

Symptom Burden and Quality of Life After Successful Ablation in Patients With Low Burden of Symptomatic Premature Ventricular Complexes

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Abstract

It is essential to enhance life quality in patients with premature ventricular complexes (PVCs) with the use of radiofrequency ablation (RFA). The aim of the study was to assess symptom burden and life quality in patients with a low PVC burden following RFA. 31 individuals with a low PVC burden in whom RFA was indicated were included in the study. At baseline and after a year following RFA, the Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA) scale was used for appraisal. A 24-hour Holter electrocardiogram was used to detect recurrent PVCs 12 months after the RFA intervention. ASTA scores related to symptom burden, including the near-syncope score, health-related quality of life (HRQOL) scales pertaining to physical and mental health, and consequently the total HRQOL score, were all diminished a year after RFA ($p < 0.001$). The ASTA score for syncope symptoms was also reduced ($p < 0.05$). A fall in mean PVC burden was seen from 8.0% to 0.8% ($p < 0.001$). The long-term clinical endpoint in individuals with a low PVC burden following RFA is reported. Symptom load, life quality and ultimate PVC burden were all enhanced. Additional studies incorporating longer follow-up and monitoring periods, respectively, would be beneficial.

Introduction

In patients with premature ventricular complexes (PVCs), life quality can be enhanced by radiofrequency ablation (RFA)¹. Objectives of cardiac rehabilitation include diminishing symptomatology and attaining superior levels of physical activity and overall health².

In routine clinical work, PVCs are the most frequent cardiac dysrhythmia encountered, with a prevalence of 1.1% being documented in a telemedicine study performed in Makassar City³. A further study noted PVCs in 1% and 40-75% of individuals on 12-lead and Holter electrocardiography, respectively⁴. PVCs are more common in patients of more advanced years; frequencies of a minimum of one PVC detected on 24-hour cardiac recordings were 16.7% in well individuals below the age of 30 years, and up to 69% in those above the age of 75 years⁵.

Within the overall population, the impact of PVCs on the establishment of congestive cardiac impairment or fatality is unclear. Nevertheless, a number of publications have implied that the likelihood of sudden cardiac demise, cardiovascular morbidity and systolic left ventricular impairment may be exacerbated by numerous PVCs⁶. In addition, patients may present with palpitations, fatigue, chest discomfort, dizziness, loss of consciousness and symptoms of cardiac impairment. Although these issues are common in patients with a high burden of PVCs, low PVC frequency, i.e. $< 5000/24$ hours, can also generate significant symptomatology and merit treatment⁷.

Earlier clinical studies have demonstrated that an impairment in left ventricular ejection fraction (LVEF) may be associated with a higher than mean burden of PVCs. Interestingly, the frequency of PVCs did not always predict left ventricular function, with patients with a high PVC burden displaying normal cardiac performance whereas cardiomyopathy related to PVCs was at times seen in subjects with a relatively

small PVC burden⁸⁻¹⁰. Currently, no specific estimate of PVC burden has been determined to be a reliable predictor of cardiac dysfunction^{7 11-13} although an arbitrary cut-off parameter of 10% PVCs with respect to the overall heart rate, as opposed to the absolute PVC frequency, has been employed in a number of studies¹¹¹⁴.

RFA is an efficacious therapeutic intervention for PVCs. Contemporary pharmaceutical agents for dysrhythmias are not always effective and may have an adverse side effect profile¹⁵. Clinical recommendations published by the European Society of Cardiology (2015) and the American Heart Association/American College of Cardiology (2017) relating to the care of individuals with ventricular dysrhythmia and sudden cardiac death prevention advise the use of RFA in patients who present with PVCs that give rise to symptoms, reduced LVEF and in whom anti-arrhythmic agents fail¹⁶¹⁷.

A number of studies have provided evidence regarding the non-subjective positive endpoints following the use of RFA in individuals with a high PVC burden, although PVCs were noted to recur after a post-procedural surveillance period of at least six months^{8 11 12 18}. One retrospective study followed up 44 individuals who had received RFA for a symptomatic high PVC burden for over a year; monitoring determined a positive outcome rate following RFA of 75%¹⁹. PVCs, arising from either a different or identical pre-ablation focus, recurred in 18.2% and 6.8% patients, respectively.

RFA does not influence mortality statistics, and therefore its clinical endpoints should be judged in relation to subjective changes in patient symptomatology. Few studies have evaluated the application of RFA in individuals who have few PVCS, particularly with respect to their symptoms and life quality. A low PVC burden may provoke symptomatology; some individuals may exhibit clinical evidence of reduced LVEF. The current research has appraised the utility of RFA with respect to the symptomatic load and life quality of individuals with symptoms pertaining to a low PVC burden. The data presented can be utilized as a foundation for establishing the utility of RFA in the clinical care of this patient cohort.

Methods

Study design

An observational, single-centre, cohort study was performed in order to assess the outcome of individuals with a low burden of PVCs treated at either the Medical Faculty of Hasanuddin University or the Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia. The study was conducted between January and December, 2019. The study was approved by Commission on Health Research Ethics Medical Faculty of Hasanuddin University RSPTN with protocol number UH20020106. All participant will be informed of the research aims and objectives, and that confidentiality will be maintained throughout the study. Information and consent form provided at baseline and participant will be free to withdraw from the research at any time. All methods were performed in accordance with the Declaration of Helsinki.

Patient characteristics

All 31 study participants had a low PVC burden, as evaluated by 24-hour Holter electrocardiography and defined as $\leq 10\%$ PVCs per 24-hour period. Indications for RFA included continuing symptoms despite use of anti-arrhythmic agents, failure to withstand medication and patient choice. Study exclusion criteria encompassed those who had undergone former RFA or who had additional coexistent rhythm disturbances. Patient demographics were documented, i.e., gender, age, weight, height, body mass index (BMI) and additional comorbidities.

Echocardiography

2-dimensional echocardiography was carried out before and after RFA intervention. LVEF and left ventricular end-diastolic dimension (LVEDd) were computed according to the Simpson method from an M-mode image obtained in the parasternal long axis plane.

Radiofrequency ablation

Following written informed consent, all patients underwent electro anatomical mapping and radiofrequency catheter ablation of the PVC foci per standard laboratory protocol and the judgment of the operator. Mapping and ablation were performed with 7Fr quadripolar electrodes and a deflectable-curve, temperature-guided ablation catheter. Activation mapping was used with 3-dimensional mapping system. Attempts were made to record an earliest endocardial activation at least 30 ms before the onset of the QRS complex from the ectopic site. The aim was to achieve a 11/12 or 12/12 identical pace mapping. Once VPCs were localized, radiofrequency power of 20 to 40 W to maintain the temperature at the catheter tip of 50°C was delivered. After ablation, all patients were kept under observation for 30 min. Successful ablation was defined as complete elimination of spontaneous or inducible PVC¹.

Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia scale

The Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia scale (ASTA) scale was utilized in order to evaluate subjects' symptom load and impact on life quality prior to and 12 months after RFA, the latter in conjunction with a further 24-hour Holter electrocardiogram in order to identify recurrent PVCs. The questionnaire was split into three sections, which assessed: (i) the most recent arrhythmic event and ongoing drug therapy; (ii) the symptom load according to a 9-item 4-point response scale (the ASTA symptom scale); and (iii) life quality using a 6- and a 7-item subscale, i.e. 13 items in total, comprising similar 4-point response rankings, i.e. the ASTA Health-Related Quality of Life (HRQOL) scale. The second section also encompassed enquiries regarding the prevalence of events relating to PVCs, the mean length of symptoms and the most enduring event, together with any history of associated loss of

consciousness, dizziness or palpitations. The ASTA HRQOL evaluation generated scores ranging between 0 and 100; the latter indicated a high symptom load and greater impact of the PVC burden on life quality^{20 21}.

Statistical analysis

The Statistical Package for the Social Sciences software was used for data analysis. Mean \pm standard deviation, together with minimal and maximal scores are presented for the continuous variables; frequencies are provided for the categorical data. Life quality pre- and post-RFA was compared using a paired simple t-test. Significance was defined as a p value < 0.05.

Results

The study sample included 19 females (61.4%) and 12 males (38.7%). Mean age was 43.0 years; age range was 17 -74 years. Mean weight was 61.7 kg, height, 160.0 cm, and BMI, 24.3 kg/cm². Comorbid factors were absent in 51.6%; hypertension, coronary heart disease and diabetes mellitus were present in 38.7%, 6.5% and 3.2%, respectively. Anti-arrhythmic medication was prescribed prior to RFA; 26 patients (83.9%) were on beta blockers, 4 (12.9%) were on amiodarone, and 1 (3.2%) was receiving a calcium channel blocker.

A 24-hour Holter monitor was conducted prior to the RFA intervention. The majority of PVCs, 45.2%, originated from the anteroseptal right ventricular outflow tract (RVOT). Additional common foci included the posteroseptal RVOT in 38.7% and anteroseptal left ventricular outflow tract (LVOT) in 6.5%. 3.2% subjects exhibited PVCs derived from the anterolateral RVOT, posterior RVOT and HIS. Patient demographics are illustrated in Table 1.

Table 1. Patient characteristics

Variables	Min/Max	Mean \pm SD	Number of respondents (n=31)	%
Sex				
Male			12	38.7
Female			19	61.3
Age (years)	17/74	43.0 \pm 14.4		
Weight (kg)	43/84	61.7 \pm 9.8		
Height (cm)	149/173	160.0 \pm 6.7		
BMI (kg/cm ²)	17.7/30.8	24.3 \pm 3.7		
Comorbid factors				
None			16	51.6
Coronary heart disease			2	6.5
Hypertension			12	38.7
Diabetes mellitus			1	3.2
Anti-arrhythmic drugs				
Beta blocker			26	83.9
Calcium channel blocker			1	3.2
Amiodarone			4	12.9
PVC locations				
RVOT anteroseptal			14	45.2
RVOT posteroseptal			12	38.7
RVOT posterior			1	3.2
RVOT anterolateral			1	3.2
LVOT anteroseptal			2	6.5
HIS			1	3.2

Echocardiographic findings from baseline and a year after RFA are displayed in Table 2. Mean baseline and 12-month follow-up LVEFs were 62.9% (29.0-76.0 %) and 64.2% (35.5-73%), respectively. Pre- and 12-month post-ablation LVEDd were 43.8 mm (36.0-67.0 mm) and 45.0 mm (40.0-67.0 mm). No differences were detected following the intervention. Prior to the procedure, the mean PVC burden was 8.0%. In contrast, 12 months following RFA, the mean PVC burden detected was markedly reduced, i.e.0.8% (range: 0-5.6%) (p<0.001).

Table 2. Comparison of echocardiographic parameters and PVC burden before and after ablation

Variable	Min-Max	Mean \pm S.D	Min-Max	Mean \pm S.D	p value*
Ejection fraction (%)	29.0 – 76.0	62.9 \pm 7.7	35.5-73.0	64.2 \pm 6.91	0.505
LVEDd (mm)	36.0 - 67.0	43.8 \pm 5.3	40.0-67.0	45.0 \pm 5.22	0.384
PVC burden (%)	4.3 - 10.0	8.0 \pm 1.5	0.0-5.6	0.80 \pm 1.49	< 0.001

*Paired t-test for comparison before and after ablation

Changes in symptom burden and quality of life 12 months after radiofrequency ablation

The symptom load evaluated with the use of the ASTA score demonstrated a reduction from 39.1 to 2.1 (range: 0-21.0) following RFA (Table 3). Baseline ASTA near-syncope score was 7.5; this dropped to 0 following the intervention, with no participants reporting symptoms of near-syncope or syncope during the surveillance period. All the symptom burdens measured on the ASTA score decreased (p<0.05).

Life quality was also evaluated at baseline and at one year following RFA, yielding HRQOL physical subscale values of 30.7 and 0.3 (range: 0-9.1), respectively. The mental HRQOL additionally diminished following RFA, with baseline and post-intervention values of 32.7 and 2.7 (range: 0-21.1), respectively. Thus, post-RFA, the total HRQOL scale score decreased from 32.5 to 1.5, indicating a notable improvement in life quality ($p < 0.001$).

Table 3. Symptom burden and quality of life before and 12 months after ablation

Variable	Min-Max	Mean±S.D	Min-Max	Mean±S.D	p value*
ASTA symptom burden	17.8-75.0	39.1 ±14.98	0.0-21.0	2.1 ±4.34	<0.001
ASTA symptom near-syncope	0.0-75.0	7.5 ±22.54	0.0-0.0	0.00 ±0.00	<0.001
ASTA symptom syncope	0.0-85.7	2.8 ±15.39	0.0-0.0	0.00 ±0.00	<0.005
Physical subscale HRQOL	4.5-86.3	30.70 ±17.72	0.0-9.1	0.30 ±1.66	<0.001
Mental subscale HRQOL	15.7-89.4	32.7 ±21.52	0.0-21.1	2.7 ±5.46	<0.001
Total scale HRQOL	10.0-87.5	32.5 ±19.37	0.0-12.5	1.50 ±3.12	<0.001

*Paired t-test for comparison before and after ablation

Recurrence of PVCs 12 months after ablation

If the burden of PVCs remained over 80% of the baseline value on the 24-hour Holter electrocardiogram after 12 months or PVCs noted on the monitor were symptomatic, the RFA was deemed to be a failure and PVCs to have recurred. Ten of the 30 participants who underwent RFA exhibited PVCs on the follow-up 24-hour Holter recording, of whom 5 were described as having a good ablation outcome with an 80% reduction in PVCs, and 5 were considered to have a poor procedural endpoint, with a PVC burden fall of less than 80%. Eight subjects fulfilled the parameters for PVC recurrence, whereas the remaining two did not as their PVCs had been ameliorated by over 80%. Despite the evident PVCs, these individuals reported no symptoms. Thus, the proportion of subjects who presented with recurrent PVCs was documented to be 26.6% (8/30) (Table 4).

Table 4. Distribution of subjects showing PVCs 12 months after ablation and symptoms category

Ablation results category	n=10	Symptomatic	Asymptomatic
Good ($\geq 80\%$)	5 (50%)	3	2
Poor ($< 80\%$)	5 (50%)	3	2

Discussion

Characteristics of symptomatic low burden PVC patients undergoing ablation procedures

In this patient sample, the proportion of females experiencing symptoms from a low PVC burden was higher than males. Gender differences in the prevalence of PVCs have been reported in previous studies, e.g. the ARIC study and a study published by Kerola et al.²²; both concluded that being male increased the likelihood of PVCs. The results from the current study concur with several studies pertaining to the incidence of PVCs^{23 24 25}. Of 30 patients with numerous PVCs who were treated with RFA, females reported a higher number of related symptoms. It is possible that the latter show a heightened awareness of milder disturbances associated with PVCs and are therefore more likely to present than males, although to date, there are no data to support this theory.

PVCs can be detected in individuals at any life stage, but research has implied that they become more common with advancing years. In this study, the mean age of the population with low burden PVCs was over 40 years. A similar mean age was noted by Darrieux et al.²⁶ in 30 patients who were treated with RFA for symptomatic multiple PVCs. The observation of age being a predictor of symptomatic PVC prevalence was also reported by a number of other researchers^{24,25,27}, and could be associated with the overall heightened cardiovascular risk profile in the elderly, together with the onset of additional generalized symptomatology that leads individuals to seek clinical review.

The PVC site is strongly associated with symptom prevalence, a positive interventional outcome and a reduced rate of complications. Despite an underlying structurally normal heart, Darrieux et al.²⁶ affirmed that PVCs arising from the ROVT (PVC-RVOT) were most likely to generate symptoms^{23 27}. Farzaneh et al.²⁸ noted that 80% of individuals with PVC-RVOT were free from structural cardiac pathology. Earlier research findings are in keeping with the current study. Despite the fact that patients with a low PVC burden were selected for this study, the majority had PVCs originating from the RVOT. All the subjects reported symptoms; only a single individual was noted to have underlying cardiac structural abnormality. These observations are disparate to those found by Xu et al.²⁹; these authors reported the presence of a high PVC burden in patients with PVC-RVOT.

It has been demonstrated that individuals with an impaired LVEF have a greater average PVC burden than those with an LVEF within the normal range, i.e. 29-37% and 8-13%, respectively^{11 14}. Cardiomyopathy precipitated by PVCs has been occasionally noted in subjects with relatively few PVCs⁸. The data presented in the current study are in agreement, in that the participants with a mean PVC burden of 8% demonstrated a normal LVEF of 62.9% and LVEDd of 43.8 mm on echocardiography. These two parameters remained stable following RFA indicative of the absence of PVC-related cardiac impairment prior to the procedure.

Only a single individual was noted to have a low LVEF of 29% and dilated LVEDd of 67 mm prior to RFA owing to concurrent coronary artery disease. Subjects in whom a reduced LVEF was identified only demonstrated a rise of LVEF of up to 15% on the yearly follow-up scan, despite a positive outcome from RFA defined by the drop in PVC burden from 9.8% to 0%. PVC-related cardiomyopathy is presumed if the diminished baseline LVEF rises by a minimum of 15% or returns to the normal range, i.e. > 50%, following

RFA¹¹. It was therefore surmised that the cardiac impairment seen in this individual was unlikely to be a result of PVCs or concomitant structural cardiac pathology.

Changes in symptom burden and quality of life in low burden PVC patients 12 months after ablation

It was observed that both symptom load and life quality improved within the year after RFA in patients with a low initial PVC burden, which was in keeping with the recorded reduction in PVC burden following the procedure. Earlier studies have additionally demonstrated the success of RFA in diminishing PVC frequency, and in alleviating symptoms and enhancing life quality in patients with a relatively high PVC burden^{1 30}. In one study in which 30 patients with a high PVC burden causing symptoms underwent RFA, PVC frequency and symptoms were reduced and a superior life quality was reported a year following the intervention²⁴; these were similar results to those obtained in the current study on subjects with a low PVC burden. At follow-up, two-thirds of patients were symptom-free; in the remaining third, their symptoms had been ameliorated and they reported no physical or psychological disruptions to their life quality.

Changes in PVC burden 12 months after ablation

Earlier work has presented evidence to demonstrate that RFA has a higher efficacy than pharmaceutical therapy for the eradication of PVCs. However, these studies were generally performed on individuals with a high PVC burden. Specialist recommendations published by the European Heart Rhythm Association (2014) relating to ventricular dysrhythmias have advised RFA in individuals who remain symptomatic in the face of medical therapy or who have non-permanent impaired left ventricular function related to PVCs.

The current study has demonstrated a fall in PVC prevalence a year following RFA as documented using 24-hour Holter monitoring. These data are in keeping with former research on populations with a high PVC burden^{8,12,13,31}. In a study of 30 patients, a fall in the high PVC burden of 23.1% to 1% was noted at 3-4 months follow-up³². A similar decrease in high PVC burden, from 19% to 1.1% was noted in 50 individuals in a study published by Baser et al.²⁵.

Recurrence incidence 12 months after ablation of low burden PVC patients

Statistics have revealed that individuals who exhibit over 12 PVCs on a daily basis have an increased mortality rate from all etiologies and a higher number of in-patient admissions for cardiac pathologies, including myocardial infarctions, when judged against subjects with a lower number of PVCs⁶. A RFA intervention is deemed successful if the PVC burden were diminished by 80% of the baseline total^{11 25}. There is a range of parameters that have been used to determine PVC resumption following RFA; current research has predominantly used populations with a high PVC burden. The definition of recurrence in this study was failure to decrease the PVC burden by 80% of the baseline value as recognized by 24-hour Holter electrocardiography, or the resumption of PVC-related symptomatology documented during the Holter monitoring period.

According to the above criteria, 26.6% were noted to have recurrent PVCs a year after RFA. A number of earlier researchers have demonstrated the frequency of PVC recurrence following RFA to be between 10-20%, although it was slightly higher in one study²⁴, which documented a recurrence rate of 26% (8/30 participants). Patients with recurring PVCs reported symptoms, although on additional analysis, the residual symptomatology was less intense than prior to RFA and failed to impact life quality. Those who were deemed to have recurrent PVCs owing to less than 80% PVC reduction but who were symptom-free implied that the subjective parameters relating to the presence or absence of symptoms could not be utilized in isolation.

Strengths and limitations of the study

The life quality of individuals with a low PVC burden who underwent PVC was assessed. This research therefore forms the foundation for establishing the application of RFA in this patient cohort. Subjective bias from patients self-completing the questionnaire cannot be entirely excluded. Furthermore, the Holter system utilized was only a seven-lead system, which has restrictions with respect to recognizing the focal loci of PVCs in those individuals in whom recurrence was suspected. This is significant, as RFA may have been effective in ablating earlier PVCs but detected de novo PVCs may have arisen from a different site.

Conclusions

In patients with a low PVC burden, RFA offered a symptom burden reduction and enhanced life quality after a year following the intervention. The PVC burden was diminished at this juncture; PVC recurrence was identified in 26.6% subjects.

Thus, it can be concluded that patients with a low PVC burden but who experience symptoms should be treated with RFA. A more prolonged monitoring period is favored, i.e. a minimum of 48 hours. Additional studies are merited to establish the impact of RFA on the burden of symptoms and life quality in patients with only a low PVC burden; patients should be followed up long-term and studies should incorporate larger population sizes.

Declarations

Ethics approval and consent to participate

The Commission on Health Research Ethics Medical Faculty of Hasanuddin University RSPTN gave ethical approval for this research (protocol number: UH20020106). All study subjects were provided information pertaining to the aims and objectives of the study; their anonymity was guaranteed. Informed consent was obtained from all participants at baseline. Subjects were reassured that they could leave the study at any juncture.

Consent for Publication

Not applicable

Availability of data and material

Datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The author (s) declare no competing interests.

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Authors contributions

The manuscript was written by all the authors. MA, PK and MNIS were responsible for study design, data collection, analysis and interpretation, and manuscript drafting. PT, IJP and SMZ contributed to data analysis and interpretation, and the writing of the manuscript. The final manuscript was read, critiqued, revised and ultimately approved by all authors.

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