Frequent Premature Ventricular Complexes Originating from the Right Ventricular Outflow Tract Are Associated with Left Ventricular Dysfunction

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Background: Recent case series have shown reversal of left ventricular (LV) dysfunction after catheter ablation of frequent premature ventricular complexes (PVCs) originating from the right ventricular outflow tract (RVOT). We conducted a retrospective study to evaluate the prevalence of patients with frequent RVOT PVCs (≥ 10 per hour) and LV dysfunction.

Methods: RVOT PVC was defined as PVC with left bundle branch block morphology and inferior axis on a 12-lead ECG. We included patients with frequent RVOT PVCs on 24-hours Holter monitor who had a recent evaluation of LV function. Patients with structural heart disease, including obstructive coronary artery disease, were excluded. Patients were divided into three groups based on the number of PVCs ($<1000/24$ hour, $1000\text{--}10,000/24$ hour, $\geq 10,000/24$ hour), and the prevalence of LV dysfunction was evaluated in each group.

Results: Our analysis included 108 patients: 24 patients had $<1000\text{PVCs}/24$ hour, 55 patients had $1000\text{--}10,000\text{PVCs}/24$ hour, and 29 patients had $\geq 10,000\text{PVCs}/24$ hour. The prevalence of LV dysfunction was 4%, 12%, and 34%, respectively ($P = 0.02$). With logistic regression analysis, non-sustained ventricular tachycardia was an independent predictor of LV dysfunction with odds ratio of 3.6 (1.3–10.1).

Conclusion: We demonstrated a significant association between frequent RVOT PVCs and LV dysfunction in patients without structural heart disease.

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premature ventricular complex; tachycardia-induced cardiomyopathy;
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Left ventricular (LV) dysfunction secondary to tachycardia has been termed "tachycardia-induced cardiomyopathy."¹ This syndrome has been described in association with a variety of arrhythmias, including atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia, and ventricular tachycardia (VT).²

Premature ventricular complexes (PVCs) and short bursts of nonsustained VT in the absence of structural heart disease usually originate in the right ventricular outflow tract (RVOT). Recently, several case reports^{3–5} and case series^{6,7} demonstrated the reversal of LV dysfunction after catheter ablation of the RVOT focus in patients with frequent RVOT PVCs. The true prevalence of LV dysfunction in an unselected population of patients

with idiopathic PVCs and nonsustained VT has not been well documented.

The purpose of this study is to describe the prevalence and predictors of LV dysfunction in patients with frequent RVOT PVCs.

METHODS

Study Population

We reviewed all 24-hour Holter monitors performed at our institution from January 2001 to August 2006 to identify patients with frequent (≥ 10 PVCs per hour) RVOT PVCs. RVOT PVCs were defined as PVCs with left bundle branch morphology and inferior axis, as identified on the 12-lead

Figure 1. RVOT PVC was defined as PVC with left bundle branch block and inferior axis.

tracing from the Holter recording (Fig. 1). Patients who had other morphology of PVCs were included if a majority (>80%) were RVOT PVCs. Patients with sustained supraventricular tachycardia, atrial fibrillation, or a pacemaker were excluded.

Evaluation of Left Ventricular Function

Clinical information including the assessment of LV function was obtained retrospectively from the medical records. Patients who had echocardiography or ECG-gated SPECT within 1 year were included. LV function was evaluated during sinus beats. Normal LV function was defined as LV ejection fraction $\geq 55\%$ by echocardiography or LV ejection fraction $\geq 45\%$ by SPECT. Patients with history of ischemic heart disease, structural heart disease, LV dysfunction with segmental wall motion abnormality on echocardiography, or with other apparent

cause of left ventricular dysfunction (i.e., alcohol, HIV) were excluded.

Statistical Analysis

Continuous variables are described as mean $\pm$ SD. Patients were divided into three groups based on the number of PVCs; <1000 PVCs/24 hours (Group 1), 1000–10,000 PVCs/24 hours (Group 2), and $\geq 10,000$ PVCs/24 hours (Group 3). Chi-Square analysis was used to compare results between the groups. Univariate analysis was performed to evaluate the following factors for association with LV dysfunction: age, gender, the number of PVCs, the presence of nonsustained VT (≥ 3 consecutive PVCs), the mean heart rate, and the presence of PVCs with other morphologies. Median score was used to analyze the number of PVCs for nonparametric distribution. Logistic regression analysis

Figure 2. Study population.

was performed using above factors. A value of $P < 0.05$ was considered statistically significant.

RESULTS

There were 3091 Holter monitor recordings during the study period at our institution. Of these, 429 patients had frequent PVCs, and 172 patients had PVCs with RVOT morphology. Recent evaluation of LV function was available in 127 patients (120 echocardiography and 5 gated SPECT). The mean interval between Holter monitor and evaluation of LV function was 2.0 ± 2.9 months (0–12 months). Significant coronary artery disease was found in 11 patients (5 history of myocardial infarction, 4 history of coronary artery bypass surgery, 2 mul-

tivessel coronary artery disease requiring coronary bypass surgery), other structural heart disease was found in 4 patients, and other cause of LV dysfunction was found in 4 patients. After all exclusions, 108 patients were included in the analysis (Fig. 2); 24 patients in Group 1, 55 patients in Group 2, and 29 patients in Group 3. Mean age was 50 ± 16 years, and 31% were men. (Table 1).

Statistically significant differences in the prevalence of LV dysfunction based on the number of PVCs were found. The prevalence of LV dysfunction was 4%, 12%, and 34% in Group 1, 2, and 3 respectively ($P = 0.02$) (Fig. 3). In addition to the number of PVCs, the presence of nonsustained ventricular tachycardia (NSVT) was also associated with LV dysfunction. Age and gender were not

Table 1. Characteristics of Study Patients

	Group1 ($<1000/24h$)	Group2 ($1000-10,000/24\text{ hour}$)	Group3 ($>10,000/24\text{ hour}$)
	[n = 24]	[n = 55]	[n = 29]
Age	47 ± 16	52 ± 17	48 ± 15
Male	21%	36%	31%
PVCs	641 ± 247	3722 ± 2453	$22,537 \pm 8615$
NSVT*	4%	16%	48%
Other PVCs	17%	15%	33%

The differences of age and gender were not statistically significant. NSVT = nonsustained ventricular tachycardia.

* $P < 0.01$.

Figure 3. The prevalence of LV dysfunction in each group.

associated with LV dysfunction. The presence of PVC with different morphology was not associated with LV dysfunction (Table 2).

With logistic regression analysis, using more than 10,000 PVCs and the presence of NSVT, the presence of NSVT was the only predictor of LV dysfunction. The odds ratio for LV dysfunction in patients with NSVT was 3.6 with 95% confidence interval of 1.3–10.1 (P = 0.0146).

DISCUSSION

Isolated RVOT PVCs without structural heart disease have been regarded as a clinically benign arrhythmia.⁸ However, an association with LV dys-

function has been suggested recently. Tachycardia-induced cardiomyopathy is a well-recognized cause of LV dysfunction.^{1,2} In addition to atrial fibrillation and supraventricular tachycardia, idiopathic RVOT VT has been proposed as a cause of reversible LV dysfunction.⁹ Since the first case of reversal of LV dysfunction after ablation of frequent RVOT PVCs was reported in the year 2000,³ several additional reports have been published^{4–6} in support of this finding.

Takemoto et al. reported 40 patients who underwent ablation of RVOT PVCs. Left ventricular ejection fraction and dimensions were worse in patients if more than 20% of their QRS complexes were PVCs.⁶ In their study, >20,000 PVCs /24 hours were associated with LV dysfunction. Interestingly, improvement of LV end-diastolic dimension and end-systolic dimension after ablation of frequent monomorphic PVCs in patients with normal LV function was demonstrated in another study.¹⁰ Duffee et al. initially described four patients with more than 20,000 PVCs (morphology not reported) over 24 hours and a cardiomyopathy, in which LV dysfunction improved after suppression of PVCs by the use of either amiodarone or beta-blocker.¹¹

Although the mechanisms of LV dysfunction in patients with frequent RVOT PVCs are not well understood, several mechanisms have been proposed. One theory is that an RVOT PVC reverses the direction of LV contraction. Most of the reported cases of

Table 2. Factors Associated with LV Dysfunction
 Univariate Analysis to Evaluate the Association between other Holter Variables and LV Dysfunction

	Normal LVF [n = 87]	LV Dysfunction [n = 21]	P Value
Age	49 ± 16	52 ± 16	0.53
Male	26 (30%)	8 (38%)	0.47
#PVCs	6822 ± 9456	13,341 ± 11,020	0.004
NSVT	15 (20%)	9 (40%)	0.012
Mean HR	77 ± 13	81 ± 12	0.17
Other PVCs	15 (17%)	4 (19%)	0.98

LVF = left ventricular function; #PVCs = the number of PVCs per 24 hour; NSVT = nonsustained ventricular tachycardia, the presence of NSVT; HR = heart rate.

reversible LV dysfunction after ablation of frequent PVCs are from the RVOT, and only one case of PVCs with right bundle branch block morphology and reversible LV dysfunction has been reported.¹² Reversibility of LV dysfunction may be solely a function of heart rate, but in our study, the mean heart rate was not associated with LV dysfunction.

We found a statistically significant association between the number of PVCs and the prevalence of LV dysfunction in patients without structural heart disease. Thirty-four percent of patients with more than 10,000PVCs/24 hour had LV dysfunction, and the presence of NSVT was an independent predictor for LV dysfunction. This retrospective study shows only a correlation between PVC frequency and LV dysfunction; it does not demonstrate causality. Further, 26% of patients were excluded because of a lack of recent evaluation of LV function. This may bias the findings in favor of an association, as patients at "low risk" of LV dysfunction may not have been referred for echocardiography. Also, given the retrospective nature, we could not fully evaluate patient symptoms and the treatment status. In addition, the 12-lead ECG was used to diagnose "RVOT" PVCs. Without intracardiac mapping, the definitive RVOT origin cannot be determined.¹³ Still, this study serves to strengthen the relationship between frequent PVCs from RVOT and LV dysfunction.

CONCLUSION

The current analysis demonstrated association of frequent RVOT PVCs with LV dysfunction in patients without structural heart disease. Further prospective studies may examine whether treatment of these PVCs can prevent and reverse cardiomyopathy associated with these arrhythmias.

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