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Original Article

The Short-term Post-Ablation Outcome of Patients With Low-Burden Premature Ventricular Complexes

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ABSTRACT

Background: The management of low-burden premature ventricular complexes (PVCs) (<10%) is currently a matter of debate among clinicians. Several small studies have shown an increased risk for left ventricular dysfunction in a lower PVC burden. Radiofrequency ablation is known to have favorable effects on PVC frequencies and left ventricular dysfunction. However, data are scarce regarding ablation in patients with low-burden PVCs, especially its benefits on symptom burden and the quality of life. This study aimed to compare symptom burden and the quality of life before and 6 months after ablation.

Methods: Thirty-one patients with low-burden PVCs who underwent radiofrequency ablation were assessed. The ASTA (Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia) was used to assess symptom burden and the quality of life in the patients. The score was calculated before and 6 months after ablation.

Results: Significant differences existed in the mean scores before and 6 months after ablation concerning the ASTA burden scale symptom score (38.83 vs 4.45; $P<0.05$), the ASTA health-related quality of life (HRQoL) physical subscale (30.30 vs 1.91; $P<0.05$), the ASTA HRQoL mental subscale (32.41 vs 4.51; $P<0.05$), and the ASTA HRQoL total scale (32.09 vs 2.90; $P<0.05$).

Conclusions: Radiofrequency ablation was associated with a favorable outcome in terms of symptom burden and the quality of life in our patients with low-burden PVCs in the short term. ***(Iranian Heart Journal 2021; 22(4): 25-33)***

KEYWORDS: Premature ventricular complexes, Low burden, Radiofrequency ablation

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Premature ventricular complexes (PVCs) constitute an early depolarization originating from the ventricles. PVCs comprise a common electrocardiographic (ECG) finding in the general population. In several epidemiological studies on healthy people, the prevalence of PVCs has been found to range from 1% to 4% on 12-lead ECGs and from 40% to 75% on ambulatory ECGs.[1,2] PVCs are often found in association

with the presence of structural heart diseases and an increased risk of cardiovascular diseases and sudden death. However, PVCs can also occur in patients even without underlying heart diseases. Various studies have shown that frequent PVCs increase the risk of sudden death, cardiovascular events, and left ventricular dysfunction.[3, 4]

Previous research has shown that PVCs can cause dysfunction and progressive left ventricular dilatation.[5,6] The mechanisms thought to play a role in mediating left ventricular dysfunction by PVCs include disturbances in calcium hemostasis, increased oxygen consumption, and ventricular dysfunction. Therefore, the management guidelines from the European Society of Cardiology (ESC) in 2015 and the American Heart Association (AHA)/American College of Cardiology (ACC) in 2017 recommend prescribing medications or actions to suppress PVCs in symptomatic individuals whether or not they have left ventricular dysfunction.[7, 8]

PVC burden is a predictor that is considered to play a major role in determining whether a PVC will cause left ventricular dysfunction. Studies on patients with PVCs have reported that a PVC burden exceeding 24% is independently associated with the incidence of PVC-induced cardiomyopathy.[9] Recent investigations reporting a lower PVC burden (8%) have demonstrated earlier systolic dysfunction based on global longitudinal strain examinations.[10] Kanei et al[11] reported that the prevalence of left ventricular dysfunction in patients with PVCs fewer than 1000 within 24 hours was 4% in their study. Dukes et al[12] reported in a study performed by Holter monitoring on 1139 subjects that more than half of the patients with a PVC burden of 3% had heart failure within 5 years. Lin et al[13] stated that PVCs more than 12 per day were independent predictors of mortality and hospitalization due to any cause, hospitalization due to cardiovascular diseases, and new-onset heart failure in their study population. Symptoms are not limited to patients with high-burden PVCs only; those with a lower PVC burden (<5000/24 h) can be very symptomatic and require further action.[14] There is a dearth of data on ablation in patients with low-burden PVCs, especially as regards the benefits of ablation on symptom burden and the quality of life. A study by Shanmugam et al[14] reported that there was an improvement in the left ventricular function in cardiomyopathy patients with a PVC burden of 4% after ablation. Recalling symptoms can occur in patients who had low-burden PVCs and have started to show earlier signs of left ventricular dysfunction.

The present study aimed to compare symptom burden and the quality of life before and 6 months after ablation with a view to determining the benefits of radiofrequency ablation in terms of symptom burden and the quality of life for patients with low-burden PVCs.

METHODS

The present observational, single-center, cohort study was conducted from January through December 2019. The study population was composed of all patients with low-burden PVCs who were planned for ablation because of refractoriness to antiarrhythmic treatment, patient intolerance, and patient preference. PVC burden assessment was carried out based on the results of a 24-hour Holter ECG. A low-burden PVC was defined as a maximum PVC burden of 10% within 24 hours. Patients with a history of previous ablation and patients with other concomitant arrhythmias were excluded from this study. The patients' baseline status such as sex, age, weight, height, the body mass index (BMI), and comorbid factors were recorded.

Two-dimensional echocardiography was performed prior to ablation. The results concerning the left ventricular ejection fraction (LVEF) and the left ventricular end-diastolic dimension (LVEDd) were recorded

through calculations in the M-mode parasternal long-axis view and the Simpson method.

This study used the Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA) to assess symptom burden and the quality of life in the low-burden PVC patients included in the study. The ASTA questionnaire is a validated questionnaire divided into 3 separate parts. Part I evaluates patients' latest episodes of arrhythmias and current medications. Part II assesses burden symptoms and features a 9-item symptom scale with a 4-point response scale (the ASTA symptom scale). Outside of the symptom scale, there are questions with regard to the frequency of arrhythmia episodes, the average and the longest duration of an arrhythmia episode, and experience of near syncope, syncope, and palpitations in connection with arrhythmias. Part III assesses the health-related quality of life (HRQoL) via a 13-item scale, with the same 4-point response scale (the ASTA HRQoL scale) as for the symptom scale. The ASTA HRQoL scale is divided into a 7-item physical subscale and a 6-item mental subscale. Values range from 0 to 100, and higher scores reflect a higher symptom burden and a worse effect on HRQoL due to the arrhythmia.[15, 16]

The ASTA scale score was calculated at baseline before the ablation procedure and 6 months afterward. In addition, 10-second 12-lead ECGs were obtained to assess the presence of PVC recurrences 6 months after ablation.

Statistical Analysis

The data obtained were analyzed by computer using the Statistical Package for Social Science (SPSS) program. Categorical data were presented in the form of frequencies. Categorical data were carried out through the analysis of the mean, the median, the minimum, the maximum, and the standard deviation. The paired-sample *t* test was used to compare the quality of life before and 6 months after ablation. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

Thirty-one subjects met the study inclusion and exclusion criteria. The study population's basic characteristics (viz, sex, age, weight, height, BMI, and comorbid factors), PVC burden, and echocardiography findings (viz, LVEF and LVEDd) before ablation are presented in Table 1.

As is demonstrated in Table 1, the study population had a female preponderance (19 [61.3%] vs 12 [38.7%]). The mean age of the sample was 43.06 years. The youngest and oldest subjects were 17 and 74 years old, respectively. The average body weight was 61.71 kg, the mean height was 160.85 cm, and the mean BMI was 24.3 kg/cm^2. More than half of the total sample had no comorbid factors, while the most comorbid factor was hypertension (38.7%), followed by coronary heart disease (6.5%) and type II diabetes mellitus (3.2%).

Apropos of echocardiography findings, the mean LVEF was 62.8%, and the mean LVEDd was 43.7 mm. Only 1 subject was found to have a decreased LVEF (=29%) and an increased LVEDd (=67 mm). The mean PVC burden was 7.9%. The lowest and highest PVC burden values were 4.3% and 10%, respectively. At the time of ablation, based on the results of the ablation report, most of the PVC origins were from the anteroseptal right ventricular outflow tract (RVOT) (45.2%), followed by the posteroseptal RVOT (38.7%) and the anteroseptal LVOT (6.5%). There were also some other origins such as the anterolateral RVOT, the posterior RVOT, and the His bundle.

Six months after ablation, 12-lead ECG was performed in 22 subjects. (Technical reasons precluded this examination in 9 patients.)

Eight of the 22 subjects exhibited PVCs with a volume of 1 to 2 PVCs at an average of 0.41±0.5 in 10 seconds on a 12-lead ECG. Additionally, there were 7 subjects (31.8%) with 1 PVC and 1 subject (4.5%) with 2 PVCs; the remaining 14 subjects (63.6%) showed no PVCs within 10 seconds of 12-lead ECG.

The ASTA Scale Score Before and 6 Months Post Ablation

The assessment of symptom burden and the quality of life was carried out before and 6 months after ablation using the ASTA questionnaire. The ASTA scale scores before and 6 months after ablation can be seen in Table 2.

The ASTA symptom burden scale score shows how severely the symptoms of PVCs affect subjects. The lowest score obtained was 17.8, while the highest score was 75 with a mean of 38.83. Six months after ablation, 19 patients (61.2%) still had symptoms with an ASTA symptom burden scale ranging from 4.0 to 46.0.

The ASTA near-syncope scale and the ASTA symptom syncope scale score are based on the presence or absence of near-syncope or syncope symptoms. Our results revealed 3 subjects with this symptom with a mean score of 7.25 and 2.76. After ablation, this symptom never occurred.

The ASTA HRQoL score consists of 2 subscales that assess the effects of arrhythmias on the quality of life both physically and mentally. The results of the interview showed that the majority of the 31 subjects experienced disturbances in carrying out daily activities, decreased physical abilities, diminished concentration, sleep disturbances, and anxiety due to the arrhythmias that they experienced to different degrees.

Based on the calculation of the ASTA scale score, the decrease in the mean ASTA symptom burden scale was 88.52%, the mean ASTA HRQoL physical subscale was 93.71%, the mean mental subscale was 86.08%, and the total scale was 90.09%. The statistical analyses using the *t* test found a significant difference in the mean ASTA burden scale symptom score before and 6 months after ablation (38.83 vs 4.45; $P<0.05$), the ASTA HRQoL physical subscale (30.30 vs 1.91; $P<0.05$), the ASTA HRQoL mental subscale (32.41 vs 4.51; $P<0.05$), and the ASTA HRQoL total scale (32.09 vs 2.90; $P<0.05$). However, no statistically significant differences were found between the ASTA symptom near-syncope scale and the ASTA symptom syncope scale.

Table 1. Baseline characteristics of the study population

Variables	n (%)	Min/Max	Mean±SD
Sex Male Female	 12. (38.7%) 19 (61.3%)		
Age, y		17/74	43.0±14.4
Weight, kg		43/84	61.7±9.8
Height, cm		149/173	160.8±6.7
Body mass index, kg/cm^2		17.7/30.8	24.35±3.7
Comorbid Factors None Coronary artery disease Hypertension Type II diabetes mellitus	 16 (51.6%) 2 (6.5%) 12 (38.7%) 1 (3.2%)		
Echocardiography Ejection fraction (%) LVEDd (mm)		 29.0/76.0 36/76	 62.83±7.7 43.7±5.3
PVC burden (%)		4.3/10.0	7.95±1.5

PVC Origin			
RVOT anteroseptal	14 (45.2%)		
RVOT anterolateral	1 (3.2%)		
RVOT posterior	1 (3.2%)		
RVOT posteroseptal	12 (38.7%)		
LVOT anteroseptal	2 (6.5%)		
His bundle	1 (3.2%)		

PVC, Premature ventricular complex; RVOT, Right ventricular outflow tract; LVEDd, Left ventricular end-diastolic dimension

Table 2. ASTA scale score before and 6 months after ablation

ASTA Scale	Before Ablation	6 Months Post Ablation	*P*-value
ASTA symptom burden scale	Min/max 17.8/75.0 38.83±14.98	Min/max 0/46.4 4.45±8.54	<0.05
ASTA symptom near syncope	Min/max 0/75 7.25±22.50	Min/max 0/0 0±0	0.083
ASTA symptom syncope	Min/max 0/85.7 2.76±15.30	Min/max 0/0 0±0	0.780
ASTA HRQOL			
physical subscale	Min/max 4.5/86.3 30.30±17.72	Min/max 0/31.8 1.91±6.18	<0.05
Mental subscale	Min/max 15.7/89.4 32.41±21.52	Min/max 0/31.5 4.51±7.09	<0.05
Total scale	Min/max 10/87.5 32.09±19.37	Min/max 0/32.5 2.90±6.22	<0.05

DISCUSSION

PVCs are ventricular arrhythmias that tend to be benign or harmless, especially in patients without structural heart diseases. In general, individuals with PVCs do not feel any symptoms; nonetheless, a few also experience various kinds of symptoms that prompt them to seek medical attention. Symptoms can range from mild (eg, palpitations, dizziness, chest discomfort, and chest pain) to severe (eg, syncope). PVCs have long-term effects such as increased hospitalization, increased incidence rates of heart failure, and increased cardiovascular disease mortality. This of course cannot be separated from the frequency or burden of the PVC itself. Research shows a linear correlation between PVC burden (the frequency of PVCs within 24 hours) and symptoms, hospitalization, and cardiovascular mortality. What has been discussed so far is a PVC that induces cardiomyopathy.[13] Baman et al[9] reported that a PVC burden of greater than 24% had a sensitivity of 78% and a specificity of 79% in predicting PVC-induced cardiomyopathy. Therefore, PVC burden is often used as a reference in PVC management.

Handling symptomatic PVCs is not always easy since many patients have to take long-term antiarrhythmic medications, which are sometimes ineffective and cause many side effects. Radiofrequency ablation may be an alternative treatment for PVCs. Guidelines from the ESC in 2015 and the AHA/ACC in 2017 recommend that ablation be performed in patients with symptomatic PVCs, for which the administration of antiarrhythmic drugs fails to confer satisfactory results, or patients who cannot tolerate antiarrhythmic drugs (especially those with a PVC burden exceeding 20% to 24%.[7,8] Many studies have shown that radiofrequency ablation can reduce symptoms, diminish the frequency of PVCs within 24 hours, and improve LVEF in PVC-induced cardiomyopathy. Latchamsetty et al,[17] in a multicenter study on patients with a PVC burden exceeding 20±13%, concluded that ablation was an effective strategy in eliminating PVCs and

restoring the cardiac function in PVC-induced cardiomyopathy.

The management of low-burden PVCs (<10%) is currently a matter of debate among clinicians. Indeed, the existing literature contains a paucity of information on both symptoms and long-term effects. Several studies and case reports have reported that cardiomyopathy is also found at a PVC burden of less than 10%. Yarlagadda et al[18] reported cardiomyopathy in a patient with a PVC frequency of only 5500 per day. Shanmugam et al[14] reported a significant resolution of decreased left ventricular systolic function after radiofrequency ablation in patients with PVCs occurring fewer than 5000 per day. Lie et al[10] assessed PVC burden and its relationship with myocardial function and concluded that more than 8% of PVC burden was associated with an impaired systolic function by global longitudinal strain. In terms of symptoms and their effects on the quality of life, Huang et al[19] reported that there was no statistically significant difference between a PVC burden of less than 10% and a burden ranging between 10% and 20%.

Our study aimed to assess symptom burden and the quality of life in the short term (6 mon) in patients with low-burden PVCs (burden <10%). We found improvements in symptom burden and the quality of life within 6 months after ablation, where there was a statistically significant difference between the ASTA scores (the symptom burden scale and the HRQoL scale) before and 6 months after ablation.

There are differences between the 2 sexes concerning the incidence of PVCs. The results of the ARIC study and a study by Kerola et al[20] showed that being male was one of the predictors of PVC occurrence. In contrast, in our study, low-burden PVCs occurred more frequently among women, which is consistent with the findings of a study by Sirichand et al,[21] who reported that the symptomatic PVC incidence was more common in women. This is presumably because women tend to be more sensitive to milder symptoms of PVCs and seek medical attention more often. However, there is no specific research on this matter.

PVCs can occur at any age, from infancy to old age. Based on our study data, the mean age of patients with low-burden PVCs was over 40 years, with the youngest being 17 years. The ARIC cohort study associated old age with the presence of at least 1 PVC every 2 minutes of ECG recording.[22] This is consistent with a population-based study conducted by Sirichand et al,[21] who concluded that the incidence of ventricular arrhythmias increased with age. This is probably related to an increase in cardiovascular risk factors in general, as well as the emergence of other nonspecific symptoms, which prompt individuals to seek medical attention.

There is some information on the association between anthropometric profiles such as weight, height, and BMI and the incidence of PVCs, especially low-burden PVCs. Based on our data, the average BMI was 24.35±3.7 kg/cm^2, but there were 14 subjects with BMI exceeding 25 kg/cm^2. Obesity itself is considered a risk factor for arrhythmias. This is thought to be related to several factors such as hypoxia, hypercapnia, electrolyte disturbances, ventricular hypertrophy, coronary heart disease, obstructive and sleep apnea.[23] A previous study reported that metabolic syndromes were associated with the recurrence rate of outflow tract PVCs in patients without structural heart diseases. [24]

Cardiovascular risk factors such as hypertension, type II diabetes mellitus, and coronary heart disease are often associated with the incidence of PVCs insofar as these diseases cause structural changes at both macro and micro levels. In this study, we

found that more than half of the total subjects (51.6%) did not have this risk factor. This is also supported by echocardiography, which revealed only 1 subject with a decreased LVEF and an increased LVEDd, although this subject had coronary heart disease comorbidities. Therefore, we cannot conclude that there was PVC-induced cardiomyopathy.

The origin of PVCs is closely related to PVC burden and is associated with the incidence of PVC-induced cardiomyopathy. Xu et al[25] reported that PVCs derived from the RVOT had a higher PVC burden than PVCs from other origins. A previous study by Takemoto et al[5] indicated that PVCs derived from the RVOT were a possible cause of LV dysfunction and heart failure. However, there was no significant correlation between the origin of this PVC and the severity of symptoms. In our study, most of the subjects had PVCs derived from the RVOT (90.3%), with only 6.5% originating from the LVOT and 3.2% from the His bundle, which chimes in with the findings of a study by Farzaneh et al,[26] who reported that in patients without structural heart diseases, 80% of PVCs came from the RVOT, with the remaining 20% coming from the LVOT.

Although PVCs are generally benign, the symptoms they cause (eg, palpitations, chest pain, dizziness, near-syncope, and syncope) can affect the quality of life to varying degrees. Ablation significantly reduces the frequency of PVCs. Huang et al[19] reported that ablation improved the quality of life in their PVC patients and decreased overall costs. Pytcowski et al[27] reported a significant improvement in the quality of life after ablation in patients with frequent PVCs. In patients with low-burden PVCs for whom we performed a quality of life assessment, ablation improved the quality of life both physically and mentally at 6 months when compared with before ablation. Although some patients experienced insignificant improvements in their quality of life and still experienced symptoms less frequently, overall, after we conducted statistical tests there was a significant improvement ($P<0.05$).

In this study, we did not conduct further analyses of the causes or factors affecting PVC recurrence. Based on a study by Baser et al,[28] the acute success rate of PVC ablation was 74%, and this predictor of success was determined by the presence or absence of predominant PVCs within 12 hours after ablation. Latchamsetty et al[17] reported an acute ablation success rate of 84% at follow-up. In their investigation, the success rate at a mean follow-up of 20 months was 71%, of which 19% were still on antiarrhythmic drugs. Latchamsetty and colleagues also reported that the predictors of long-term success and failure were the origin of PVCs: PVCs derived from the RVOT had a higher success rate, while epicardial and multifocal PVCs were considered predictors of long-term failure.

In light of the results of the current investigation, we maintain that ablation in patients with symptomatic low-burden PVCs provides benefits and outcomes in terms of improving symptom burden and the quality of life that are comparable with patients with high-burden PVCs. The presence or absence of symptoms and how much it influences the quality of life of patients with PVCs should be considered one of the parameters in determining the PVC treatment strategy. The treatment should be thoroughly explained to the patient, who should also be offered reassurances and be given thorough evaluations, before a decision is made as to which method of treatment to choose.

Limitations

The most important limitations of this study are its relatively low number of samples and its short follow-up duration. The fact that our study was a single-center investigation precludes the generalizability of the results.

A longer-term follow-up including Holter ECG 6 months post-ablation is required to assess efficacy and recurrence in more detail for a better assessment of the role of ablation in patients with low-burden PVCs.

CONCLUSIONS

Radiofrequency ablation was associated with favorable short-term outcomes in terms of symptom burden and the quality of life in our patients with low-burden PVCs.

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