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Original Article

Comparison of right ventricular global longitudinal strain between pacemaker lead position in patients with permanent pacemaker

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Abstract

Background: The implantation of a permanent pacemaker (PPM) can reduce right ventricular function. Echocardiography using speckle tracking can detect a decrease in right ventricular function earlier. The value of right ventricular global longitudinal strain (RVGLS) based on the location of the pacemaker lead between the apex and non-apex was currently unknown, although the placement of the correct pacemaker lead location was very important for evaluating right ventricular dysfunction to prevent right heart failure. This study aims to determine the comparison of RVGLS between pacemaker lead positions in patients with a permanent pacemaker.

Methods: This study was a nested case-control study to assess the comparison of RVGLS between pacemaker lead positions in patients with a permanent pacemaker. The study was divided into the right ventricular apex group (RVA) and the non-right ventricular apex group (NRVA). This study used data from the pacemaker registry and medical records of patients who had undergone pacemaker implantation since June 2021. The Shapiro-Wilk normality test was performed before analyzing all numerical data, followed by an independent t-test or Mann-Whitney test to determine the differences between groups.

Results: In this study, there were 38 patients with permanent pacemakers, consisting of 18 samples with the RVA group and 20 samples with the NRVA group. In this study, no significant differences were found in age, sex, diagnosis, comorbidities, therapy, pacemaker mode, baseline QRS duration, pacing burden, puncture site, and initial echocardiography between of two groups. There was a significant difference in paced QRS duration between the RVA and RVNA groups (160 + 20 ms vs 140 + 28 ms, p=0.024). Based on statistical analysis, there was a significant difference in the value of RVGLS in the RVA group compared to the RVNA group (-14.87 + 4.48% vs -18.40 + 3.21%, p=0.015).

Conclusions: The position of the apex right ventricular lead resulted in a lower value of RVGLS compared to the position of the non-apex right ventricular lead.

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Keywords: *Pacemaker lead, right ventricular function, right ventricular global longitudinal strain.*

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Introduction

The prevalence of permanent pacemakers is estimated to reach 1.25 million each year worldwide. In 2016, there were 500,000 pacemaker implantations in Europe. In Indonesia, the Asia Pacific Heart Rhythm Association (APHRS) reported 1,342 permanent pacemaker implantations in 2021.[1-2] Long-term effects of pacemaker implantation were heart failure, atrial fibrillation, increased mortality, and morbidity. The incidence of right heart failure has been reported at 22% cases after one year of pacemaker implantation. The mechanism of right ventricular dysfunction in permanent pacemakers is debatable to this day.[3-4] Several studies have shown that the position of the pacemaker lead in the right ventricular apex is associated with the occurrence of right heart failure. A study by Yu et al. showed that lead-associated tricuspid regurgitation and electrical asynchrony are higher at the right ventricular apex than at non-ventricular leads' apex.[5-6]

Early detection of right ventricular dysfunction was mandatory. Conventional echocardiography has some limitations, such as being operator-dependent, time-consuming, and detecting when it is clinically manifested.[7-8] The global longitudinal strain parameter of the right ventricle with speckle tracking echocardiography has been reported to be able to detect the presence of subclinical right ventricular dysfunction earlier and more sensitively than conventional parameters.[8-10]

The value of global longitudinal strain based on the location of the pacemaker lead between the apex and non-apex is still unknown; on the other hand, the placement of the correct lead location is essential for evaluating right ventricular dysfunction to prevent right heart failure. This study aims to determine the comparison of RVGLS between pacemaker lead positions in permanent pacemaker patients.

Methods

This was a nested case-control study for the determination of comparison of RVGLS between pacemaker lead positions in patients who underwent pacemaker implantation from June 2021 to October 2023. Inclusion criteria were patients who had an echocardiography initial due to permanent pacemaker implantation (PPI) and echocardiography data after 6-12 months of PPI. We exclude patients with LV and RV dysfunction at echocardiography, significant valve disease, history of tachyarrhythmia, documented acute coronary syndrome during PPI, and poor echocardiographic windows.

Study Population

The total population was 83 patients. There are 51 patients who met the inclusion criteria. Three samples were excluded because the ejection fraction function on the initial echocardiogram was below 50%. The samples that were excluded were 2 samples in the RVA group and 1 sample in the NRVA group. In order to have the same number of samples and follow the required sample size according to the sample size formula, a random sampling was carried out in the NRVA group using the Microsoft Excel application with the RANDBETWEEN formula for 20 samples, so that the total sample in the study was 38 samples.

Pacing Procedure

Patients underwent dual-chamber or single-chamber implantation by operator preference under fluoroscopy in the catheterization laboratory. Pacemaker leads were inserted using a subclavian venous, axillary venous, or cephalic venous cutdown approach. Right atrial leads were implanted in the RA appendage, RV leads were implanted in the RV apex groups or the non-RV apex group (RVOT, Septal, and His-Bundle). Pacing burden was measured at interrogate evaluation 6-12 month after PPI.

ECG and Echocardiography

Standard echocardiography was performed using Vivid 7 Ultrasound with a 3.5 MHz multiphase-array probe. Patients are in the lateral decubitus position on the left. The 2D-guided M-mode method was used to determine chamber dimensions, while the Simpson's method was used to measure LVEF. 2D RV pictures were obtained from apical four-chamber or RV focus views. We measured the tricuspid annulus's Doppler imaging systolic velocity. The average segmental strain was used to determine the GLS. The endocardial border along the RV apex and the free wall to the tricuspid valve annulus were identified, and the RV peak systolic longitudinal strain was calculated using an interface. The program automatically separates three RV free wall and three septal wall segments and calculates the longitudinal peak systolic strain; the RVGLS was determined as the average of these longitudinal peak systolic strains after a region of interest covering the breadth of the myocardium was defined.

Statistical Analysis

Data with normal distribution are presented as mean value ± SD. Data with abnormal distribution are presented as median and minimum-maximum. The chi-square test was used to compare categorical data. An unpaired t-test was performed

on numeric data with normal distribution. Mann-Whitney was performed on numeric data with abnormal distribution. A P-value <0.05 was considered statistically significant. Bland-Altman method of comparison was used to assess inter-observer variability. The analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Mac version 25.

Results

Patients Clinical Characteristic

The baseline characteristics of the study population are shown in Table 1. Paced QRS duration of the RVA group after evaluation (6-12 months after PPI) was significantly different from the NRVA group with p=0.024. The baseline values of LVEF, TAPSE, and RVGLS did not differ substantially between the two groups.

Comparison of echocardiographic values of the RVA pacemaker group and the NRVA pacemaker group

According to Table 2, the RVGLS of the NRVA group is higher than the RVGLS of the RVA group with a p-value of 0.015; this difference is statistically significant. Table 2 also explains that there were no significant differences in the values between the RVA and NRVA groups on other echocardiographic parameters such as LVEF, TAPSE, RV FAC, RVS', PAcct, TRV, TVG, PVR, RA area, RV basal diameter, and severity of TR.

Intra-observer and inter-observer variability

The evaluation of intra-observer and inter-observer variability using the Bland-Altman method showed good agreement in the examination of global longitudinal strain of the right ventricle. No significant differences were found between intra- and inter-observer (p>0.05), and the data were 100% within the 95% limit of agreement.

Table 1. Baseline characteristics.

Variable	RVA (n = 18)	NRVA (n = 20)	p-value
Age (year), median (minimum-maximum)	61 (49-85)	62 (20-81)	0.661[b]
Sex, n (%)			
Male	4 (22)	8 (40)	0.307[a]
Female	14 (78)	12 (60)	
Pacing indication, n (%)			
Sinus node dysfunction (SND)	5 (27)	6 (30)	0.880[a]
AV block	13 (73)	14 (70)	
Co-morbid risk factor, n (%)			
Hypertension	8 (44)	11 (55)	0.516[a]
Diabetes Mellitus	4 (22)	2 (10)	0.395[a]
Dyslipidemia	6 (33)	4 (20)	0.287[a]
Smoker	2 (11)	5 (25)	0.410[a]
Medication, n (%)			
Angiotensin converting enzyme inhibitor (ACE-I)	3 (16)	2 (10)	0.448[a]
Angiotensin receptor blocker (ARB)	5 (27)	9 (45)	0.272[a]
B-blocker			
Calcium channel blocker	6 (33)	7 (35)	0.914[a]
Statin	2 (11)	4 (20)	0.663[a]
Antiplatelet	2 (11)	2 (10)	1.000[a]
Diuretic	0	2 (10)	0.488[a]
Pacing Mode, n (%)	2 (11)	2 (10)	1.000[a]
VVI	13 (72)	17 (85)	0.438[a]
DDD	5 (27)	3 (15)	
ECG: QRS duration (ms)			
Baseline QRS duration, median (minimum-maximum)	80 (40-120)	80 (40-120)	1.000[b]
Paced QRS duration after implant, median (minimum-maximum)	160 (80-180)	140 (60-160)	**0.024[b]**
Pacing burden, n (%)			
≤ 50%	6 (33)	3 (15)	0.260[a]
> 50%	12 (67)	17 (85)	

Variable	RVA (n = 18)	NRVA (n = 20)	p-value
Site Puncture, n (%)			
V. Subclavia	16 (88)	13 (65)	0.074[a]
V. Aksilaris	2 (12)	2 (10)	
V. Cephalica	0	5 (25)	
Echocardiography baseline			
LV EF (%), mean±SD	59.50 ± 10.58	63.55 ± 8.31	0.196[c]
TAPSE (cm), mean±SD	2.13 ± 0.35	2.08 ± 0.30	0.618[c]
Right ventricular global longitudinal strain (%), median (minimum-maximum)	-21.50 (-20 up to -24.5)	-21.5 (-20.2 up to -23.5)	0.736[b]

[a]chi square test
[b]Mann-Whitney test
[c]Independent sample t-test

Table 2. Echocardiography of the pacemaker lead on follow-up.

Variable	RVA (n = 18)	NRVA (n = 20)	p-value
LV EF (%), mean±SD	62.56 ± 6.50	64.55 ± 6.31	0.344[c]
Right ventricular global longitudinal (%), mean±SD	-14.87 ± 4.48	-18.40 ± 3.21	**0.015[c]***
TAPSE (cm), mean±SD	2.08 ± 0.31	2.33 ± 0.49	0.073[c]
RV FAC (%), median (minimum-maximum)	44 (35-54)	47.50 (36-73)	0.341[b]
RVS' (cm/s), median (minimum-maximum)	12 (10-14)	12 (10-21)	0.201[b]
PAccT (ms), mean±SD	111.39 ± 24.9	123.35 ± 23.12	0.134[c]
TR Vmax (m/s), median (minimum-maximum)	2.15 (1.2-3.3)	2.1 (1.2-2.9)	0.297[b]
TVG (mmHg), median (minimum-maximum)	19 (6-43)	19.06 (6-68)	0.608[b]
PVR, mean±SD	2.05 ± 0.32	1.92 ± 0.69	0.475[c]
RA area, mean±SD	20.23 ± 3.04	18.49 ± 5.93	0.269[c]
RV basal diameter, mean±SD	34.83 ± 5.75	37.25 ± 5.62	0.199[c]
TR severity			
Mild	17	20	0.474
Moderate	1	-	
Severe	-	-	

[b]Mann-Whitney test
[c]Independent sample t-test

Discussion

This study showed that there were differences in the values of RVGLS in the groups of right ventricular apex pacemakers and non-right ventricular apex pacemakers, with an average value of -14.87 ± 4.48% in the RVA group and -18.40 ± 3.21% in the NRVA group. The results of this study are also supported by the results of study by Solima, et al., which reported a decrease in global longitudinal strain of the right ventricle after 6 months of RVA pacemaker implantation compared to the control group with a value of right ventricular GLS of -14.623 ± 4.295% compared to

the control group with a value of right ventricular GLS of -20.37 ± 1.987%.[11]

Several studies have also reported a decrease in right ventricular function after permanent pacemaker implantation. A study by Sinkar et al. reported a decrease in RVEF of 2.8% after 6 months of RVA pacemaker implantation. A study by Gupta et al. reported a decrease in right ventricular myocardial performance index and TAPSE after 6 months of RVA pacemaker implantation. These studies concluded that there is a decrease in right ventricular function in RVA pacemakers based on the assessment of right ventricular function by conventional echocardiography. Several studies have reported that a decrease in right ventricular function is associated with electrical asynchrony, mechanical asynchrony, and lead-associated tricuspid regurgitation.[3-4]

A study by Soliman et al. showed that right ventricular dysfunction is associated with electromechanical changes, such as a decrease in conduction velocity and mechanical asynchrony. Right ventricular apex pacemakers also cause faster activation in the apical segment and slowing in the basal segment, resulting in decreased right ventricular function, also known as intraventricular asynchrony. Because a significant difference in QRS duration was found in the RVA and NRVA groups (160 + 20 ms in RVA and 140 + 28 ms in NRVA) after implantation of permanent pacemakers, intraventricular asynchrony could be one of the factors causing a decrease in global longitudinal strain of the right ventricle in this study.[11]

Other studies also show that right ventricular apex pacemakers have a wider QRS duration, resulting in more non-physiological ventricular activation, mechanical asynchrony, electrical asynchrony, higher myocardial perfusion defects, and decreased right ventricular function. Electrical impulses from right ventricular pacemakers originate from the right ventricle and spread through the myocardium, not through the His-Purkinje conduction system, resulting in a wider QRS complex like in LBBB. Pacemakers with wider QRS will increase the risk of heart failure compared to patients with narrower QRS, so the selection of non-right ventricular apex pacemakers is preferred in the prevention of long-term comorbidities.[10, 12-13]

A study by Yu YJ, et al., reported a higher risk of tricuspid regurgitation in the RVA group compared to the NRVA group due to lead impact with the posterior valve. However, this was not found in this study because there was no statistically significant difference in the degree of tricuspid regurgitation in both groups. This may be because the study by Yu YJ, et al., conducted an echocardiographic evaluation with a longer duration of up to 55 months in the RVA group.[6]

There were no statistically significant differences in conventional echocardiographic parameters during evaluation in the RVA and NRVA groups. The results of a study by Yu YJ, et al., showed that there were no statistically significant differences in conventional right ventricular function in the RVA and NRVA groups after pacemaker implantation. A study by Chen JY, et al., also showed that there were no differences in conventional right ventricular function values in patients with apical and septal pacemaker lead implantation after 3-6 months.[6, 14]

Beyond early subclinical changes detected by strain, several studies suggest that right-ventricular apical (RVA) pacing may carry less favorable long-term consequences compared with non-apical sites. RVA pacing has been associated with wider QRS and greater electromechanical desynchrony, factors linked to adverse remodeling and progression of tricuspid regurgitation (TR) due to lead–leaflet interaction and altered RV mechanics.[5-6] Comparative data also indicate better mechanical performance with non-apical sites such as septal/RVOT pacing,[12] while experimental work shows early maladaptive molecular changes after RVA pacing that plausibly precede clinical dysfunction.[13] Although our study was not powered for clinical endpoints, the lower (less negative) RVGLS in the RVA group is consistent with these mechanistic concerns and may represent an early marker of subsequent adverse remodeling.

This study is the first study to assess the differences in global longitudinal strain values of the right ventricle in patients with RVA pacemakers and NRVA pacemakers in Indonesia. The results of this study are expected to be used as a basis for further research on the relationship between the position of the pacemaker lead and right heart function over a longer period of time and with a larger sample size, making it one of the efforts to conduct early screening to prevent the occurrence of heart failure in patients with permanent pacemakers. This study is also expected to help clinicians in choosing the position of the pacemaker lead in pacemaker implantation.

Limitations

Although this study has shown differences in the values of global longitudinal strain of the right ventricle based on the position of the permanent pacemaker lead, the researchers are aware that there are still some shortcomings in this study. In

this study, our follow-up was limited to 6–12 months, and we did not collect long-term clinical outcomes (e.g., heart failure hospitalization, mortality), serial TR progression, or pacing-induced cardiomyopathy. As such, we cannot determine whether the observed RVGLS differences translate into long-term adverse events or clinically significant TR. The sample size and single-center design further limit the detection of infrequent outcomes. The ECG conditions at the time of the echocardiographic examination were not differentiated, whether in the condition of ECG pacing or ECG on beat. This study also did not assess the interrogate characteristics in patients with pacemakers, such as impedance values, R wave, and amplitude.

Conclusion

Our study compared right ventricular global longitudinal strain between the RVA and NRVA groups. There were no significant differences of characteristic groups except for paced QRS duration between the right ventricular apex pacemaker group and the non-right ventricular apex pacemaker group. The right ventricular apex pacemaker groups have lower global longitudinal strain values than the non-right ventricular apex pacemaker groups.

List of Abbreviations

APHRS	Asia Pacific Heart Rhythm Society
ECG	Electrocardiography
LVEF	Left Ventricular Ejection Fraction
NRVA	Non-Right Ventricular Apex
PPI	Permanent Pacemaker Implantation
PPM	Permanent Pacemaker
PVR	Pulmonary Vascular Resistance
RVA	Right Ventricular Apex
RVFAC	Right Ventricular Fractional Area Change
RVGLS	Right Ventricular Global Longitudinal Strain
RVOT	Right Ventricular Outflow Tract
TAPSE	Tricuspid Annular Plane Systolic Excursion
TR	Tricuspid Regurgitation

Ethical Clearance

All methods were carried out by relevant guidelines and regulations after obtaining approval and recommendations from the Ethics Committee Review Board of Dr. M. Djamil General Hospital, with reference number LB.02.02/5.7/299/2023.

Publication Approval

All authors consent to the publication of this manuscript.

Authors' Contributions

MF contributed to the study's conception and design, data collection, analysis and interpretation, as well as drafting and critically revising the manuscript for important intellectual content. HER and MY provided critical supervision and intellectual input. RM offered supervision with a particular focus on statistical analysis and research methodology.

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Conflict of Interest

None.

Availability of Data and Materials

Not applicable.

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