

## Assessment of Ventricular Function after Permanent Pacing: Tissue Doppler Echocardiographic Study

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### Abstract

**Background:** Although the fact that ventricular pacing is highly beneficial in the treatment of various types of symptomatic bradycardia, RVA pacing has harmful effects on both LV diastolic and systolic parameters of both conventional and Tissue Doppler echocardiography.

**Patients and Methods:** This study was conducted on 120 patients who were scheduled for permanent cardiac pacing (73 Single Chamber VVI and 47 Dual Chamber DDD pacing) in order to assess ventricular function by conventional echocardiography and Pulsed tissue Doppler echocardiography after pacemaker implantation of both groups within 1,3 and 6 months. We assess systolic parameters (EF, FS and S'), diastolic parameters (E, A, E/A ratio, E deceleration by pulsed MV flow, E', A' and E/E' of septal and lateral MV annulus) and Tie index (LVMPI and RVMPI) as parameter for systolic and diastolic performance of both ventricles.

**Results:** As regards LV systolic function; highly significant decline of EF/FS of both groups ( $P < 0.001$ ), highly significant decrease of S' of VVI group with less significant decrease with DDD ( $P 0.002$  for lateral MV annulus and  $0.011$  for septal MV annulus). As regards LV diastolic function: highly significant decrease E/A ratio ( $P < 0.001$ ), increase MV deceleration ( $p < 0.001$ ) and significant increase of E/E' ( $P 0.002$  for lateral MV annulus and  $< 0.001$  for septal MV annulus) after VVI group with less significant decrease of E/A ratio ( $P 0.042$ ), less significant increase of MV deceleration ( $P 0.038$ ), less significant increase of E/E' ( $P 0.34$  Lateral and  $0.015$  for septal) of DDD group. As Regards RV function: Highly significant decrease of E/A of tricuspid flow ( $P < 0.001$ ) and increase E deceleration ( $P < 0.001$ ) and increase E/E' ratio ( $p < 0.001$ ) with VVI group with less significant decrease of tricuspid E/A ratio ( $P 0.045$ ), increase E deceleration ( $P 0.045$ ) and increase of E/E' ( $P 0.034$ ) of DDD group. As regards ventricular performance: Highly significant increase of Tie index of both LV and RV with both groups ( $p < 0.001$ ).

**Conclusion:** Chronic RV pacing induces LV/RV dysfunction regardless pacing Mode (VVI or DDD) that can be assessed by more accurate and sensitive parameters of systolic and diastolic dysfunction with tissue Doppler echocardiography.

**Keywords:** Permanent Cardiac Pacemaker; Tissue Doppler Echocardiography; Systolic Performance; Diastolic Performance; RV Apical Pacing

### Abbreviations

EF: Ejection Fraction; FS: Fractional Shortening; MV: Mitral Valve; TV: Tricuspid Valve

### Introduction

Permanent cardiac pacemaker is widely recognized as beneficial in the treatment of various types of symptomatic bradycardia [1].

Although the fact that ventricular pacing is highly beneficial in patients with completely blocked intrinsic conduction, it does not resemble nature [2].

During recent years there has been a focus on the negative effects associated with long-term pacing of the apex of the right ventricle (RV) [3].

Ventricular pacing induces an abnormal electrical activation leading to mechanical dyssynchrony as with LBBB [4] with subsequent detrimental effects on LV pump function, LV remodeling, and increased risk of heart failure [5-10] atrial fibrillation and death [3].

As regards type of pacing, single chamber ventricular pacing VVI has been demonstrated to be associated with a significant negative inotropic effect and with an increased rate of congestive heart failure [11].

Ideally, pacing should correct arrhythmia with preservation of AV synchrony without adversely affecting ventricular synchrony [12].

There is also a preference and superiority for dual-chamber pacing in patients with any degree of systolic dysfunction and/or diastolic dysfunction in whom the maintenance of AV synchrony is more necessary for preserving optimal hemodynamics than heart rate alone [13,14].

RVA pacing has harmful effects on both LV diastolic and systolic parameters of both conventional and Tissue Doppler echocardiography even in patients with normal LV function [15].

Tissue Doppler imaging (TDI) provides an alternative superior technique to evaluate global and regional systolic LV function, abnormal LV relaxation [16] and ventricular synchrony [17,18].

In the assessment of LV diastolic function, TDI provides valuable information [16] by the ratio of transmitral early peak flow velocity (E) over early diastolic mitral annulus velocity (E') (E/E') which is more reliable for diagnosing diastolic dysfunction [19-21].

One of the most important clinical applications of TDI is the assessment of global LV systolic function; by measuring the myocardial peak systolic velocities of the mitral valve annulus (S) at several locations and to derive an average of them [22].

There is an excellent correlation between systolic mitral annulus velocity  $S_m$  and LV ejection fraction [23].

Also, Tei index is another non-invasive Doppler-derived index which assesses both systolic and diastolic myocardial performance [24].

Increased value of Tei index correlated significantly with the clinical status of LV dysfunction and proved to be more informative than the systolic function indices [25].

### Patients and Methods

This study was done on 120 patients admitted in the Cardiology Department of Specialized Medical Hospital, Faculty of Medicine; Mansoura University; during the period from March 2013 to March 2015 for permanent cardiac pacemaker implantation.

It was done after approval of the local ethics committee and the patient's informed consent was obtained.

This study is a descriptive cross-sectional prospective study that was conducted on 120 patients who were scheduled for permanent cardiac pacing (Single Chamber VVI or Dual Chamber DDD pacing) in order to assess ventricular function by tissue Doppler echocardiography after pacemaker implantation within 1,3 and 6 months.

These patients were divided into divided into 2 groups:

1. **Group I:** 73 Patients with single chamber VVI pacemaker with mean age ( $68.9 \pm 7$ ) years; it included 61 patients with sinus rhythm and 12 patients with AF.

**2. Group II:** 47 Patients with dual chamber DDD pacemaker with mean age ( $60.3 \pm 10.5$ ) years; all of them with sinus rhythm.

All the ventricular leads were positioned in the right ventricular apex, via trans-venous approach under fluoroscopic guidance and all the atrial leads were active-fixation leads placed in the right atrial appendage.

Patients with lost Follow Up, died patient through the Follow Up, Poor transthoracic echocardiographic window and image quality, no informed consent, terminal End-stage CKD or Liver disease and terminal end-stage malignancy were excluded from the study.

### Methods

All patients included in the study were subjected to the following:

- History tacking concerned to the symptoms related to brady-arrythmia (Syncope/presyncope) and symptoms suggesting pacemaker syndrome with follow up visits (NYHA dyspnea grade), basal resting surface 12 leads ECG was done for all the patients before implantation
- Echocardiographic Study Protocol: Using General electric System Vivid -5 machine with tissue Doppler imaging capability with (2.5 - 5) MHZ probe.
- Initial baseline pre-procedure echocardiographic evaluation of ventricular function mainly LV by transthoracic conventional echocardiography and pulsed tissue Doppler echocardiography, followed by serial follow up assessment after 1, 3 and 6 M. after permanent cardiac pacing of both groups (VVI and DDD) by the same parameters that will be described in details.

### Transthoracic conventional echo doppler protocol

All standard views were obtained according to American Society of Echocardiography recommendation [26] focusing on assessment of ventricular function.

### Transthoracic conventional echocardiographic M-mode

The following measures were obtained by M-Mode mid-LV parasternal long or short axis views to measure LVEDD, LVESD, EF and FS.

### Pulsed wave doppler of mitral valve

Pulsed-wave (PW) Doppler is performed in the apical 4-chamber view to obtain mitral inflow velocities to assess LV filling. A 1-mm to 3-mm sample volume is placed 1 cm distal to the MV annulus or between the leaflet tips during diastole [27] to measure the following:

E wave velocity (cm) (Early diastole positive wave), A wave velocity (cm) (Late diastolic positive wave, atrial contraction), E deceleration (m/sec) and E /A ratio.

### Pulsed doppler of tricuspid valve

Pulsed-wave (PW) Doppler is performed from the apical 4-chamber view to obtain Tricuspid inflow velocities to assess RV filling by the same parameters of MV pulsed flow.

### Pulsed wave tissue doppler imaging protocol

The sample volume was placed at the lateral, septal (medial) annulus of Mitral valve and the lateral annulus of Tricuspid valve.

The measurements were best performed in the apical 4 chambers view, where Doppler angles are well aligned with the lateral and septal MV annulus.

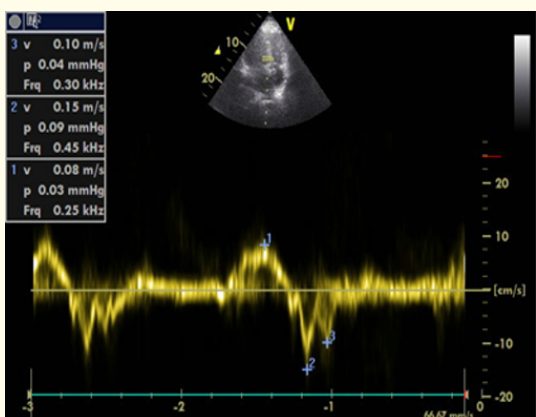


Figure 1: Pulsed tissue doppler of septal MV annulus, measuring S', E' and A'.

For each annular site, we measured peak TDI velocities as the following:

- Positive systolic wave velocity (S') m/sec.
- 2 negative diastolic waves velocities: Early diastolic filling velocity (E') m/sec and Late diastolic filling velocity (A') m/sec.
- E/E' ratio = Transthoracic conventional Pulsed Doppler E velocity/Tissue Doppler pulsed E' velocity of the related annulus (Normal Value > 10 for lateral MV annulus and > 15 for septal MV annulus) [26].
- Tie index: We obtain the Myocardial Performance Index (MPI) by Pulsed tissue Doppler technique that calculated by this equation: LV MPI in our study was calculated by tissue Doppler as this equation: LV Tie index = (MCO - ET)/ET [28,29]; as MCO time (Mitral valve closure-to-opening time) (a): The interval between mitral valve closure and opening is equal to the sum of (IRT + ET + ICT). Left ventricular ET (b) was measured as duration of S' wave by Tissue Doppler imaging. ICT+IRT were obtained by subtracting (b) from (a). So, the TEI index was calculated as (a - b) /b [21,28].

**Pulsed tissue doppler of tricuspid lateral annular**

The measurements were best performed in the apical 4 chambers view, where Doppler angles are well aligned with the lateral Tricuspid annulus.

The sample volume was placed at the lateral annulus of Tricuspid valve we measured peak TDI velocities by the same parameters of MV annulus with assessment of S', E', A', E/E' ratio and RMPI.

RMPI by tissue Doppler was calculated by the same technique of LV tie index: RMPI = (IVRT + IVCT)/ET = (TCO - ET)/ET [29] as TCO, tricuspid valve closure-to-opening time. Normal mean value by Tissue Doppler about 0.38 ± 0.08 [30], RMPI > 0.54 by DTI indicate RV dysfunction [27].

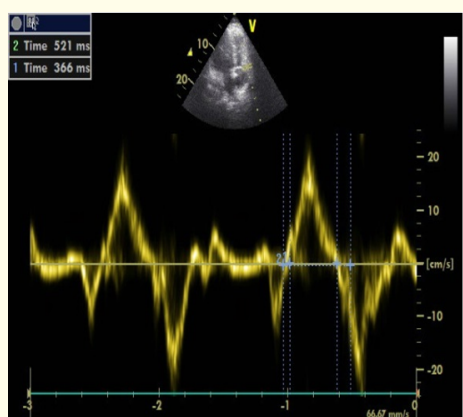


Figure 2: Show pulsed tissue doppler of lateral TV annulus to measure RMPI.

**Statistical analysis**

All statistical analyses were performed using SPSS for windows version 20.0 (SPSS, Chicago, IL). Continuous data were expressed as mean ± standard deviation (SD), while categorical data were expressed in number and percentage. The comparisons of the echo parameters at baseline and at post 1 and post 2 were tested using the repeated measure differences among the groups were determined using one way analysis of variance (ANOVA test) for continuous data. The comparisons of the continuous data between the two groups were determined by independent samples Student’s t test while chi square test is used for the comparison between categorical data. Statistical significance was set at  $p < 0.05$ .

**Results**

The patients of this study are divided into 2 groups with different demographic and clinical data as described in table 1:

	Type of pacing		Student’s t test	
	VVI (n = 73)	DDD (n = 47)	t	p
	Mean ± SD	Mean ± SD		
Age (years)	68.9 ± 7	60.3 ± 10.5	5.393	< 0.001
Sex (n, %)				
Females	40, 54.8%	26, 55.3%	0.003	0.955
Males	33, 45.2%	21, 44.7%		
Hypertension (n, %)	62, 84.9%	38, 80.9%	0.343	0.558
DM (n, %)	36, 49.3%	19, 40.4%	0.910	0.340
Renal impairment (n, %)	3, 4.1%	0, 0%	1.981	0.159
Rhythm (n, %)				
Sinus	62, 84.9%	47, 100%	7.797	0.005
AF	11, 15.1%	0, 0%		
Rate	38.1 ± 4.8	40.2 ± 4.4	2.446	0.016
QRS	138.1 ± 19.1	126.4 ± 18.6	3.314	< 0.001

**Table 1:** Comparison of the clinical & demographic data of patients with VVI and DDD pacing.

Data expressed as (n, %) as (number of patients, Percentage) and Mean ± SD, DM: Diabetes; AF: Atrial Fibrillation.

**1. Group I:** Patients with single ventricular chamber pacemaker VVI

- a. It included 73 Patients (60.8%).
- b. Their mean age (68.9 ± 7) years.
- c. It included males (33) and females (40).
- d. It included 62 patients with basal sinus rhythm (84.9%) and 11 patients with AF (15.1%) with mean basal pre-procedure heart rate (38.1 ± 4.8) beats/Min with mean QRS duration (138.1 ± 19.1) msec.
- e. It included 62 patients had hypertension, 36 patients with DM, 3 patients with renal impairment.

**2. Group II:** Patients with dual chamber permanent pacemaker DDD

- a. It included 47 Patients (39.2%).
- b. Their mean age (60.3 ± 10.5) years.
- c. It included males (21) and females [26].
- d. It included 47 patients with basal sinus rhythm (100%) and no patients with basal AF rhythm (0%) with mean basal pre-procedure heart rate (40.2 ± 4.4) beats/Min with mean QRS duration (126.4 ± 18.6) msec.
- e. It included 38 patients had hypertension, 19 patients with DM, No patients with renal impairment.

Firstly, As regards LV dimensions and systolic function by conventional echocardiography after pacing, there was significant increase LVESD of both groups with less significance with DDD arm (P value < 0.001 of VVI group and 0.008 of DDD group) with significant increase of LVEDD of VVI group (P value < 0.001) with non-significant increase of the DDD group (P value 0.155) during follow up period of the study up to 6 months.

There was significant impairment of LV systolic function by serial follow up of both groups after permanent pacemaker implantation either VVI or DDD, represented by highly significant decrease of EF and FS of both groups (P value < 0.001) as described in table 2.

		Pre	Post (1)	Post (2)	Post (3)	F	P
LVEDD (cm)	VVI	5.2 ± 0.5	5.3 ± 0.6	5.49 ± 0.6	5.59 ± 0.6	6.887	< 0.001
	DDD	5.3 ± 0.7	5.4 ± 0.6	5.52 ± 0.6	5.67 ± 0.6	1.767	0.155
LVESD (cm)	VVI	3.3 ± 0.6	3.48 ± 0.6	3.69 ± 0.6	3.8 ± 0.6	10.022	< 0.001
	DDD	3.3 ± 0.6	3.52 ± 0.6	3.64 ± 0.6	3.7 ± 0.6	4.073	0.008
EF (%)	VVI	65.2 ± 6.5	62.6 ± 6.7	60.1 ± 6.5	58.3 ± 6.6	15.246	< 0.001
	DDD	66.3 ± 7.4	63.6 ± 7.7	61.2 ± 7.8	59.3 ± 7.8	7.321	< 0.001
FS (%)	VVI	36 ± 5.3	34 ± 4.9	31.9 ± 4.7	30.9 ± 6	80.083	< 0.001
	DDD	36.9 ± 5.5	34.8 ± 5.4	32.8 ± 5.2	31.5 ± 4.5	53.969	< 0.001

**Table 2:** The change of left ventricular parameters of patients with VVI and DDD pacing during the follow up period.

F test (ANOVA= analysis of variance). Data expressed as Mean ± SD. P value < 0.001 means highly significant difference. LVEDD: LV End-Diastolic Dimensions; LVESD: LV End-Systolic Dimension; EF: Ejection fraction; FS: Fractional shortening; Post1: After 1 month; Post 2: After 3 months; Post 3: After 6 months.

As regards pulsed flow of MV, there were parameters suggesting LV diastolic dysfunction presenting (as shown in table 3 as:

		Pre	Post (1)	Post (2)	Post (3)	F	P
MVE velocity (m/sec)	VVI	0.9 ± 0.3	0.73 ± 0.3	0.67 ± 0.3	0.64 ± 0.3	10.950	< 0.001
	DDD	0.87 ± 0.3	0.83 ± 0.2	0.78 ± 0.2	0.76 ± 0.2	2.898	0.036
MV A velocity (m/sec)	VVI	0.81 ± 0.3	0.88 ± 0.2	0.91 ± 0.3	0.93 ± 0.3	2.598	0.052
	DDD	0.80 ± 0.4	0.85 ± 0.3	0.88 ± 0.2	0.90 ± 0.2	1.674	0.173
MV E/A ratio	VVI	1.2 ± 0.5	0.97 ± 0.4	0.69 ± 0.7	0.67 ± 0.5	16.138	< 0.001
	DDD	1.22 ± 0.5	1.09 ± 0.6	0.94 ± 0.6	0.92 ± 0.6	2.793	0.042
MV E deceleration (ms)	VVI	186 ± 97.9	193.3 ± 54.1	214.7 ± 63.3	243.9 ± 64.1	9.424	< 0.001
	DDD	184.4 ± 64.4	188.0 ± 71.5	191.8 ± 53.2	218 ± 57.6	2.858	0.038

**Table 3:** The change of mitral valve parameters of patients with VVI and DDD pacing during the follow up period.

- Highly significant decline of E velocity (P < 0.001), highly significant decrease of E/A ratio (P < 0.001) with highly significant increase of MV E deceleration (P < 0.001) after VVI pacemaker implantation.
- Less significant decline of E velocity (P 0.036), less significant decrease of E/A ratio (P 0.042) with less significant increase of MV E deceleration (P 0.038) after DDD pacemaker implantation compared to VVI group, suggesting more prominent LV diastolic dysfunction after VVI group.

Similarly, As regards pulsed flow of TV, there were parameters suggesting RV diastolic dysfunction presenting:

- Highly significant decline of E velocity (P < 0.001), highly significant decrease of E/A ratio (P < 0.001) with highly significant increase of MV E deceleration (P < 0.001) after VVI pacemaker implantation.

- Less significant decline of E velocity (P 0.021), less significant decrease of E/A ratio (P 0.045) as shown in figure 3 with less significant increase of MV E deceleration (P 0.045) after DDD pacemaker implantation compared to VVI group, suggesting also more prominent RV diastolic dysfunction after VVI group.



Figure 3: The change of the tricuspid valve E/A ratio of patients with VVI and DDD pacing during the follow up period.

As regards Pulsed Tissue Doppler parameters of MV annulus (Lateral/Septal) after pacing of both groups, as shown in table 3 the study reported that:

- There was highly significant decline of S' velocity of both lateral/septal MV annuli after VVI pacemaker (P < 0.001/< 0.001) with less significance after DDD pacemaker (P 0.002/0.011) suggesting decrease of LV systolic function after both group of pacing with higher significance with VVI arm as shown in figure 4.
- There was highly significant decrease of E' velocity of MV annulus (Lateral/Septal) (P < 0.001 of both) with significant increase of E/E' of both MV annuli (P 0.002/< 0.001) after VVI pacing, implicating significant diastolic dysfunction and LV filling pressure.
- There was also less significant decrease of E' velocity of MV annulus (Lateral/Septal) (P 0.046/ 0.034) with less significant increase of E/E' of both MV annuli (P 0.034/0.015) after DDD pacing.
- There was highly significant increase of LV myocardial performance index (Tei index of both MV annuli) after pacing of both groups (VVI and DDD) with P value < 0.001 as shown in figure 5 supporting impairment of LV systolic and diastolic performance after both groups.

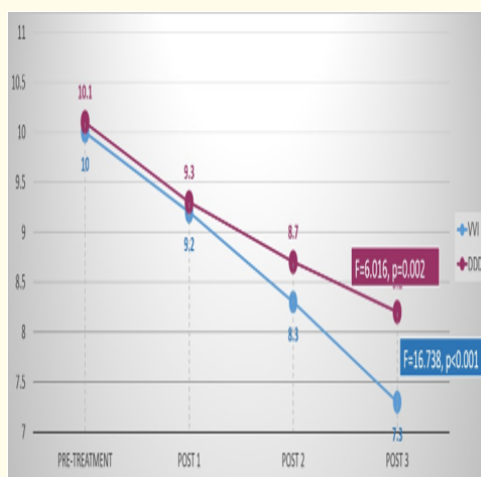


Figure 4: The change of the Lateral annulus Mitral valve S velocity of patients with VVI and DDD pacing during the follow up period.



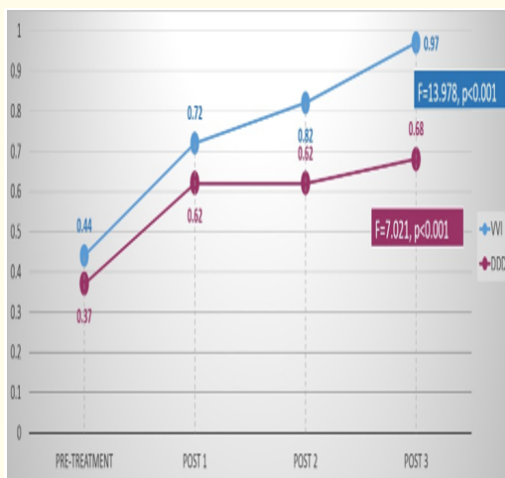


Figure 5: The change of the septal annulus Mitral valve Tei index of patients with VVI and DDD pacing during the follow up period.

Finally, as regards Pulsed Tissue Doppler parameters of TV lateral annulus:

- There was higher significant decrease of S' after VVI arm, compared to DDD arm (P 0.003 vs 0.011).
- There was highly significant decrease of E' velocity (P < 0.001) and highly significant increase of E/E' TV (P < 0.001) after VVI pacemaker.
- On the other hand, there was less significant decrease of E' (P 0.042) and highly significant increase of E/E' TV (P < 0.001) after DDD pacemaker as described in figure 6.
- Also, there was highly significant increase of RMPI (RV myocardial performance index, Tei index of TV) after VVI implantation (P < 0.001) with less significance after DDD group (P 0.014) as shown in figure 7.
- These parameters suggestion RV systolic and diastolic dysfunction after cardiac pacing of both groups with prominent significance after VVI pacemaker implantation.

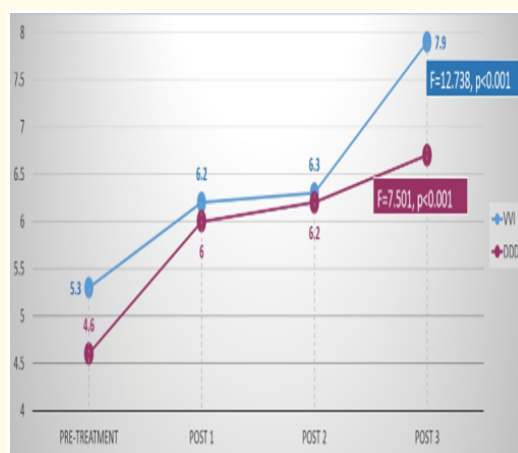


Figure 6: The change of the E of pulsed TCV / Lat TCV E' amplitude of patients with VVI and DDD pacing during the follow up period.



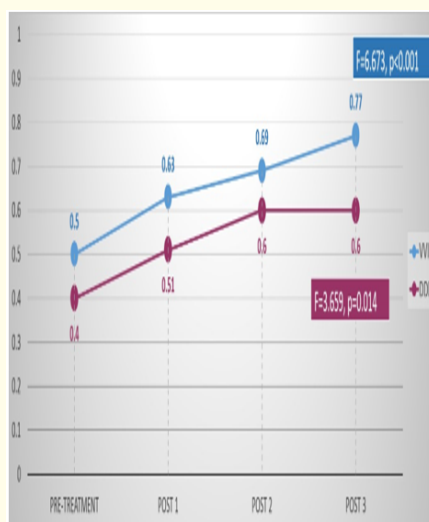


Figure 7: The change of the Lateral annulus Tricuspid valve Tei index of patients with VVI and DDD pacing during the follow up period.

		Pre	Post (1)	Post (2)	Post (3)	F	P
S' lateral MV (cm/sec)	VVI	10 ± 2.5	9.2 ± 2.6	8.3 ± 2.2	7.3 ± 2.4	16.738	< 0.001
	DDD	10.1 ± 2.4	9.3 ± 2.5	8.7 ± 2.0	8.2 ± 2.1	2.898	0.002
E' lateral MV (cm/sec)	VVI	11.5 ± 5.0	10.2 ± 4.7	9.1 ± 4.7	8.1 ± 5.5	6.272	< 0.001
	DDD	11.4 ± 3.24	10.7 ± 3.4	10.5 ± 3.2	9.9 ± 3.4	2.713	0.046
A' lateral MV (cm/sec)	VVI	10.1 ± 4.1	11.1 ± 3.6	11.7 ± 3.6	12.5 ± 6.1	3.738	0.012
	DDD	10.2 ± 3.8	10.5 ± 3.2	11.2 ± 3.9	12.1 ± 3.5	2.572	0.056
E/E' lateral MV	VVI	8.7 ± 5.0	10.1 ± 4.7	10.2 ± 4.7	11.9 ± 5.4	5.095	0.002
	DDD	8.2 ± 3.2	8.1 ± 3.2	8.7 ± 3.4	9.9 ± 3.4	2.943	0.034
Lateral MV Tei index	VVI	0.47 ± 0.53	0.72 ± 0.43	0.79 ± 0.32	0.95 ± 0.44	15.291	< 0.001
	DDD	0.42 ± 0.45	0.63 ± 0.59	0.65 ± 0.34	0.71 ± 0.32	6.063	< 0.001

Table 4: The change of lateral annulus mitral valve parameters of patients with VVI and DDD pacing during the follow up period.

S': Positive Systolic Wave; E': Early Diastolic Wave; A': Late Diastolic Atrial Contraction Wave; E/E': Pulsed MV E/E' of Pulsed Tissue Doppler of Lateral MV Annulus; MV: Mitral Valve.

		Pre	Post (1)	Post (2)	Post (3)	F	P
S' septal MV (cm/sec)	VVI	9.8 ± 2.5	8.4 ± 2.6	7.7 ± 2.6	6.9 ± 2.7	16.330	< 0.001
	DDD	9.9 ± 3.1	8.7 ± 3.0	8.3 ± 2.6	8.0 ± 3.0	3.806	0.011
E' septal MV (cm/sec)	VVI	9.0 ± 5.8	8.0 ± 3.0	7.6 ± 2.7	6.2 ± 3.2	6.535	< 0.001
	DDD	8.6 ± 2.6	7.8 ± 1.8	7.7 ± 1.9	7.3 ± 2.3	2.951	0.034
A' septal MV (cm/sec)	VVI	10 ± 3.0	10.3 ± 3.4	11.2 ± 3.8	12.5 ± 4.0	7.214	< 0.001
	DDD	9.8 ± 3.1	10.1 ± 3.0	10.4 ± 2.8	10.6 ± 3.3	0.617	0.605
E/E' septal MV	VVI	9.9 ± 6.9	12.5 ± 5.7	12.8 ± 5.3	14.0 ± 5.9	6.085	< 0.001
	DDD	9.1 ± 3.5	9.5 ± 2.6	10.9 ± 4.5	11.2 ± 4.1	3.563	0.015
Septal MV Tei index	VVI	0.44 ± 0.41	0.72 ± 0.30	0.82 ± 0.40	0.97 ± 0.79	13.978	< 0.001
	DDD	0.37 ± 0.35	0.62 ± 0.40	0.62 ± 0.30	0.68 ± 0.37	7.021	< 0.001

Table 5: The change of septal mitral valve annulus parameters of patients with VVI and DDD pacing during the follow up period.

		Pre	POST1	POST2	POST3	F	P
S' lateral TV (cm/sec)	VVI	13.4 ± 3.9	12.1 ± 4.0	11.8 ± 4.0	10.9 ± 4.4	4.693	0.003
	DDD	14.1 ± 2.8	13.1 ± 2.7	12.8 ± 2.7	12.3 ± 2.4	3.842	0.011
E' lateral TV (cm/sec)	VVI	13.7 ± 4.1	11.1 ± 3.9	10.4 ± 3.6	9.3 ± 4.0	16.740	< 0.001
	DDD	12.8 ± 6.2	12.6 ± 3.1	11.4 ± 3.3	10.7 ± 2.6	2.850	0.039
A' lateral TV (cm/sec)	VVI	12.3 ± 4.6	14.7 ± 4.7	16.7 ± 4.7	17.9 ± 4.7	21.364	< 0.001
	DDD	12.5 ± 6.3	14.2 ± 4.7	16.1 ± 4.9	16.2 ± 4.8	2.780	0.042
E/E' lateral TV	VVI	5.3 ± 3.0	6.2 ± 2.3	6.3 ± 2.2	7.9 ± 2.8	12.738	< 0.001
	DDD	4.6 ± 2.2	6.0 ± 2.2	6.2 ± 2.2	6.7 ± 2.4	7.501	< 0.001
Lateral TV Tei index (RMPI)	VVI	0.50 ± 0.47	0.63 ± 0.31	0.69 ± 0.30	0.77 ± 0.40	6.673	< 0.001
	DDD	0.40 ± 0.29	0.51 ± 0.36	0.60 ± 0.40	0.60 ± 0.30	3.659	< 0.001

**Table 6:** The change of lateral TCV annulus parameters of patients with VVI and DDD pacing during the follow up period.

**Discussion**

Several studies have demonstrated the deleterious consequences of short, mid and long-term RVA pacing on both systolic and diastolic LV function, especially in the presence of CHF [15].

Tantengco., *et al.* [6] had provided parallel evidence of Doppler echocardiography-derived variables of global LV systolic and diastolic function in patients who had long-term RV apical pacing.

However, a few of these studies used TDI technique instead of conventional echocardiography for this purpose [15].

So, in our study we decide to detect the harmful effects RVA pacing on ventricular function by Pulsed Tissue Doppler echocardiography in comparison with conventional echocardiographic parameters of systolic and diastolic ventricular dysfunction.

**RV pacing affects LV systolic function**

Left ventricular EF is a surrogate parameter that describes myocardial pump function [31].

In our study there was statistically highly significant decrease of EF and FS with both groups of pacing (VVI and DDD groups) (P value of both groups < 0.001).

In consistent of our results, there are several studies have reported that RV apical pacing is associated with de-crease in LV ejection fraction [10,32-34] and heart failure [35].

In our study there was statistically highly significant increase of both LV end-systolic and LV end-diastolic internal dimensions in VVI group over time (P value < 0.001) within repeated measurements of left ventricular throughout the follow up until 6 Months, with statistically significant increase of LV end-diastolic dimensions (P value 0.008) with non-significant increase of LV end-systolic (P value 0.155) in DDD group over time.

Our results were consistent with that of previous studies [15,36,37].

Dwivedi., *et al.* [38] studied 48 patients with VVI pacing and reported statistically significant decline of EF at 6 months after (P < 0.05) with significant increase of left ventricular end diastolic dimension and left ventricular end systolic dimension by 6 months (P < 0.05).

Fang., *et al.* [39] also found a significant decrease in EF after RV pacing.

Barold and Herweg [40] reported that the detrimental effects of long-term RVA pacing may occur in patients with normal and abnormal LV ejection fractions (LVEF) as documented in our study population that included patients with basal normal and impaired EF before pacemaker implantation.

In contrast to our results, Boucher, *et al.* [41] reported no significant change in EF with VP.

Similarly, Sagar, *et al.* [42] showed opposite results that long-term right ventricular apical pacing had no detrimental effect on ventricular function.

Also, Algazzara, *et al.* [43] reported that there was no statistically significant difference in left ventricular EF (P value > 0.19), end systolic LV dimensions (P value > 0.069) and end diastolic dimensions (P value > 0.078) between both groups over time

In our study, RV pacing regardless mode of pacing results in impaired of LV function due to RV apical pacing of majority of our cases, these results are consistent with other studies [36,44,45].

In our study, we found no significant valuable advantages of DDD pacemaker over single ventricular VVI pacing due long-term pacing from right ventricular apex in both groups as reported [46,47].

On the other hand; Styliadis, *et al.* [48] reported that Left ventricular fractional shortening (FS) and both ventricular sizes remained unchanged with no change throughout the period of evaluation up to 12M after DDD pacemaker implantation. These results were related to optimization of Atrio-Ventricular Interval (AVI).

In the opposite of our results, Kindermann, *et al.* [49] documented modest improvement of Doppler echocardiographic indexes of ventricular function (EF and Tie index) after DDD pacing due to better AV sequencing. This improvement was achieved due to RV septal pacing (in half of the patients), optimization of drug therapy and cardioversion of atrial fibrillation.

S' wave by pulsed tissue Doppler is another predictor of systolic dysfunction [50].

In our study, there was significant decline of S' amplitude of both septal and lateral MV annulus after pacing of both groups, similarly as documented by Fang, *et al.* and Algazzar, *et al.* [39,43,50].

### RV pacing affects LV diastolic function

In most of studies, stress has been on systolic function of LV after long term pacing while data regarding the diastolic function is conflicting [38].

In our study there was evidence suggesting diastolic dysfunction of both ventricles after VVI pacing that was documented by statistically highly significant decrease of E amplitude of MV flow (P value < 0.001), highly significant decrease of E/A ratio of MV flow (P value < 0.001) and highly significant increase of E deceleration (P value < 0.001) with VVI group, these results are consistent with Tantengco, *et al.* [6] and Yu, *et al.* [17].

In comparison to DDD group, there was less significant decrease of MV E amplitude (P value 0.036), less significant decrease of E/A ratio (P value 0.042) and less significant increase of MV E deceleration (P value 0.038), these results are similar to D'Andrea, *et al* [51].

In contrast, Vardas, *et al.* [52] found no difference in the diastolic Doppler indices after DDD pacemaker implantation.

Also, Forwalt, *et al.* [53] observed that RV apical pacing resulted in acute systolic dyssynchrony with preserved diastolic synchrony but this study was limited due to its immediate or acute diastolic parameters results.

As regards Tissue Doppler parameters: in our study there was statistically significant decrease of MV E' amplitude of lateral and septal MV annuli with significant increase of E/E' ratio of both groups of pacing (VVI and DDD).

These results were consistent with other studies as Lin, *et al.* [54], Moarref, *et al.* [15] and Mitov, *et al* [55].

Also, Ortega, *et al.* [56] reported that Chronic RV apical pacing impaired diastolic indices in the lateral mitral annulus by decrease E' amplitude and increase E/E' ratio.

This was due to slowed/delayed LV relaxation and prolonged the isovolumetric relaxation time, which led to the decreased  $E'$  with increased LV filling pressure resulted in LA compensatory contraction and the increased  $A'$ .

Our results were found to be inconsistent with Kojuri, *et al.* [51] who found that no significant changes in  $E'$  and  $A'$  by pulsed tissue Doppler between DDD and VVI.

Naegeli, *et al.* [14] documented that no significant changes in transmitral flow deceleration time and the  $E/E'$  ratio between DDD and VVI mode

### RV pacing affects LV global performance

RVA pacing has deleterious effects on both LV systolic and diastolic parameters of not only conventional echocardiography but also TDI even in patients with normal LV function [15].

Tie index is the most accurate parameter for the detection of impairment of combined diastolic and systolic performance [56] and correlates well with known invasive indices of LV systolic and diastolic functions [43].

In our study there was evidence of LV systolic and diastolic dysfunction documented by conventional and tissue Doppler echocardiographic parameters as described before, these data were correlated with statistically significant increase of Tie index of septal and lateral MV annuli after RV pacing of both groups (VVI and DDD) (P value < 0.001).

Similarly, in another study on 12 patients with RVA pacing, resulted in a significant reduction in global LV function after 18M. documented by increase of Tie index [32].

Also, Choi, *et al.* [57] documented that Tie index significantly increased after 12 months of implantation of VVI pacemakers of 40 patients.

On the same way, Algazzar, *et al.* [43] showed increase in myocardial performance index in both groups (DDD and VVI).

These results due to RV paced patients had significantly longer isovolumic contraction times, which is likely a consequence of slower pressure development during a dyssynchronous LV contraction leading to limitation of the time available for adequate systolic ejection and diastolic filling (shorter ejection time).

### RV dysfunction parameters

In our study, there was evidence of RV diastolic dysfunction after pacing regardless mode reported by significant decrease of E velocity of TV flow, increase E/A ratio, increase E deceleration time with increase  $E/E'$  ratio indicating high RA pressure and RV filling pressure with consistent results with Dwivedi, *et al* [38].

Also, in our study there was evidence of Impaired RV systolic function after pacing of both modes by significant decrease of  $S'$  and significant increase of RV MPI (Tie index) indication impairment of RV systolic and diastolic performance as reported by another study by Ichiki, *et al* [58].

### Study Limitations

- Short-duration and restrictive range of FU (6 months), high cumulative pacing in all patients (>90%) and the limited number of patients, respectively.
- Inability of programming of all pacemaker patients to optimize AV interval and hysteresis parameters to decrease RV pacing amount.
- Other factors affecting on systolic or diastolic ventricular function were not excluded as DM, HTN, Ischemia or valvular, etc.

### Conclusion

- a) Chronic RVA pacing induces LV/RV dysfunction regardless pacing Mode (VVI or DDD), irrespective of basal ventricular function. So, it is recommended to minimize RV pacing (mainly apical site) and search for another alternative pacing sites

- b) Tissue Doppler imaging (TDI) provides an alternative superior technique to evaluate systolic and diastolic ventricular function after cardiac pacing.

So, in the near future there will be a need to reassess and recorrect our current practice in permanent cardiac pacing with choosing the right ventricular apex as our preferred site for chronic pacing in any patient who is candidate for permanent pacemaker.

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