Cryoablation for Ventricular Arrhythmias Arising From the Papillary Muscles of the Left Ventricle Guided by Intracardiac Echocardiography and Image Integration

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ABSTRACT

OBJECTIVES This case series reports outcomes and complications of catheter cryoablation at the papillary muscles (PM) of the left ventricle (LV).

BACKGROUND Catheter radiofrequency ablation is an effective treatment for ventricular arrhythmias (VAs) arising from the PM of the LV. The use of cryoablation at PMs has not been described.

METHODS Ten patients (70% men; median age: 38 years [range: 34 to 45 years]) with drug-refractory premature ventricular contractions or ventricular tachycardia underwent catheter cryoablation. VAs were localized using 3-dimensional (3D) mapping, multidetector computed tomography, and intracardiac echocardiography, with arrhythmia foci being mapped at either the anterolateral PM or posteromedial papillary muscle (PMPM) of the LV. Focal ablation, up to 240 s with freeze-thaw-freeze cycles was performed using an 8-mm cryoablation catheter via a transmitral approach.

RESULTS Termination of ventricular arrhythmia was observed in all 10 patients during ablation. Median follow-up was 6 months after ablation. The PMPM had higher prevalence of clinical arrhythmias (100% PMPM VAs vs. 10% anterolateral PM VAs). The PM base was the most frequent site of origin of the arrhythmias (60% of patients). Pace-mapping showed ≥11/12 match in all treated PM at the site of effective lesion. All VAs arising from the base of the PM showed Purkinje potentials. There were no post-procedure complications. VA recurred in 1 patient.

CONCLUSIONS Cryoablation for arrhythmias arising from the PMs of the LV can be performed, and is a safe and effective alternative energy source for ablation. (J Am Coll Cardiol EP 2015;1:509–16) © 2015 by the American College of Cardiology Foundation.
concern during procedures (4–7). Acute mitral valve dysfunction due to PM injury is a major concern while delivering RF energy at PMs, although it has not yet been reported.

This is the first case series describing the use of cryoenergy for the treatment of ventricular tachycardia (VT) and premature ventricular contractions (PVCs) localized at the PMs of the LV, with the aid of intracardiac echocardiography (ICE) and image integration.

METHODS

The study population was drawn from 71 consecutive patients (49% male; median age, 42 years [range: 28 to 54 years]) with symptomatic idiopathic sustained VT (n = 9), nonsustained VT (n = 18), or PVC (n = 44) referred for catheter ablation to the Buenos Aires Cardiovascular Institute (Buenos Aires, Argentina) between January 2014 and April 2015. The sites of origin of VAs included the right ventricular (RV) outflow tract (RVOT) in 45 patients (63%), aortic root in 3 (4%), aortomital continuity in 5 (7%), mitral annulus in 1 (1.5%), fascicles of the left bundle branch in 2 (3%), anterolateral PM in 1 (1.5%), posteromedial papillary muscle (PMPM) in 10 (14%), and other sites in 3 (4%). This case series retrospectively included 10 patients with symptomatic and drug-refractory VAs originated at the PMs of the LV. Each patient gave written informed consent, and all antiarrhythmic drugs were discontinued for ≥5 half-lives before the study.

All patients underwent electrophysiological study and catheter ablation. Catheter ablation was performed under conscious sedation. For mapping and pacing, standard multi-electrode catheters were placed in the coronary sinus, His bundle region, and RV apex through the right femoral vein. An 8-mm cryoablation catheter was advanced into the LV through a transeptal and transmural approach. Arrhythmia induction was attempted by programmed electrical stimulation from the RV apex, RVOT, and coronary sinus, with 1, 2, and 3 extrastimuli introduced after an 8-beat drive train, if necessary, with the addition of an isoproterenol infusion. Intravenous heparin was administered to maintain an activated clotting time of ≥300 s.

IMAGING. A 2-dimensional ICE prove (ViewFlex, St. Jude Medical Inc., St. Paul, Minnesota) was advanced toward the right atrium (home view) and RVOT sequentially. The ICE 2-dimensional catheter was positioned toward the RVOT and rotated in a clockwise fashion to visualize the different LV structures.

By ICE direct visualization, we attributed 3 segments to each PM to specify the origin and catheter position of the VAs: the apex, which corresponded with the most distal third of the PM, at the point of insertion of the chords; the body, representing the intermediate third of the PM; and the proximal third of the PM, in contact with the LV wall, was considered the PMs base (Figure 1). Continuous ICE monitoring was performed for possible complications. Special attention was paid to PM injury and mitral valve dysfunction. Catheter position, contact, and stability were also assessed through this method.

Multidetector computed tomography (MDCT) was performed with a 64-detector Phillips Brilliance (Phillips Medical Systems, Best, the Netherlands) <15 days before catheter ablation. No ionic contrast material was used (Optiray 350 mg/ml) and scanning was performed with a collimated slice thickness of 0.9 mm. Prospective electrocardiographic gating at 75% of the R-R interval was performed to eliminate cardiac motion artifacts and reduce radiation dose. Integration of the cardiac MDCT image into the mapping system was performed.

SEGMENTATION. Raw MDCT data were loaded into the 3D electroanatomic system equipped with an image integration module (EnSiteVelocity 3.0.1.1, St. Jude Medical Inc.). The segmentation process has been described elsewhere (8). The accuracy of this technique has been validated in previous studies (9,10). The 3D structures of the LV were segmented. The 3D reconstructed LV and PM images were then registered.

REGISTRATION. Previously acquired 3D model (MDCT images) were aligned with the NavX system. Fiducial point pairs were created by an operator identifying and selecting locations on the NavX system, and matching these on the MDCT model to the same anatomic area. Matching of the fiducial points created on the NavX system was confirmed by ICE. Fiduciary points from the base, body, and apex of the PMs were obtained and matched to the MDCT images during shell construction (11). Figure 2 shows the final 3D anatomy obtained from the 3D reconstructed MDCT images after fusing them with the fiduciary points obtained by ICE imaging.

MAPPING AND CRYOABLATION. Activation and pacemapping was performed in all cases to identify the site of the VA origin. The VAs electrograms to QRS
interval was measured systematically (Figure 3). Electroanatomic 3D LV anatomic shells and activation maps (EnSite Velocity, St. Jude Medical Inc.) of the LV were obtained in all cases. No voltage maps were performed. Pace mapping was performed at a pacing cycle of 600 milliseconds and stimulus amplitude of 1 mA greater than the late diastolic threshold. We used 2 different pacemapping criteria: 1) paced QRS match of $\frac{11}{12}$ leads; and 2) a pace mapping score determined from the R/S ratio and fine notch of the QRS in the 12-lead electrocardiogram (ECG) as previously reported (perfect pace mapping $= 24$ points) (12).Notch was defined as a high frequency component of either the upstroke or the downstroke of the QRS at any lead.

Cryoenergy was delivered at myocardial sites exhibiting the earliest bipolar activity or local unipolar QS pattern or at a Purkinje network with an early activity preceding the QRS onset for $\geq 25$ ms during the VA (Figure 4) at pace mapping areas exhibiting QRS match of $\geq 11/12$ or a pace mapping score of $\geq 20$. If pacemapping showed a QRS match of $\geq 11/12$ and a score of $\geq 20$ due to discrepancies in fine notch matching, cryoenergy was delivered anyway. Focal ablation was performed with an 8-mm cryoablation catheter (Freezor MAX 3, Medtronic, Inc., Minneapolis, Minnesota). When a reduction in the incidence of VT or PVCs was observed cryoenergy was delivered for up to 240 s with 2 freeze-thaw-freeze cycles; otherwise, cryoenergy delivery was terminated, and the catheter was repositioned. The endpoint of the catheter ablation was the elimination and noninducibility of VAs during isoproterenol infusion (2 to 10 $\mu$g/min) and burst pacing from the RV to a cycle length as short as 300 ms. Procedural success was defined as abolition of inducible or spontaneous ventricular arrhythmia.

**ECG ANALYSIS.** Twelve-lead ECGs during the VAs and pace mapping were recorded digitally at a sweep speed of 100 to 200 mm/s in all patients for offline analysis. The QRS duration and axis, notching, and R/S transition in precordial leads were measured with electronic calipers (EP-WorkMate 4.2 System, St. Jude Medical Inc.) by 2 experienced investigators blinded to the site of the origin. If there were discrepancies between those results, they were adjudicated by a third investigator.

**FOLLOW-UP.** All patients were monitored continuously for 24 h after the ablation procedure. Electrocardiography and echocardiography were performed before discharge in all patients. Follow-up information was obtained from direct evaluation in our arrhythmia clinic. Patients underwent 24-h Holter monitoring and baseline electrocardiography before and 1, 3, and 6 months after the procedure. Arrhythmia burden was assessed before and after catheter ablation. All patients who reported symptoms underwent Holter monitoring to document the cause of symptoms. Successful long-term catheter ablation was defined
as a significant reduction or absence of the clinical arrhythmia at 1, 3, and 6 months of follow-up. Significant reduction of the clinical arrhythmia was defined as Holter burden reduction of the clinical VA by ≥50% when compared with Holter recordings prior catheter ablation. No antiarrhythmic drugs were continued after catheter ablation unless VA recurred. All patients underwent echocardiography with color Doppler at discharge and 30 days after the ablation to evaluate the mitral valve, specifically the degree of mitral regurgitation.

STATISTICAL ANALYSIS. Variables with nonnormal distributions were expressed as median values with the interquartile range (IQR). Categorical variables were presented as numbers and percentages.

RESULTS

PATIENT CHARACTERISTICS. Ten patients underwent PM VAs catheter ablation. The median age was 38 years (IQR: 34 to 45 years) and 70% were males. The median left ejection fraction was 55% (IQR: 55% to 58%). None of the patients presented underlying cardiomyopathy. Only 1 patient had mitral valve prolapse of the posterior leaflet with moderate regurgitation. This was the only patient exhibiting VAs at both the anterolateral and PMPM. Only 3 patients were treated with antiarrhythmic drugs before catheter ablation (Table 1). All patients were drug free after cryoablation. The population baseline characteristics are summarized in Table 1.

PROCEDURAL OUTCOMES. Termination of the arrhythmia was observed in all patients without further inducibility (100% procedural success rate). There were no intraoperative complications. Catheter stability was achieved in all patients. The PMPM had higher prevalence of clinical arrhythmias (100% PMPM VAs vs. 10% anterolateral PM VAs). Only 1 patient had PVCs originating at the anterolateral PM. That same patient also presented with a NSVT arising from the PMPM. The PM base was the most frequent site of origin of VAs (n = 6). Pace mapping showed a ≥11/12 match in all treated PMs at the site of effective lesion. Purkinje potentials (PP) were observed in 6 patients. All patients who presented the site of effective lesion at the base of the PM also showed PP. In those patients where PP were not observed (n = 4), the effective lesion site was located at the body or apex. Total fluoroscopy time was 14 min (IQR: 9 to 17 min) and total procedure time was 124 min (IQR: 100 to 142 min).

LONG-TERM OUTCOMES. Patients were seen in routine follow-up at 1, 3, 6, and 12 months after catheter ablation (median follow-up, 6 months; IQR: 4 to 10 months). Follow-up Holter monitors were placed once for 24 h at 1, 3, and 6 months after cryoablation. All patients reported immediate improvement in symptoms at the first month of follow-up and no evidence of postprocedure complications assessed by cardiac ultrasound. Only 1 patient had recurrent symptomatic VT during the first week after the procedure and required a second catheter ablation with RF energy. One patient had PVC-induced cardiomyopathy (left ejection fraction of 45%) with 40% Holter burden despite flecainide treatment. After PM cryoablation, Holter burden was reduced 50%, the patient
remained asymptomatic, and left ejection fraction improved to 54% without the use of antiarrhythmic drugs. The remaining patients had no evidence of recurrent arrhythmias during Holter monitoring at the 1-, 3-, and 6-month follow-ups (Table 2). No patient required antiarrhythmic drugs after ablation.

**ECG ANALYSIS.** The mean QRS duration was 146 ms (IQR: 138 to 150 ms). VAs with an RSr pattern were
more frequent at the base of PM (57.1%, n = 4), whereas an rSR pattern was more frequent at the body (66.7%; n = 2). There was no correlation between early or late precordial RS transition and the site of effective lesion at the base, body or apex of the PM. Electrocardiographic and procedural characteristics are summed up in Table 3.

**DISCUSSION**

**MAIN FINDINGS.** This study demonstrates that cryoablation has a favorable success rate and low recurrence rate for ablation of ventricular arrhythmias arising from the LV PMs. Catheter stability was achieved in all cases due to cryocatheter adherence to the myocardium, which is a potential advantage over the use of RF ablation. Mitral valve regurgitation or PM injury or rupture was not observed. The PMPM was the most arrhythmogenic and the most frequent site of origin of the VAs was at the base of the PMs. Discrepancies between pace mapping match of ≥11/12 and pace mapping score were observed in 2 patients. Both exhibited perfect paced QRS match with the clinical VA but poor pace mapping score. This was attributed to the presence of notching during pace-mapping as compared with the clinical VA, accounting for a lower score. It is controversial whether PPs can be identified at the effective ablation site. Good et al. (13) reported the presence of PP in all treated PM VAs, whereas Doppalapudi et al. (14) did not identify PP at the effective ablation site. No information about the specific site of VA origin at the PM (apex, body, or base) was provided in these studies. In our study, PP were seen in 60% of VAs, and only in those with VAs originating at the base of the PM. This finding may suggest that the Purkinje network may not extend further from the base of the PM, hence the absence of PP at the body or apex. It has been reported that ablation at sites with excellent pace mapping is usually unsuccessful (15), suggesting that the site of VA origin may be located away from the breakout site, which can be recognized as the site with the best pace map. In our case series, cryoablation at sites with excellent pace mapping was always successful. It has also been reported that almost one-half of these patients present multiple VT morphologies (15), which may be due to the presence of multiple exit sites. The patients included in this study presented only single VAs morphology.

**RF ENERGY.** Because of ventricular thickness, higher power settings are often required for LV catheter ablation when using RF energy (16). Catheter irrigation is often used to cool the ablation electrode such that more power can be delivered without being limited by the formation of thrombus at the catheter-tissue interface (17). Excessive intramyocardial heating can produce steam formation and abrupt volume expansion, which may be audible as steam pops (18). Pops are capable of causing deep tissue tears, and patients with ventricular perforations are more likely to require surgical repair (19). A potential complication during RF ablation is mitral valve dysfunction by injury or rupture of the PMs, especially when using irrigated tip ablation catheters, although this has not yet been reported.

**CRYOENERGY.** Cryoablation has been reported as a safe alternative for catheter ablation in idiopathic VT arising from the RVOT, aortic cusps, and epicardium (20,21). Cryothermal safety profile is attributed to the mechanism of tissue destruction (22). Histology of chronic lesions shows well-demarcated lesions with minimal tissue disruption and preserved underlying

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**Table 1** Baseline Patient Demographics and Follow-Up

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<th>Age, yrs</th>
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<th>CMP</th>
<th>AADs</th>
<th>VA</th>
<th>VAM</th>
<th>Follow-Up (months)</th>
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<td>M</td>
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AADs = antiarrhythmic drugs used before catheter ablation; AADs CA = antiarrhythmic drugs used after catheter ablation; CMP = cardiomyopathy; Diltz = diltiazem; Flec = flecainide; Isch = ischemic; LVEF = left ejection fraction; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular contraction; Rec = recurrence of the clinical arrhythmia after catheter ablation; Sot = sotalol; TM = tachycardiac myopathy; VA = clinical presentation of the ventricular arrhythmia; VAM = number of morphologies of the clinical arrhythmia; VT = ventricular tachycardia.

**Table 2** Holter Burden of Clinical Arrhythmias During Follow-Up

<table>
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<tr>
<th>Patient #</th>
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<th>HB-1 Mo</th>
<th>HB-3 Mo</th>
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HB-1 Mo = Holter burden of the clinical arrhythmia at 1 month after cryoablation; HB-3 Mo = at 3 months; HB-6 Mo = at 6 months; HB-PCA = Holter burden of the clinical arrhythmia previous to cryoablation; other abbreviations as in Table 1.
architecture. Catheter stabilization during ablation at the PMs is a major consideration. Stabilization is achieved due to catheter-tissue adherence after reaching temperatures of \(-80\^\circ\)C.

**IMAGING TECHNIQUES.** Cardiac multi-imaging integration constitutes an important tool for PM ablation, providing an accurate anatomy, and aiding catheter manipulation during the ablation procedure. ICE represents a key element in our study guiding the manipulation during the ablation procedure. ICE provides an accurate anatomy, and aiding catheter stabilization during ablation.

**TABLE 3 Electrocardiographic and Procedural Characteristics**

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A = anterolateral; Axis = QRS electrical axis; EL = location of the effective lesion site; FT = fluoroscopy time; I = inferior; Induction = induction of the clinical arrhythmia; Is = isoproterenol; NCL = number of cryolesions; P = posterior medial; PM = papillary muscle; PMs = pace mapping score; PP = presence of Purkinje potentials; PS = programmed stimulation; PT = procedural time; QRSd = duration of the QRS interval in milliseconds; QRS-P = QRS morphology; RS = precordial transition from R to S; S = superior; Sp = spontaneous; VEGM-QRS = interval between the earliest activation (VEGM) during the clinical arrhythmia and the QRS, at the effective lesion site.

Recently, Latchamsetty et al. (31) showed that PVCs originating in the PMs were associated with low RF ablation success rates (60%), high recurrence rate, long procedure times, and the delivery of large amounts of RF energy. Our case series shows the safety and feasibility of catheter cryoablation in arrhythmias from the LV PMs, providing catheter adherence and preservation of ultrastructural integrity.

**STUDY LIMITATIONS.** The small number of patients in our report does not allow for any outcome to be statistically representative. This is due in part to the fact that patients with PM arrhythmias represent a small subset of subjects referred for ablation, making them less suitable for larger studies. Voltage mapping has not been performed in any of the patients.

This is not a comparative study so no comparison can be performed with RF catheter ablation, which is the most used technique in this subset of patients.

**CONCLUSIONS**

This case series demonstrated that catheter cryoablation for ventricular arrhythmias originating at the PMs of the LV is technically feasible, safe and effective. Catheter stability was always achieved with cryoablation.

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Cryoablation for Ventricular Arrhythmias

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Catheter cryoablation can be used to eliminate ventricular arrhythmias originating at the PMs of the LV with high success rates and without complications. Imaging techniques are diagnostic and therapeutic corner stones in these patients.

TRANSLATIONAL OUTLOOK: Although this is a small case series with a relatively short follow-up, longer term studies may provide further data regarding long-term benefits of cryoablation.

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