Multicenter Outcomes for Catheter Ablation of Idiopathic Premature Ventricular Complexes

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ABSTRACT

OBJECTIVES This study reports multicenter outcomes and complications for catheter ablation of premature ventricular complexes (PVCs) and investigates predictors of procedural success, as well as development of PVC-induced cardiomyopathy.

BACKGROUND Catheter ablation of frequent idiopathic PVCs is used to eliminate symptoms and treat PVC-induced cardiomyopathy. Large-scale multicenter outcomes and complication rates have not been reported.

METHODS This retrospective cohort study included 1,185 patients (55% female; mean age 52 ± 15 years; mean ejection fraction 55 ± 10%; mean PVC burden 20 ± 13%) who underwent catheter ablation for idiopathic PVCs at 8 centers between 2004 and 2013. The following factors were evaluated: patient demographics, procedural characteristics, complication rates, and clinical outcomes.

RESULTS Acute procedural success was achieved in 84% of patients. In centers at which patients were followed up routinely with post-ablation Holter monitoring, continued success at clinical follow-up without use of antiarrhythmic drugs was 71%. Including the use of antiarrhythmic medications, the success rate at a mean of 1.9 years of follow-up was 85%. In a multivariate analysis, the significant predictors of acute success were PVC location and number of distinct PVC configurations (p < 0.03). The only significant predictor of continued success at clinical follow-up was a right ventricular outflow tract PVC location (p < 0.01). In 245 patients (21%) with PVC-induced cardiomyopathy, the mean ejection fraction improved from 38% to 50% (p < 0.01) after ablation. Independent predictors for development of PVC-induced cardiomyopathy were male gender, PVC burden, lack of symptoms, and epicardial PVC origin (p < 0.05). The overall complication rate was 5.2% (2.4% major complications and 2.8% minor complications), and complications were most commonly related to vascular access (2.8%). There was no procedure-related mortality.

CONCLUSIONS Catheter ablation of frequent PVCs is a low-risk and often effective treatment strategy to eliminate PVCs and associated symptoms. In patients with PVC-induced cardiomyopathy, cardiac function is frequently restored after successful ablation. (J Am Coll Cardiol EP 2015;1:116–23) © 2015 by the American College of Cardiology Foundation.
In addition to causing potentially debilitating symptoms, idiopathic premature ventricular complexes (PVCs) can cause significant left ventricular (LV) dysfunction or dilation (1). Single-center studies have demonstrated that catheter ablation is superior to pharmacological therapy for decreasing PVC burden and improving cardiac function (2–4).

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Larger scale multicenter studies evaluating the safety and efficacy of ablation have been lacking. Furthermore, data are limited on the relationship between specific PVC sites of origin or the number of PVC foci and outcomes. The purpose of this multicenter study was to assess outcomes and complications of catheter ablation of idiopathic PVCs and to determine the predictors of acute and long-term efficacy.

METHODS

We retrospectively analyzed 1,185 patients who underwent radiofrequency catheter ablation for frequent idiopathic PVCs at 8 international centers between 2004 and 2013. The presence of structural heart disease was evaluated by echocardiogram, exercise stress testing, cardiac catheterization, and/or cardiac magnetic resonance imaging (MRI). Patients with a history of prior infarcts or delayed enhancement identified by cardiac MRI were excluded. Patients with decreased LV ejection fraction or LV dilation without a known cause other than the PVCs were included in the study. Patient demographics, ejection fraction, PVC burden, medical therapy, the number and origin of PVCs, procedural details, complications, and outcomes were collected. Data regarding antiarrhythmic drug use after ablation were also collected. Beta-blockers and calcium channel blockers were not included in the antiarrhythmic medications in this study.

A baseline ejection fraction <50% was considered to be evidence of a PVC-induced cardiomyopathy. The origin of PVCs was classified as right ventricular outflow tract (RVOT), aortic cusps, epicardium, or papillary muscles. If PVCs did not originate from any of these locations, they were defined as having “other” origin. An epicardial origin was considered to be present if there was an early activation time or a matching pace map within the coronary venous system or the epicardial space as accessed through a subxyphoid puncture. Complications were classified as major or minor. Major complications included any complication that required procedural intervention, blood transfusion, or prolonged hospitalization or resulted in long-term clinical effects. All other complications were considered minor.

Acute procedural success was defined as the elimination of the targeted PVC(s) at the termination of the procedure at least 30 min after the last ablation. Clinical success was evaluated at centers where 24- to 48-h Holter monitoring was performed routinely during follow-up and was defined as at least an 80% decrease in PVC burden. Holter monitoring was performed 3 to 6 months post-ablation, and further monitoring was performed at the discretion of the clinician based on symptom recurrence or finding of PVCs on an electrocardiogram (ECG).

STATISTICAL ANALYSIS. Continuous variables were expressed as mean ± SD. Discrete variables were compared using the Fisher exact test or by chi-square
analysis as appropriate, and continuous variables were compared using 2-group Student t test. For comparison among multiple groups, analysis of variance was used for comparison of continuous variables with post-hoc testing comparing all pairwise group combinations. Bonferroni correction was used to correct for the number of pairwise comparisons.

To evaluate predictors of ablation outcomes and development of cardiomyopathy, univariate logistic regression was performed to identify potential predictors. Parameters that were associated with a p value <0.1 were entered into a multivariate logistic regression analysis to assess whether they were independent predictors. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). The long-term outcomes analysis did not adjust for correlation within centers because the within-center correlation was low at 0.01. A p value <0.05 was considered significant. Statistical analyses were performed using R version 2.15.1 and StatView version 5.01 (SAS Institute, Cary, North Carolina).

RESULTS

PATIENT AND PVC CHARACTERISTICS. Among the 1,185 patients in this study, 55% were female, the mean age was 52 ± 15 years, and the mean LV ejection fraction was 55 ± 10% (Table 1). The mean pre-ablation PVC burden was 20 ± 13%. The most common site of PVC origin was the RVOT (45%). Multiple PVC configurations were present in 18% of patients, and the mean number of PVCs per patient was 1.7. The interquartile range of PVCs among patients with multiple PVCs was 2 to 4. The majority of patients (90%) had symptoms relating to their PVCs. A total of 245 patients (21%) had an ejection fraction <50%.

PROCEDURAL TIMES. For all procedures, the mean procedure time was 198 ± 115 min, mean fluoroscopy time was 30 ± 24 min, and mean radiofrequency energy application time was 12 ± 11 min (Table 2). Procedure and fluoroscopy times were lowest for patients with PVCs from the RVOT (157 ± 97 min and 20 ± 17 min, respectively, p < 0.01). Patients with a single PVC configuration had shorter procedure, fluoroscopy, and radiofrequency times compared with patients who had multiple PVCs (p < 0.01). Patients in whom PVCs originated from the papillary muscles and epicardium had longer procedure times (249 ± 109 min and 249 ± 117 min, respectively) and fluoroscopy times (40 ± 21 min and 48 ± 27 min, respectively) than did patients with PVCs from the RVOT or the aortic cusps (p < 0.01). Patients with PVCs from the papillary muscle had the longest radiofrequency energy time (26 ± 19 min) compared with other locations (p < 0.01).

PROCEDURAL OUTCOMES. Acute procedural success was achieved overall in 84% of patients (Figure 1). The highest success rate was in patients with PVCs from the RVOT (93%), and the lowest success rate was in patients with epicardial PVCs (67%) (Figure 1). By multivariate analysis, epicardial location (OR: 0.49; 95% CI: 0.27 to 0.91; p = 0.02), RVOT location (OR: 3.78; 95% CI: 1.87 to 7.6; p < 0.01), and number of PVC configurations (OR: 0.89 for each additional PVC configuration; 95% CI: 0.82 to 0.98; p = 0.01) were independently predictive of acute procedural outcome (Figure 2).

Follow-up data were evaluated for 490 patients at centers at which Holter monitoring was performed routinely after ablation to assess procedural efficacy. Mean follow-up duration in these patients was 20.2 ± 21.7 months. At clinical follow-up without the use of antiarrhythmic drugs, 71% of patients at centers at which Holter monitoring was performed routinely had at least an 80% decrease in PVC burden for all PVC locations. Patients with PVCs originating from the papillary muscle had the lowest success rate (60%), and patients with PVCs originating from the RVOT had the highest success rate (82%). A total of 19% of patients were receiving antiarrhythmic drugs at follow-up. Including those using antiarrhythmic drugs, 85% of patients experienced a decrease in PVC burden of at least 80%. The only predictor of clinical success without antiarrhythmic drugs at follow-up was an RVOT location (OR: 2.28; 95% CI: 1.41 to 3.67; p < 0.01).

In patients for whom Holter monitoring was not routinely performed and for whom success was determined by resolution of symptoms and lack of

### Table 1: Patient Characteristics (N = 1,185)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (n%)</th>
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<tbody>
<tr>
<td>Age, yrs</td>
<td>52 ± 15</td>
</tr>
<tr>
<td>Female</td>
<td>55</td>
</tr>
<tr>
<td>Hypertension</td>
<td>37</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>9</td>
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<tr>
<td>PVC burden (pre-ablation), %</td>
<td>20 ± 13</td>
</tr>
<tr>
<td>Ejection fraction (pre-ablation), %</td>
<td>55 ± 10</td>
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<tr>
<td>PVC-induced cardiomyopathy</td>
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<tr>
<td>Site of origin</td>
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<tr>
<td>RVOT</td>
<td>45</td>
</tr>
<tr>
<td>Cusp</td>
<td>15</td>
</tr>
<tr>
<td>PAP</td>
<td>5</td>
</tr>
<tr>
<td>Epicardial</td>
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<tr>
<td>Other</td>
<td>24</td>
</tr>
<tr>
<td>Single PVC configuration</td>
<td>82</td>
</tr>
</tbody>
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Values are mean ± SD or %. *Pre-ablation PVC burden and ejection fraction data were available in 73% and 96% of the population, respectively.

PAP = papillary muscle; PVC = premature ventricular complex; RVOT = right ventricular outflow tract.
PVCs on ECGs, follow-up data were available for an additional 432 patients. Reported success rates in these patients at a mean follow-up duration of 20.4/21.5 months were 75% without the use of antiarrhythmic drugs and 81% including the use of antiarrhythmic drugs. These values were not significantly different compared with the group for whom Holter monitoring was performed routinely (p > 0.05).

In the total cohort, repeat ablation procedures were necessary in 259 patients (22%), most commonly with PVCs from the epicardium (38%) and papillary muscle (36%). The total number of procedures per patient ranged from 1 to 6, with a mean of 1.3 procedures per patient. Patients with epicardial and papillary muscle PVCs underwent a mean of 1.6 and 1.5 procedures, respectively.

**PVC-INDUCED CARDIOMYOPATHY.** Data on baseline ejection fraction were available in 96.2% of patients. In this study, 245 patients (21%) with an ejection fraction <50% underwent PVC ablation. Independent predictors for PVC-induced cardiomyopathy by multivariate logistic regression analysis included male gender, lack of symptoms, high PVC burden, and an epicardial PVC location (Figure 3). Post-ablation, the mean PVC burden in these patients decreased from 27% to 5% (p < 0.01), and mean ejection fraction increased from 38% to 50%. Among patients with a cardiomyopathy who underwent ablation, 15% experienced worsening or no improvement in ejection fraction, 18% experienced <10% increase in ejection fraction, and 67% experienced ≥10% increase in ejection fraction.

<table>
<thead>
<tr>
<th>TABLE 2 Procedure Times</th>
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<tbody>
<tr>
<td>PVC Location</td>
</tr>
<tr>
<td>Procedure duration, min</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
</tr>
<tr>
<td>Radiofrequency time, min</td>
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</tbody>
</table>

Values are mean ± SD. Listed p values are based on testing for all groups having the same mean or proportion. After Bonferroni correction, significant differences were found between the following groups for each variable: RVOT and cusp, RVOT and papillary, RVOT and epicardial, cusp and papillary, cusp and epicardial, single vs. multiple; RVOT and cusp, RVOT and papillary, RVOT and epicardial, cusp and papillary, cusp and epicardial, single vs. multiple; RVOT and papillary, cusp and papillary, papillary and epicardial, single vs. multiple.

Abbreviations as in Table 1.
COMPLICATIONS. Among the 1,185 patients, a total of 62 complications occurred (5.2%), with 29 major complications (2.4%) and 33 minor complications (2.8%) (Figure 4). The most common complications were related to vascular access, with 33 patients (2.8%) having groin-related complications, 15 (1.3%) of whom required transfusion or surgical intervention. Nine patients (0.8%) had pericardial tamponade requiring pericardiocentesis, and 3 patients had small hemodynamically stable effusions that were managed conservatively. A single patient experienced permanent atrioventricular block. No patients experienced perioperative stroke, and no patients died.

Major complication rates were similar across different PVC locations but overall were highest for epicardial PVCs at 4.2%. The majority of these complications consisted of pericardial tamponade that required drainage. Among the 17 patients who underwent epicardial ablation with use of a subxyphoid approach, 1 patient experienced tamponade that was successfully drained percutaneously. Ablation of PVCs from the RVOT had the lowest overall major complication rate (2.1%).

DISCUSSION

MAIN FINDINGS. This study is the first large-scale, multicenter analysis of outcomes of ablation of idiopathic PVCs. The overall acute success rate of PVC ablation was 84%. During clinical follow-up, the success rate declined to 71% without the use of
antiarrhythmic drug therapy and was 85% with the use of antiarrhythmic drugs. A PVC origin from the RVOT was the only independent predictor of an acute successful outcome, whereas an epicardial origin and multifocal PVCs were predictive of procedural failure. Male sex, increasing PVC burden, asymptomatic PVCs, and an epicardial PVC origin were independent predictors for development of PVC-induced cardiomyopathy. The only significant predictor for long-term procedural success post-ablation was an RVOT PVC origin. Major complications occurred in 2.4% of patients, and none was fatal.

PVC ABLATION AND OUTCOMES. The data from this study show that ablation for idiopathic PVCs is often effective in reducing or eliminating symptomatic PVCs and treating PVC-induced cardiomyopathy. The highest success rate and a trend toward the lowest complication rate were observed in patients with PVCs originating from the RVOT. On the other hand, an epicardial PVC origin was associated with the lowest success rate and with a trend toward the highest complication rate. Similarly, multifocal PVCs are associated with higher failure rates and longer procedure durations. When counseling patients with frequent PVCs about treatment options, the site of origin and number of PVC configurations need to be considered.

Prior studies have reported similar success rates for epicardial sites of PVC origin even without using an epicardial subxyphoid approach (5,6). More recently the subxyphoid approach has been questioned given the lack of additional benefit and a higher complication rate compared with an ablation approach from within the coronary venous system and surrounding structures (7). Medical therapy might be preferable as the initial therapy in patients with epicardial PVCs unless medical therapy is not desired or PVC-induced cardiomyopathy is present.

PVCs originating in the papillary muscles also tended to be associated with a lower ablation success rate. Papillary muscle PVCs have a high recurrence rate and require long procedure times and delivery of larger amounts of radiofrequency energy. For these arrhythmias, it has been demonstrated that intracardiac echocardiography is helpful in guiding the procedure (8,9). Intracardiac echocardiography was not uniformly used in the patients in this study, which may in part explain the lower success rate for ablation of papillary muscle PVCs.

It is important to recognize the potential for PVC recurrence after an apparently successful ablation procedure. In addition to papillary muscle PVCs, recurrent PVCs during follow-up were particularly prevalent among patients with PVCs originating in the aortic cusps. A potential reason for this finding may be the lower power settings that often are used in the aortic cusps to minimize the risk of complications.

PVC-INDUCED CARDIOMYOPATHY. Several predictors for PVC-induced cardiomyopathy have previously been described, including a high PVC burden of >24%, asymptomatic status associated with frequent PVCs, a broad PVC-QRS complex >150 ms, the presence

FIGURE 4 Distribution of Major Complications (Total 2.4%)

Groin complications constituted more than one-half of all major complications after ablation. Cardiac tamponade was the next most common major complication at a rate of 0.8%.
of interpolated PVCs, and an epicardial PVC origin (1,10–12). In this large study, several of these predictors were confirmed, and male gender was also identified as an independent predictor of PVC-induced cardiomyopathy. Identification of male gender as a predictor during multivariate analysis was possible because of the large amount of data available in the present study, whereas in smaller single-center studies, male gender was only found to be predictive in univariate analyses (11,12). Knowledge of these predictors is important when counseling patients about their therapeutic options, especially if they are asymptomatic, have a high PVC burden, and have normal LV function.

This study confirmed the findings of several single-center studies in which improvement in LV function was seen when PVCs were successfully ablated (12–15). Whether such an improvement can be achieved with medical therapy remains to be seen and is the subject of ongoing clinical trials.

STUDY LIMITATIONS. The patients in this study were primarily from tertiary referral centers and may not reflect other patient populations. Furthermore, the procedures were performed by experienced operators, and the reported outcomes may be different for centers with less experienced operators. Holter monitoring at follow-up was not available at all participating centers. However, when long-term data in patients with Holter monitoring at follow-up were compared with long-term data in patients without Holter monitoring at follow-up, the success rates were not significantly different. Because most patients had symptomatic PVCs, resolution of symptoms in these patients likely reflects successful outcome at follow-up. Because of the large number of patients and centers, certain data such as PVC QRS width were not available for many patients. The definition of PVC-induced cardiomyopathy in this study is based on a lack of other underlying structural heart disease but is subject to the limitations of available diagnostic studies, which may not unequivocally preclude the existence of other myocardial disease. Echocardiographic analysis of LV function was not performed in an echocardiographic core laboratory. Furthermore, LV dimensions were also not available for the entire cohort of patients with LV dysfunction. Data on duration of PVCs and cardiomyopathy were limited and were not included in the analysis. Quantitative assessment of symptom improvement after ablation was not performed uniformly across centers and thus was not able to be compared.

CONCLUSIONS

Frequent PVCs can be treated with a high rate of success and a low complication rate with radiofrequency ablation. Patients with PVCs originating in the RVOT have the highest success rate and a low complication rate. An epicardial PVC site of origin has a lower success rate, trends toward a higher procedural complication rate, and has an increased rate of PVC-induced cardiomyopathy. In patients with PVC-induced cardiomyopathy, successful ablation frequently restores LV function.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Catheter ablation can frequently be used to eliminate frequent idiopathic premature ventricular complexes with low overall complication rates. PVC-induced cardiomyopathy is frequently reversed after successful catheter ablation.

TRANSLATIONAL OUTLOOK: Although this is a relatively short-term study, longer term studies, particularly in patients with PVC-induced cardiomyopathy, can provide further data regarding the long-term benefits of ablation.
REFERENCES


KEY WORDS ablation, cardiomyopathy, complications, outcomes, premature ventricular complexes