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Catheter ablation of idiopathic outflow tract ventricular arrhythmias with low intraprocedural burden guided by pace mapping

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BACKGROUND There are limited data comparing ablation outcomes in patients with low intraprocedural burden of ventricular arrhythmias (VA) undergoing a pace mapping (PM)-guided strategy vs those with high burden guided by standard activation mapping strategy (non-PM).

OBJECTIVE We sought to determine if catheter ablation-guided by PM of low-intraprocedural-burden idiopathic outflow tract VA would be noninferior compared to non-PM-guided ablation.

METHODS Outcomes of catheter ablation of idiopathic outflow tract VA in 22 patients with a low burden of intraprocedural VA using PM-guided ablation were compared to 44 patients with a high burden of intraprocedural VA undergoing ablation using standard techniques.

RESULTS Sixty-six patients were included (age 46.5 ± 14.8 years; 68% female, left ventricular ejection fraction $59\% \pm 5\%$). Within the PM group, 24-hour preprocedure premature ventricular complex (PVC) burden was 9.5% (interquartile range [IQR] 4%–13.8%), number of pace maps 33.6 ± 18.5 , surface area of $\geq 95\%$ pace map correlation 1.9 ± 1.2 cm², with best pace map correlation

96% (IQR 92%–97%). Within the non-PM group, 24-hour preprocedure PVC burden was 13.5% (IQR 6.6%–30%), earliest activation time -33.7 ± 9.9 ms. Procedural duration, general anesthesia administration, fluoroscopy dose, and complications were all comparable. Following final procedure, 24-hour VA burden (PM 0% [IQR 0–2.4%] vs non-PM 0% [IQR 0–4.2%], $P = .98$), along with VA-free survival at 6-month follow-up (PM 77% vs non-PM 71%, $P = .77$), were both comparable.

CONCLUSION In patients with low intraprocedural burden of outflow tract VA, PM-guided catheter ablation can accurately identify the VA site of origin, leading to outcomes comparable to those achieved with standard ablation techniques.

KEYWORDS Catheter ablation; Idiopathic; Outflow tract; Pace mapping; Ventricular arrhythmia

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Introduction

Catheter ablation is highly efficacious in the treatment of idiopathic outflow tract ventricular arrhythmia (VA). It can relieve symptoms related to arrhythmia, reduce high VA burden, restore ventricular function in VA-related cardiomyopathy, and cure premature ventricular complex (PVC)-triggered ventricular fibrillation.¹ Mechanistically, outflow tract VAs predominantly occur owing to focal automaticity or triggered activity and are most commonly idiopathic in etiology. Standard ablation techniques rely on frequent, spontaneous

intraprocedural VA or reliable provocation, allowing for activation mapping. Pace mapping (PM) can be used to supplement activation mapping.² Contemporary electroanatomic mapping (EAM) systems have sophisticated algorithms that can accurately correlate the paced QRS morphology with the clinical VA. Paucity of VA at the time of ablation is not uncommon, with daily variability in VA burden, sedation, and general anesthesia all impacting VA provocation. In such situations, ablation may be guided primarily by PM. Relying predominantly on this approach can be limited by several factors, including unreliable pace capture, inferior pace map spatial resolution compared to activation mapping,³ intramural VA focus resulting in poor pace map correlation on the endocardial surface, and uncertainty regarding acute success. Recently several studies have sought to

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KEY FINDINGS

- Highly symptomatic premature ventricular complexes (PVCs) that are relatively quiescent on the scheduled day of catheter ablation is a common clinical problem
- Catheter ablation guided solely by a pace mapping strategy in these patients can result in equivalent outcomes, compared to standard ablation techniques in patients with higher intraprocedural burden of PVCs, with comparable procedure times and complication rates

describe outcomes in patients with a low intraprocedural burden of idiopathic PVCs in whom primarily a PM approach was employed. Although results are encouraging, these studies are limited by a small number of patients, with reported freedom from clinical VA between 79% and 100%, during medium-term follow-up.^{4,5}

In this study we sought to compare outcomes among patients with low intraprocedural burden of idiopathic outflow tract VA who received ablation guided by a PM approach vs patients with frequent intraprocedural idiopathic outflow tract VA undergoing standard activation-guided ablation (non-PM). We hypothesized that the 2 techniques would have comparable outcomes.

Methods

Between April 2016 and June 2020, 66 consecutive patients underwent catheter ablation of idiopathic outflow tract VA at a single tertiary referral center (Westmead Hospital, Sydney, Australia) and were included in this retrospective analysis. To meet inclusion criteria, patients were required to have a diagnosis of idiopathic outflow tract PVC or ventricular tachycardia (VT), treated by catheter ablation. Patients with evidence of structural heart disease were excluded, apart from those deemed to have PVC-induced cardiomyopathy. Patients with idiopathic VA originating from the coronary cusps (but not left ventricular outflow tract) and intracardiac areas other than the outflow tracts were also excluded. These patients were excluded based on VA electrocardiogram (ECG) morphology or if the site of best PM correlation or earliest activation was in a coronary cusp or non-outflow tract location. Patients who required additional ablation from a coronary cusp for a VA focus with best PM correlation or earliest activation in an outflow tract site (that was not in the coronary cusps), where the focus was likely intramural, were included in the study.

Transthoracic echocardiography ± cardiac magnetic resonance imaging was performed on all patients prior to procedure, to assess for structural heart disease and define ventricular function. Where relevant, investigations to exclude ischemic heart disease were performed, including 1 or a combination of stress echocardiography, computed tomography coronary angiography, or invasive coronary

angiography. Patients were deemed to have structural heart disease if they had any of the following: (1) ischemic heart disease, defined as either significant coronary artery disease (>70% stenosis), prior coronary artery revascularization, evidence of myocardial ischemia, or prior myocardial infarction; or (2) nonischemic cardiomyopathy, defined as either evidence of a nonischemic cardiomyopathic disease diagnosed on multimodality imaging (including transthoracic echocardiography, cardiac magnetic resonance imaging, prior EAM) or VA not consistent with an idiopathic arrhythmia.

All patients gave written informed consent for the procedure. The study analysis was performed according to protocols approved by the Western Sydney Local Health District Human Research Ethics Committee and in keeping with the Helsinki Declaration guidelines on human research.

Mapping

Figure 1 outlines the procedural workflow used in our study. Antiarrhythmic drugs (AADs) were ceased at least 5 half-lives prior to the procedure, except in the case of an emergent indication or amiodarone, where the half-life is considerably longer than 5 days. Procedures were performed under conscious sedation whenever possible using a combination of low-dose midazolam with or without low doses of fentanyl, to aid VA inducibility. When this was not practical, general anesthesia was used at the discretion of the operator and anesthesiologist; this typically involved anesthesia induction using propofol, followed by remifentanyl.

Vascular access was obtained under ultrasound guidance. An SL3 sheath (Abbott Medical, Abbott Park, IL) was used to perform coronary sinus venography and insertion of a decapolar catheter into the coronary sinus. A quadripolar catheter was deployed to the right ventricle (RV) apex. Systemic anticoagulation was administered after sheath insertion using intravenous unfractionated heparin to maintain an activated clotting time of ≥ 400 seconds prior to left ventricle (LV) access or ≥ 250 seconds for RV access, unless an epicardial approach was planned. If an epicardial approach was planned, anticoagulation was commenced after safe epicardial access was established. The endocardial LV was accessed transeptally (Large curve AgilisTM; Abbott Medical), or retrogradely (SL1 8.5F; Abbott Medical), or both. In 1 patient with previously failed endocardial catheter ablation and suspected intramural/epicardial substrate, epicardial access (via a percutaneous approach) was obtained. Coronary angiography was performed prior to epicardial ablation to avoid coronary artery injury. High-output pacing (10 mA and 9 ms output) was performed to exclude phrenic nerve stimulation.

Three-dimensional EAM of the RV, LV, or both was performed using either the CARTO® (Biosense Webster, Inc, Diamond Bar, CA) or EnSite PrecisionTM (Abbott Medical) EAM systems. In the EAM system and Cardiolab EP recording system, band-pass filtering was performed at 30–500 Hz. An endocardial and/or epicardial 3-dimensional shell

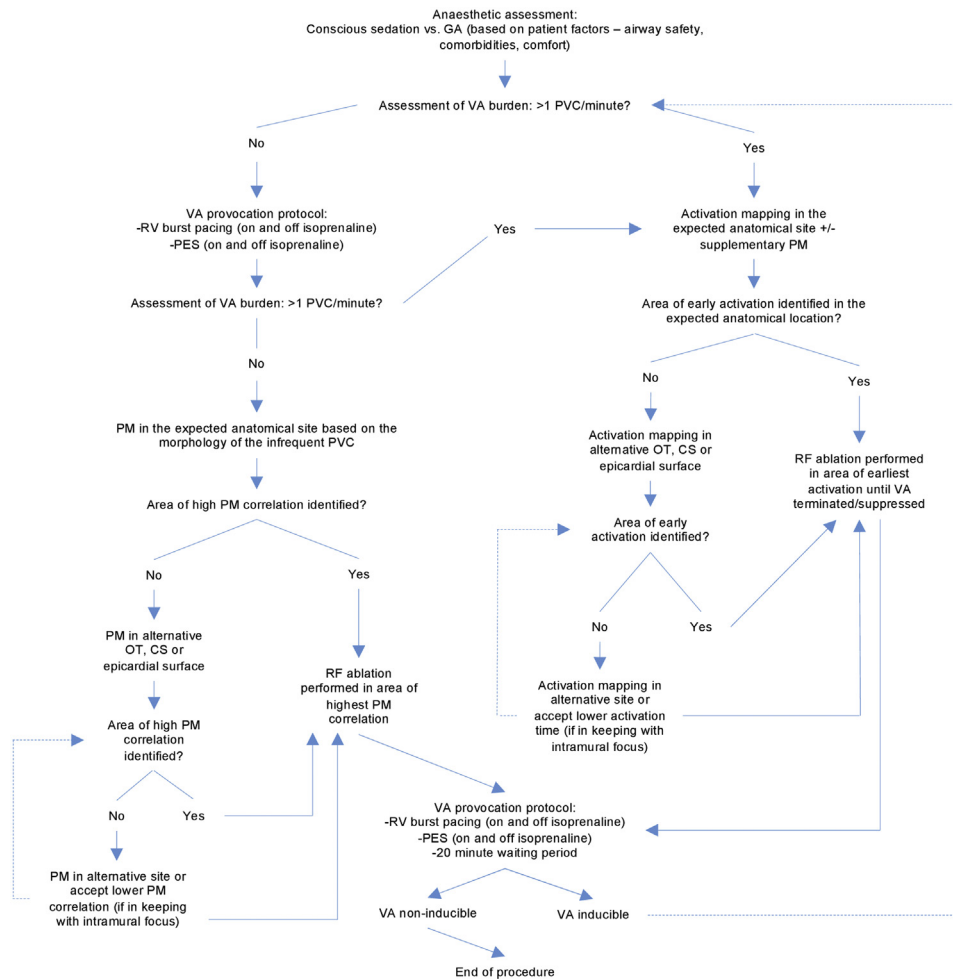


Figure 1 Flowchart outlining the procedural workflow adopted for each patient. CS = coronary sinus; GA = general anesthesia; OT = outflow tract; PES = programmed electrical stimulation; PM = pace mapping; PVC = premature ventricular complex; RV = right ventricle; VA = ventricular arrhythmia.

of chamber geometry was constructed for the ventricle of interest, with electrogram recordings during the patient's native rhythm (sinus or paced rhythm). The chamber mapped was based on the characteristics of the induced or spontaneously occurring VA. Intracardiac echocardiography (ICE) was used where feasible, with or without image integration where possible (CARTO; Biosense Webster, Inc).

VA provocation protocol

Patients were allocated to receive PM- or non-PM-guided ablation based on the intraprocedural burden of VA. When the targeted VA was too scarce to permit activation mapping, several provocation maneuvers were employed before a PM technique was assigned. Initially, burst RV pacing down to ventricular refractoriness was performed from the RV apex. This was then repeated on the highest tolerated dose of isoprenaline (up to 40 $\mu\text{G}/\text{min}$) with hemodynamic support to maintain perfusion pressure. This typically involved an intravenous infusion of metaraminol and/or noradrenaline, titrated according to blood pressure. Programmed electrical stimulation was then performed from at least 2 RV sites using a 400 ms drive train with 4 extrastimuli beginning at 300 ms,

decrementing by 10 ms down to ventricular refractoriness. Isoprenaline was initially commenced at 10 $\mu\text{G}/\text{min}$, with the programmed electrical stimulation and RV burst pacing protocol repeated after incrementing the isoprenaline dose by 10 $\mu\text{G}/\text{min}$. Sustained VT was defined as monomorphic VA with duration >10 seconds.

If, despite this provocation protocol, the paucity of VA remained too low to permit activation, defined as <1 PVC per minute, then PM-guided ablation was performed. The same VA provocation protocol was repeated post ablation.

Pace mapping protocol

The starting anatomical location was determined based on the morphology of the clinical VA documented on the preprocedural ECG or that seen infrequently at the start of the procedure. Bipolar pacing from the ablation catheter at a fixed rate of 600 ms (or 10 ms below baseline rate) with an output of 2 mA and 2 ms pulse width was performed. Tissue contact was confirmed by ensuring a contact force (CF) of ≥ 10 g and, where available, through direct visualization of the catheter tip with ICE. In regions where no pace capture was obtained, the pacing output was increased to 10 mA and

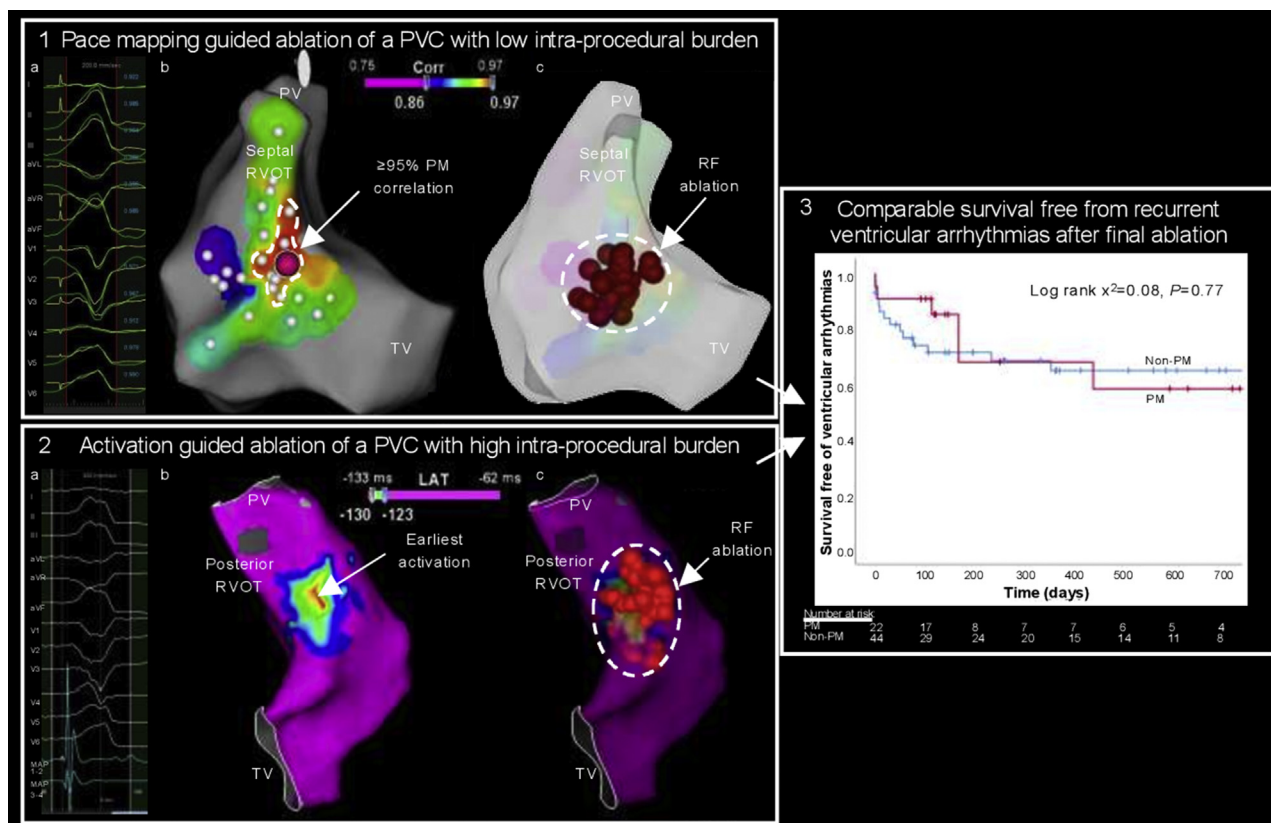


Figure 2 Pace mapping (PM)-guided ablation of a premature ventricular complex (PVC) with low intraprocedural burden originating from the inferior septal right ventricular outflow tract (RVOT) (1a–c), and activation-guided ablation of a PVC with high intraprocedural burden originating from the posterior RVOT (2a–c). Survival analysis demonstrated comparable freedom from recurrent ventricular arrhythmias at 6 months (3). **1a–c:** The clinical PVC template (green) with the paced beat morphology (yellow) can be seen (1a); there is a 97% pace map correlation. The right ventricle (RV) geometry is depicted in a left posterior view with the pace map correlation displayed in 1b. Each white dot represents an area of PM with correlation $\geq 86\%$ and the colors represent accuracy of pace map correlation to the clinical PVC morphology (purple = lowest to red = highest). The area encircled with a white dotted line represents the surface area with $\geq 95\%$ PM; the pink dot represents the best PM of 97% and corresponds to the paced morphology in 1a. Image 1c represents the area of radiofrequency (RF) ablation (red dots), encompassing the area of high PM correlation. **2a–c:** Image 2a shows the clinical PVC as recorded through the surface electrocardiogram leads with the earliest signal (-47 ms before onset of QRS) recorded from the distal electrode of the ablation catheter (MAP 1–2). The RV geometry is depicted in a right lateral view in images 2b and 2c. In image 2b, the purple area represents anatomical locations where the ablation catheter signal was recorded later than -123 ms before the CARTO reference point. The blue, green, yellow, and red region corresponds to an area in the posterior RVOT where the ablation catheter signal was recorded earlier than -123 ms before the CARTO reference point. Image 2c depicts the ablation performed (red dots) in this area of early activation. **3:** Survival free of recurrent ventricular arrhythmias after final procedure; PM (red), non-PM (blue). Survival free from recurrent ventricular arrhythmias was comparable between the 2 groups at 6 months. LAT = local activation time; PV = pulmonary valve; TV = tricuspid valve.

2 ms, and then further to 10 mA and 9 ms if required. No capture at this high output was tagged as an area of electrically inexcitable myocardium (typically, the valve annuli or areas of prior ablation). Captured beats were analyzed using algorithms on the relevant EAM systems (PASO® for CARTO [Biosense Webster]; Score map for EnSite Precision [Abbott Medical]). This technique involved clear delineation of an area of high pace map correlation (ideally $>90\%$). This was achieved by defining areas of poor pace map correlation, which improved in all directions towards the area of best pace map correlation (Figure 2). The region of high pace map correlation ($\geq 90\%$) was then treated with radiofrequency (RF) ablation. When high pace map areas were not located in the expected location, the technique was repeated in an adjacent anatomical site. Recognition of intramural foci prompted the

operator to accept lower pace map correlations (the lowest best accepted pace map correlation was 81%), perform longer duration of ablation with surrounding consolidatory lesions, and/or perform ablation from an adjacent site in a different chamber.

Patients with an intraprocedural burden of VA high enough to permit activation mapping underwent a standard approach to their ablation, guided by activation mapping using the ablation catheter (33/44 [75%]), or alternatively using a multielectrode mapping catheter (11/44 [25%]). This approach could be supported by PM at the discretion of the operator, as per guidelines.¹ Areas of ablation were performed where the signal on the distal electrode of the ablation catheter was earliest to onset of the PVC/VT QRS (activation mapping).

Table 1 Baseline patient characteristics

	PM (n = 22)	Non-PM (n = 44)	P value
Age, mean \pm SD (years)	47.3 \pm 12	45.3 \pm 15.8	.6
Sex: Female, n (%)	15 (68)	30 (68)	1
LVEF, mean \pm SD (%)	60 \pm 2	58 \pm 6	.13
Number of failed AADs pre-index procedure, median (IQR)	1 (0–1)	1 (0–1)	.65
Failed amiodarone pre-index procedure, n (%)	0 (0)	1 (2)	.51
PVC-induced cardiomyopathy, n (%)	0 (0)	4 (9)	.15
PVC as indication for procedure, n/N procedures (%)	16/25 (64)	28/48 (58)	.62
Sustained VT as indication for procedure (including VT storm), n/N procedures (%)	9/25 (36)	20/48 (42)	.62
VT storm as indication for procedure, n/N procedures (%)	0/25 (0)	3/48 (7)	.18
Comorbidities, n (%):			
Diabetes mellitus	1 (5)	4 (9)	.57
Hypertension	4 (18)	9 (21)	.78
Chronic lung disease [†]	1 (5)	2 (5)	1
Obstructive sleep apnea	2 (9)	3 (7)	.78
CKD [‡]	0 (0)	0 (0)	-
Atrial fibrillation/flutter	1 (5)	4 (9)	.57
Previous stroke	1 (5)	0 (0)	.14
Obesity	2 (9)	5 (11)	.8

AAD = antiarrhythmic drug; CKD = chronic kidney disease; IQR = interquartile range; LVEF = left ventricular ejection fraction; PM = pace mapping; PVC = premature ventricular complex; SD = standard deviation; VT = ventricular tachycardia.

[†]Chronic lung disease includes asthma, chronic obstructive pulmonary disease, bronchiectasis, pulmonary fibrosis, and amiodarone-induced lung disease.

[‡]CKD was defined as baseline eGFR <60 mL/min/1.73 m²

Ablation

RF ablation was performed using a 3.5-mm-tip open-irrigation catheter ThermoCool® SmartTouch® SurroundFlow® (Biosense Webster Inc), or the TactiCath™ SE catheter (Abbott Medical). Ablation was routinely delivered with a CF of ≥ 10 grams. RF energy of up to 50 watts was delivered, aiming for an impedance drop of between 10 and 20 ohms. When available, real-time visualization of the catheter tip using ICE guided ablation, ensuring adequate tissue contact and catheter stability along with lesion formation.

In the PM-guided ablation group, ablation was performed until the region of best 5%–10% PM correlation was completely treated with ablation lesions, as defined by the above ablation parameters and the EAM system. In the non-PM group, ablation was guided by cessation and noninducibility of VA, with acute success defined as the noninducibility of any PVCs/VT and failure defined as persisting or inducible clinical/spontaneous VA despite ablation. Following ablation with both techniques, the complete VA provocation protocol was repeated (Figure 1).

Follow-up

All patients underwent a 24-hour period of cardiac monitoring immediately following the procedure. After discharge, patients were followed up through a combination of outpatient clinical reviews, 5-day Holter monitoring (4–6 weeks

after ablation), or an implantable loop recorder. In the latter, patients were enrolled in a remote monitoring service, managed either by Westmead Hospital or referring cardiologist. All implantable loop recorder activations were recorded, logged, and transmitted to the clinic, which prompted an in-office visit for detailed evaluation of clinical and device data. Hospital medical records and outpatient clinic assessments were used to complete clinical follow-up. Follow-up was defined as the time from final ablation procedure to the last documented clinical review.

In follow-up, outcomes were reported as follows:

VA-free survival:

- PVC recurrence, defined as failure to reduce PVC burden by >80% on Holter monitoring,⁵ or symptomatic recurrence of PVCs captured on ECG/cardiac monitoring;
- Sustained VA recurrence, defined as any sustained VA greater than or equal to 30 seconds, VA resulting in hospitalization, or need for repeat ablation procedure.

Outcomes were reported after the final procedure.

Definition of major complications

Major complications were defined as any major vascular complications requiring transfusion, endovascular or surgical treatment, any thromboembolic event (including stroke, systemic or pulmonary emboli), atrioventricular block, pericardial effusion requiring intervention, heart failure,

Table 2 Procedural characteristics

	PM (n = 22)	Non-PM (n = 44)	P value
Total number of ablation procedures performed, no. of patients/no. of procedures (%)	22/25 (88%)	44/48 (92%)	.58
Number (%) of patients undergoing:			
1 procedure	20 (91)	39 (89)	.8
2–3 procedures	2 (9)	5 (11)	.8
Number of VT/PVCs targeted with ablation per procedure, median (IQR)	1 (1–1)	1 (1–1)	.74
Procedure duration, mean ± SD (min)	206.3 ± 64.3	221 ± 48.1	.28
Fluoroscopy dose in Gy.cm ² , median (IQR)	5.1 (1.7–25.2)	5.5 (2.1–15.1)	.98
RF ablation duration, median (IQR) (min)	9 (6.8–12.2)	13.4 (7.4–23.5)	.04
RF ablation surface area, median (IQR) (cm ²)	2.4 (1.9–3.2)	3.3 (2.4–4.3)	.03
Total PM surface area, mean ± SD (cm ²)	9.3 ± 6	-	-
≥90% pace map correlation surface area, mean ± SD (cm ²)	3.6 ± 2.2	-	-
≥95% pace map correlation surface area, mean ± SD (cm ²)	1.9 ± 1.2	-	-
Number of PM points, mean ± SD	33.6 ± 18.5	-	-
Best PM point %, median (IQR)	96 (92–97)	96 (94–98)	.71
Earliest activation time pre-QRS, mean ± SD (ms)	-	-33.7 ± 9.9	-
Number of AADs after final procedure, median (IQR)	0 (0–1)	0 (0–1)	.34
Number on amiodarone after final procedure, n (%)	0 (0)	0 (0)	-
Number of procedures when epicardial ablation performed, n/N procedures (%)	1/25 (4)	1/48 (2)	.62
ICE used in procedure, n/N procedures (%)	10/25 (40)	15/48 (31)	.45
CF-sensing catheters used in procedure, n/N procedures (%)	20/25 (80)	26/48 (54)	.03
Major procedural complications, n/N procedures (%)	1/25 (4)	0/48 (0)	.17

AAD = antiarrhythmic drug; CF = contact force; ICE = intracardiac echocardiography; IQR = interquartile range; PM = pace mapping; PVCs = premature ventricular complexes; RF = radiofrequency; SD = standard deviation; VT = ventricular tachycardia.

electromechanical dissociation, or coronary or phrenic injury.

Statistical analysis

SPSS version 25 (IBM Corp, Armonk, NY) was used for analysis. Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed; median and 25%–75% interquartile range (IQR) or full ranges were used if the data were clearly skewed. Continuous variables were compared using a Student *t* test when normally distributed, or a Mann-Whitney *U* test when they were not normally distributed. χ^2 or Fisher exact test was used when comparing categorical variables. Survival free of VA was estimated using the Kaplan-Meier method and the log-rank χ^2 method. Cox proportional hazard models were created to determine predictors of VA recurrence. Hazard ratios (HRs) and 95% confidence intervals (CIs) were used to express risk of VA recurrence. A 2-tailed *P* value of <.05 was considered statistically significant.

Results

Baseline characteristics

Baseline characteristics are summarized in Table 1. There were no significant differences in age, sex, prior AAD use, and comorbidities between the 2 groups. There were 4 patients with PVC-induced cardiomyopathy in the non-PM group, resulting in a numerically lower mean LV ejection fraction in this group, which did not reach statistical significance (60% ± 2% vs 58% ± 6%, *P* = .13). Median 24-hour preprocedure PVC burdens were comparable (PM 9.5% [IQR 4%–13.8%] vs non-PM 13.5% [IQR 6.6%–30%], *P* = .38).

Procedural characteristics

Procedural characteristics are summarized in Table 2. There was a comparable proportion of patients undergoing a single procedure in the 2 groups; 88% vs 92% (*P* = .58). Indication for ablation was PVCs in the majority of patients; 64% vs 59% (*P* = .68). Conscious sedation was used for the mapping

Table 3 Anatomical locations of ablated ventricular arrhythmias

Anatomical site of ablation	PM (n=22)	Non-PM (n=44)	P value
RVOT, n/N inducible VA (%):			
Lateral free wall	4/30 (13)	4/59 (7)	.35
Anterior free wall	4/30 (13)	11/59 (19)	.48
Septum	5/30 (17)	11/59 (19)	.82
Anterior septal	8/30 (27)	10/59 (17)	.27
Posterior septal	5/30 (17)	6/59 (10)	.35
Posterior	2/30 (7)	2/59 (3)	.38
Tricuspid annulus, n/N inducible VA (%)	0/30 (0)	2/59 (3)	.34
LVOT, n/N inducible VA (%):			
Aortomitral continuity	0/30 (0)	6/59 (10)	.08
Anterior LVOT	1/30 (3)	1/59 (2)	.77
Posterior LVOT	0/30 (0)	1/59 (2)	.44
Septal LVOT	0/30 (0)	0/59 (0)	-
Multiple chambers, n/N inducible VA (%):			
Endocardial septal RVOT and LVOT	0/30 (0)	2/59 (3)	.34
Epicardial and endocardial RVOT free wall	1/30 (3)	0/59 (0)	.18
Coronary cusp and endocardial RVOT	0/30 (0)	1/59 (2)	.44
Coronary cusp and aortomitral continuity	0/30 (0)	1/59 (2)	.44
Coronary sinus and aortomitral continuity	0/30 (0)	1/59 (2)	.44

LVOT = left ventricular outflow tract; PM = pace mapping; RVOT = right ventricular outflow tract; VA = ventricular arrhythmia.

component of the procedure in 40% of the PM and 40% of the non-PM procedures. There were 4 procedures in the PM group and 1 in the non-PM group, which required conversion from conscious sedation to general anesthesia for the ablation component of the procedure. Within the PM group, the mean number of pace map points was 33.6 ± 18.5 , with a median best pace map correlation of 96% (IQR 92%–97%) and mean $\geq 95\%$ pace map correlation surface area of $1.9 \pm 1.2 \text{ cm}^2$. Within the non-PM group, the mean earliest activation time was $-33.7 \pm 9.9 \text{ ms}$ and 25 of 44 (57%) patients also received PM in the area of earliest activation, with a median best pace map correlation of 96% (IQR 94%–98%).

RF ablation time was significantly shorter in the PM compared to non-PM group (9 [IQR 6.8–12.2] minutes vs 13.4 [IQR 7.4–24.6] minutes, $P = .04$). Likewise, the surface area of RF ablation was smaller in the PM compared to non-PM group (2.4 [IQR 1.9–3.2] cm^2 vs 3.3 [IQR 2.4–4.3] cm^2 , $P = .03$). Procedural duration, fluoroscopy dose, and post-procedure AAD use were all comparable between the 2 groups.

Complication rates were comparable in the PM and non-PM group (4% and 0%, respectively, $P = .17$). The single complication was cardiac tamponade following PM-guided ablation in the lateral free wall of the right ventricular outflow tract (RVOT). This was treated with pericardiocentesis and did not require surgical intervention.

Table 3 describes the anatomical sites of documented VA origin in the 2 groups. Within the RVOT, VA originated from similar anatomical locations in both groups. There were fewer non-RVOT VAs in the PM group, compared to the non-PM group (1/30 [3%] vs 12/59 [20%], $P = .03$). Per patient, there was a non-statistically significant trend of patients who did not have a VA site of origin within the RVOT in the PM group, compared to the non-PM group (1/22 [5%] vs 9/44 [21%], $P = .09$).

There were 14 of 66 patients who required mapping in the coronary cusps (9% PM vs 27% non-PM, $P = .09$), of which 2 patients in the non-PM group required additional ablation from a coronary cusp (right coronary cusp for a posteroseptal RVOT VA focus and the left coronary cusp for an aortomitral

Table 4 Factors associated with VA recurrence

Variable	Univariate HR for VA recurrence (95% CI)	P value	Multivariate HR for VA recurrence (95% CI)	P value
>1 ablation procedure	8.99 (3.58–22.6)	<.001	8.19 (3.16–21.18)	<.001
Obesity	3.25 (1.17–8.99)	.02		
AAD use before ablation	2.99 (1.08–8.24)	.04	3.48 (1.17–10.35)	.03

Data include variables with a P value $<.2$ following univariate analysis and independent variables with a P value $<.05$ following multivariate analysis. AAD = antiarrhythmic drug; CI = confidence interval; HR = hazard ratio; VA = ventricular arrhythmia.

continuity VA focus). Overall, 6 of 66 (9%) patients required ablation from 2 adjacent chambers for an intramural VA focus (5% PM vs 11% non-PM, $P = .43$).

VA recurrences in follow-up

Median follow-up was 12 (IQR 4–23.6) months (PM group: 7.5 [IQR 3.9–20.7] months; non-PM group: 13.9 [IQR 4.5–25.2] months, $P = .45$). Following final procedure, 24-hour median VA burden (PM 0% [IQR 0–2.4%] vs non-PM 0% [IQR 0–4.2%], $P = .98$) and VA-free survival at 6 months (PM 77% vs non-PM 71%, $P = .77$. [Figure 2](#)) were both comparable between the 2 groups.

When patients with left ventricular outflow tract VA were excluded from survival analysis, comparable VA-free survival at 6 months remained (PM 81% vs non-PM 69%, $P = .32$; [Supplemental Figure 1](#)). In further subgroup analysis of outcomes based on mapping techniques, there was comparable VA-free survival at 6 months, between patients receiving PM \pm activation mapping ($n = 50$) and those receiving only activation mapping ($n = 16$) (74% vs 81%, $P = .43$). Similarly, there was comparable VA-free survival at 6 months between the PM and activation mapping only groups (77% vs 81%, $P = .53$).

When a 30-day “blinking” period was applied to the overall population, VA-free survival at 6 months after final ablation was again comparable between the 2 groups (PM 86% vs non-PM 91%, $P = .38$).

Independent predictors of VA recurrence were >1 ablation procedure (HR 8.19 [95% CI 3.16–21.18], $P < .001$, [Table 4](#)) and prior AAD therapy (HR 3.48 [95% CI 1.17–10.35], $P = .03$, [Table 4](#)). [Supplemental Table 1](#) describes all variables included in univariate analysis.

There were no statistically significant differences in baseline and procedural characteristics between the 2 subgroups of patients who experienced VA recurrence after final ablation ([Supplemental Table 2](#)).

In those patients with PVC-induced cardiomyopathy at baseline, follow-up transthoracic echocardiography performed at least 3 months after ablation demonstrated resolution of LV systolic function in all cases.

Discussion

This study describes the procedural parameters and outcomes of catheter ablation for idiopathic outflow tract VA in patients with low vs high intraprocedural burden of VA. We found that catheter ablation of low-intraprocedural-burden idiopathic outflow tract VA guided by a PM approach resulted in comparable medium-term outcomes compared to standard (non-PM) ablation techniques, with lower RF ablation times but similar procedure times and fluoroscopy doses.

Previous studies using primarily pace mapping to guide ablation of idiopathic VA

Shirai and colleagues⁵ recently described a similar PM approach in 24 patients with low intraprocedural burden of PVCs originating from any ventricular site. Patients

included were similar in demographics to our study, the majority with a diagnosis of idiopathic PVCs and 2 patients with impaired LV ejection fraction $<50\%$, secondary to PVC-induced cardiomyopathy. PM was performed using a 3.5-mm-tip ThermoCool ablation catheter at an output just above capture threshold. Median number of pace maps performed per procedure was 27 (17–55), and median pace map score was 97% (96%–98%), both in keeping with our study. Clinical success was determined by achieving $>80\%$ reduction in PVC burden, absence of symptoms, or no documented clinical PVCs if they were infrequently present at baseline or exercise induced. Based on these criteria, they reported a 79% success rate at a median follow-up of 9.2 (2–15) months. Unlike in our study, AAD use after ablation was not reported, patients with documented sustained VT as an indication for ablation were not included, and there was no direct comparison of outcomes against patients undergoing standard activation-guided ablation. Fedida and colleagues⁴ directly compared a PM approach with standard ablation, but the numbers were lower—12 in the PM group vs 47 in the standard ablation group—and follow-up was only 1 month. Their results demonstrated high acute success rates with 100% VA-free survival at 1 month within the low-burden PVC group.

In contrast to the above studies, Baser and colleagues⁶ described lower success rates in catheter ablation of patients with infrequent procedural PVCs compared to those with frequent PVCs (85% vs 56%, $P < .001$), with success defined at 3 months as a reduction in PVC burden $\geq 80\%$. Potential reasons for these conflicting results include the differing sites of ablation, with 17% of the low-frequency PVC patients requiring ablation in the coronary cusps compared to 0% in our study, a higher number of PVC cardiomyopathy patients (12% vs 0% in our PM group), and advancements in contemporary technologies aiding ablation in our study such as PM algorithms and the use of ICE, with the latter recently shown to be associated with improved outcomes of catheter ablation.^{7,8} Both groups also required more RF ablation than our patients (high PVC burden: 17.2 ± 12.6 minutes and low PVC burden: 17.1 ± 15 minutes), potentially suggesting a more complex group of patients compared to our study population. Choi and colleagues⁹ described higher VA recurrence in patients with noninducible sustained VT at the time of their ablation for idiopathic outflow tract VT, compared to those with inducible VT (46% vs 18%, $P = .002$). Patients with noninducible VT had infrequent PVCs mapped primarily with PM, whereas the inducible group underwent activation mapping. In contrast to our study, indication for ablation was sustained VT in all patients. PM of infrequent PVCs assumed to be from the same focus as the clinical VT is an important limitation of a PM approach, with Choi and colleagues⁹ reporting only 75% of PVCs seen in patients with inducible VT to be morphologically identical to the inducible sustained VT. In our study there were 8 patients in the PM group

with sustained VT as the indication for ablation, with PM based on mapping of an infrequent PVC, deemed to be morphologically similar to the clinical VT morphology. Among these 8 patients, 2 had early recurrence of VA within 7 days; the remaining 6 were free from VA recurrence at median follow-up.

Considerations for pace mapping–guided ablation

It is important to recognize several factors, including limitations, that are involved in adopting a PM-guided approach to catheter ablation of outflow tract VA. The method and output of pacing will influence the amount of myocardium captured by each pacing stimulus. Bipolar pacing results in less artefact interference but captures a larger area of myocardium, when compared to unipolar pacing. In our study we used bipolar pacing, at a relatively low output (2 ms and 2 mA), to try and minimize the area of captured myocardium (surface area of $\geq 95\%$ pace map $1.9 \pm 1.2 \text{ cm}^2$). In locations where pace capture is difficult to achieve at this output, increasing the output or pulse width will result in greater pace capture but with reduced accuracy in correlating the location paced to the location captured. The coronary cusps are an example of an anatomical location where higher pacing outputs may be required, but capture may not correspond with catheter tip position. For this reason, we chose to exclude patients where the VA was originating from the coronary cusps, with the recognition that these patients would likely have better outcomes with activation mapping. Higher pacing outputs may also be required to obtain capture within or above the pulmonary valve cusps. While ablation within the pulmonary valve cusps has been shown to be associated with a high long-term success rate (when using a combination of activation mapping and PM techniques in patients with RVOT morphology PVCs),¹⁰ the adoption of this supra-valvular technique might be challenging in patients where a purely PM strategy is relied upon. Furthermore, reliable pace capture and interpretation of the paced beat morphology can be impacted by catheter-induced ventricular ectopy, with a potential increase in procedural time owing to the need to manipulate the catheter slower and wait for the ectopy to settle before resuming PM.

Intramural focus of VA may lead to lower pace map correlation compared to superficial endocardial foci. Recognition of this phenomenon may only be clear following mapping in several adjacent sites, with a cut-off pace map correlation of $\leq 86\%$ previously shown to differentiate well between intramural and nonintramural sites of VA origin.¹¹ Consolidative lesions around the area of best pace map and/or ablation from an adjacent site should then be performed. Furthermore, unsuccessful ablation may shift the VA exit site, leading to subtle changes in QRS morphology without effective treatment of the true VA focus.¹² It is plausible that there were fewer patients with intramural VA focus in the PM group given the lower ablation times and fewer number requiring ablation from adjacent chambers. However, these differences could also be accounted for by the higher

use of CF-sensing catheters in the PM group, with higher CF known to correlate with larger ablation lesions,¹³ and hence potentially the need for less ablation.

PM has been shown to have a lower spatial resolution compared to activation mapping (pace map ≥ 0.94 correlation coefficient area: $1.8 \pm 0.6 \text{ cm}^2$ vs 10 ms isochronal activation area: $1.2 \pm 0.7 \text{ cm}^2$).³ The relatively high-density nature of our PM approach is important to define an area with high pace map correlation, which is bordered by progressively lower pace map sites. Although no specific number of pace map points is required, it seems feasible that a higher number will lead to more accurate identification of the highest pace map site. There was a large range of points collected in our study (10–80), reflecting varying complexities of the PM approach, different operator techniques, and diverse anatomical focus of outflow tract VA.

Acute procedural success can be difficult to define when intraprocedural burden of VA is low prior to ablation. We consistently adopted an aggressive pre- and postprocedure provocation protocol, along with at least a 20-minute wait time following last ablation, and closely monitored patients for the immediate 24-hour period on cardiac monitoring. We chose not to use a blanking period, with immediate post-procedure VA recurrence defined as a recurrence rather than procedural failure.

Study limitations

This was an unblinded, nonrandomized study on a relatively small number of patients; thus, there is potential for operator selection bias. Relying solely on a PM-guided strategy is limited perhaps most importantly by reliable pace capture of the myocardium at the site of VA origin. Where this site is located within a valve cusp or electrically inexcitable myocardium, pace capture may not be possible, or at the very least will require higher pacing outputs with subsequent reduction in the spatial resolution of the area of best pace map correlation.

All of our patients required either conscious sedation or general anesthesia during their procedure. It is likely that this will have reduced the intraprocedural burden of VA. However, maintaining patient comfort and airway safety should always be a priority, particularly in those patients with underlying respiratory conditions and obesity.

It is possible, given the single-center setting of this study, that these results may not be applicable to all electrophysiology centers.

Conclusion

Catheter ablation of idiopathic outflow tract VA using a PM approach in the setting of low intraprocedural VA burden was associated with comparable medium-term outcomes, when compared to a standard non-PM approach. Procedural duration, fluoroscopy dose, and complication rates were comparable in both groups. A multicenter study with a larger population of patients is warranted to further validate our findings.

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Disclosures

Timothy Campbell is a former employee of Biosense Webster, Inc, and has received speakers' honoraria for Biosense Webster, Inc in the last 12 months.

Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent

All patients gave written informed consent for the procedure.

Ethics Statement

The study analysis was performed according to protocols approved by the Western Sydney Local Health District Human Research Ethics Committee and in keeping with the Helsinki Declaration guidelines on human research.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hroo.2021.05.008>.

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