ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

The effect of radiofrequency catheter ablation of frequent premature ventricular complexes and arrhythmia burden on left ventricular function

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Abstract

Background: Frequent premature ventricular complexes (PVC) are related to reversible tachycardia-induced cardiomyopathy. However, the role of arrhythmia burden on the outcome of the catheter ablation has not been fully recognised.

Aim: The aim of this study was to assess the effect of catheter ablation and PVC burden in patients with and without structural heart disease (SHD) on left ventricular ejection fraction (LVEF).

Methods: Transthoracic echocardiography was done before and six months after radiofrequency catheter ablation in 109 consecutive patients (61 men, age 55 ± 17 years) with frequent PVCs. Sixty-five (59.6%) patients had underlying SHD.

Results: The catheter ablation procedure was successful in 93 (85.3%) patients. Baseline PVC burden was higher in patients with SHD (22,267 ± 12,934) compared to those without concomitant SHD (15,546 ± 7888), p = 0.005. Nevertheless, patients with LVEF ≤ 50% at baseline presented greater LVEF recovery (from 44% to 56%) than those with LVEF > 50% at baseline after catheter ablation. In both groups, the LVEF improved (p < 0.001); however, no difference was observed between patients with SHD (5.7% ± 1.37%) and without (4.6% ± 0.96%) SHD; p = 0.89. PVC burden was higher in patients with (24,350 ± 2776 PVC/day) compared to those without improvement of LVEF. In multivariate regression analysis PVC burden > 20,000/day (but not age, p = 0.95; gender, p = 0.89; presence of SHD, p = 0.53; QRS complex width of the treated PVC, p = 0.21, LVEF before ablation, p = 0.19; and site of origin, p = 0.47) predicted improvement in LVEF after successful catheter ablation (odds ratio: 3.53; 95% confidence interval: 1.15–10.75; p = 0.023).

Conclusions: Catheter ablation of frequent PVCs improves left ventricular function in multivariate analysis predicted improvement of LVEF within six months after the successful catheter ablation procedure in patients with PVC burden exceeding 20,000/24 h.

Key words: catheter ablation, left ventricular ejection fraction, structural heart disease, ventricular arrhythmia, premature ventricular complex

Kardiol Pol 2017; 75, 7: 698–704

INTRODUCTION

Frequent premature ventricular complexes (PVCs) are one of the major causes of reversible cardiomyopathy [1–3]. Tachycardia induced cardiomyopathy belongs to the acquired dilative cardiomyopathies and requires exclusion of other underlying disorders and observation of left ventricle (LV) functional improvement after achievement of arrhythmia control for diagnosis [1–3]. Frequent PVCs significantly influence the patient’s quality of life. Idiopathic PVCs in patients without structural heart disease (SHD) are usually considered benign [1–3]. Successful elimination of the PVCs, either by radiofrequency (RF),
catheter ablation, or antiarrhythmic drugs, may improve or even normalise LV systolic function [3–9]. This retrospective study was done to assess the predictors of improvement of LV function in patients with frequent PVCs.

**METHODS**

**Study population**

A total of 109 consecutive patients (62 men; mean age 56 ± 17 years) who were referred for catheter ablation of symptomatic frequent PVCs refractory to medical therapy, including beta-blockers and calcium channel blockers, and patients with subsequent LV dysfunction between January 2009 and December 2010, were included in this study. The patients with sustained ventricular tachycardia were excluded. Frequent PVCs were defined as PVC burden > 10,000/day during 24-h Holter monitoring. 24-h Holter monitoring was performed in all the patients before and 3–6 months after the ablation procedure. An effective RF ablation was defined as a procedure resulting in a reduction of the PVC burden by > 80%. SHD was ruled overestimation of LV function. LVEF < 50% was defined as abnormal. The definition of dilated LV used in the study was the end-systolic dimension of the LV > 38 mm and end-diastolic dimension > 58 mm. Example echocardiographic results are presented in Figure 2.

**Catheter ablation**

The catheter ablation procedure was done in the fasting state. All the patients gave written informed consent for the electrophysiology study and the catheter ablation procedure. All antiarrhythmic drugs (including beta-blockers and calcium channel blockers) were discontinued for at least five half-lives prior to the catheter ablation procedure. Mapping and RF catheter ablation were performed either using a 4-mm tip (Navistar, Biosense Webster, Inc., Diamond Bar, CA, USA) with a power setting of 50 W and temperature limit of 60°C, or a 3.5-mm open irrigated tip ablation catheter (Thermocool Navistar or Navistar RMT, Biosense Webster, Inc.) with a temperature limit of 48°C and a power setting of 30–40 W. Three-dimensional electroanatomical mapping was performed using CARTO-XP, CARTO-RMT, or CARTO-3 mapping systems.

The optimum ablation site was determined by activation and/or pace-mapping as described earlier in detail [10, 11]. The site of origin was defined as the earliest site of the local activation time and from which the best pace-mapping score was obtained. After the catheter ablation, orciprenaline sulphate (Alupent®, Boehringer-Ingelheim Pharma GmbH, Ingelheim am Rhein, Germany) was used to re-induce the PVCs.

**Echocardiography**

Echocardiography was performed before ablation and 3–6 months after the procedure (Fig. 1). Assessment of LV ejection fraction (LVEF) was performed using the Simpson method. Each echocardiography was analysed by two independent observers. To assess the LVEF parameter we used the second sinus beat of two consecutive sinus beats to avoid post-PVC overestimation of LV function. LVEF < 50% was defined as abnormal.

**Statistical analysis**

Variables are expressed as mean ± standard deviation (or standard error of mean), and percentage. Differences in frequency of characteristics were assessed by independent

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<th>Table 1. Baseline patients’ characteristics*</th>
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<td><strong>Group A</strong>*</td>
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<td>Percentage of LVEF recovery</td>
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*Presented as mean ± standard error of mean; † Patients with idiopathic premature ventricular complexes; ** Patients with underlying structural heart disease; ‡ Comparison between the two groups; LVEDD — left ventricular end-diastolic dimension; LVESD — left ventricular end-systolic dimension; LVESV — left ventricular end-systolic volume; LVEF — left ventricular ejection fraction; PVC burden — number of premature ventricular complex in 24-h Holter monitoring.
sample t-test for continuous variables. For discrete variables $\chi^2$ statistics (or Fisher’s exact test if applicable) were used. For non-discrete variables, we used Wilcoxon’s and Shapiro-Wilk’s tests. Predictors of LV function improvement were determined by binary multiple logistic regressions and all the variables with $p < 0.3$ in bivariable analysis were included in the final model. A two-tailed $p$-value $< 0.05$ was considered statistically significant. We used SPSS® 13.0 (SPSS Inc., Chicago, USA) for data storage and analysis.

RESULTS

Patient characteristics

Sixty-five (59.6%) patients had underlying SHD (Table 1). Twenty-six (24%) patients had an implantable cardioverter-defibrillator. Bivariate analysis showed that male gender ($p = 0.0001$), the presence of SHD ($p = 0.001$), but not PVC burden ($p > 0.05$) were associated with LV dysfunction before the catheter ablation procedure. PVCs originated from the right and LV outflow tracts in 50 (46%) and 31 (28%) patients, respectively.

Results of catheter ablation

Ablation of frequent PVCs was successful in 94 (85.4%) patients after a single catheter ablation procedure (88.6% and 83.1% in patients without and with underlying SHD, respectively; $p = 0.42$), with mean PVC burden reduction of 93% ± 11% (92 ± 10% and 90 ± 17% in patients without and with SHD; $p = 0.52$). Three patients experienced complete atrioventricular block due to ablation at high LV septum. One patient died six months after ablation due to exacerbation of heart failure.

The mean LVEF increased from 50% ± 13% to 56% ± 13% ($p < 0.01$) after catheter ablation (Fig. 3). In patients with SHD or decreased LVEF (i.e. < 50), the mean LVEF increased from 37% ± 8% to 48% ± 13% (Fig. 1A, 3A, B). Changes in other echocardiographic parameters are presented in Figure 1B–D.

Predictors of improved LV function

in multivariate analysis

We included age, gender, underlying SHD, baseline echocardiographic LVEF, site of origin, and PVC burden
in our model. In multivariate regression analysis PVC burden > 20,000/24 h (but not age, p = 0.95; gender, p = 0.89; presence of SHD, p = 0.53; baseline LVEF before ablation, 0.19; and site of origin, p = 47) predicted improvement in LVEF after successful catheter ablation (odds ratio [OR]: 3.53; 95% confidence interval [CI]: 1.15–10.75; p = 0.023). The level of echocardiographic recovery after catheter ablation was significant in dilated cardiomyopathy patients (LVEF 39.73 vs. 47.72, p < 0.001), as well as idiopathic ones (LVEF 57.9 vs. 63.49, p < 0.001). In ischaemic subjects, there were no significant LVEF changes (46.27 vs. 49.0, p = 0.2).
DISCUSSION

The main outcome of our study shows that the greater the PVC burden (cut-off value > 20,000/24 h) the better the improvement of LVEF after successful RF catheter ablation. Compared to patients with lower arrhythmia burden (< 20,000 PVC/24 h), the mentioned group had 3.5 times greater odds of LV function improvement 3–6 months after RF catheter ablation (OR: 3.53; 95% CI: 1.15–10.75; p = 0.023). Age, gender, the presence of SHD, baseline LVEF (in patients with LVEF < 50%), and the site of origin did not predict the improvement of LV function.

Tachycardia-induced cardiomyopathy (TIC) is LV dysfunction resulting from cardiac arrhythmia in the absence of concomitant SHD, which is completely or partially reversible after normalisation of cardiac rhythm [3]. Fenelon et al. [12] showed that arrhythmia duration exceeding 10% of the day is the cut-off burden of arrhythmia for TIC. They also defined the additional group of “mixed” TIC, who experience improvement of LV function after successful restoration of normal cardiac rhythm despite the presence of concomitant SHD [12]. However, the median LVEF improvement was more prominent in patients with pure TIC (ΔLVEF > 15%) compared to those with mixed TIC (ΔLVEF > 5%) [13]. The mean improvement of LV function in our patients was 8.3% ± 1.8%.

Baman et al. [14] intended to determine a cut-off PVC burden that could result in PVC-induced cardiomyopathy. The authors determined PVC burden in a group of 174 patients with idiopathic PVC with 24-h Holter monitoring. A reduced LVEF was present in 57 (33%) patients. In multivariate analysis, PVC burden > 24% (OR: 1.12; p < 0.01) was independently associated with PVC-induced cardiomyopathy [14]. Higher PVC burden (> 26%/day) with 70% sensitivity and 78% specificity was an independent marker of PVC-mediated LV dysfunction in a study by Ban et al. [15]. Yokokawa et al. [16] studied 241 patients with frequent PVCs, who were referred for catheter ablation. 180 (75%) patients experienced symptoms and 61 (25%) were asymptomatic. LV dysfunction was present in 76 (32%) patients. Symptom duration of 30 to 60 months, symptom duration > 60 months, the absence of symptoms, and PVC burden in asymptomatic patients were independent predictors of impaired LV function [16]. The 10,000 extra beats per day was the cut-off in Sekiguchi’s group study investigating the haemodynamic effects of PVCs in relation to LV dimensions and serum B-type natriuretic peptide level, which appeared to improve after RF catheter ablation [17]. Baseline PVC burden of 13% (100% sensitivity and 85% specificity) predicted more than a 5% increase in LVEF after sustained successful ablation in 80 patients assessed by Blaye-Felice et al. [20]. The studies mentioned above showed that high PVC burden is associated with impaired LV function before catheter ablation. Our study showed that PVC burden is associated not only with LV dysfunction before catheter ablation but also predicts the improvement of LVEF 3–6 months after the catheter ablation procedure.

The follow-up echocardiography in our study was performed 3–6 months after the catheter ablation procedure, which might have caused underestimation of the beneficial effect of the successful ablation procedure. Yokokawa et al. [19] studied the time course of recovery of the LV function after catheter ablation. In 87 patients (with mean LVEF 40 ± 10%) the PVC burden was reduced to < 20% in comparison to the initial PVC burden in 75 patients after the catheter ablation procedure. The majority of patients (51; 68%) with PVC-induced LV dysfunction had recovery of LV function within four months. However, in one-third (24; 32%) of patients, the recovery of LV function took more than four months (mean 12 months; range 5–45 months) [19].

In multivariate analysis, epicardial PVC focus was associated with the delayed recovery of LVEF in patients with LV dysfunction [19]. In a recently published study by Sadrone Blaye-Felice et al. [20] the PVC burden, epicardial origin, or lack of palpitations were independent factors identifying patients with tachycardiacardiomyopathy. Nevertheless, improvement of LV function, after complete PVC elimination, was not associated with the arrhythmia origin in a different study performed by Mountantonakis et al. [21]. This was also the case in our study.

Recently, an interesting analysis was performed by Doygu Bas et al. [22], showing that patients with PVC-induced cardiomyopathy have a lower degree of PVC variability during the 24-h time in comparison to patients who do not develop cardiomyopathy. Daily variability of PVC may account for even 20% difference; however, those variances in short periods of time may not significantly influence general change in ejection fraction after ablation in a 3–6-month period [22].

We observed a high prevalence of atrioventricular block. One of the reasons was the ablation region (para-Hisian in two cases), age, SHD at baseline, high New York Heart Association class symptoms, widened QRS complex, comparatively longer time of procedure.

According to the current European Society of Cardiology 2015 guidelines, frequent PVCs in patients with SHD increase the mortality rate. In symptomatic PVC patients, as well as, TIC catheter ablation and amiodarone are class II a indication. PVC burden exceeding 24% daily in patients with LV dysfunction suggests PVC-induced cardiomyopathy. Catheter ablation in such a group may restore LV function [23].

Unfortunately, our study design was retrospective. This might not sufficiently assess the success rate and LV recovery; however, it could present some trends and differences of clinical significance.

CONCLUSIONS

High PVC burden, i.e. > 20,000 PVC/day, predicts improvement of LVEF after successful catheter ablation. Compared to patients with < 20,000 PVC/day, they had 3.5 times greater
odds of improvement of LV function within six months after RF catheter ablation (OR: 3.53; 95% CI: 1.15–10.75; p = 0.023).

Age, gender, presence of SHD, baseline LVEF (in patients with LVEF < 50%), and site of origin did not predict improvement of LV function. Catheter ablation should be considered as the first-line therapy in all patients with PVC > 20,000/day and LV dysfunction [24]. Still, there are many unclear aspects of tachycardiomopathy treatment in the prevention of structural changes and long-term risk of sudden cardiac death, which necessitate further exploration [25, 26].

Conflict of interest: Oskar Kowalski and Gerhard Hindricks: Lectures for Medtronic, Biotronik, St. Jude Medical.

References
Znaczenie obciążenia arytmią i wpływu leczenia ekstrasystolii komorowej przezskórną ablacją prądem o wysokiej częstotliwości na funkcję lewej komory

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Streszczenie

Wstęp: Ekstrasystolia komorowa (PVC) może być przyczyną odwratalnej tachykardiomiopatii. Jednak wpływ stopnia obciążenia arytmią na efekty leczenia przezskórną ablacją pozostaje niejasny.

Cel: Celem badania była ocena wpływu terapii za pomocą przezskórnej ablacji i stopnia obciążenia arytmią na frakcję wyrzutową lewej komory (LVEF) u chorych z strukturalną i bez strukturalnej choroby serca.

Metody: Do badania włączono 109 kolejnych chorych (61 mężczyzn, w wieku średnio 55 ± 17 lat) z liczną PVC poddawany przezskórnej ablacji prądem o wysokiej częstotliwości. Przed zabiegiem i 6 miesięcy po nim wykonywano przezklatkowe badanie echokardiograficzne. U 59,6% osób stwierdzono współistniejącą strukturalną chorobę serca.

Wyniki: Zabieg ablacji był skuteczny u 93 (85,3%) pacjentów. Wyjściowe obciążenie arytmia było większe (22 267 ± 12 934 PVC/24 h) u osób ze strukturalną chorobą serca w porównaniu z grupą bez organicznej choroby serca (15 546 ± 7888 PVC/24 h); p = 0,005. LVEF uległa poprawie w obydwu badanych grupach (p < 0,001), jednak bez istotnej różnicy między nimi (w grupie ze strukturalną chorobą serca średnia zmiana LVEF wyniosła 5,7% ± 1,37%, a bez uszkodzenia — 4,6% ± 0,96%; p = 0,89). Niemniej jednak, u chorych z LVEF ≤ 50% przed zabiegiem obserwowano większą poprawę LVEF po ablacji (z średniej wartości LVEF 44% na 56%) w stosunku do grupy z LVEF > 50%. Obciążenie arytmia było większe u osób, u których obserwowano poprawę funkcji skurczowej lewej komory (24 350 ± 2776 PVC/24 h) w porównaniu z pacjentami (17 588 ± 1970 PVC/24 h), u których nie uzyskano poprawy. W analizie wieloczynnikowej stopień obciążenia PVC przekraczający 20 000 PVC/dobę był czynnikiem prognozowym poprawy LVEF po skutecznej przezskórnej ablacji arytmii (iloraz szans: 3,53; 95% przedział ufności: 1,15–10,75; p = 0,023). Czynnikami prognozowymi nie były: wiek (p = 0,95); płeć (p = 0,89); obecność strukturalnej choroby serca (p = 0,53), szerokość zespołu QRS dodatkowego skurczu komorowego (p = 0,21), funkcja skurczowa lewej komory przed ablacją (p = 0,19) ani miejsce wyjścia arytmii (p = 0,47).

Wnioski: Przezskórna ablacja PVC poprawia funkcję skurczową lewej komory. W opisywanej populacji skuteczne leczenie ablacją prądem o wysokiej częstotliwości poprawiało LVEF po 6 miesiącach od zabiegu wśród wszystkich chorych, a szczególnie w grupie pacjentów z obciążeniem przekraczającym 20 000 PVC/24 h.

Słowa kluczowe: ablacja prądem o wysokiej częstotliwości, frakcja wyrzutowa lewej komory, skurczowa choroba serca, arytmia komorowa, ekstrasystolia komorowa

Kardiol Pol 2017; 75, 7: 698–704