Relationship between burden of premature ventricular complexes and left ventricular function

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BACKGROUND Frequent idiopathic premature ventricular complexes (PVCs) can result in a reversible form of left ventricular dysfunction. The factors resulting in impaired left ventricular function are unclear. Whether a critical burden of PVCs can result in cardiomyopathy has not been determined.

OBJECTIVE The objective of this study was to determine a cutoff PVC burden that can result in PVC-induced cardiomyopathy.

METHODS In a consecutive group of 174 patients referred for ablation of frequent idiopathic PVCs, the PVC burden was determined by 24-hour Holter monitoring, and transthoracic echocardiograms were used to assess left ventricular function. Receiver-operator characteristic curves were constructed based on the PVC burden and on the presence or absence of reversible left ventricular dysfunction to determine a cutoff PVC burden that is associated with left ventricular dysfunction.

RESULTS A reduced left ventricular ejection fraction (mean 0.37 ± 0.10) was present in 57 of 174 patients (33%). Patients with a decreased ejection fraction had a mean PVC burden of 33% ± 13% as compared with those with normal left ventricular function 13% ± 12% ($P < .0001$). A PVC burden of >24% best separated the patient population with impaired as compared with preserved left ventricular function (sensitivity 79%, specificity 78%, area under curve 0.89) The lowest PVC burden resulting in a reversible cardiomyopathy was 10%. In multivariate analysis, PVC burden (hazard ratio 1.12, 95% confidence interval 1.08 to 1.16; $P < .01$) was independently associated with PVC-induced cardiomyopathy.

CONCLUSION A PVC burden of >24% was independently associated with PVC-induced cardiomyopathy.

KEYWORDS Premature ventricular complexes, Ablation, Cardiomyopathy

ABBREVIATIONS **CI** = confidence interval; **EF** = ejection fraction; **HR** = hazard ratio; **LV** = left ventricular; **PVC** = premature ventricular complexes; **ROC** = receiver operator characteristic; **RVOT** = right ventricular outflow tract

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Frequent ventricular ectopy in patients without structural heart disease previously was thought to be a benign finding with no prognostic significance.[1,2] However, recent studies have shown that frequent premature ventricular complexes (PVCs) can result in left ventricular (LV) dilatation[3,4] as well as a reversible cardiomyopathy.[5,6] The critical burden of PVCs required to result in cardiomyopathy is not known. The purpose of this study was to identify the critical PVC burden associated with cardiomyopathy.

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Methods

Patient characteristics

The subjects of this retrospective study were 174 consecutive patients (87 women, age 48 ± 13 years, ejection fraction [EF] 51% ± 13%) with frequent PVCs referred for catheter ablation (Table 1). One hundred forty-seven patients experienced palpitations for a mean duration of 59 ± 92 months. Seventeen patients were asymptomatic, and 10 patients had heart failure symptoms at presentation. LV dysfunction was present in 57 patients who had a mean EF of 35% ± 9%. Additionally, 42 of the 174 patients had nonsustained ventricular tachycardia, constituting <1% of the overall PVC burden.

The patients had failed to respond to a mean of 2 ± 1 antiarrhythmic medications, including beta-blockers and calcium channel blockers. Nine patients were taking amiodarone before the procedure. Coronary artery disease was ruled out by cardiac catheterization or stress testing.

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Table 1 Comparison of patients with frequent PVCs with and without cardiomyopathy

Clinical characteristics	No cardiomyopathy (n = 117)	Cardiomyopathy (n = 57)	*P* value
Male sex	52 (44)	35 (61)	.02
Age, years	48 ± 12	49 ± 12	.73
Mean duration of palpitations, months	57 ± 89	62 ± 100	.76
EF, %	59 ± 4	35 ± 9	<.01
Baseline LV end-diastolic dimension, mm	51 ± 6	57 ± 6	<.01
Baseline LV end-systolic dimension, mm	33 ± 7	42 ± 8	<.01
Therapy			
Beta-blockers/calcium channel blockers	90 (77)	44 (77)	.50
Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers	23 (20)	27 (47)	<.01
Digoxin	2 (2)	4 (7)	.06
Antiarrhythmic drug therapy including amiodarone	29 (25)	12 (21)	.83
Amiodarone	4 (3)	5 (9)	.09

Values are n (%) or mean ± SD.
EF = ejection fraction; LV = left ventricular; PVC = premature ventricular complex.

Assessment of LV function

Echocardiography was performed and the LV ejection fraction was assessed based on 2 consecutive sinus rhythm beats using the Simpson formula. If there was incessant bigeminy, the ejection fraction of the sinus rhythm beat was averaged with the ejection fraction of the PVC.[5] Echocardiography was repeated a mean of 3.7 ± 4.5 months after the ablation procedure. An ejection fraction <50% was considered abnormal. The left ventricle was considered to be dilated if the end-systolic dimension was >38 mm or the end-diastolic dimension was >58 mm. Two independent observers analyzed the ejection fraction.

Holter monitoring

Holter monitoring was performed at baseline to assess the PVC burden. The PVC burden was defined as the percentage of total beats that were PVCs. The Holter monitor was repeated 3 to 6 months postablation and later if palpitations recurred.

Electrophysiology procedure and ablation

After informed consent was obtained, 3 multipolar catheters were inserted into a femoral vein and positioned in the atrium, the His bundle, and the right ventricle. Programmed stimulation was performed to rule out inducible ventricular tachycardia with and without isoproterenol. The PVCs were mapped using activation mapping if they occurred frequently (bigeminy, trigeminy, and quadrigeminy), or pace mapping if they were not frequent. A 4-mm-tip ablation catheter (Navistar, Biosense Webster, Diamond Barr, California) or a 3.5-mm open-irrigated-tip catheter (Thermocool, Biosense Webster) was used for mapping and ablation. For right-sided procedures, 3,000 units of heparin initially were administered as a bolus, followed by 1,000 units every hour. For left-sided procedures, an initial 5,000-unit bolus was administered after arterial access was obtained, and the heparin dosage then was titrated to maintain an activated clotting time of ≥250 seconds.

Radiofrequency energy was delivered with a conventional 4-mm-tip ablation catheter in a temperature-controlled mode with a target temperature of 55°C at a power of ≤50 W. When using an irrigated-tip catheter, radiofrequency energy was applied at a power of 30 to 35 W and a maximal temperature of 45°C. Programmed ventricular stimulation before and during isoproterenol infusion (up to a rate of 20 μg/min) was repeated at the end of the procedure.

Procedural end point

The end point of the procedure was elimination of the most prevalent PVC. In patients with pleomorphic PVCs, the site of origin (SOO) of all PVCs were sought. If the SOO of the less prevalent PVCs could not be identified, the procedure was terminated.

Definitions

The criterion for an effective ablation procedure was an 80% reduction in the PVC burden. A patient was defined to have PVC-induced cardiomyopathy if an abnormal ejection fraction improved by at least 15% or normalized (ejection fraction ≥50%) after an effective ablation procedure. A PVC site of origin was considered epicardial if the earliest site of activation was recorded within the coronary venous system or in the pericardial space.

Follow-up

Patients were seen in an outpatient clinic 3, 6, and 12 to 48 months postablation. An echocardiogram was repeated if the baseline ejection fraction had been abnormal 3 to 6 months postablation. After an effective ablation, all antiarrhythmic drug therapy was discontinued if the ablation was effective. Beta-blockers and heart failure medications were continued initially and were discontinued if and when LV function and dimensions normalized. No new medications were added after an effective ablation procedure.