The effect of different pacing modes on LV global and regional longitudinal systolic strain by 2-D speckle tracking echocardiography

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Abstract

Background Inspite of the fact that the life quality improved for most patients with a cardiac pacemaker implant, the pacing induced left bundle branch block pattern can result in changes of the structure, function and hemodynamic of the heart. Methods: This study was performed on 30 patients with history of dual chamber pacemaker implantation more than 6 months duration and 30 healthy volunteers as controls. Conventional and 2-D speckle tracking echocardiography were performed to evaluate the LV global and regional systolic longitudinal strain in different pacing modes. Results: Pacemaker programming from atrial sensed-ventricular paced mode (AS-VP mode) to atrial paced-ventricular paced mode (AP-VP) showed a significant decrease in global LV longitudinal systolic strain (P value <0.05). Moreover, programming to asynchronous ventricular pacing (VVI mode) demonstrated a further significant reduction of global LV LSS when compared to other pacing modes (P value <0.05). Conclusion: Permanent RV apical pacing leads to marked changes of LV systolic function. Moreover, atrial pacing and asynchronous ventricular pacing may cause more deterioration of LV global and regional systolic longitudinal strain detected by 2-D speckle tracking echocardiography.

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Abstract

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Methods: This study was performed on 30 patients with history of dual chamber pacemaker implantation more than 6 months duration and 30 healthy volunteers as controls. Conventional and 2-D speckle tracking echocardiography were performed to evaluate the LV global and regional systolic longitudinal strain in different pacing modes.

Results: Pacemaker programming from atrial sensed-ventricular paced mode (AS-VP mode) to atrial paced-ventricular paced mode (AP-VP) showed a significant decrease in global LV longitudinal systolic strain (P value <0.05). Moreover, programming to asynchronous ventricular pacing (VVI mode) demonstrated a further significant reduction of global LV LSS when compared to other pacing modes (P value <0.05).

Conclusion: Permanent RV apical pacing leads to marked changes of LV systolic function. Moreover, atrial pacing and asynchronous ventricular pacing may cause more deterioration of LV global and regional systolic longitudinal strain detected by 2-D speckle tracking echocardiography.

Key words: pacing, strain, speckle tracking echocardiography

Background

Pacemakers are considered an effective therapy for symptomatic bradyarrhythmia caused by AV nodal and SA nodal disease.**(1)** Inspite of the fact that the life quality improved for most patients with a cardiac pacemaker implant, the pacing induced left bundle branch block pattern can result in changes of the structure, function and hemodynamic of the heart.

. **(2,3)**

In cases with RV apical pacing, the electrical wave front propagates in a slower fashion and induces electrical heterogeneity in the activation of the myocardium similar but not identical to the changes that occur with patients having inherent left bundle branch block. The electrical wave front starts with breakthrough across the interventricular septum and lastly activates the infero-posterior base of the LV.**(4,5)** This electrical pattern alters the mechanical activation of the LV during pacing of RV apex. Not only the anatomic onset of myocardial activation changes but also the resulting mechanical pattern of contraction appears to be altered. **(6)**

Badke et al., explained the mechanism of a reduced rate of change of LV pressure (dP/dt) and the asynchronous pattern of contraction that occur with apical pacing. **(7)**

The early contraction of paced area occurs at the time of low load, but then later in systole it is stretched as the final contraction occurs in lateral wall. **(7)** Moreover, the stroke volume reduced significantly as the

myocardium contracts in asynchronous pattern and this leads to right shift of the LV end-systolic pressure - volume curve. Discrepancy between the relaxation of early- and late stimulated areas shortens the filling time of LV. Thus, apical of RV apex causes ventricular dyssynchrony, impairment of both systolic and diastolic ventricular functions, elevated wall stress and energetic inefficiency. [(8)] In this study we aimed to assess LV regional and global systolic longitudinal strain by 2D STE in different pacing modes in patients with dual chamber pacemaker.

Subjects and methods

This study was performed on 30 patients with history of dual chamber pacemaker implantation (at RV apical position) more than 6 months duration and 30 healthy volunteers as controls. Subjects were included in this study after obtaining their written informed consent and acquiring the approval of the local Ethics Committee.

Inclusion criteria : 1) patients with implanted dual chamber pacemaker more than 6 months duration 2) the ventricular lead placed in the apex of RV (confirmed by fluoroscopy). 3) patients should have LV EF $>$ 50%. 4) ventricular pacing should be at least $>$ 90%.

Exclusion criteria: 1) position of ventricular lead outside the apex of RV. 2) pacemakers implanted less than 6 months duration before enrollment. 3) bad echocardiographic window. 4) previous cardiac surgery (e.g. valve replacement, CABG). 5) history of IHD or previous PCI. 6) myocardial disease as hypertrophic cardiomyopathy, restrictive cardiomyopathy. 7) significant valvular lesions.

Methods: All the subjects underwent detailed history taking, clinical examination and 12- lead ECG. A transthoracic echocardiography was done using vivid E9, general electric health care (GE Vingemed, Norway) equipped with a harmonic M5S variable frequency (1.7 – 4 MHz) phased-array transducer with the patient in the left lateral position based on American Society of Echocardiography (ASE) recommendations.

[(9)]

Conventional echocardiographic examination:

M-Mode measurements included the inter-ventricular septal thickness in diastole (IVSd), the posterior wall thickness in diastole (PWd), the LV end-diastolic diameter (LVEDD), the LV end-systolic diameter (LVESD), LV ejection fraction (EF %) and fractional shortening (FS %). As this method is inaccurate due to paradoxical septal motion caused by RV pacing; we assessed the EF using the modified biplane Simpson's method. The LVEDV and LVESV were calculated from the apical 2- and 4-chamber views. The LV ejection fraction (EF %) was automatically calculated as follows [(10)] : Ejection fraction (EF %) = (EDV-ESV)/EDV$\times$100.

2-D speckle tracking echocardiography (STE):

Apical views were adjusted at a frame rates that range from 70–100 frame/s. The patients were asked to hold breath at the end of expiration and three cardiac cycles were taken consecutively. Images were stored on the hard drive digitally for off-line analysis later. Pulsed-wave Doppler was used to record mitral and aortic velocities to determine the cardiac events timing.

The endocardial lining of these chambers was traced manually by two-dimensional strain Echo Pac software. Eventually a region of interest (ROI) involving the entire transmural wall was created automatically by the computer. The software divided each wall into three segments (basal, mid and apical). Regional and global LV longitudinal systolic strain (LSS) values were calculated.

[(11)] **Figure 1,2&3**

Pacemaker programming:

All patients underwent different programming modes for their devices and were thereby represented as 3 groups: group I (AS-VP mode): in atrial sensed and ventricular paced mode; the device sense the intrinsic atrial activity and pace the ventricles accordingly to maintain A-V synchrony, group II (AP-VP mode): in

atrial paced and ventricular paced mode; the device was programmed to initiate atrial pacing at a rate of 100 b/min followed by ventricular pacing "maintaining A-V synchrony" and group III (VVI mode): in this mode, the atrial lead is switched off and the device functions as a single chamber pacemaker delivering ventricular pacing at 100 b/min dissociated from the intrinsic atrial activity i.e. asynchronous ventricular pacing mode.

2-D STE was used to measure the global and segmental systolic longitudinal strain of the LV walls in order to compare them between controls and patients during AS-VP mode (group I). We also compared LV LSS in the patients in the three pacing modes; group I (AS-VP mode), group II (AP-VP mode) and group III (VVI mode). The comparison of LV LSS between group (AS-VP) and group (AP-VP) was done to study the indirect effects of atrial pacing on LV LSS. The comparison of LV LSS between group (AP-VP) and group (VVI) was done to study the effects of A-V synchrony on LV LSS at the same heart rate of 100 b/min.

Statistical Analysis

Results were statistically analyzed by statistical package for social science (SPSS, version 20). Student's t-test was used to indicate the significance between 2 means. Chi-Squared ($\chi 2$) test was used for comparison regarding qualitative variables. P value was considered statistically significant if < 0.05.

Results:

Our study enrolled 30 patients (18 females and 12 males) with mean age (62.600 $\pm$5.028) and 30 controls (16 females and 14 males) with mean age (59.633 $\pm$ 6.672). we didn't observe any significant difference regarding age and sex between the patients and controls (P value > 0.05). **table 1**

By comparing conventional echocardiographic parameters between the studied groups; LVEDD and LVESD didn't show any significant difference between the controls and the patients during AS-VP mode (group I) (P value > 0.05) **table 2** .

When we measured the LV ejection fraction by M- Mode, we didn't observe any statistical difference between the controls and the patients during AS-VP mode (group I) (P value > 0.05). on the contrary; we found that LV ejection fraction measured by biplane 2D Simpson's technique was significantly lower in patients during AS-VP mode (group I) than the controls (P value < 0.05) **table 2.**

By 2-D speckle tracking echocardiography; the patients during AS-VP mode (group I) had statistically significant lower global LV longitudinal systolic strain (LV LSS) when compared to the control (P Value $<$ 0.001) **table 3** .

As regard regional LV longitudinal systolic strain; most LV segments had significantly lower LSS in the patients during AS-VP mode (group I) when compared to the controls. Moreover, the apical segments had the lowest values (P value < 0.001) **table 4** .

Programming the pacemakers from AS-VP mode (group I) to AP-VP mode at rate of 100 b/min in (group II) showed a significant decrease in both global and regional LV LSS. Moreover, the programming to asynchronous ventricular pacing (VVI mode) at rate of 100 b/min in group III demonstrated a further reduction of both global and regional LV LSS when compared to both groups (P value <0.05) **table 5 ,6 & figure 4,5.**

Discussion

The use of pacemakers was shown to have a marked effect on the life quality of patients with bradyarrhythmia.**(12)** However, serious clinical consequences may occur due to myocardial dysfunction caused by apical pacing.**(13)** Pacing from implantable cardiac devices had a slower electrical conduction velocity than the normal conduction as well as abnormal sequences of myocardial activation.

(14)

One of the serious consequences of RV pacing is the development of pacing-induced cardiomyopathy (PICM) which is known as a significant drop in LV ejection fraction in a patient with high pacing percentage of RV

when no other possible cause is detected.

(15,16)

Dyssynchrony is considered one of several mechanisms that RV pacing can cause myocardial dysfunction. Pacing of RV apex leads to both inter-ventricular and intra-ventricular dyssynchrony which in turn reduces LV systolic function and leads to adverse clinical outcomes.**(17)** Long-term studies suggested that more than 40% of RV pacing in rate modulated (DDDR) mode is predictive of unfavorable events as HF hospitalization.

(3,18)

Moreover, restoration of ventricular synchrony by CRT resulted in improved systolic function of LV and improved clinical outcomes.**(19)** This suggests that the abnormal ventricular activation pattern during pacing may be the cause of LV function deterioration. **(20)**

Based on the aforementioned studies regarding the consequences of RV apical pacing on the heart and their effect on clinical outcomes, our study investigated the effect of pacing of RV on global and regional LV function using 2-D speckle tracking echocardiographic strain techniques, in comparison to controls. In addition, we evaluated the change in global LV longitudinal strain upon programming the DDD pacemaker from AS-VP mode to AP- VP mode and to VVI mode.

When we measured the LV ejection fraction by M- Mode, we didn't observe any statistical difference between the controls and the patients during AS-VP mode (group I) (P value > 0.05). on the contrary; we found that LV ejection fraction measured by biplane 2D Simpson's technique was significantly lower in patients during AS-VP mode (group I) than the controls (P value < 0.05). This can be explained as EF by M Mode is measured across the basal septal and posterior walls and is limited by excessive geometric simplification leading to inaccurate values when abnormal wall motion is present especially in the apical regions are present. **(9)** While Simpson's method is based on the summation of the smaller volumes in order to obtain the overall left ventricular volume which can provide a better evaluation of left ventricular function especially in the presence of abnormal motion of the septum during activation by RVA pacing. **(9)**

Our results coincided with **Burn et al** who provided evidence that mechanical dyssynchrony induced by RVA pacing was associated with reduced LV function even when LV function was normal prior to pacing.**(21)** Pacing of RV acutely increases intramural dyssynchrony in normal hearts. After chronic pacing, intramural dyssynchrony persists and intraventricular dyssynchrony may become evident. pacing induced LV dysfunction may be caused by intramural dyssynchrony. **(22)**

By 2-D speckle tracking echocardiography; the patients during AS-VP mode (group I) had statistically significant lower global LV longitudinal systolic strain (LV LSS) when compared to the control (P Value $<$ 0.001). As regard regional LV longitudinal systolic strain; most LV segments had significantly lower LSS in the patients during AS-VP mode (group I) when compared to the controls. Moreover, the apical segments showed the most significant difference in reduction (P value < 0.001).

Similarly; **Burn et al** observed that LV longitudinal shortening decreased acutely in a significant pattern in pacing of RV apex. Affection of longitudinal strain were even more evident than circumferential strain. Moreover, differences in strain were most evident when measured at the apex and mid-ventricle, rather than at the LV base. **(21)** Interestingly, the degree of shortening in the early-activated regions of LV was lower than in the other regions, causing a decrease in the global LV strain in pacing.**(23)** **Liu et al** studied the acute effects of RVA on LV function using real-time three-dimensional echocardiography in patients had sick sinus syndrome and they found that RVA pacing induced interventricular and intraventricular mechanical delays that led to a reduction of LV systolic function. **(24)**

Our results aligned with a study done by **Liang et al** ., who showed that RV apical pacing resulted in a decrease in longitudinal strain values near pacing sites (apical segments) compared to remote regions (middle and base segments) indicating that RV apex pacing has an unfavorable impact on the LV strain. **(25)** **Chin et al** used global longitudinal systolic strain as a predictor of RVA pacing induced cardiomyopathy (PICM).

In their study, PICM was defined as LVEF decrease [?]10% from the preimplant EF that results in LVEF <50%. They concluded that PICM was evidenced by reduced global longitudinal strain values in patients with subclinical LV systolic dysfunction. These patients warrant closer follow-up with a lower threshold for biventricular pacing.

(26)

In our study; programming the pacemakers from AS-VP mode (group I) to AP-VP mode at rate of 100 b/min in (group II) showed a significant decrease in both global and regional LV LSS.

Hettrick et al observed that atrial pacing has been shown to reduce overall LV stroke volume due to impaired filling caused by atrial dysfunction. **(27)** In **Liang et al** . study, atrial pacing in DDD mode resulted in sub-optimal ventricular diastolic filling and consequently stroke volume compared to intrinsic atrial derived rhythm in VDD mode. In addition, they also demonstrated atrial mechanical dysfunction reflected by decreased active atrial strain caused by atrial pacing in DDD mode.**(25)** In their study, although LVEF was not statistically different between VDD (ventricular only pacing) and DDD (dual chamber pacing) modes, the more sensitive strain measurements demonstrated statistically significant differences in global strain of LV. This indicated that LV systolic function is indeed lower in DDD mode due to direct deleterious effect of atrial pacing on the atrium leading to indirect effects on the LV strain. Therefore, they concluded that atrial pacing in DDD mode led to atrial dysfunction causing decreased LV preload and consequently reduced LV systolic mechanics, resulting in sub-optimal LV performance when compared to VDD mode.

(25)

In our study; the programming to asynchronous ventricular pacing (VVI mode) at rate of 100 b/min in group III demonstrated a further reduction of both global and regional LV LSS when compared to both groups (P value <0.05).

Dual chamber pacing during AS-VP mode maintains physiological A-V synchrony. This is important as atrial contribution to ventricular filling is extremely valuable as result of LV diastolic and systolic pacing induced dysfunction. Loss of A-V synchrony during VVI mode has a deleterious impact on ventricular filling and may even lead to occasional simultaneous atrioventricular contractions which can lead to pacemaker syndrome. A sub-study of the Mode Selection Trial (MOST) showed that pacing of RV was strongly associated with heart failure, hospitalization and atrial fibrillation in both "physiologic pacing" (dual-chamber pacing: n = 707) and ventricular pacing (single-chamber ventricular pacing: n = 632). They observed that ventricular pacing > 40% in DDD group and >80% in VVI group was closely related to heart failure and hospitalization.

(3,12)

Conclusion:

Permanent RV apical pacing leads to marked changes of LV systolic function. Moreover, atrial pacing and asynchronous ventricular pacing may cause more deterioration of LV global and regional systolic longitudinal strain detected by 2-D speckle tracking echocardiography.

Limitations: The sample size was relatively small and data resulting from this study should be considered as preliminary observations. Larger studies with a greater number of patients should be conducted to validate our results. Coronary angiography wasn't performed to rule out coronary artery disease as an additional cause that can affect strain values. This was due to absence of indications for further coronary evaluation.

Abbreviations: 2-D: two dimensional, AP: atrial paced, AS: atrial sensed, ASE: American society of echocardiography, A-V: atrioventricular, CABG: coronary artery bypass graft, CIED: cardiac implanted electronic devices, CRT: cardiac resynchronization therapy, DDDR: dual chamber pacemaker with rate modulation ,ECG: electrocardiogram, EF: Ejection fraction, FS: fractional shortening, HF : heart failure, IHD: ischemic heart disease, IVSd: interventricular septum diastolic thickness, LBBB: left bundle branch block, LV: left ventricle, LV LSS: left ventricular longitudinal systolic strain, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter, LVEDV: left ventricular end diastolic

volume, LVESV: left ventricular end systolic volume, MOST: Mode Selection Trial, PICM: pacing induced cardiomyopathy, PCI: percutaneous coronary intervention, PWd: posterior wall diastolic thickness, ROI: region of interest, RV: right ventricle, RVA: right ventricular apical, SA: sinoatrial, SD: standard deviation, STE: speckle tracking echocardiography, VP: ventricular paced, VVI: Single-chamber ventricular pacing

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Tables

Table 1: Demographic data of the studied subjects:

		Controls n=30	Patients n=30	t-test	P-value
Age	**Mean ±SD**	59.633 ± 6.672	62.600 ±5.028	-1.945	0.057
Sex	**Male Female**	**N (%)**	**N (%)**	$\mathbf{X^2}$	**P-value**
		14 (46.6%) 16 (53.4%)	12 (40%) 18 (60%)	2.347	0.988

Table 2: Comparison of conventional echocardiographic parameters between the controls and

the patients during AS-VP mode (group I)

	Controls n=30	**Patients n=30**	**t -test**	**P-value**
Controls n=30 Patients n=30 t -test P-value mean ±SD mean ±SD				
IVSd $_{cm}$ 1.073 ±0. 126 1.087 ± 0.120 -0.421 0.675				
PWd $_{cm}$ 1.073 ± 0.126 1.087 ± 0.117 -0.426 0.672				
LVEDD $_{cm}$ 4.893 ± 0.466 4.933 ± 0.459 -0.335 0.739				
LVESD $_{cm}$ 2.910 ± 0.378 3.053 ± 0.417 -1.395 0.168				
FS $_{\%}$ 36.367±4.499 34.600 ± 3.169 1.758 0.084 **EF $_{\%}$ by M-Mode** 66.300 ± 4.921 64.433 ± 3.491 1.695 0.096 **EF by 2D Simpson's technique** 64.123 ± 3.325 57.867 ±3.360 18.033 **0.021***				

Table 3: Comparison between the controls and the patients during AS-VP mode (group I) regarding global left ventricular longitudinal systolic strain

	Controls n=30	**Patients n=30**	**t -test**	**P-value**
Global LV LSS (Mean ±SD)	-18.090 ± 2.200	-13.450 ±3.302	-6.405	**<0.001***

LV LSS: left ventricular longitudinal systolic strain

Table 4: Comparison between the controls and the patients during AS-VP mode (group I) regarding regional left ventricular longitudinal systolic strain

Regional LV LSS	Regional LV LSS	Controls n=30	Patients n=30	t -test	P-value
		(mean ±SD)	(mean ±SD)		
Inferoseptal wall	**Basal**	-14.600±3.490	-13.344±3.896	-1.315	0.194
	Mid	-16.967±2.953	-15.066±3.606	-2.233	**0.029***
	Apical	-21.700±4.268	-16.862±6.607	-3.369	**<0.001***
Lateral wall	**Basal**	-17.733±3.226	-13.272±3.961	-4.784	**<0.001***
	Mid	-18.300±2.168	-13.194±4.569	-5.531	**<0.001***
	Apical	-20.967±3.567	-14.678±7.323	-4.228	**<0.001***
Inferior wall	**Basal**	-16.567±4.539	-12.976±3.730	-3.348	**0.001***
	Mid	-18.567±2.239	-14.264±3.954	-5.186	**<0.001***
	Apical	-20.567±4.183	-14.352±6.958	-4.193	**<0.001***
Anterior wall	**Basal**	-16.533±3.451	-14.580±4.394	-1.915	0.060
	Mid	-17.067±3.226	-12.302±4.662	-4.604	**<0.001***
	Apical	-18.900±5.598	-10.815±7.470	-4.744	**<0.001***
Posterior wall	**Basal**	-16.500±3.794	-15.035±5.039	-1.272	0.209
	Mid	-17.600±3.158	-13.136±5.234	-3.999	**<0.001***
	Apical	-20.400±5.946	-12.239±7.119	-4.819	**<0.001***
Anteroseptal wall	**Basal**	-15.467±4.091	-12.812±4.041	-2.529	**0.014***
	Mid	-17.833±2.972	-13.767±4.946	-3.860	**<0.001***
	Apical	-20.967±6.049	-13.699±6.664	-4.423	**<0.001***

LV LSS: left ventricular longitudinal systolic strain

Table 5: Comparison between the patients during AS-VP mode (group I), AP-VP mode (group II) and VVI mode (group III) regarding global LV longitudinal systolic strain

	Patients$_{(n=30)}$	**Patients$_{(n=30)}$**	**Patients$_{(n=30)}$**	**ANOVA**	**ANOVA**
	Group I (AS-VP)	**Group II (AP-VP)**	**Group III (VVI)**	**F**	**P-value**
Global LV LSS (mean ±SD)	-13.450± 3.302	-11.456 ±2.729	-10.738 ±2.563	7.133	**0.001***

AS-VP: atrial sensed – ventricular paced, AP-VP: atrial paced – ventricular paced, VVI: ventricular sense – ventricular pace with inhibitory response, LV LSS: Left ventricular longitudinal systolic strain

Table 6: Comparison between the patients during AS-VP mode (group I), AP-VP mode (group II) and VVI mode (group III) regarding regional LV longitudinal systolic strain

LV LSS	Group I (AS-VP)	Group II (AP-VP)	Group III (VVI)	ANOVA (F)	P-value
	mean ±SD	**mean ±SD**	**mean ±SD**		
Inferoseptal wall	-15.092±3.698	-11.777±4.261	-10.211±3.830	12.018	**<0.001***
Lateral wall	-13.715±4.399	-12.670±4.175	-9.896±3.916	6.727	**0.002***
Inferior wall	-13.865±4.409	-12.162±4.705	-10.532±4.241	4.199	**0.018***

LV LSS	Group I (AS-VP)	Group II (AP-VP)	Group III (VVI)	ANOVA (F)	P-value
Anterior wall	-12.565±4.552	-10.503±3.866	-9.791±4.206	3.502	**0.034***
Posterior wall	-13.470±4.962	-11.029±3.389	-10.456±4.303	4.221	**0.018***
Anteroseptal wall	-13.426±4.659	-9.183±3.945	-8.434±3.485	13.203	**<0.001***

AS-VP: atrial sensed – ventricular paced, AP-VP: atrial paced – ventricular paced, VVI: ventricular sense – ventricular pace with inhibitory response, LV LSS: Left ventricular longitudinal systolic strain

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`figures.pdf` available at https://authorea.com/users/468706/articles/562096-the-effect-of-different-pacing-modes-on-lv-global-and-regional-longitudinal-systolic-strain-by-2-d-speckle-tracking-echocardiography