The Influence of Right Ventricular Pacing Location, Pacing Burden and Paced QRS Duration to Subclinical Left Ventricular Systolic Dysfunction as Shown by Global Longitudinal Strain Echocardiography

Mohammad Iqbal[1], Gadih R. Endamatriza[1], Irene Lampita[1], Sindy Hendrawansyah[1], Sidhi Laksono[2], Melawati Hasan[1], Chaerul Achmad[1], Giky Karwiky[1], Hanna Goenawan[3], Mohammad R. Akbar[1], Arief S. Kartasasmita[4]

[1] Department of Cardiology and Vascular Medicine, Faculty of Medicine University of Padjadjaran, Bandung, Indonesia.

[2] Faculty of Medicine, University of Muhammadiyah Prof Dr Hamka, South Jakarta, Indonesia.

[3] Departement of Biomedical Sciences, Division of Physiology, Faculty of Medicine University of Padjadjaran, Bandung, Indonesia.

[4] Faculty of Medicine University of Padjadjaran, Bandung, Indonesia.

Corresponding Author:

Mohammad Iqbal, MD. Department of Cardiology and Vascular Medicine, Universitas Padjadjaran. Jalan Eyckman 38, Bandung 40161, Indonesia. E-mail: mohammadiqbal178@gmail.com; dr_mohammadiqbal@yahoo.com.

ABSTRAK

Latar belakang: *Pemacuan ventrikel kanan/ right ventricle (RV) yang berkepanjangan berhubungan dengan gangguan fungsi ventrikel kiri/ left ventricle (LV). Beberapa studi menunjukkan bahwa posisi lead, presentasi pemacuan dan durasi QRS saat pemacuan dapat mempengaruhi fungsi sistolik LV. Gangguan LV subklinikal bahkan dapat timbul lebih dini setelah pemasangan permanent pacemaker (PPM). Studi ini bertujuan untuk mendeteksi gangguan awal sistolik LV subklinikal yang diukur dengan global longitudinal strain (GLS) dengan menggunakan speckle tracking echocardiography (STE) 1 bulan paska pemasangan PPM.* ***Metode:*** *Studi single center, metode kohort prospektif dengan kriteria inklusi pada penelitian ini adalah semua pasien dengan indikasi implantasi PPM dengan fungsi sistolik LV awal normal. Variabel pada penelitian ini adalah posisi sadapan (apeks RV dibandingkan dengan right ventricular outflow tract (RVOT), persentase pemacuan (≤40% vs >40%) dan durasi QRS selama pemacuan (≤150ms dan >150ms). Perubahan (delta) GLS diukur sebelum dan satu bulan setelah implantasi PPM.* ***Hasil:*** *Pada 37 pasien dalam penelitian ini, terdapat perbedaan yang signifikan antara GLS sebelum (-20,30 SB 3,38) dan setelah (-16,93 SB 3,47) implantasi PPM (p=<0,001). Tidak terdapat perbedaan yang signifikan pada delta GLS baik antara pasien dengan posisi sadapan pada apeks RV vs RVOT ((2,30 (0,00-10,50) vs 2,95(0,10-8,30), p=0,648) ataupun antara pasien dengan durasi QRS selama pemacuan ≤150ms vs >150ms ((1,70 (0,30-8,30) vs 3,45(0,0-10,5)), p=0,266). Sementara itu, terdapat perbedaan delta GLS yang signifikan antara pasien dengan persentase pemacuan ≤40% vs> 40% ((Rata-rata 1,92 SB 1,37 vs 3,98 SB 3,04)), p=0,007). Analisis lebih lanjut menunjukkan bahwa persentase pemacuan hanya akan mempengaruhi delta GLS pada kelompok dengan pemacuan apeks RV (≤40% (1,58 SB 0,59) vs >40% (4,67 SB 3,47), p=0,008) dan tidak mempengaruhi delta GLS pada kelompok dengan pemacuan RVOT (≤40% (2.32 SB 1.98) vs >40%(3.29 SB 2.48), p=0.446).* ***Kesimpulan:*** *Disfungsi sistolik LV subklinis menurun secara signifikan satu bulan setelah implantasi alat pacu jantung yang ditunjukkan oleh penurunan GLS. Persentase pemacuan >40% merupakan faktor yang berhubungan dengan penurunan GLS satu bulan setelah implantasi PPM, terutama ketika sadapan ditempatkan pada apeks RV.*

Kata kunci: *Right ventricular pacing, global longitudinal strain, lead position, pacing percentage, QRS duration during pacing.*

ABSTRACT

Background: *Prolonged pacing of the right ventricle (RV) is associated with left ventricular (LV) systolic dysfunction. Several studies have shown that the RV pacing location, pacing burden (percentage), and paced QRS duration may affect LV systolic function. Subclinical LV dysfunction may occur early after implantation of a permanent pacemaker (PPM). Therefore, this study aims to detect early subclinical LV systolic dysfunction measured by global longitudinal strain (GLS) using speckle tracking echocardiography (STE) at one month after PPM implantation.* ***Methods:*** *A single-center, prospective cohort study was conducted, and all patients indicated for PPM implantation with preserved LV systolic function were included. Data of RV pacing location (RV apical vs right ventricular outflow tract (RVOT), pacing burden (percentage) (≤40% vs >40%), and paced QRS duration (≤150 ms and >150 ms) were obtained. The change of GLS was also measured before and one month after PPM implantation (delta GLS).* ***Results:*** *37 patients were enrolled in this study, which demonstrated significant difference between GLS before (-20.30 SD 3.38) and after (-16.93 SD 3.47) PPM implantation (p=<0.001). There were no significant difference in delta GLS either between patients with RV pacing location on RV apical vs RVOT ((2.30 (0.00–10.50) vs 2.95(0.10–8.30), p=0.648) or between patient with paced QRS duration ≤150ms vs >150ms ((1.70 (0.30–8.30) vs 3.45 (0.0–10.5)), p=0.266). Meanwhile, there was a significant difference of delta GLS between patients with pacing burden ≤40% vs >40% (Mean 1.92 SD 1.37 vs 3.98 SD 3.04), p=0.007). Further analysis found that pacing burden only affected the delta GLS in group with apical RV pacing (≤40% (1.58 SD 0.59) vs > 40% (4.67 SD 3.47), p = 0.008) and did not affect the delta GLS in group with RVOT pacing (≤40% (2.32 SD 1.98) vs > 40% (3.29 SD 2.48), p = 0.446).* ***Conclusion:*** *The pacing parameter, particularly pacing burden > 40% may induce the subclinical LV systolic dysfunction after one month of pacemaker implantation as shown by decline of GLS, especially when the RV pacing location was placed on apical.*

Keywords: *Right ventricular pacing location, global longitudinal strain, pacing burden, paced QRS duration.*

INTRODUCTION

Pacemaker implantation is the mainstay treatment for symptomatic bradycardia.[1] However, prolonged right ventricular (RV) pacing has been reported to be associated with left ventricular (LV) systolic dysfunction. The reported incidence of heart failure after RV pacing varied between 3-31% after 1-3 years of PPM implantation.[2-6] Also, right ventricular pacing creates a non-physiological activation sequence, and the impulse conduction velocity is slower compared to normal conduction, leading to electrical and mechanical dyssynchrony in the LV.[7-9] Some studies showed that RV pacing position (apical vs right ventricular outflow tract (RVOT)), pacing burden (percentage) and paced QRS duration may lead to LV systolic dysfunction.[2, 10-15]

Echocardiography is the most widely used non-invasive modality to evaluate LV function because of its portability, low risk, and comparatively high temporal resolution.[16, 17] Furthermore, global longitudinal strain (GLS) using 2D echocardiography has high sensitivity (92%) and specificity (89%) for detecting early-stage of LV systolic dysfunction, therefore it can be used to detect subclinical LV systolic dysfunction.[18] In this study, GLS was assessed before and one month after PPM implantation. In addition, the effect of RV pacing position, pacing burden, and paced QRS duration on the changes of GLS within 1 month was also assessed.

METHODS

This is a prospective cohort study, and a total of 50 patients who underwent pacemaker implantation for symptomatic bradycardia at Hasan Sadikin Hospital were prospectively enrolled between May 1, 2018 and January 31, 2019. The patient's inclusion criteria were >18 years, have preserved LV ejection fraction (EF≥ 50%), and have normal QRS duration (≤120

ms) before implantation PPM. This study has been approved by the Ethical Committee of Hasan Sadikin Hospital, Bandung (Ref. no. LB.02.01/X.6.5/67/2019).

Meanwhile, those with history of acute coronary syndrome, valvular heart disease, congenital heart disease, and congenital AV block before implantation and during follow-up were excluded. Also, patients with sinus node disease who implanted AAI were excluded. Those with poor echocardiography window and insufficient image tracking in more than one segment during GLS measurement were also excluded. In addition, GLS was measured within one week before implantation (as baseline GLS) and one month after implantation. The delta GLS is defined as a change of GLS value before and after implantation. The LV systolic dysfunction is defined as the significance of decline GLS (delta GLS) before and one month after implantation that measured by the statistic analyzed (Paired T-test).

ECHOCARDIOGRAPHY AND GLOBAL LONGITUDINAL STRAIN

A detailed echocardiographic evaluation was performed before and after one month of pacemaker implantation using Vivid S6 and Vivid 7 (GE Vingmed Ultrasound AS, Horten, Norway). Echocardiographic calculations of chamber quantification were quantified in accordance with The American Society of Echocardiography 2015 recommendations.[19] In addition, cardiac anatomy and valvular were defined through standard transthoracic study, and the biplane Simpson`s rule was used to calculate LV ejection fraction (LVEF).

Cardiac images were obtained at a rate of 50-70 frames per second (fps) from apical long-axis, apical two and four chambers view (16 segment AHA/ASE model). All raw data were stored and transferred for offline analysis to a workstation with EchoPAC 201 Version software. A region-of-interest was semi-manually traced and the software calculated the mean global strain values for all predetermined LV segments (**Figure 1**). The GLS measurement was taken during paced rhythm beat. Also, all echocardiographic imaging and strain values measurements were carried out by a single cardiologist specialized in echocardiography who was blinded to pacing interrogation results.

PACEMAKER IMPLANTATION AND ELECTROCARDIOGRAPHY

In sinus node disease patients, (Atrio-ventricular) AV node function was tested before

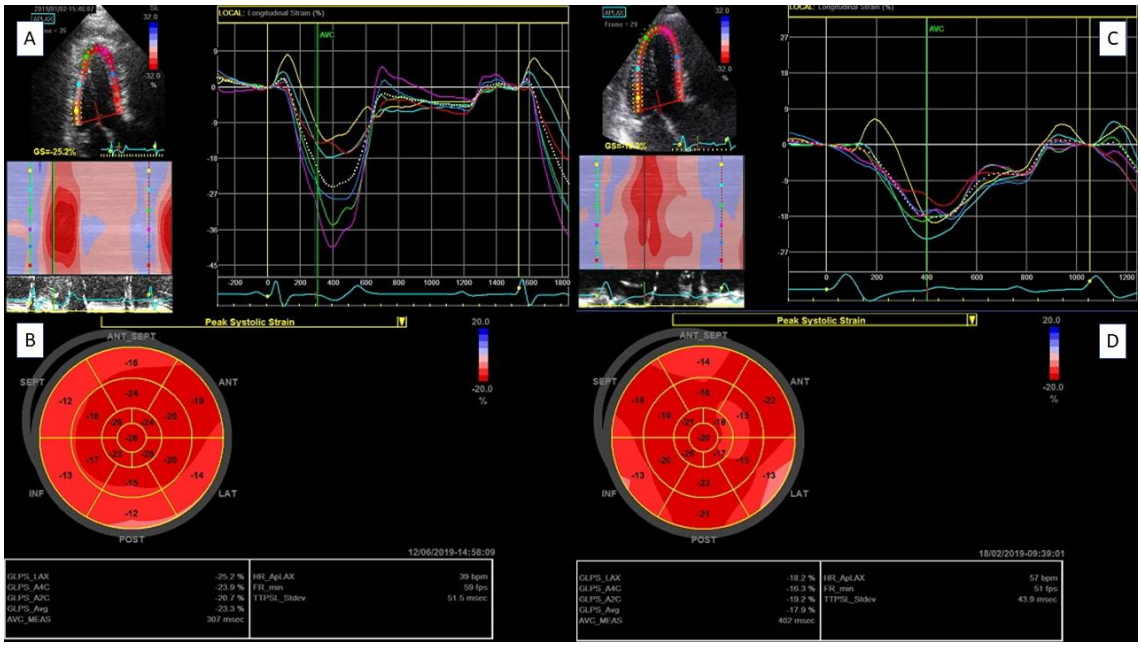

Figure 1. Global longitudinal strain at one week before pacemaker implantation (A and B), and one month after pacemaker implantation (C and D), corresponding strain curves are shown (A and C). The average GLS value at one week before pacemaker implantation is -23.3% (B), and the value is significantly decreased to -17.9% at one month after pacemaker implantation (D).

pacemaker implantation. Incremental atrial pacing was used to determine whether the patient had subclinical/impending AV block or AV node disease. When the atrial incremental atrial pacing showed AV 1:1 conduction in rate pacing >130 beats per mins, AAI was implanted. AV 1:1 conduction means that each capture atrial pacing was conducted to the ventricle. We excluded a patient who implants with AAI. In case of no 1:1 AV conduction with incremental atrial pacing in rate <130 beats per mins, it may suggest that patient had subclinical/ impending AV block or AV node disease. In such patient, VVI or DDI was advised over the AAI. The lower rate of VVI was determined according to baseline patient heart rate. For example, when the patient had a sinus node disease (with intermittent sinus pause), and the baseline heart rate was about 55-60 BPM, the lower rate was set at 50 BPM. This setting was important to avoid unnecessary RV pacing. In dual-chamber pacemaker, the AV interval was set up in the default setting (paced AV interval was 150 ms and sensed AV interval 120 ms). Meanwhile, in case of the prolonged PR interval, AV interval was set up (max of 250 ms) according to the physician's decision to reduced unnecessary RV pacing.

All pacemaker implantation was carried out by an experienced operator. Either RV apical or right ventricular outflow tract (RVOT) pacing was achieved with an active fixation lead. Furthermore, the appropriate positioning of the lead was fluoroscopically confirmed at the time of implantation and by the QRS axis (during pacing) from ECG recorded after implantation (**Figure 2**). Right ventricle apical (RV apical) positions were considered when the QRS axis in inferior leads are predominantly negative, and RVOT positions were considered when QRS axis in inferior leads of ECG are predominantly positive. The pacing burden (percentage pacing) and other pacemaker parameters were determined from stored data after one month of follow-up. A standard 12 lead surface ECG was obtained at 25 mm/s. The paced QRS duration was defined as the length of time from the beginning of the pacing artifact (spike) to the end of the QRS complex. The QRS duration was measured using a digital caliper (KW06-351, Krisbow). The recorder QRS duration was the longest measured from all 12 leads of ECG. The pacing burden (percentage) was categorized into 2 groups with a cutoff of 40%. The paced QRS duration was categorized into 2 groups with a cutoff of 150 ms.

STATISTICAL ANALYSIS

The Shapiro-Wilk test was used to assess all the data distribution (normality data). Continuous variables were expressed as means (standard deviations), or median (range) when data were

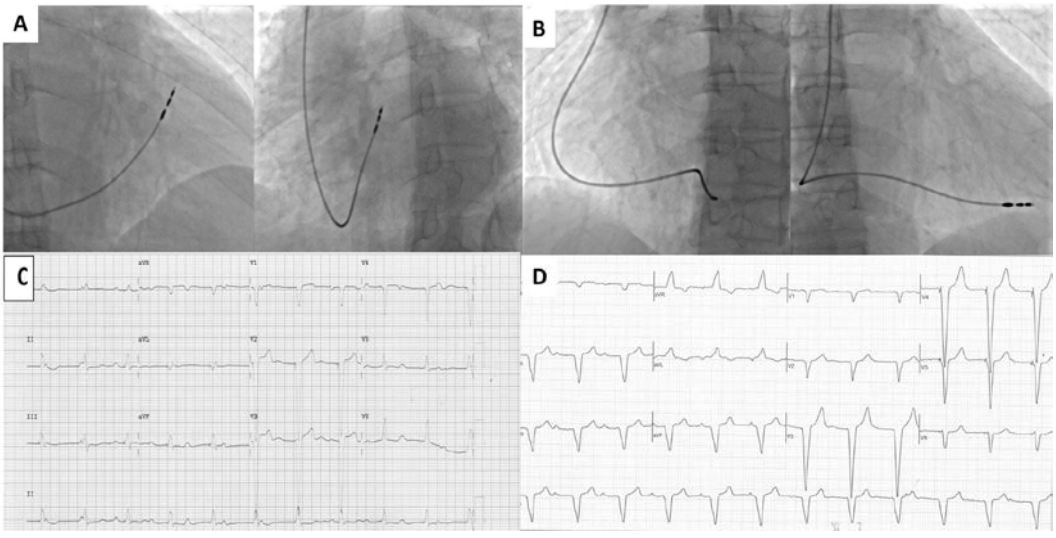

Figure 2. RAO 35' and LAO 40' position showed lead position on RVOT (A), confirmed by predominant positive axis of QRS in inferior leads, with the QRS duration 140 ms (B). RAO 35' and LAO 40' position showed lead position on RV apical (C), confirmed by predominant negative axis of QRS in inferior leads, with the QRS duration 166 ms (D). RAO : right anterior oblique, LAO: left anterior oblique.

not normally distributed. Categorical data were summarized as frequencies and percentages. Student's t-test or Mann-Whitney U test were the statistical methods used for paired or unpaired data depend on the normality data. Also, all probability values were deemed statistically significant at a level of ≤0.05. Statistical analyses were performed with SPSS, version 25.0 (SPSS, Inc, Chicago, IL, USA).

RESULTS

Patient Characteristics

50 consecutive patients were enrolled, and a total of 13 were excluded due to poor echocardiography window (10 patients) and lost to follow-up (3 patients). Finally, 37 patients were studied; 13 male and 24 female with averages ages of 66 (SD 12) years. The majority of the population was female (64.9%), and hypertension was the most common comorbidity. The most frequent indication for pacing was total AV block (62.2%). The lead distributions were placed 19 patients at RV apical and 18 patients at RVOT. Almost all the implanted pacemakers were single-chambered VVI (83.8%). Patient characteristics are shown in **Table 1**.

Table 1. Baseline characteristics.

Characteristics	n=37
Age (y.o), mean (SD)	66 (12)
Sex, n %	
- Male	13 (35.1)
- Female	24 (64.9)
Diagnosis, n (%)	
- Sinus node disease (SND)	14 (37.8)
- Total AV block	23 (62.2)
Comorbid, n (%)	
- Hypertension	28 (75.7)
- Diabetes Mellitus	3 (8.1)
- Dyslipidemia	1 (2.7)
- Coronary artery disease	4 (10.8)
- Smoker	3 (8.1)
Medication used, n (%)	
- Calcium channel blocker	16 (43.2)
- Statin	2 (5.4)
- Angiotensin Converting Enzym inhibitor (ACE-I)	6 (16.2)
- Angiotensin Receptor Blocker (ARB)	6 (16.2)
- Antiplatelet	4 (10.8)
- Diuretic	2 (5.4)
Pacemaker mode, n (%)	
- VVI	31 (83.8)
- DDD	6 (16.2)
RV pacing location, n (%)	
- RV apical	19 (51.4)
- RVOT	18 (48.6)
QRS duration (ms)	
- Baseline QRS duration, mean (SD)	104 (19)
- Paced QRS duration	151 (128-189)
Pacing burden (Cumulative pacing rate %)	78.7 (5.7-100)

GLS: Global longitudinal strain; RV: Right ventricle; RVOT: Right ventricular outflow tract

Left ventricle systolic function and chamber remodelling

Neither LVEF and left ventricular internal diameter at systolic (LVIDd) showed significant changes statistically before and after implantation (p=0.23 and p=0.35, respectively). Furthermore, GLS showed significant changes before and after one month of implantation (- 20.30 SD 3.38 vs -16.93 SD 3.47, p<0.001) (**Table 2**).

The effect of RV pacing position, pacing burden, and paced QRS duration on global longitudinal strain

Several parameters that may affect GLS at one month were examined, including RV pacing location, pacing burden, and paced QRS duration. The value of delta GLS (before and after implantation) between RV pacing location of RV apical vs RVOT ((2.30 (0.00–10.50) vs 2.95 (0.10–8.30), p=0.648) and paced QRS duration of <150 ms vs >150 ms ((1.70 (0.30–8.30) vs 3.45 (0.0–10.5)), p=0.266) did not significantly different. However, there was a significant difference of delta GLS between patient with pacing burden <40% vs > 40% (1.92 SD 1.37 vs 3.98 SD 3.04, p = 0.007). Whereas patients with pacing burden > 40% have worsened GLS (**Table 3**).

This finding was further analyzed to determine the effect of pacing burden on GLS based on RV pacing location. It was found that the pacing burden only affected delta GLS when it was > 40% when RV pacing was placed on apical (≤40% (1.58 SD 0.59) vs > 40% (4.67 SD 3.47), p = 0.008), and did not affect the delta GLS in group with RVOT pacing (≤40% (2.32 SD 1.98) vs > 40% (3.29 SD 2.48), p = 0.446) (**Table 4**).

DISCUSSION

This is the first study in Indonesia that describes GLS in the population of patients who

Table 2. Systolic function and chamber remodeling.

Variables	Baseline n=37 mean (SD)	1 month after implantation n=37 mean (SD)	p- value#
LVEF	67.46 (4.71)	66.27 (6.96)	0.230
GLS	- 20.30 (3.38)	-16.93 (3.47)	<0.001
LVIDd	46.20 (5.52)	46.71 (4.66)	0.350
LVIDs	28.3 (5)	29.08 (5.2)	0.141
LV mass index	126.7 (41.1)	120.9 (39.2)	0.266
LV volume index	67.9 (21.09)	63.1 (16.88)	0.058
LA dimension	36.9 (7.21)	37.7 (5.98)	0.298

Paired T-test; LVEF: Left ventricle ejection fraction; GLS: Global longitudinal strain; LVIDd: Left ventricle internal diameter at diastolic; LVISd: left ventricle internal diameter at systolic; LV: left ventricle; LA : left atrial

Table 3. Effect of several parameters on delta GLS.

Variables	Delta GLS	p-value
Lead placement-median		
RV apical (n = 19)	2.3 (0.00 – 10.50)	0.648†
RVOT (n =18)	2.95 (0.10 – 8.30)	
Paced QRS duration-median		
≤150 ms (n = 17)	1.70 (0.30 – 8.30)	0.266†
>150 ms (n = 20)	3.45 (0.0 – 10.5)	
Pacing percentage-mean (SD)		
≤40 % (n = 11)	1.92 (1.37)	0.007††
>40 % (n = 26)	3.98 (3.04)	

†Mann-U Whitney test, ††Unpaired t-test.
GLS: Global longitudinal strain; RV: Right ventricle; RVOT: Right ventricular outflow tract.
Note: delta GLS was a changed of GLS that measured before and after 1 month of implantation

Table 4. Effect of pacing percentage and lead position on delta GLS.

Variable	Pacing percentage (%)		p-value††
	≤40% n=11	>40% n=26	
Delta GLS, mean (SD)			
RV apical	1.58 (0.59)	4.67 (3.47)	0.008
RVOT	2.32 (1.98)	3.29 (2.48)	0.446

††Unpaired t-test; GLS: Global longitudinal strain; RV: Right ventricle; RVOT: Right ventricular outflow tract.
Note: delta GLS was a changed of GLS that measured before and after 1 month of implantation.

underwent PPM implantation. This study showed that LVEF and LVIDd did not show significant changes one month after implantation (**Table 3**). This finding may suggest that the macroscopic anatomical remodeling may not be seen within one month after implantation. The previous study also has a similar finding that there was no significant difference of LVEF within one month after implantation, and also the changing of LVID may be seen later in longer follow-up [20,21]

However, subclinical LV systolic dysfunction can already be found using GLS, one month after implantation. Furthermore, this study showed that subclinical LV systolic dysfunction already occurred as early as one month after implantation. Meanwhile, previous studies showed consistent results. Ahmed et al.[20] found that a decrease in GLS at one month correlated with the incidence of pacemaker induced cardiomyopathy (PICM) after 1 year. However, the difference compared to this study was that they only included patients with RV apical pacing. Also, RV pacing on RVOT and several parameters were not analyzed in that study (pacing percentage and QRS duration during pacing). Meanwhile, Algazaar et al. has shown worse GLS in patients with RV apical pacing compared with septum after six months of follow up. The RVOT pacing site in this study was also slightly higher than the septum.[9]

The vector of the QRS axis in normal condition was superior to inferior, made predominant positive QRS in inferior leads. Therefore, RVOT pacing location might be "more" similar to the physiologic condition in terms of a vector of QRS, compared to RV apical pacing. However, our study showed no difference between RVOT pacing and RV apical pacing (p = 0.648). The effect of RV pacing location is only significant if combined with the pacing burden (**Table 4**). The explanations of this finding probably due to; (1). The RV pacing location may affect the GLS depend on the time burden and duration. The more frequent RV apical pacing

occurs, the more non-physiologic axis that may induce LV systolic dysfunction, (2). It was still possible that RV pacing location might be the independent factor to predict the decline of GLS in long-term follow-up.

Our study showed significant changes of GLS related to pacing burden ≥ 40% in the apical RV pacing group, which occurred within one month after implantation. In contrast, Dudoniene et al.[22] did not find any difference in GLS between apical RV and septal pacing during three months follow-up period. Although both groups have shown significantly worse GLS compared to baseline. Also, the difference of pacing site between mid septum and more physiological pacing site (RVOT) used in this study may be the reason for this discrepancy. Thus far, studies regarding the effect of pacing location on LV performance showed conflicting results. Therefore, further studies are needed to answer this problem. Previous studies only included patients with dependent RV pacing (>90% pacing) because they aimed to study the effect of pacing location but not burden on GLS.[9,20] Meanwhile, other studies addressing the effect of pacing burden on GLS were not found. Subsequently, it was assumed that pacing burden >40 % means that the incidence of non-physiological pacing will be more frequent and worsen the intra-ventricular and inter-ventricular dyssynchrony. Our study used the cut-off value pacing burden of 40%, following the results from the previous study[2,24]. Also, ventricular activation by pacemaker results in heterogenic electrical activation through each myocardial segment. In addition, frequent pacing has been shown to increase the risk of heart failure and hospitalization.[23]

Our study showed that the greater GLS changes were seen in the group with paced QRS duration > 150 ms, although not statistically significant. Previous studies showed consistent results regarding paced QRS duration. They found that wider paced QRS duration correlated with worse LV systolic function that measured by LVEF, in long-term follow up (one year) and increase the risk of heart failure.[24,25] Also, Khursid et al. found that pacing burden >20% and paced QRS duration ≥ 150 ms increased the risk of PICM. This study also correlated the paced QRS duration in long-term LVEF (mean follow-up 2.5 years).[26] To the best of our knowledge, our study is the first study that examined the effect of paced QRS duration on early changes of GLS. Our study showed that the correlation between delta GLS and paced QRS duration is not statistically significant, even if the trend of correlation might be seen. This result is probably due to the shorter follow-up duration compared to the previous studies. It may be speculated that paced QRS duration may affect the delta GLS in longer follow-up. Therefore, a longer follow was needed to confirm this finding.

Data showed that subclinical LV dysfunction occurred as early as one month after pacemaker implantation which could be detected by GLS. In fact, worse GLS after pacemaker implantation has been associated with PICM in the future.[20] However, to the best of our knowledge, there is no data or consensus to state the absolute delta GLS in patients before and after pacemaker implantation. The previous study used the delta GLS to state the significance of GLS changes. The study by Xu et al.[27] showed that the significant delta GLS before and after implantation (-16.6 + 1.2 to – 14.9 + 1.8) within one month would predict cardiomyopathy later. Ahmed et al.[20] also found a similar finding that the significant delta GLS (-16.3 + 0.5 to -12.6 + 0.5) within one month will predict LV systolic dysfunction later that showed by reduced EF. Our study showed that decline delta GLS was comparable (or even greater) (**Table 2**) compared to the previous study. Therefore, we assumed that based on our result and also previous study[20,27], the delta GLS >2 (become less negative within one month) will be useful for early detection of LV systolic dysfunction. Therefore, GLS needed to be evaluated before and after implantation, especially in the patient with a pacing burden > 40% and lead paced on RV apical, as showed by our study. However, the current practice does not incorporate GLS as a consideration either to upgrade the pacemaker into cardiac resynchronization therapy (CRT) or predict which patient will develop heart failure. Therefore, GLS inclusion

can be argued in future practice to predict clinical LV systolic dysfunction. The significant decline of GLS as showed by delta GLS in our study may be an important finding in clinical practice. It may be beneficial that a patient with implanted PPM to check and reprogram the PPM more frequently, especially in a patient who had significant delta GLS in a short term period. The patient should be warned of the clinical heart failure symptoms in the future, and if so, upgrading the PPM to CRT may be considered. Furthermore, the physician may set up the pacemaker to avoid unnecessary RV pacing (eg. set up appropriate lower rate limit of VVI pacemaker or appropriate setting of AV delay in DDD pacemaker) or even to do more physiological pacing, such as "bundle of his" pacing in purpose to prevent or delay PICM.

Study Limitation

This study has several limitations. First, a multivariable analysis could not be conducted due to a limited number of samples. Second, it only examined the short-term effect of pacemaker implantation. Third, a Cardiac CT examination to determine the precise RV pacing location was not performed. The decision of which patients were included in RV apical or RVOT group was only based on fluoroscopy image and confirmed by QRS axis in inferior leads. Fourth, the pacemaker majority was VVI. Therefore, it could not be analyzed whether maintaining AV synchrony (in DDD) may affect GLS or not. However, the burden of VVI >80% made the population in our study more homogeneous. Furthermore, this is the first study to analyze the effect of implantation parameters on early changes of early subclinical LV systolic dysfunction that measured by GLS.

CONCLUSION

The pacing parameter, particularly pacing burden >40% may induce the subclinical LV systolic dysfunction after one month of pacemaker implantation as shown by decline of GLS, especially when the RV pacing location was placed on apical.

CONFLICT OF INTEREST

All authors declare no conflict of interest related to this study.

REFERENCES

1. Brignole M, Auricchio A, Baron-Esquivias G, et al. ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Eur Heart J. 2013;34(29):2281-329.
2. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation. 2003;107:2932-7.
3. Nahlawi M, Waligora M, Spies SM, et al. Left ventricular function during and after right ventricular pacing. J Am Coll Cardiol. 2004;44(9):1883-8.
4. Dreger H, Maethner K, Bondke H,et al. Pacing-induced cardiomyopathy in patients with right ventricular stimulation for 15 years. EP Eur. 2012;14(2):238-42.
5. Thackray SDR, Witte KK, Nikitin N, et al. The prevalence of heart failure and asymptomatic left ventricular systolic dysfunction in a typical regional pacemaker population. Eur Heart J. 2003;24(12):1143-52.
6. Zhang X H, Chen H, Siu C W, et al. New-onset heart failure after permanent right ventricular apical pacing in patients with acquired high-grade atrioventricular block and normal left ventricular function. J Cardiovasc Electrophysiol. 2008;19(2):136-41.
7. Prinzen FW, Vernooy K, Lumen J, et al. Physiology of cardiac pacing and resynchronization. In: Kenneth A Ellenbogen GNK, Chu Pak Lau, Bruce L Wilkoff, Angelo Aurichio, eds. Clinical cardiac pacing, Defibrillator and resychronization therapy. 5th ed. Philadephia: Elsevier; 2017. p. 213-46.
8. Inoue K, Okayama H, Nishimura K, et al. Right ventricular septal pacing preserves global left ventricular longitudinal function in comparison with apical pacing. Circ J. 2011;75(7):1609-15.
9. Algazzar AS, Katta AA, Ahmed KS, et al. Changes in left ventricular global and regional longitudinal strain during right ventricular pacing. Cardiol Res. 2016;7(1):17-24.
10. Kiehl EL, Makki T, Kumar R, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. Heart Rhythm. 2016;13:2272–8.
11. Andersen HR, Nielsen JC, Thomsen PEB, et al. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet. 1997;350(9086):1210-6.

12. Tse H-F, Yu C, Wong K-K, et al. Functional abnormalities in patients with permanent right ventricular pacing : The effect of sites of electrical stimulation. J Am Coll Cardiol. 2002;40(8):1451-8.
13. Shimony A, Eisenberg MJ, Filion KB, et al. Beneficial effects of right ventricular non-apical vs. Apical pacing: A systematic review and meta-analysis of randomized-controlled trials. Europace. 2012;14(1):81-91.
14. Kikuchi M, Tanno K, Miyoshi F, et al. Long-term effectiveness of right septal pacing vs. Right apical pacing in patients with atrioventricular block. J Arrhytmia. 2012;28(4):214-8.
15. Chen S, Yin Y, Lan X, et al. Paced QRS duration as a predictor for clinical heart failure events during right ventricular apical pacing in patients with idiopathic complete atrioventricular block: results from an observational cohort study (PREDICT-HF). Eur J Heart Fail. 2013;15:352-9.
16. Salm LP, Schuijf JD, de Roos A, et al. Global and regional left ventricular function assessment with 16-detector row CT: Comparison with echocardiography and cardiovascular magnetic resonance. Eur J Echocardiogr. 2006;7(4):308-14.
17. III JG, Tanaka H. Echocardiographic assessment of myocardial strain. J Am Coll Cardiol. 2011;58(14):1401–13.
18. Reisner SA, Lysyansky P, Agmon Y, et al. Global longitudinal strain: a novel index of left ventricular systolic function. J Am Soc Echocardiogr. 2004;17(6):630-3.
19. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;16(3):233-71.
20. Ahmed FZ, Motwani M, Cunnington C, et al. One-month global longitudinal strain identifies patients who will develop pacing-induced left ventricular dysfunction over time: The pacing and ventricular dysfunction (PAVD) study. PLOS ONE. 2017;12(1):e0162072.
21. Silva RT, Martinelli Filho M, de Oliveira JC, et al. Ventricular remodeling in right ventricular apical pacing. Arq Bras Cardiol. 2007;88(2):152-8.
22. Baronaite-Dudoniene K, Vaskelyte J, Puodziukynas A, et al. Evaluation of left ventricular longitudinal function and synchrony after dual chamber pacemaker implantation. Medicina. 2014;50(6):340-4.
23. Murakami Y, Tsuboi N, Inden Y, et al. Difference in percentage of ventricular pacing between two algorithms for minimizing ventricular pacing: results of the IDEAL RVP (Identify the Best Algorithm for Reducing Unnecessary Right Ventricular Pacing) study. Europace. 2010;12(1):96-102.
24. Sharma G, Shetkar SS, Patel CD, et al. Paced QRS duration predicts left ventricular function in patients with permanent pacemakers e One-year follow-up study using equilibrium radionuclide angiography (ERNA). Indian Pacing Electrophysiol J. 2015;15(2):90-5.
25. Nakamura H, Mine T, Kanemori T, et al. Effect of right ventricular pacing site on QRS Width. Asian Cardiovascular and Throracic Annals. 2011;19(5):339-45.
26. Khurshid S, Liang JJ, Owens A, et al. Longer paced QRS duration is associated with increased prevalence of right ventricular pacing-induced cardiomyopathy. J Cardiovasc Electrophysiol. 2016;27(10):1174-9.
27. Xu H, Li J, Bao Z, Xu C, Zhang Y, Liu H,Yang J. Early change in global longitudinal strain is an independent predictor of left ventricular adverse remodelling in patients with right ventricular apical pacing. Heart Lung Circ. 2019;28(12):1780-7.