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Right Ventricular Dysfunction in High Burden Idiopathic Inferior Axis Premature Ventricular Contraction Population

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ABSTRACT – Some previous studies stated that high burden premature ventricular contractions (PVC) can be a risk factor for right ventricular dysfunction as similar to left ventricular dysfunction in general. There has been no previous specific study that analyzed how large percentage of idiopathic inferior axis PVC burden that could lead to right ventricular (RV) dysfunction. The purpose of this study was to evaluate if there was an association between idiopathic inferior axis PVC burden percentage and RV dysfunction using speckle tracking echocardiography. From January 1st to March 31st, 2023, a cross-sectional observational study of 24 patients with a high burden of idiopathic inferior axis PVC underwent right ventricular global longitudinal strain (GLS) and free wall longitudinal strain (FWLS) using speckle tracking echocardiography in the outpatient clinic of National Cardiovascular Center Harapan Kita (NCCHK). Using right ventricular GLS and FWLS, a statistical analysis was done to determine the association between the percentage of idiopathic inferior axis PVC burden and RV dysfunction. The percentage of females in the 24 research subjects was larger than males (17 persons compared to 7 people), with the majority of PVC morphology being inferior axis and left bundle branch block (LBBB) pattern (83.3%). In this study cohort, the average proportion of PVC burden is 18.6 ± 9.6%. The percentage of PVC burden was found to be bivariately associated with RV dysfunction via the RV GLS parameter ($p = 0.031$), but multivariate analysis revealed no independent association with RV dysfunction ($p = 0.063$, OR 1.18, 95% CI 0.99 - 1.41). In both bivariate and multivariate analyses, the proportion of PVC burden exhibited no connection with RV dysfunction via RV FWLS characteristics. In individuals with a high burden of idiopathic inferior axis PVC, there is no independent association between the proportion of PVC burden and RV dysfunction.

Index terms – Free Wall Longitudinal Strain, Global Longitudinal Strain, High Burden, Idiopathic, Axis,

Premature Ventricular Contraction, Right Ventricular Dysfunction

1. Introduction

The occurrence of premature contractions (PVC) is very common, including in populations of healthy people and people with heart disease. Increasing age, blood pressure, history of heart disease, low physical activity, and smoking each can be a predictor of the frequency of PVC. PVC is generally asymptomatic, but can cause clinical symptoms such as palpitations, shortness of breath, presyncope and fatigue. The basic potential mechanisms postulated so far are automaticity, triggered activity, and re-entry. The increased frequency of PVC may be a risk factor for heart failure and death.[1], [2]

The phenomenon of PVCs can be evaluated through clinical history, physical examination and 12-lead electrocardiography (ECG). A basic examination to determine the source of PVC and the PVC burden figure in percentage terms can be done with a 12-lead Holter ECG for a minimum of 24 hours. PVCs in the absence of underlying cardiac structural abnormalities are termed idiopathic PVCs, with the majority (up to 70-80%) originating in the right ventricular outflow tract (RVOT). An ambulatory monitor is needed to measure the frequency of PVCs for at least 24 hours, if the PVC burden reaches ≥ 5%, then it is an indication for ablation, especially in symptomatic patients. Diagnostic investigations in the form of imaging such as echocardiography and cardiac magnetic resonance imaging (cMRI) can help evaluate structural abnormalities of the heart.[1], [2]

Patients with high burden PVC without structural abnormalities of the heart can usually still have symptoms in the form of palpitations, easily fatigue and dizziness, whereas patients with PVCs who are already accompanied by significant left ventricular (LV) dysfunction may present with clinical symptoms of acute heart failure. Several previous studies suggested that there was a relationship between high burden idiopathic PVCs and complications in the form of LV dysfunction (decreased ejection fraction to < 50%), or known as PVC-associated cardiomyopathy (PIC), which has an impact on increasing mortality rates, the incidence of myocardial infarction, heart failure, and death. With varying burden figures as a risk factor for PIC occurrence, the 5% of burden is currently the lowest cut off value to be the limit number that has a risk of PIC occurrence.[2], [3], [4], [5]

The concept of LV dysfunction induced by high PVC burden with restoration of LV function after PVC elimination / ablation is well understood, but isolated RV systolic dysfunction induced by high PVC burden is still very limited. There is a case report by Berruezo A. et al (2018) which showed that there was an improvement or normalization of the geometric parameters (RVOT diameter) and RV function and wall motion through echocardiography after 1 year of PVC ablation, this concept is in accordance with the definition of PIC in LV dysfunction cases. Another recent study from Uhm J.S. et al (2022) also showed that patients with RV dysfunction based on GLS and FAC examinations had a higher PVC burden compared to PVC patients without RV dysfunction.[5], [6]

There are many modalities in measuring RV function that can provide information for decreased systolic function, including the speckle tracking method. In the relationship between echocardiographic findings and arrhythmias, Fonseca M. et al. (2020) showed from his research that patients with high-burden idiopathic PVCs originating from the RVOT had lower RV Global Longitudinal Strain (GLS) and Free Wall Longitudinal Strain (FWLS) findings compared to controls. In addition there is a study from Kirkels F.P. et al (2021), that the RV GLS examination in which it can measure parameters of deformation pattern and RV mechanical dispersion, with the findings of the abnormality apparently independently associated with the incidence of malignant ventricular arrhythmias, so that the GLS examination is appropriate to be used as a benchmark for RV function through echocardiography in cases arrhythmias, including their ability to detect subtle and early movement abnormalities.[7], [8], [9] Currently in Indonesia, there are still no studies regarding the association between the percentage of idiopathic inferior axis PVC burden and decreased RV function, so researchers are trying to conduct research that is one step further by analyzing the association between the percentage of PVC burden and the incidence of RV dysfunction using echocardiography in inferior axis idiopathic PVC patients at NCCHK.

2. Methods

2.1 Study Design and Participants

The study design is observational cross-sectional, and the data will be presented in a descriptive and analytic form. The study was conducted at NCCHK in January - March 2023. The population for this study were idiopathic inferior axis PVCs with a PVC burden of ≥ 5% who underwent RV speckle tracking echocardiography at the Echocardiography Polyclinic at NCCHK. The minimum sample required is 18 samples entirely based on the previous similar reference from Uhm et al. The subjects of this study were inferior axis idiopathic PVC patients with a PVC burden of ≥ 5% who underwent speckle tracking echocardiography (GLS and FWLS) of the RV in NCCHK.

The inclusion criteria were as follows: 1. Age ≥ 17-year-old; 2. Subject with inferior axis idiopathic PVC; and PVC burden ≥ 5%. The exclusion criteria were as follows: 1. Subject with non-sinus rhythm as underlying rhythm; 2. Multifocal PVC without predominance source; 3. Very high PVC burden (> 50%); 4. History of prior PVC ablation; 5. Subject with valvular heart disease and/or congenital heart disease; 6. Left ventricular ejection fraction < 50%; 7. Heart failure with preserved ejection fraction (HFrEF); 7. Subject with poor echo window; 8. Hyperthyroid status; 9. Chronic obstructive pulmonary disorder (COPD); and 10. Pulmonary hypertension.

2.2 Ethical Approval

Formal ethical clearance for the protocol of the study was required, and it obtained from the Institutional Review Board (IRB) of NCCHK in accordance with the declaration with Nuremberg Code and Declaration of Helsinki.

2.3 Study Procedures

Patients with PVCs who meet the inclusion criteria and no exclusion criteria were found would be recruited as research participants by filling out a consent form. After obtaining approval, a RV GLS and FWLS examination was scheduled in the echocardiography room at NCCHK. The observation period and data analysis was carried out in the range of March – April 2023. The study subjects were recruited consecutively, who were diagnosed as idiopathic PVCs at the outpatient clinic of NCCHK, without any history / suspicion of clinical symptoms and signs that lead to structural heart disease or coronary arterial disease. Furthermore, calculating the PVC burden and determining the morphology of PVC using the PVC axis and bundle branch block morphology from the 12-lead Holter ECG.

All subjects who met the inclusion and exclusion criteria were given a consent form. After agreeing to participate as a research subject, the subject would then have holter ECG data taken and speckle tracking echocardiography measurements taken. Patients who are included in the inclusion criteria with 12-lead Holter ECG results that have been validated by arrhythmia consultant at NCCHK as high burden idiopathic PVCs would be subject to echocardiography examination within 1-7 days afterward. Speckle tracking echocardiography examination was carried out by a third party who did not know the patient's clinical data, namely by technicians from the Non-Invasive Diagnostic and Cardiovascular Imaging Division of NCCHK. Speckle tracking echocardiographic examinations performed were the GLS and FWLS. In the RV GLS measurement, this measurement used the Speckle Tracking method, with normal GLS < -21% and FWLS < -20%.[10]

2.4 Statistical Methods

All research data was then entered into the PVC registry. The process of analyzing the significance of each variable data carried out using an unpaired T-test and analysis of confounding variables using a multivariate testing with the logistic regression method. Data processing and analysis using the SPSS for Windows v.26 application. Statistical significance was expressed with a *p* value < 0.05.

3. Results

The number of high burden PVC patients obtained from the results of a Holter examination with data that allowed them to be taken at NCCHK in the period of 1 October 2022 – 31 March 2023 was 59 patients. From the exclusion criteria, it was found that only 24 patients met the requirements as the study sample population. Final data analysis was performed on these 24 people to determine the association between the percentage of PVC burden and RV dysfunction.

In this study, the average age of the research subjects was 42.3 ± 14.1 years. The proportion of female sex is higher than male (17 people compared to 7 people). Based on the results of the 12-lead Holter ECG examination parameters, the median percentage of PVC burden was found to be an average of 18.6 ± 9.6%. From the study subjects, the majority obtained PVC with inferior axis left bundle branch block (LBBB) in 20 patients (83.3%). Patients with episode of persistent ventricular tachycardia (VT) and non-sustained VT (NSVT) were both found in 2 patients each (8.3%).

In anti-arrhythmic medication that the patient had been taking until the time of the echocardiographic examination, 1 patient (4.2%) received oral Amiodarone, 7 patients (29.2%) took Non-Dihydropyridine (Non-DHP) calcium antagonist, and 17 patients (70.8%) took beta blockers. In examining RV function using speckle tracking echocardiography, it was found that the median GLS result was -18.6% with a minimum value of -5.9% and a maximum value of - 24.7%, and a median FWLS result of -20.1% with a minimum value of 40.9% and a maximum value of -28.1%.

Table 1. Baseline Characteristics of Research Subjects

Parameters	Value (n = 24)
Demographic	
Age	42,3 ± 14,1
Gender	
Female	17 (70,8%)
Male	7 (29,2%)
Concomittant Disease	
Hipertension	5 (20,8%)
Diabetes Mellitus	1 (4,2%)
Dyslipidaemia	2 (8,3%)
Holter Parameters	
PVC Burden (%)	18,6 ± 9,6
PVC Circadian Variability	
Fast Rate	15 (62,5%)
Slow Rate	0 (0%)
Independent Rate	9 (37,5%)
PVC QRS Duration (ms)	150 (140 – 160)
Interpolated PVC	
Yes	5 (20,8%)

No	19 (79,2%)
Shortest Coupling Interval (ms)	
≤ 360	13 (54,2%)
> 360	11 (45,8%)
Coefficient of PVC Variation	
> 35%	9 (37,5)
≤ 35%	15 (62,5)
PVC Morphology	
LBBB	20 (83,3%)
Non-LBBB	4 (16,7%)
VT Episodes	
Sustained	2 (8,3%)
Non-Sustained	2 (8,3%)
No	20 (83,4%)
Medication	
Amiodarone	1 (4,2%)
Calcium Channel Blocker (CCB)	7 (29,2%)
Beta Blocker	17 (70,8%)
Anti-Hypertension	6 (25,0%)
Echocardiography Result	
RV GLS (%)	18,6 (5,9 – 24,7)
< 21%	14 (58,3%)
≥ 21%	10 (41,7%)
RV FWLS (%)	20,1 (40,9 – 28,1)
< 20%	11 (45,8%)
≥ 20%	13 (54,2%)
TAPSE (mm)	19,4 ± 5,2
< 17 mm	7 (29,2%)
≥ 17 mm	17 (70,8%)
3D RVEF (%)	41,6 ± 9,6
< 45%	13 (54,2%)
≥ 45%	11 (45,8%)
LV EDD (mm)	47,3 ± 4,8
LVEF (%)	63,5 ± 6,4
E/e' average	7,01 (4,72 – 13,60)

The results of the bivariate analysis showed that there was an association with a statistically significant mean difference between the percentage of PVC burden in the population of study subjects with RV dysfunction and populations with normal RV function through the GLS parameter, whereas from the FWLS parameter no significant relationship was found. Of the other variables, it was found that only consumption of beta-blocker had a significant association with RV dysfunction through GLS parameters.

Table 2. Bivariate analysis of RV dysfunction based on GLS

Variable	Normal (n = 10)	RV Dysfunction (n = 14)	*P Value*
Demographic			
Age	40,8 ± 13,9	43,4 ± 14,6	0,671
Gender			
Female	7 (70,0)	10 (71,4)	1,000
Male	3 (30,0)	4 (28,6)	
Concomittant Disease			
Hipertension	1 (10,0)	4 (28,6)	0,358
Diabetes Mellitus	0 (0)	1 (7,1)	1,000
Dyslipidaemia	0 (0)	2 (14,3)	0,493
Holter Parameters			

PVC Burden (%)	13,7 ± 7,7	22,1 ± 9,5	**0,031***
	PVC Circadian Variability		
Fast Rate	6 (60,0)	9 (64,3)	1,000
Independent Rate	4 (40,0)	5 (35,7)	
PVC QRS Duration (ms)	155 (140 – 160)	150 (140 – 160)	0,657
Interpolated PVC			
Yes	8 (80,0)	11 (78,6)	1,000
No	2 (20,0)	3 (21,4)	
	Shortest Coupling Interval (ms)		
≤ 360	7 (70,0)	4 (28,6)	0,095
> 360	3 (30,0)	10 (71,4)	
	Coefficient of PVC Variation		
> 35%	5 (50,0)	4 (28,6)	0,403
≤ 35%	5 (50,0)	10 (71,4)	
PVC Morphology			
LBBB	8 (80,0)	12 (85,7)	1,000
Non-LBBB	2 (20,0)	2 (14,3)	
VT Episodes			
Yes	1 (10,0)	3 (21,4)	0,615
No	9 (90,0)	11 (78,6)	
Medication			
Amiodarone	0 (0)	1 (7,1)	1,000
Calcium Channel Blocker (CCB)	2 (20,0)	5 (35,7)	0,653
Beta Blocker	10 (100,0)	7 (50,0)	**0,019***
Anti-Hypertension	3 (30,0)	3 (21,4)	0,665

Table 3. Bivariate analysis of RV dysfunction based on FWLS

Variable	Normal (n = 13)	RV Dysfunction (n = 11)	*P Value*
Demographic			
Age	40,5 ± 16,3	44,4 ± 11,4	0,519
Gender			
Female	9 (69,2)	8 (72,7)	1,000
Male	4 (30,8)	3 (27,3)	
Concomittant Disease			
Hipertension	2 (15,4)	3 (27,3)	0,630
Diabetes Mellitus	0 (0)	1 (9,1)	0,458
Dyslipidaemia	0 (0)	2 (18,2)	0,199
Holter Parameters			
PVC Burden (%)	16,5 ± 9,4	21,1 ± 9,6	0,247
PVC Circadian Variability			
Fast Rate	8 (61,5)	7 (63,6)	1,00
Independent Rate	5 (38,5)	4 (36,4)	
PVC QRS Duration (ms)	150 (140 – 160)	150 (140 – 160)	0,660
Interpolated PVC			1,000
Yes	10 (76,9)	9 (81,8)	
No	3 (23,1)	2 (18,2)	
Shortest Coupling Interval (ms)			
≤ 360	6 (46,2)	5 (45,5)	1,000
> 360	7 (53,8)	6 (54,5)	
Coefficient of PVC Variation			
> 35%	5 (38,5)	4 (36,4)	1,000

≤ 35%	8 (61,5)	7 (63,6)	
PVC Morphology			
LBBB	10 (76,9)	10 (90,9)	0,596
Non-LBBB	3 (23,1)	1 (9,1)	
VT Episodes			
Yes	2 (15,4)	2 (18,2)	1,000
No	11 (84,6)	9 (81,8)	
Medication			
Amiodarone	0 (0)	1 (9,1)	0,458
Calcium Channel Blocker (CCB)	3 (23,1)	4 (36,4)	0,659
Beta Blocker	11 (84,6)	6 (54,5)	0,182
Anti-Hypertension	4 (30,8)	2 (18,2)	0,649

Multivariate analysis was conducted for PVC burden, shortest coupling interval and beta blocker medication to analyze the independence of each of these variables on RV dysfunction. Based on the results of multivariate analysis, there were no variables that had significant significance independently of RV dysfunction, including the percentage of PVC burden.

Table 4. Multivariate analysis of RV dysfunction based on GLS

Variable	Univariate	*P Value*	Multivariate	*P Value*
	OR (95% CI)		OR (95% CI)	
PVC Burden (%)	1.14 (0,99 – 1,30)	**0,051**	1,18 (0,99 - 1,41)	0,063
Shortest Coupling Interval	5,83 (0,98 – 34,64)	0,095	-	-
Beta Blocker	n/a	**0,019**	n/a	0,999

4. Discussion

The results of the analysis of the basic characteristics of the population in this study showed that the sex of patients with high-burden PVC was more female than male (17 compared to 7 patients). Previous research is also consistent with this study by stating that the prevalence of female is higher, and other sources also state that the population of female with PVCs is more likely to have symptomatic manifestations of PVCs, so they tend to be diagnosed more easily and more frequently than male.[6], [11]

From this study, the average percentage of PVC burden was 18.6 ± 9.6%. From the existing literature it has been stated that a PVC burden of 5% is included as a high burden PVC, which has a risk for left ventricular dysfunction and includes indications for ablation management. It was also mentioned in previous studies that the best cut-off rate for PVC burden, which is currently a predictor of left ventricular cardiomyopathy, is 24% (sensitivity 79% and specificity 78%).[2], [12] So with an average rate of around 18%, in general the population in this study is at risk for LV and/or RV dysfunction events, with the main target of this study being to prove the relationship between the percentage of PVC burden on right ventricular function through examination. echocardiography.

On the results of echocardiographic examination of the study subjects, the median value of the parameters GLS -18.6% and FWLS -20.1% was obtained which showed that the median result was still below the normal reference value. With an overview of these characteristics, it can be shown that the population of this study has a median number that corresponds to the condition of RV PIC, with findings from the GLS parameter, 14 people with RV dysfunction were found and from the FWLS parameter, 11 people with RV dysfunction were found. The main hypotheses that are thought to play a role in the mechanism of PIC are mechanical ventricular dyssynchrony and increased oxygen consumption, with these several theories underlying the mechanism:[13], [14], [15]

1. The mechanical efficiency disturbances of the heart globally
2. Significant changes in myocardial blood flow
3. Local changes in myocardial protein expression
4. Associated high burden PVC to PIC in LV cases. May cause dilation and impaired ventricular function, which is similar to the mechanism of LBBB or chronic RV pacing
5. Associated with very high PVC burden. The mechanism is similar to that of tachycardia-induced cardiomyopathy (TIC)

In connection with the variable anti-arrhythmic drugs in this study, a study conducted by Tang JKK et al (2021) with research subjects in patients with a high burden of idiopathic PVC (> 5%), stated that administration of beta-blocker or CCB drugs does have limited effectiveness compared to class I and III anti-arrhythmics in the treatment of PVCs, but a reduction in PVC burden can be achieved by as much as 30.5% compared to the previous percentage of PVC burden, so that the beta-blocker class remains the drug of choice in the therapy of high burden PVC.[16]

Another study from Demir S. et al (2022) stated that 61 patients (32.1%) in their study who consumed beta blockers had a minimum reduction of PVC burden of 50%. From this study, it was found that beta blockers were also found to have a significant relationship to RV dysfunction through GLS parameters, with a characteristic description of all patients with normal RV GLS results as many as 10 people, all taking beta blockers, whereas in the subject population in this study with the results of RV dysfunction, only 7 people took beta blockers out of a total of 14 research subjects. From this description, it can be concluded that there is a significant difference between the population with RV dysfunction and normal RV function, but the results of the multivariate analysis did not find a significant independent association between consumption of beta blockers and RV dysfunction, so beta blockers cannot be used as a predictor of protective factor against RV dysfunction in this study population.[17]

The results of bivariate analysis in this study revealed a significant difference in the average burden of PVC between the group of study subjects with RV dysfunction and the group of study subjects with normal RV function indicated that a large percentage of high burden PVC was found to have an association with RV dysfunction through GLS parameter, described that the intrinsic function of the myocardial impairment of the RV. As it is known that the GLS examination is superior in detecting subtle myocardial dysfunction compared to the ejection fraction, so it is described that the GLS can be a benchmark for subclinical RV dysfunction. The results of this study are consistent with research by Fonseca et al (2021) where all research subjects were patients with a PVC burden > 10% and from the RVOT foci, with an average GLS result of -19.4 ± 4%, so it was significantly lower than controls in the form of patients who underwent slow pathway ablation in cases of supraventricular tachycardia (SVT) without any history of PVCs.[8], [12], [18]

In relation to this study, the GLS examination represents the average longitudinal strain component of the myocardium and it has been reported from several studies that the use of GLS is believed to be very helpful in its ability to identify myocardial dysfunction in an early, subtle, and subclinical manner even though the ejection fraction rate is still within normal limits. The results of a study by Cittar et al (2021) also support the role of RV GLS in cases of non-ischemic cardiomyopathy, such as tachycardiomyopathy, also mentioning that RV GLS examination has a significant prognostic role in the risk of major cardiovascular events, because it was found that a decrease in GLS results correlate with late gadolinium enhancement (LGE) findings in patients with an estimated major cardiovascular event outcome of 29% at 3 years. Thus, RV GLS is recommended as a prognostic factor in the non-ischemic cardiomyopathy population.[18], [19], [20], [21]

Previous studies have succeeded in suggesting that a PVC burden up to 24% can be used as the best cut off limit as a predictor of LV PIC events, and in fact other previous studies have also suggested that a PVC burden < 24% can still cause LV PIV.[13], [14] Then with the data on the average percentage of PVC burden reaching around 18% from the results of this study, it could already be a sign as a risk factor for RV dysfunction in patients. In another study by Delgado et al (2010), the results are consistent with this study with a description of the results in the form of differences in RV GLS results between patients with a PVC burden > 20% compared to patients with a PVC burden < 20% although the results are not statistically significant (-23.3 ± 6.0% vs. -25.2 ± 8.3%, *p* = 0.3).[22], [23]

Some studies have stated that GLS and FWLS together can be used as a good diagnostic tool in evaluating the function of the RV, including in patients with cardiomyopathy or heart failure. The free wall segment parameter measured in the FWLS examination is also included in the GLS examination because the GLS includes the RV segment globally, both the free wall and septal segments. Even so, the findings of the GLS and FWLS results can still be found differences because the RV GLS may be influenced by the condition of the LV because the interventricular septum measured in the RV GLS is also an integral part of the LV. In the results of the bivariate analysis of this study, to analyze the association between the percentage of PVC burden and RV dysfunction, there were differences in the results of GLS and FWLS. Even though the GLS parameters showed an association significancy, it was not found to be significant in FWLS parameters (p = 0.247).[24] It is suspected that there is a possibility that the parameter findings on the RV GLS will still have an influence from the condition of the LV, in which in this study the LV only measured the ejection fraction without examining the GLS. Based on the results of this study, even though the multivariate analysis was not statistically significant (OR 1.18, 95% CI 0.99-1.41, p = 0.063), so that independently it did not have a significant relationship, but it has quite good numbers in those trends so that the percentage of burden PVC together with clinical considerations could still be a good benchmark as a risk factor for RV dysfunction. This is supported by the high PVC burden which can be used as a measure of suspicion of the risk of persistent malignant ventricular arrhythmias and the need for implantable cardioverter defibrillators in ARVC cases. This is based on the difficulty of predicting the difference between RV PIC and ARVC in patients at the initial diagnosis. As the results of research by Gasperetti A. et al (2022), in ARVC patients with a PVC burden up to 3000 in 24 hours and the presence of non-sustained VT events, it is stated that they have a > 40% risk of persistent ventricular arrhythmia events within 12 months, therefore a high percentage of PVC burden can still be assessed as an important risk factor.[25], [26], [27]

4.1 Study Limitation

This research is a single centered cross-sectional observational study conducted in a short period of time, i.e. < 6 months of study period, so it is necessary to conduct a longer research period with a larger sample population to strengthen the results of this study. This study could not include the onset or duration of the study subjects experiencing PVCs because of the difficulty in determining the exact time of PVCs based on complaints.

5. Conclusions

Percentage of PVC burden has no significant association with right ventricular dysfunction in the population of high burden idiopathic inferior axis PVC patients as measured by speckle tracking echocardiography.

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References

[1] G. M. Marcus, "Evaluation and Management of Premature Ventricular Complexes," *Circulation*, vol. 141, no. 17, pp. 1404–1418, Apr. 2020, doi: 10.1161/CIRCULATIONAHA.119.042434.

[2] A. W. G. J. Oomen, L. R. C. Dekker, and A. Meijer, "Catheter ablation of symptomatic idiopathic ventricular arrhythmias : A five-year single-centre experience," *Neth Heart J*, vol. 26, no. 4, pp. 210–216, Apr. 2018, doi: 10.1007/s12471-018-1085-5.

[3] K. Baser *et al.*, "Recurrence of PVCs in patients with PVC-induced cardiomyopathy," *Heart Rhythm*, vol. 12, no. 7, pp. 1519–1523, Jul. 2015, doi: 10.1016/j.hrthm.2015.03.027.

[4] L. Capulzini *et al.*, "Acute and one year outcome of premature ventricular contraction ablation guided by contact force and automated pacemapping software," *J Arrhythm*, vol. 35, no. 3, pp. 542–549, Jun. 2019, doi: 10.1002/joa3.12194.

[5] A. Berruezo, E. Efimova, J. Acosta, and B. Jáuregui, "Isolated, premature ventricular complex-induced right ventricular dysfunction mimicking arrhythmogenic right ventricular cardiomyopathy," *HeartRhythm Case Rep*, vol. 4, no. 6, pp. 222–226, Jun. 2018, doi: 10.1016/j.hrcr.2018.02.006.

[6] J.-S. Uhm *et al.*, "Effects of Ablation on Right Ventricular Function in Right Ventricular Outflow Tract Premature Ventricular Complexes," *SSRN Journal*, 2022, doi: 10.2139/ssrn.4157165.

[7] D. A. Morris *et al.*, "Normal range and usefulness of right ventricular systolic strain to detect subtle right ventricular systolic abnormalities in patients with heart failure: a multicentre study," *Eur Heart J Cardiovasc Imaging*, vol. 18, no. 2, pp. 212–223, Feb. 2017, doi: 10.1093/ehjci/jew011.

[8] M. Fonseca *et al.*, "Premature ventricular contractions of the right ventricular outflow tract: is there an incipient underlying disease? New insights from a speckle tracking echocardiography study," *Indian Pacing Electrophysiol J*, vol. 21, no. 3, pp. 147–152, 2021, doi: 10.1016/j.ipej.2021.02.007.

[9] F. P. Kirkels *et al.*, "Right Ventricular Functional Abnormalities in Arrhythmogenic Cardiomyopathy: Association With Life-Threatening Ventricular Arrhythmias," *JACC Cardiovasc Imaging*, vol. 14, no. 5, pp. 900–910, May 2021, doi: 10.1016/j.jcmg.2020.12.028.

[10] A. Kossaify, "Echocardiographic Assessment of the Right Ventricle, from the Conventional Approach to Speckle Tracking and Three-Dimensional Imaging, and Insights into the 'Right Way' to Explore the Forgotten Chamber," *Clin Med Insights Cardiol*, vol. 9, pp. 65–75, 2015, doi: 10.4137/CMC.S27462.

[11] R. Latchamsetty and F. Bogun, "Premature Ventricular Complex-induced Cardiomyopathy," *Rev Esp Cardiol (Engl Ed)*, vol. 69, no. 4, pp. 365–369, Apr. 2016, doi: 10.1016/j.rec.2015.12.015.

[12] Ø. H. Lie *et al.*, "Lower than expected burden of premature ventricular contractions impairs myocardial function," *ESC Heart Fail*, vol. 4, no. 4, pp. 585–594, Nov. 2017, doi: 10.1002/ehf2.12180.

[13] A. Lee, T. E. Walters, E. P. Gerstenfeld, and H. M. Haqqani, "Frequent Ventricular Ectopy: Implications and Outcomes," *Heart Lung Circ*, vol. 28, no. 1, pp. 178–190, Jan. 2019, doi: 10.1016/j.hlc.2018.09.009.

[14] J. G. Panizo, S. Barra, G. Mellor, P. Heck, and S. Agarwal, "Premature Ventricular Complex-induced Cardiomyopathy," *Arrhythm Electrophysiol Rev*, vol. 7, no. 2, pp. 128–134, Jun. 2018, doi: 10.15420/aer.2018.23.2.

[15] R. K. Yarlagadda *et al.*, "Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract," *Circulation*, vol. 112, no. 8, pp. 1092–1097, Aug. 2005, doi: 10.1161/CIRCULATIONAHA.105.546432.

[16] J. K. K. Tang *et al.*, "Effectiveness of medical therapy for treatment of idiopathic frequent premature ventricular complexes," *J Cardiovasc Electrophysiol*, vol. 32, no. 8, pp. 2246–2253, Aug. 2021, doi: 10.1111/jce.15150.

[17] S. Demir *et al.*, "Predictors of positive response to beta-blockers for treatment of premature ventricular complexes," *J Electrocardiol*, vol. 70, pp. 50–55, 2022, doi: 10.1016/j.jelectrocard.2021.11.036.

[18] C. Szymanski, F. Lévy, and C. Tribouilloy, "Should LVEF be replaced by global longitudinal strain?," *Heart*, vol. 100, no. 21, pp. 1655–1656, Nov. 2014, doi: 10.1136/heartjnl-2014-306186.

[19] M. Cittar *et al.*, "Prognostic Significance of Feature-Tracking Right Ventricular Global Longitudinal Strain in Non-ischemic Dilated Cardiomyopathy," *Front Cardiovasc Med*, vol. 8, p. 765274, 2021, doi: 10.3389/fcvm.2021.765274.

[20] M. Perazzolo Marra *et al.*, "Impact of the presence and amount of myocardial fibrosis by cardiac magnetic resonance on arrhythmic outcome and sudden cardiac death in nonischemic dilated cardiomyopathy," *Heart Rhythm*, vol. 11, no. 5, pp. 856–863, May 2014, doi: 10.1016/j.hrthm.2014.01.014.

[21] A. Gulati *et al.*, "Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy," *JAMA*, vol. 309, no. 9, pp. 896–908, Mar. 2013, doi: 10.1001/jama.2013.1363.

[22] V. Delgado *et al.*, "Assessment of left ventricular dyssynchrony by speckle tracking strain imaging comparison between longitudinal, circumferential, and radial strain in cardiac resynchronization therapy," *J Am Coll Cardiol*, vol. 51, no. 20, pp. 1944–1952, May 2008, doi: 10.1016/j.jacc.2008.02.040.

[23] V. Delgado, "Novel cardiac imaging technologies : implications in clinical decision making." Corrected Publisher's Version, Nov. 11, 2010. [Online]. Available: https://hdl.handle.net/1887/16139

[24] E. Carluccio *et al.*, "Superior Prognostic Value of Right Ventricular Free Wall Compared to Global Longitudinal Strain in Patients With Heart Failure," *J Am Soc Echocardiogr*, vol. 32, no. 7, pp. 836-844.e1, Jul. 2019, doi: 10.1016/j.echo.2019.02.011.

[25] A. Gasperetti *et al.*, "Association of Premature Ventricular Contraction Burden on Serial Holter Monitoring With Arrhythmic Risk in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy," *JAMA Cardiol*, vol. 7, no. 4, pp. 378–385, Apr. 2022, doi: 10.1001/jamacardio.2021.6016.

[26] J. Cadrin-Tourigny *et al.*, "A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy," *Eur Heart J*, vol. 40, no. 23, pp. 1850–1858, Jun. 2019, doi: 10.1093/eurheartj/ehz103.

[27] H. Calkins, D. Corrado, and F. Marcus, "Risk Stratification in Arrhythmogenic Right Ventricular Cardiomyopathy," *Circulation*, vol. 136, no. 21, pp. 2068–2082, Nov. 2017, doi: 10.1161/CIRCULATIONAHA.117.030792.