrence rates in this study were low and contrasted with the findings from a smaller study by Zheng et al. where no relationship was identified, this observation has also been reported by the recently published BRAVE randomized trial of ablation versus hydroquinidine therapy in high risk Brugada patients [43, 44]. This trial found that there were no further arrhythmic events if the spontaneous or induced Brugada pattern was eliminated, but if there was also an early repolarisation pattern outside the RVOT they were at higher risk of VF recurrence [44]. This could in part be due to a lack of definition of "normalization" of the ECG or the existence of pro-arrhythmic substrate in early repolarization sites (see below). Robust ECG markers are required to standardise practice and establish the degree of normalisation necessary to prevent VF recurrence and indicate sufficient substrate modification has been performed. Sites corresponding to ECG early repolarisation patterns outside the RVOT can be identified (local fractionated electrograms) and targeted. Indeed, Cheniti et al. [45] has also shown that a subset of patients with Brugada syndrome present with an abnormal substrate extending onto the LV epicardium (45% of 22 cases) and inferior RV that is associated with *SCN5A* mutations and multigenic variants. Nademanee et al. [46] later reported they no longer use either non-inducible VT/VF or normalization of the Brugada ECG pattern but the best and only end point is to eliminate all substrate areas that harbor abnormal low-voltage fractionated signals detected after sodium channel blocker challenge. This is important as there is a risk in administering repeated ajmaline boluses to test for Brugada ECG eradication as the drug has an elimination half-life of 95 minutes and this can be toxic causing electromechanical dissociation. Hence, if one is considering this strategy, lower doses should be administered after the initial dose depending on procedure duration and the predicted remaining circulating dose.

Further studies are also necessary to formally determine whether a negative response to programmed ventricular stimulation (PVS) should also be included as a procedural endpoint. In a meta-analysis of 14 studies with a total of 709 patients catheter ablation resulted in non-

inducibility of VF in 91% of patients and resolution of type 1 patterns in 95%, leading to 87% of patients free of ventricular arrhythmia at a mean follow up period of 2.5 years [47]. Endocardial unipolar voltage abnormalities may predict ventricular fibrillation inducibility during PVS and therefore could have applications in risk stratification as they may correlate with areas of structural abnormalities with arrhythmogenic potential such as fibrosis [48, 49]. Whether they may also identify distant epicardial scar and therefore target regions for an epicardial approach, remains uncertain [48, 50].

A substrate-based approach could be further supplemented by advanced electrocardiogram or imaging strategies and improved mapping techniques. A recent study identified steep repolarization heterogeneities in sinus rhythm in all Brugada patients but no controls, which correlated with the location of a rotational VF beat at induction and was abolished in 94.3% of patients that underwent ablation [51]. Larger prospective studies could investigate the use of ECG imaging to detect repolarization heterogeneities and targets for ablation.

LONG-TERM OUTCOMES:

It is recognized that long-term data for ablation in Brugada syndrome is limited. In a meta-analysis by Kotake et al. [37], of 56 studies and 388 patients the pooled incidence of non-inducibility of ventricular arrhythmia was 87% with acute resolution of a type 1 ECG pattern in 74.5% of cases, with only 17.6% of cases of recurrence of ventricular arrhythmia [37]. While this is consistent with previous findings, the weighted mean follow-up was only 28 months [37, 52]. Recently, the results from the BRAVE prospective multicenter two arm randomized clinical trial in symptomatic patients with Brugada syndrome was published. Symptomatic Brugada syndrome was defined very strictly by the presence of a type 1 ECG pattern with or without sodium channel blocker challenge, along with one or more of the following: 1) aborted cardiac arrest, 2) documented VF episodes, 3) agonal respiration during sleep with difficulty arousing, 4) unexplained syncope with malignant characteristics, or 5) seizures suspected to be of arrhythmic origin. The ablation group had significantly fewer VF events (HR, 0.288) over 3 years of follow-up compared with controls (no ablation or quinidine) and at the interim analysis, early trial termination due to favourable outcomes was recommended by the study safety meeting [44]. Both a trigger and substrate-guided approach was performed with PVS before and after ablation. The endpoint was defined as elimination of any PVC's identified as VF triggers and ablation of all substrates (with unmasking using ajmaline) having targeted all abnormal fractionated electrograms. After ablation, 83% of patients were VF free and without

ICD therapies at the end of the follow up period. All patients without concomitant early repolarization remain free of VF after a single ablation except 1 patient whose type 1 Brugada ECG pattern persisted after ablation. While this study provides support for the efficacy of arrhythmogenic substrate-based VT ablation in Brugada, it does not compare outcomes with a patient group stable on quinidine and despite recent publication of another randomized study (Pappone et al. [53]), additional trials with longer term data are urgently needed.

SAFETY CONSIDERATIONS:

As endocardial ablation is insufficient for a significant proportion of patients, epicardial access is required typically by subxiphoid puncture. A safety meta-analysis by Kotake et al. [37] including 56 studies and 388 Brugada patients, reported pericarditis or pericardial effusion in 9.3% of cases that were all managed with either medication or a pericardial drain. There were no periprocedural deaths. Similarly, pericardial effusion was the only major procedural complication reported in the BRAVO study (overall complication rate 1%) [39]. These studies are however limited by their relatively small size and likely impacted by bias from being performed at experienced and high-volume centres. The risks of epicardial puncture can be mitigated by utilising C02 insufflation to lift the pericardium from the epicardial surface and minimise the risk of RV perforation with access [54].

Acute procedural complications rates are 1%–17.5% for epicardial VT ablation in ischaemic and non-ischaemic cardiomyopathies with additional complications are reported including pneumothorax, phrenic nerve injury, myocardial infarction and very rarely oesophageal injury [40, 55, 56]. To reduce these risks, it is recommended to perform phrenic nerve capture testing and selective coronary angiography when anticipating ablation near coronary arteries [40]. It is essential that safety data is gathered from all centres performing VT ablation for Brugada and that risk scores used for other cardiac conditions (e.g., the PAINSED score [57]) are validated in this patient group as predictors of complications and long-term mortality may differ.

FUTURE APPROACHES:

The identification of patients that would benefit the most from an ablation strategy needs to be addressed. There is a significant amount of variability in the inclusion criteria between studies currently reported (Table 1) [58]. These are predominantly observational and to make substantial advances and implement in clinical guidelines, additional efforts are needed to establish international randomized controlled trials.

It remains undetermined whether ablation is a potential management strategy in patients without recurrent ICD therapy, which is associated with increased morbidity and adverse psychological effects that need to be balanced with the complexity of an epicardial approach and the associated risks and costs. ICD implantation remains the gold standard for protection against sudden death in Brugada patients however it does not target the underlying arrhythmogenic substrate. Li et al have compared outcomes of catheter ablation in patients with and without ICD implantation, the latter having declined a device [59]. They reported fewer events in the ablation group (5.6% vs. 54.5%) however this study should be interpreted with caution. This study was small (n = 40), the ICD group were older (mean age 47.8 vs. 38.8 years) and they had a greater proportion of cardiac arrests (45.5% vs. 22.2%) prior to recruitment [59]. Therefore, they may have been at higher risk of arrhythmic events compared to the catheter ablation group. The study also highlights increasing interest in the application of VT ablation outside of existing inclusion criteria recommended in current international guidelines. In a published survey, 36% of included centres consider ventricular ablation as a first line therapy for recurrent ventricular arrhythmia and 17% would also consider ablation for patients with high-risk features (symptoms, ECG findings, inducibility at programmed ventricular stimulation) but without documented arrhythmia [60]. Indeed, given the findings of the BRULOOP study showing implantable loop recorders detects arrhythmic events in only 30% of symptomatic Brugada patients with ventricular arrhythmia only documented in 7% of cases, one must exercise caution in determining which patients will benefit most from ablation [61].

Evidence is needed from randomized control trials to support an expanding the application of catheter ablation, particularly in individuals asymptomatic at presentation where the risk of arrhythmic events is low. Risk scores such as the Predicting Arrhythmic evenT [62], Sieira [63], Shanghai Score System [64] and BRUGADA-RISK [65] score could be tested to more effectively identify patients with most to gain from an invasive strategy. The proposed scoring systems and thresholds to consider patients at high risk of ventricular arrhythmia to warrant ablation are highlighted in Table 2. Studying asymptomatic resting type 1 Brugada cases will require sizeable international studies including southeast Asia as event rates are so low — a sample size of around 600 patients would be required to demonstrate the expected reduction of VF risk at 5 years from 5% with no therapy to 1% with ablation therapy [66]. There has been no study of the impact of genotype on efficacy or safety of VT ablation. This is likely due to the relatively small proportion of pathogenic variant carriers included in existing studies (13% and 35% in the randomized trials by Nademanee et al. [44] and Pappone et al. [53], respectively). This need to be considered in the design of future randomized studies.

CONCLUSIONS

There is a growing evidence base illustrating the efficacy of ablation in symptomatic Brugada Syndrome especially with clearly documented ventricular arrhythmia episodes. However, the number of studies remains limited with a lack of long-term data on outcomes with randomized control trials. The identification of patients that may benefit (including those perceived to be slightly lower risk) and technical challenges (e.g., safe subxiphoid access) remain. These issues need to be addressed to ensure a robust evidence base to undertake ablation in Brugada Syndrome especially in asymptomatic subjects.

Article information

Conflict of interest: WJY acknowledges the NIHR Integrated Academic Training programme, which supports his Academic Clinical Lectureship post. PDL is supported by UCL/UCLH Biomedicine NIHR and British Heart Foundation. Educational grants and speaker fees, advisory boards from Boston Scientific, Abbott.

Funding: None.

REFERENCES

1. Probst V, Veltmann C, Eckardt L, et al. Long-term prognosis of patients diagnosed with Brugada syndrome: Results from the FINGER Brugada Syndrome Registry. Circulation. 2010; 121(5): 635–643, doi: 10.1161/CIRCULATIONAHA.109.887026, indexed in Pubmed: 20100972.
2. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: A distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol. 1992; 20(6): 1391–1396, doi: 10.1016/0735-1097(92)90253-j, indexed in Pubmed: 1309182.
3. Hunuk B, Kepez A, Erdogan O. Prevalence of Brugada-type electrocardiogram pattern by recording right precordial leads at higher intercostal spaces. Europace. 2013; 15(4): 590–594, doi: 10.1093/europace/eus211, indexed in Pubmed: 22767008.

4. Wilde AAM, Amin AS, Morita H, et al. Use, misuse, and pitfalls of the drug challenge test in the diagnosis of the Brugada syndrome. Eur Heart J. 2023; 44(27): 2427–2439, doi: 10.1093/eurheartj/ehad295, indexed in Pubmed: 37345279.
5. Antzelevitch C, Yan GX, Ackerman MJ, et al. J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge. Heart Rhythm. 2016; 13(10): e295–e324, doi: 10.1016/j.hrthm.2016.05.024, indexed in Pubmed: 27423412.
6. Brugada J, Campuzano O, Arbelo E, et al. Present status of Brugada syndrome: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018; 72(9): 1046–1059, doi: 10.1016/j.jacc.2018.06.037, indexed in Pubmed: 30139433.
7. Vutthikraivit W, Rattanawong P, Putthapiban P, et al. Worldwide prevalence of Brugada syndrome: A systematic review and meta-analysis. Acta Cardiol Sin. 2018; 34(3): 267–277, doi: 10.6515/ACS.201805_34(3).20180302B, indexed in Pubmed: 29844648.
8. Milman A, Andorin A, Gourraud JB, et al. Age of first arrhythmic event in Brugada syndrome: Data from the SABRUS (Survey on Arrhythmic Events in Brugada Syndrome) in 678 patients. Circ Arrhythm Electrophysiol. 2017; 10(12): e005222, doi: 10.1161/CIRCEP.117.005222, indexed in Pubmed: 29254945.
9. Rattanawong P, Kewcharoen J, Kanitsoraphan C, et al. The utility of drug challenge testing in Brugada syndrome: A systematic review and meta-analysis. J Cardiovasc Electrophysiol. 2020; 31(9): 2474–2483, doi: 10.1111/jce.14631, indexed in Pubmed: 32573844.
10. Camkiran V, Ozden O, Atar I. Long-term follow-up of patients with Brugada syndrome: Foremost risk factors associated with overall arrhythmic events. Medicine (Baltimore). 2024; 103(18): e37990, doi: 10.1097/MD.0000000000037990, indexed in Pubmed: 38701276.
11. Wu W, Tian Li, Ke J, et al. Risk factors for cardiac events in patients with Brugada syndrome: A PRISMA-compliant meta-analysis and systematic review. Medicine (Baltimore). 2016; 95(30): e4214, doi: 10.1097/MD.0000000000004214, indexed in Pubmed: 27472692.
12. Biernacka EK, Osadnik T, Bilińska ZT, et al. Genetic testing for inherited cardiovascular diseases. A position statement of the Polish Cardiac Society endorsed by Polish Society of Human Genetics and Cardiovascular Patient Communities. Pol Heart J. 2024; 82(5): 569–593, doi: 10.33963/v.phj.100490, indexed in Pubmed: 38712785.
13. Watanabe H, Minamino T. Genetics of Brugada syndrome. J Hum Genet. 2015; 61(1): 57–60, doi: 10.1038/jhg.2015.97, indexed in Pubmed: 26223181.

14. Kukavica D, Trancuccio A, Mazzanti A, et al. Nonmodifiable risk factors predict outcomes in Brugada syndrome. J Am Coll Cardiol. 2024; 84(21): 2087–2098, doi: 10.1016/j.jacc.2024.07.037, indexed in Pubmed: 39387761.
15. Probst V, Wilde AAM, Barc J, et al. SCN5A mutations and the role of genetic background in the pathophysiology of Brugada syndrome. Circ Cardiovasc Genet. 2009; 2(6): 552–557, doi: 10.1161/CIRCGENETICS.109.853374, indexed in Pubmed: 20031634.
16. Lambiase PD, Ahmed AK, Ciaccio EJ, et al. High-density substrate mapping in Brugada syndrome: Combined role of conduction and repolarization heterogeneities in arrhythmogenesis. Circulation. 2009; 120(2): 106–117, doi: 10.1161/CIRCULATIONAHA.108.771401, indexed in Pubmed: 19564561.
17. Wülfers EM, Moss R, Lehrmann H, et al. Whole-heart computational modelling provides further mechanistic insights into ST-elevation in Brugada syndrome. Int J Cardiol Heart Vasc. 2024; 51: 101373, doi: 10.1016/j.ijcha.2024.101373, indexed in Pubmed: 38464963.
18. Nademanee K, Raju H, de Noronha SV, et al. Fibrosis, connexin-43, and conduction abnormalities in the Brugada syndrome. J Am Coll Cardiol. 2015; 66(18): 1976–1986, doi: 10.1016/j.jacc.2015.08.862, indexed in Pubmed: 26516000.
19. Konigstein M, Rosso R, Topaz G, et al. Drug-induced Brugada syndrome: Clinical characteristics and risk factors. Heart Rhythm. 2016; 13(5): 1083–1087, doi: 10.1016/j.hrthm.2016.03.016, indexed in Pubmed: 27131070.
20. Postema PG, Wolpert C, Amin AS, et al. Drugs and Brugada syndrome patients: Review of the literature, recommendations, and an up-to-date website (www.brugadadrugs.org). Heart Rhythm. 2009; 6(9): 1335–1341, doi: 10.1016/j.hrthm.2009.07.002, indexed in Pubmed: 19716089.
21. Mizusawa Y, Morita H, Adler A, et al. Prognostic significance of fever-induced Brugada syndrome. Heart Rhythm. 2016; 13(7): 1515–1520, doi: 10.1016/j.hrthm.2016.03.044, indexed in Pubmed: 27033637.
22. Zeppenfeld K, Tfelt-Hansen J, de Riva M, 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(40): 3997–4126, doi: 10.1093/eurheartj/ehac262, indexed in Pubmed: 36017572.
23. Belhassen B, Rahkovich M, Michowitz Y, et al. Management of Brugada syndrome: Thirty-three-year experience using electrophysiologically guided therapy with class 1A

antiarrhythmic drugs. Circ Arrhythm Electrophysiol. 2015; 8(6): 1393–1402, doi: 10.1161/CIRCEP.115.003109, indexed in Pubmed: 26354972.

24. Belhassen B, Glick A, Viskin S. Efficacy of quinidine in high-risk patients with Brugada syndrome. Circulation. 2004; 110(13): 1731–1737, doi: 10.1161/01.CIR.0000143159.30585.90, indexed in Pubmed: 15381640.
25. Hermida JS, Denjoy I, Clerc J, et al. Hydroquinidine therapy in Brugada syndrome. J Am Coll Cardiol. 2004; 43(10): 1853–1860, doi: 10.1016/j.jacc.2003.12.046, indexed in Pubmed: 15145111.
26. Mazzanti A, Tenuta E, Marino M, et al. Efficacy and limitations of quinidine in patients with Brugada syndrome. Circulation: Arrhythmia and Electrophysiology. 2019; 12(5): e007143, doi: 10.1161/circep.118.007143.
27. Rakza R, Groussin P, Benali K, et al. Quinidine for ventricular arrhythmias: A comprehensive review. Trends Cardiovasc Med. 2025; 35(2): 73–81, doi: 10.1016/j.tcm.2024.07.003, indexed in Pubmed: 39079606.
28. Anguera I, García-Alberola A, Dallaglio P, et al. Shock reduction with long-term quinidine in patients with Brugada syndrome and malignant ventricular arrhythmia episodes. J Am Coll Cardiol. 2016; 67(13): 1653–1654, doi: 10.1016/j.jacc.2016.01.042, indexed in Pubmed: 27150692.
29. Darmon JP, Bettouche S, Deswardt P, et al. Radiofrequency ablation of ventricular fibrillation and multiple right and left atrial tachycardia in a patient with Brugada syndrome. J Interv Card Electrophysiol. 2004; 11(3): 205–209, doi: 10.1023/B:JICE.0000048571.19462.54, indexed in Pubmed: 15548887.
30. Haïssaguerre M, Shoda M, Jaïs P, et al. Mapping and ablation of idiopathic ventricular fibrillation. Circulation. 2002; 106(8): 962–967, doi: 10.1161/01.cir.0000027564.55739.b1, indexed in Pubmed: 12186801.
31. Nademanee K, Veerakul G, Chandanamattha P, et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. Circulation. 2011; 123(12): 1270–1279, doi: 10.1161/CIRCULATIONAHA.110.972612, indexed in Pubmed: 21403098.
32. Haïssaguerre M, Extramiana F, Hocini M, et al. Mapping and ablation of ventricular fibrillation associated with long-QT and Brugada syndromes. Circulation. 2003; 108(8): 925–928, doi: 10.1161/01.CIR.0000088781.99943.95, indexed in Pubmed: 12925452.

33. Morita H, Zipes DP, Morita ST, et al. Epicardial ablation eliminates ventricular arrhythmias in an experimental model of Brugada syndrome. Heart Rhythm. 2009; 6(5): 665–671, doi: 10.1016/j.hrthm.2009.01.007, indexed in Pubmed: 19328041.
34. McBenedict B, Alphonse B, Devan JN, et al. Advances and challenges in the management of Brugada syndrome: A comprehensive review. Cureus. 2024; 16(6): e61837, doi: 10.7759/cureus.61837, indexed in Pubmed: 38975383.
35. Shan Q, Yang B, Chen M, et al. Short-term normalization of ventricular repolarization by transcatheter ablation in a patient with suspected Brugada syndrome. J Interv Card Electrophysiol. 2008; 21(1): 53–57, doi: 10.1007/s10840-007-9193-y, indexed in Pubmed: 18299974.
36. Pappone C, Brugada J, Vicedomini G, et al. Electrical substrate elimination in 135 consecutive patients with Brugada syndrome. Circ Arrhythm Electrophysiol. 2017; 10(5): e005053, doi: 10.1161/CIRCEP.117.005053, indexed in Pubmed: 28500178.
37. Kotake Y, Barua S, Kazi S, et al. Efficacy and safety of catheter ablation for Brugada syndrome: An updated systematic review. Clin Res Cardiol. 2023; 112(12): 1715–1726, doi: 10.1007/s00392-022-02020-3, indexed in Pubmed: 35451610.
38. Sunsaneewitayakul B, Yao Y, Thamaree S, et al. Endocardial mapping and catheter ablation for ventricular fibrillation prevention in Brugada syndrome. J Cardiovasc Electrophysiol. 2012; 23 Suppl 1: S10–S16, doi: 10.1111/j.1540-8167.2012.02433.x, indexed in Pubmed: 22988965.
39. Nademanee K, Chung FP, Sacher F, et al. Long-term outcomes of Brugada substrate ablation: A report from BRAVO (Brugada Ablation of VF Substrate Ongoing Multicenter Registry). Circulation. 2023; 147(21): 1568–1578, doi: 10.1161/CIRCULATIONAHA.122.063367, indexed in Pubmed: 36960730.
40. Arya A, Di Biase L, Bazán V, et al. Epicardial ventricular arrhythmia ablation: A clinical consensus statement of the European Heart Rhythm Association of the European Society of Cardiology and the Heart Rhythm Society, the Asian Pacific Heart Rhythm Society, the Latin American Heart Rhythm Society, and the Canadian Heart Rhythm Society. Europace. 2025; 27(4): euaf055, doi: 10.1093/europace/euaf055, indexed in Pubmed: 40163515.
41. Pappone C, Santinelli V, Mecarocci V, et al. New electromechanical substrate abnormalities in high-risk patients with Brugada syndrome. Heart Rhythm. 2020; 17(4): 637–645, doi: 10.1016/j.hrthm.2019.11.019, indexed in Pubmed: 31756528.

42. Chung FP, Raharjo SB, Lin YJ, et al. A novel method to enhance phenotype, epicardial functional substrates, and ventricular tachyarrhythmias in Brugada syndrome. Heart Rhythm. 2017; 14(4): 508–517, doi: 10.1016/j.hrthm.2017.01.006, indexed in Pubmed: 28065832.
43. Zhang P, Tung R, Zhang Z, et al. Characterization of the epicardial substrate for catheter ablation of Brugada syndrome. Heart Rhythm. 2016; 13(11): 2151–2158, doi: 10.1016/j.hrthm.2016.07.025, indexed in Pubmed: 27453126.
44. Nademanee K, Wongcharoen W, Chimparlee N, et al. Brugada syndrome ablation for the prevention of ventricular fibrillation episodes (BRAVE). Heart Rhythm. 2025 [Epub ahead of print], doi: 10.1016/j.hrthm.2025.04.033, indexed in Pubmed: 40294736.
45. Cheniti G, Haissaguerre M, Dina C, et al. Left ventricular abnormal substrate in Brugada syndrome. JACC Clin Electrophysiol. 2023; 9(10): 2041–2051, doi: 10.1016/j.jacep.2023.05.039, indexed in Pubmed: 37480873.
46. Nademanee K, Hocini M, Haïssaguerre M. Epicardial substrate ablation for Brugada syndrome. Heart Rhythm. 2017; 14(3): 457–461, doi: 10.1016/j.hrthm.2016.12.001, indexed in Pubmed: 27979714.
47. Doundoulakis I, Chiotis S, Pannone L, et al. Catheter ablation as an adjunctive therapy to ICD implantation in Brugada syndrome. Eur Heart J Qual Care Clin Outcomes. 2024; 10(7): 590–601, doi: 10.1093/ehjqcco/qcae040, indexed in Pubmed: 38777620.
48. Letsas KP, Vlachos K, Efremidis M, et al. Right ventricular outflow tract endocardial unipolar substrate mapping: Implications in risk stratification of Brugada syndrome. Rev Cardiovasc Med. 2022; 23(2): 44, doi: 10.31083/j.rcm2302044, indexed in Pubmed: 35229535.
49. Massé S, Downar E, Chauhan V, et al. Ventricular fibrillation in myopathic human hearts: Mechanistic insights from in vivo global endocardial and epicardial mapping. Am J Physiol Heart Circ Physiol. 2007; 292(6): H2589–H2597, doi: 10.1152/ajpheart.01336.2006, indexed in Pubmed: 17259437.
50. Bazan V, Frankel DS, Santangeli P, et al. Three-dimensional myocardial scar characterization from the endocardium: Usefulness of endocardial unipolar electroanatomic mapping. J Cardiovasc Electrophysiol. 2019; 30(3): 427–437, doi: 10.1111/jce.13842, indexed in Pubmed: 30614100.
51. Pannone L, Della Rocca DG, Vergara P, et al. In vivo mapping of human ventricular fibrillation in Brugada syndrome: The role of repolarization heterogeneity. Circ

Arrhythm Electrophysiol. 2024; 17(12): e013290, doi: 10.1161/CIRCEP.124.013290, indexed in Pubmed: 39624903.

52. Mamiya K, Inden Y, Yanagisawa S, et al. Dynamic changes in electrocardiogram parameters after epicardial substrate catheter ablation of Brugada syndrome. Circ J. 2021; 85(8): 1283–1293, doi: 10.1253/circj.CJ-20-1060, indexed in Pubmed: 33692251.
53. Pappone C, Ciconte G, Vicedomini G, et al. Epicardial ablation in high-risk Brugada syndrome to prevent ventricular fibrillation: Results from a randomized clinical trial. Europace. 2025; 27(5): euaf097, doi: 10.1093/europace/euaf097, indexed in Pubmed: 40401314.
54. Silberbauer J, Gomes J, O'Nunain S, et al. Coronary vein exit and carbon dioxide insufflation to facilitate subxiphoid epicardial access for ventricular mapping and ablation: First experience. JACC Clin Electrophysiol. 2017; 3(5): 514–521, doi: 10.1016/j.jacep.2016.11.002, indexed in Pubmed: 29759609.
55. Romero J, Cerrud-Rodriguez RC, Di Biase L, et al. Combined endocardial-epicardial versus endocardial catheter ablation alone for ventricular tachycardia in structural heart disease: A systematic review and meta-analysis. JACC Clin Electrophysiol. 2019; 5(1): 13–24, doi: 10.1016/j.jacep.2018.08.010, indexed in Pubmed: 30678778.
56. Tarantino N, Della Rocca DG, Faggioni M, et al. Epicardial ablation complications. Card Electrophysiol Clin. 2020; 12(3): 409–418, doi: 10.1016/j.ccep.2020.06.004, indexed in Pubmed: 32771194.
57. Darma A, Bertagnolli L, Dinov B, et al. Predictors of long-term mortality after catheter ablation of ventricular tachycardia in a contemporary cohort of patients with structural heart disease. Europace. 2020; 22(11): 1672–1679, doi: 10.1093/europace/euaa189, indexed in Pubmed: 32830252.
58. Karlinski Vizentin V, Ferreira Felix I, Pivato da Fonseca R, et al. Epicardial substrate ablation in patients with symptomatic Brugada syndrome: An updated systematic review and single-arm meta-analysis. Heart Rhythm. 2025 [Epub ahead of print], doi: 10.1016/j.hrthm.2025.01.006, indexed in Pubmed: 39800093.
59. Li Le, Ding L, Zhou L, et al. Outcomes of catheter ablation in high-risk patients with Brugada syndrome refusing an implantable cardioverter defibrillator implantation. Europace. 2023; 26(1): euad318, doi: 10.1093/europace/euad318, indexed in Pubmed: 37889958.

60. Conte G, Scherr D, Lenarczyk R, et al. Diagnosis, family screening, and treatment of inherited arrhythmogenic diseases in Europe: Results of the European Heart Rhythm Association Survey. Europace. 2020; 22(12): 1904–1910, doi: 10.1093/europace/euaa223, indexed in Pubmed: 33367591.
61. Bergonti M, Sacher F, Arbelo E, et al. Implantable loop recorders in patients with Brugada syndrome: the BruLoop study. Eur Heart J. 2024; 45(14): 1255–1265, doi: 10.1093/eurheartj/ehae133, indexed in Pubmed: 38445836.
62. Rattanawong P, Mattanapojanat N, Mead-Harvey C, et al. Predicting arrhythmic event score in Brugada syndrome: Worldwide pooled analysis with internal and external validation. Heart Rhythm. 2023; 20(10): 1358–1367, doi: 10.1016/j.hrthm.2023.06.013, indexed in Pubmed: 37355026.
63. Sieira J, Conte G, Ciconte G, et al. A score model to predict risk of events in patients with Brugada syndrome. Eur Heart J. 2017; 38(22): 1756–1763, doi: 10.1093/eurheartj/ehx119, indexed in Pubmed: 28379344.
64. Kawada S, Morita H, Antzelevitch C, et al. Shanghai score system for diagnosis of Brugada syndrome: Validation of the score system and system and reclassification of the patients. JACC Clin Electrophysiol. 2018; 4(6): 724–730, doi: 10.1016/j.jacep.2018.02.009, indexed in Pubmed: 29929664.
65. Honarbakhsh S, Providencia R, Garcia-Hernandez J, et al. A primary prevention clinical risk score model for patients with Brugada syndrome (BRUGADA-RISK). JACC Clin Electrophysiol. 2021; 7(2): 210–222, doi: 10.1016/j.jacep.2020.08.032, indexed in Pubmed: 33602402.
66. Viskin S, Rosso R. Treatment of Brugada syndrome in 2023: Know where you come from to know where you are going. Circulation. 2023; 147(21): 1579–1581, doi: 10.1161/CIRCULATIONAHA.123.064673, indexed in Pubmed: 37216435.
67. Brugada J, Pappone C, Berruezo A, et al. Brugada syndrome phenotype elimination by epicardial substrate ablation. Circ Arrhythm Electrophysiol. 2015; 8(6): 1373–1381, doi: 10.1161/CIRCEP.115.003220, indexed in Pubmed: 26291334.
68. Shelke A, Tachil A, Saggu D, et al. Catheter ablation for electrical storm in Brugada syndrome: Results of substrate based ablation. Indian Heart J. 2018; 70(2): 296–302, doi: 10.1016/j.ihj.2017.07.019, indexed in Pubmed: 29716710.
69. Nademanee K, Haissaguerre M, Hocini M, et al. Mapping and ablation of ventricular fibrillation associated with early repolarization syndrome. Circulation. 2019; 140(18):

1477–1490, doi: 10.1161/CIRCULATIONAHA.118.039022, indexed in Pubmed: 31542949.

70. Salghetti F, de Asmundis C, Sieira J, et al. Hybrid thoracoscopic epicardial ablation of right ventricular outflow tract in patients with Brugada syndrome. Heart Rhythm. 2019; 16(6): 879–887, doi: 10.1016/j.hrthm.2018.12.026, indexed in Pubmed: 30594641.
71. Kamakura T, Cochet H, Juhoor M, et al. Role of endocardial ablation in eliminating an epicardial arrhythmogenic substrate in patients with Brugada syndrome. Heart Rhythm. 2021; 18(10): 1673–1681, doi: 10.1016/j.hrthm.2021.06.1188, indexed in Pubmed: 34182174.
72. Haissaguerre M, Cheniti G, Hocini M, et al. Purkinje network and myocardial substrate at the onset of human ventricular fibrillation: Implications for catheter ablation. Eur Heart J. 2022; 43(12): 1234–1247, doi: 10.1093/eurheartj/ehab893, indexed in Pubmed: 35134898.
73. Santinelli V, Ciconte G, Manguso F, et al. High-risk Brugada syndrome: Factors associated with arrhythmia recurrence and benefits of epicardial ablation in addition to implantable cardioverter defibrillator implantation. Europace. 2023; 26(1): euae019, doi: 10.1093/europace/euae019, indexed in Pubmed: 38252933.
74. Talib AK, Takagi M, Shimane A, et al. Efficacy of endocardial ablation of drug-resistant ventricular fibrillation in Brugada syndrome: Long-term outcome. Circ Arrhythm Electrophysiol. 2018; 11(8): e005631, doi: 10.1161/CIRCEP.117.005631, indexed in Pubmed: 30354308.

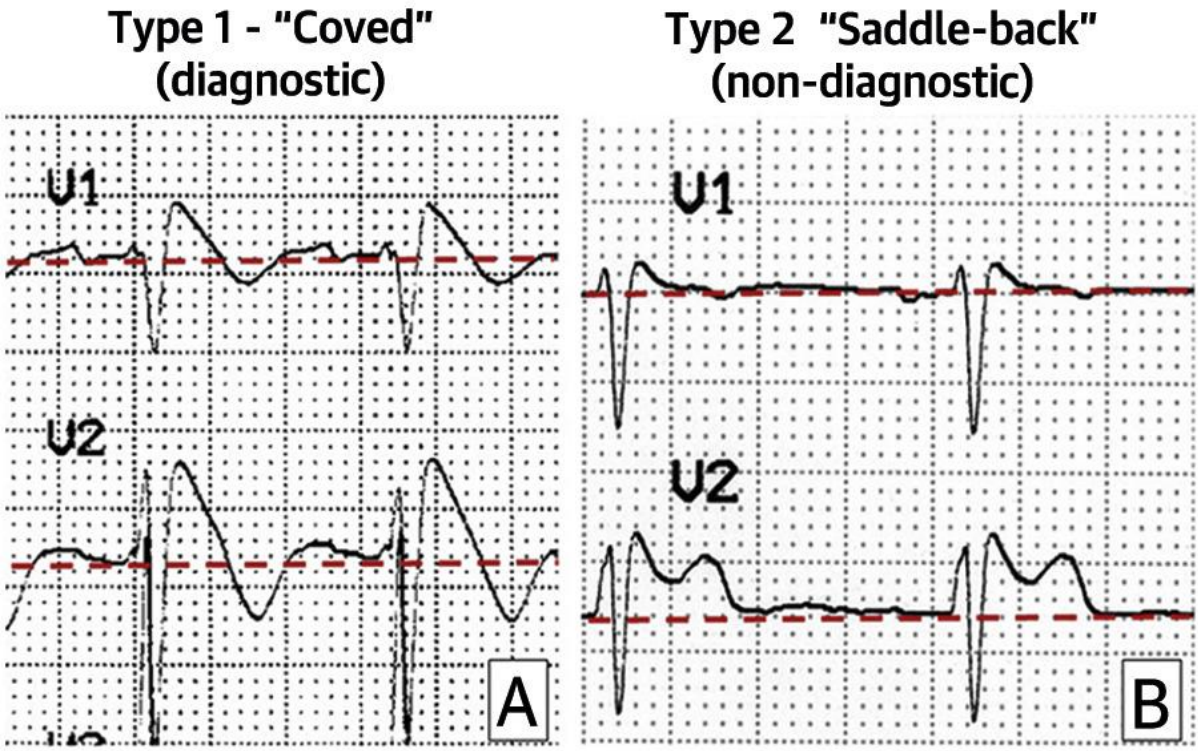

Figure 1. Electrocardiographic patterns in Brugada syndrome. **A.** Type 1 Brugada pattern with J-point elevation and a coved ST segment ≥0.2 mV. **B.** Type 2 Brugada pattern with saddle-shaped ST segment elevation ≥0.2 mV. Reused with permission [6]

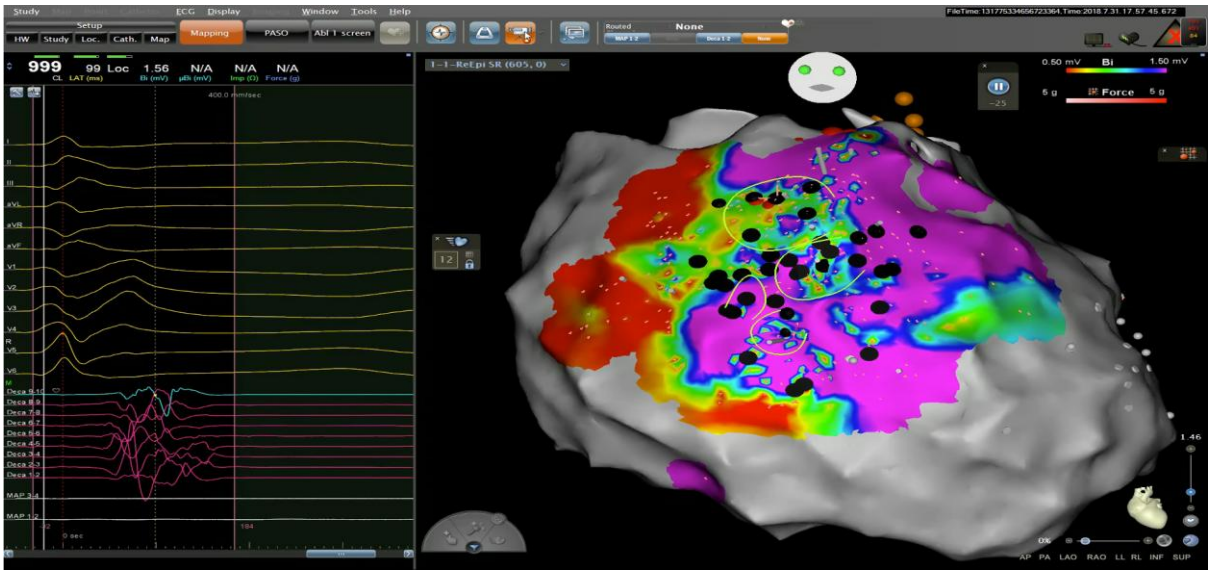

Figure 2. Epicardial substrate ablation targeting late and fractionated potentials. Epicardial substrate ablation for multiple appropriate shocks in the setting of poorly tolerated quinidine. Scattered areas of low voltage were observed in the epicardial right ventricular outflow tract consistent with regions of fibrosis. Late potentials and prolonged fractionated electrograms extending beyond the surface electrocardiogram QRS were targeted (see example in lower panel purple signals on left)

Table 1. Summary of published studies reporting outcomes for VT ablation in Brugada syndrome

First author	Year	Sample size	% male sex	Average age	Inclusion	Endo/Epi	Trigger or Substrate	SCB used	Duration of follow up	No. of patients with VT/VF during follow up after ablation	Procedural complications
Nademanee [31]	2011	9	100%	38 years	Spontaneous or drug-induced type 1 pattern with: 1) recurrent VF despite medical therapy	Combination	Substrate	None reported	Mean 20 months (± 6 months)	1 (11.1%)	Pericarditis (2×)
Sunsaneewitayakul [38]	2012	10	100%	Median 25 years (20–27 years)	Spontaneous or drug-induced type 1 pattern with either:	Endocardium	Primarily substrate but PVC triggers targets if	Flecainide	30 months for 3 patients,	4 (40%)	Right bundle branch block (1×)

					1) documented VF 2) polymorphic VT 3) syncope 4) nocturnal agonal respiration		also present		12 months for 1 patient		
Brugada [67]	2015	14	100%	39 years	Spontaneous or drug-induced type 1 pattern with either: 1) symptoms secondary to ventricular arrhythmia 2) high vulnerability for ventricular arrhythmia induction at	Combination	Substrate	Flecainide infusion (2 mg/kg in 10 mins)	Median 5 months (range 3.5–5.3)	0 (0%)	Pericarditis (1×)

					electrophysiology study						
Zhang [43]	2016	11	100%	Mean 48 years (± 16 years)	Spontaneous or drug-induced type 1 pattern with either: 1) documented VT/VF 2) syncope	Combination	Substrate	Procainamide (1g *i.v.* over 30 mins) or propafenone (1.5 mg/kg/10min)	Mean 25 months (± 11 months)	3 (27%)	Pericarditis (2×)
Chung [42]	2017	15	100%	Mean 41 years (± 10 years)	Spontaneous or drug-induced type 1 pattern with either: 1) aborted cardiac arrest 2) documented VT/VF	Combination	PVC triggers and substrate modification	Flecainide	Mean 18 months (± 9 months)	1 (6.7%)	None

Pappone [36]	2017	135	79%	Mean 40 years	Spontaneous or drug-induced type 1 pattern referred for an electrophysiology study with potential indication for VT/VF catheter ablation	Combination	Substrate	Ajmaline (1 mg/kg in 5 minutes)	Median 10 months (range 3–13)	2 (1.5%)	Pericardial effusion (5×) managed with medication only
Shelke [68]	2017	5	80%	Mean 29 (± 3.9 years)	Spontaneous type 1 patterns with electrical storm despite medical therapy	Combination	Substrate (due to insufficient PVCs in all)	Procainamide (10 mg/kg over 30 mins) for 3 patients	Median 46 months (range 4–81)	1 (20%)	Pericarditis (2×) Pericardial effusion (1×, same patient)
Nademanee [69]	2019	33 with early repolarisation and Brugada	92% (full cohort)	Median 37 years (± 14 years),	Early repolarisation study focused. However included	Combination	Primarily substrate but PVC triggers targets if	None reported	Mean 31 months (± 26 months)	14 (33%), full cohort	Pericardial effusion (1×)

		pattern, 7 with ER pattern only		full cohort	patients with ER and Brugada pattern (spontaneous or drug-induced) with either: 1) recurrent VF episodes 2) cardiac or unknown syncope 3) agonal respiration during sleep		also present				
Salghetti [70]	2019	36	72%	Mean 37 years (± 16 years)	Diagnosis of Brugada syndrome and calculate risk of VT/VF of >6% at 5 years (based on risk	Epicardial	Hybrid epicardial substrate approach	Ajmaline	Mean 16 months (± 8 months)	2 (5.6%)	Cardiac tamponade (1×)

					score by Sieira et al. [63])						
Kamakura [71]	2021	16	94%	Mean 44 years (± 13 years)	Spontaneous or drug-induced type 1 pattern and at least 1 documented episode of VT/VF	Combination	Substrate	None reported	Mean 29 months (± 29 months)	7 (44%)	None
Mamiya [52]	2021	11 in ablation group, 16 with ICD only	100%	Mean 45 years (full cohort)	Diagnosis of Brugada syndrome with recurrent VF episodes and ICD shock therapy	Combination	Substrate guided	Pilsicainide (*i.v.* 50 mg)	Mean 42 months	8 (72.7%), ablation group	None
Haissaguerre [72]	2022	19 patients with Brugada syndrome	100%	Mean 45 years (± 11 years)	Diagnosis of Brugada syndrome with previous documented VF	Combination	Combined VF triggers and substrate guided	None reported	Mean 58 months	6 (35%)	Cardiac tamponade (1×) in total cohort (including

											cardiomyopathies)
Li [59]	2023	40 (18 underwent CA)	89%	Mean 39 years (± 9 years)	VF or syncope, spontaneous type 1	Combination	Primarily substrate but PVC triggers targets if also present	Propafenone (1.5 mg/kg/10 min)	Median 46.2 months (17.5–73.7)	1 (5.5%)	Cardiac tamponade (1×)
Santinelli [73]	2024	206 patients	69%	Mean 40.5 years (± 11.6 years)	Spontaneous or drug-induced type 1 pattern with either 1) no concomitant ER ECG pattern 2) aborted cardiac arrest or malignant syncope	Combination	Substrate-guided	Ajmaline	Median 40 months (24–58)	1 (0.5%)	None

					3) ICD implantation 4) diagnostic work up for syncope without documented VT/VF 5) negative coronary angiography						
Nademanee [44]	2025	25 in ablation group, 25 in control arm	100%	43 years (ablation group)	Spontaneous or drug-induced type 1 pattern with either: 1) aborted cardiac arrest 2) documented VF 3) agonal respiration during sleep	Combination	PVC triggers if present and substrate mapping	Ajmaline	36 months	5 (20%)	Haemo-pericardium (1×)

					with difficulty arousing 4) unexplained malignant syncope 5) seizures suspected of arrhythmic origin						
Pappone [53]	2025	26 in ablation group, 14 in control arm	83%	Mean 43.7 years (± 12.1 years)	Spontaneous or drug-induced type 1 pattern with either: 1) aborted cardiac arrest 2) appropriate ICD therapy for VF	Combination	Substrate-guided	Ajmaline	Median 48.4 months	1 (after single procedure, 3.8%)	Pericarditis (1×) Pericardial effusion requiring drain (1×)
Talib [74]	2018	21 patients	90.50 %	Mean 43 years	Spontaneous or drug-induced type 1 pattern with	Endocardial	PVC triggers if present and	Pilsicainide	Mean 56 months	7 (33.3%)	Steam pop during RVOT ablation

				(± 14 years)	documented VF/VT storm or recurrent ICD shocks despite medical therapy		substrate mapping		(± 37 months)		without sequelae (1×) Transient RBBB (2×)

Abbreviations: ECG, electrocardiogram; ER, early repolarization; ICD, implantable cardioverter-defibrillator; *i.v.*, intravenous; PVC, premature ventricular complex; RBBB, right bundle branch block; VF, ventricular fibrillation; VT, ventricular tachycardia

Table 2. Examples of Brugada risk scores

Predicting Arrhythmic evenT (PAT) score	Points	Sieira score	Points	Shanghai score system	Points	BRUGADA-RISK score	Points
ECG markers		ECG markers		ECG markers		Spontaneous type 1 Brugada pattern	14
T-peak to T-end ≥100 ms	5	Spontaneous type 1	1	A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5	Arrhythmic syncope	12
Prolonged PR ≥200 ms	4	Sinus node disease	3	B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3	Early repolarisation in peripheral leads	12
Fragmented QRS	3	History		C. Type 2 or 3 Brugada ECG pattern converting with drug challenge	2	Type 1 Brugada pattern in peripheral leads	9

Type 1 in peripheral leads	3	Aborted SCD	4	Clinical history			
aVR sign	3	Syncope	2	A. Unexplained cardiac arrest or documented VF/polymorphic VT	3		
Early repolarization in inferolateral leads	3	Inducible electrophysiology study	2	B. Nocturnal agonal respirations	2		
Spontaneous type 1	2	Early familial SCD	1	C. Suspected arrhythmic syncope	2		
History				D. Syncope of unclear mechanism/unclear etiology	1		
Arrhythmic syncope	5			E. Atrial flutter/fibrillation in patients <30 years without alternative etiology	0.5		
Unexplained syncope	5			Family history			
Family history of SCD at age <40 years	2			A. First- or second-degree relative with definite BrS	2		
Atrial fibrillation	2			B. Suspicious SCD (with Brugada features) in first- or second-degree relative	1		
Laboratory tests				C. Unexplained SCD <45 years in first- or second-degree relative	0.5		

Positive electrophysiological study	2			Genotype			
Positive *SCN5A*	2			A. Probable pathogenic mutation in BrS susceptibility gene	0.5		
Score to define high risk	≥10	Score to define high risk	≥2	Score to define high risk	≥5.5	Score to define high risk	≥21

Abbreviations: BrS, Brugada syndrome; ECG, electrocardiogram; SCD, sudden cardiac death; other — see Table 1