Right Ventricular Apical versus Septal Pacing Impact on Left Ventricular Synchrony and Function

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Abstract: Background: Right ventricular (RV) pacing alters left ventricular (LV) mechanical activation, resulting in adverse impacts on LV function. Alternative RV septal pacing results in narrower QRS duration and may be more physiologic than RV apical pacing. This study was aimed to investigate the effect of RV apical (RVA) and septal pacing (RVS) on LV synchrony and function. Patients and methods: 40 patients clinically indicated for dual chamber pacing were included, subjected to conventional M-mode and 2-D echocardiography with following parameters looked for: left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), ejection fraction (EF%), fractional shortening (FS%), cardiac output (CO L/m) and tissue Doppler imaging to assess LV dyssynchrony baseline study on temporary RV apical pacing. Then patients were divided randomly into two groups: GroupI: 20 patients underwent permanent RV apical pacing. GroupII: 20 patients underwent permanent RV septal pacing. QRS duration, Electrical parameters including RV stimulation threshold, R wave, and ventricular lead impedance together with fluoroscopic time were measured in every patient. Both groups were followed up within one week and at least 6 months after implantation by echocardiography, and tissue Doppler imaging. Results: QRS duration was significantly narrower in pts with septal pacing compared to RV apical pacing (148.85±6.89 Vs 162.1±5.98, P < 0.001). Electrical parameters at implant were satisfactory for all patients and no patients required lead repositioning. There were no significant differences in the RV mean stimulation threshold, R-wave sensing, lead impedance and fluoroscopic time between the RV apical and RV septal lead positioning. Within one week following implantation there was no significant difference in LVEDD, LVESD, LVEF, CO and LV mechanical delay. On follow up, in RV septal paced patients compared to RV apical paced patients LVEDD(cm) was lower (4.73±0.59 Vs 4.94±0.61, P value= 0.27), LVESD(cm) was significantly lower (3.02±0.37 Vs 3.42±0.45, P value= 0.004), LVEF(%) was significantly higher (69±8Vs 62±7, P value= 0.006), CO (L/min) was significantly higher (4.88±0.29 Vs 4.5±0.62, P value= 0.019),LV lateral to septal delay was significantly lower (72±5 Vs 83±6, P value< 0.001). Conclusion: Long term RV septal pacing is feasible, reliable and efficient associated with less adverse effects on LV synchrony and function compared to long term RV apical pacing.
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Key words: RV septal pacing, RV apical pacing, LV dyssynchrony.

1. Introduction

Emerging evidence suggests that prolonged pacing from the right ventricular (RV) apex may lead to progressive left ventricle (LV) dysfunction, exacerbation of heart failure, atrial fibrillation (AF), and increased mortality[1,2] The mechanism behind the negative hemodynamic effects of RV apical pacing appears to be related to abnormal ventricular activation and contraction, ultimately resulting in LV remodeling[3,4]. This deleterious effect has led to a growing interest in alternate ventricular pacing sites with a more favorable hemodynamic profile.

Among the possible RV pacing sites, the septum, particularly at the mid right ventricle and outflow tract (RVOT), appears to be particularly attractive.

The hypothesis is that RV septal pacing allows a more physiological activation of the ventricles. During normal atrio-ventricular conduction, the inter-ventricular septum and the lateral wall of the LV are almost simultaneously activated. The activation wave front then advances from the base to the apical region producing a narrow QRS complex on the surface electrocardiogram (ECG) [5].

In contrast during RV apical pacing, the impulse advances toward the base area through the slow conducting myocardium with the ventricular free wall being the last to be activated. The results a broad QRS complex on the surface ECG [6,7].

With RV septal pacing, a more physiological pattern of ventricular activation should be achieved, thus avoiding the deleterious effects of RV apical pacing [8,9]. It is important to recognize that non-septal sites such as the RV free wall be avoided as this is theoretically the worst area to pace.

Aim of work

This study was initiated prospectively to evaluate:

- The feasibility and efficacy of RV septal pacing.

- The effect of RV apical versus RV septal pacing on LV systolic function and intra ventricular delay.

2. Patients & Methods

Study population:

Forty patients were included (21 males, 19 females, mean age of 54±7.2 years) in the self controlled study .All patients were admitted to the Critical Care Medicine Department, Cairo University from August 2009 to October 2011clinically indicated for dual chamber pacing.

Inclusion criteria:

Patients who were clinically indicated for dual chamber pacing with second or third degree heart block with preserved LV function(LVEF>50%).

Exclusion criteria:

- Presence of LV dysfunction (LVEF<50%).
- Pre-existing permanent cardiac pacemaker or ICD.
- Presence of hypertrophic obstructive cardiomyopathy.
- Recent cardiac surgery (≤30 days).
- Recent myocardial infarction (≤30 days).
- Patient inability or unwillingness to comply with study protocol and required study visit schedule.
- Concomitant research study whose protocol would conflict or affect the outcome of this study.
- Patients not expected to survive for the duration of the study follow-up due to co-morbid medical condition.

Methods:

The studied pts while they were on temporary RV apical pacing were subjected to baseline assessment included:

- Full History taking, Full Clinical examination and Full laboratory investigations.
- Chest radiograph and Electrocardiogram.
- Conventional echocardiographic examination and Tissue Doppler imaging.

Then, the selected patients were randomly divided into two groups:

Group I: 20 patients were subjected to permanent RV apical pacing.

Group II: 20 patients were subjected to permanent RV septal pacing.

Electrical parameters including mean stimulation threshold, R-wave, lead impedance together with fluoroscopic time at implant were measured.

Both groups were followed up within one week and at least 6 months later following implantation by:

- Electrocardiogram with special attention to QRS duration.
- Echocardiography to assess LV function.
- Tissue Doppler imaging to assess LV dyssynchrony

Permanent cardiac pacing implantation technique:

- The procedure was done in the cardiac catheterization laboratory. All patients were lightly sedated with midazolam 5mg total dose nd pethidine 50 mg total dose. Anti thrombotic drugs and food were withhold for at least 8 hours.
- The skin on the left subclavian region was sterilized thoroughly with betadine then was covered by sterile skin pad to help manipulation of the leads under complete aseptic condition.
- Physiologic dual-chamber cardiac pacemaker was implanted. The atrial lead was positioned in the right arterial appendage, and ventricular lead in the apical region of the right ventricle with fine adjusting of position to get lowest pacing threshold and best sensing P and R amplitude respectively. In septal pacing The same procedure as RVA pacing but the ventricular lead was implanted at the RVOT septal wall using screw-in ventricular lead.The position of the leads were controlled by fluoroscopy and surface ECG confirmed QRS axis normalization (0 to 90 degree)

At implant the following parameters were measured:

The fluoroscopic time consumed in the whole procedure (min), the bipolar stimulation threshold (v), R –wave sensing (mv) and the ventricular lead impedance (Ohm).

Electrocardiogram:

The QRS duration was measured from the first intrinsic deflection of the QRS complex to the terminal isoelectric component of the complex in sinus rhythm and from the first evoked QRS intrinsic deflection to the terminal isoelectric component during pacing "The longest QRS duration noted in any of the six limb leads was used".

Echocardiographic examination:

Images were obtained from each part of the examination together with standard lead-II of ECG and were stored on videotape for subsequent analysis. A 3.5 MHz. transducer of ATL5000,

coloured machine was used for imaging in the following sequence

1. M- mode and two dimensional (2-D) echocardiography: To measure the LV dimensions and LV ejection fraction, then the cross-sectional area (CSA) of the left ventricular outflow tract was automatically computed.
2. The Doppler study: Cardiac output was measured using a pulsed-Doppler focused on the left ventricular outflow tract to measure velocity time integral (VTI). For each pacing mode, three consecutive cardiac cycles were analyzed and averaged.

Cardiac output was automatically calculated "CO (L\min.)= VTI x LVOT CSA x HR".

The most frequently variables measured by the echocardiography to assess global LV function included: LVEDD (cm), LVESD (cm), LVFS %, LVEF % and CO (L/min)

Tissue Doppler imaging:

Using the same machine with incorporated TDI software

TDI was done in the pulsed modality from the apical 4 chamber view to assess the electromechanical delay in each wall as to evaluate the LV intra-ventricular synchrony.

Regional electromechanical delay (ms):

For each wall we measured the time elapsing between the beginning of the QRS or the pacing spike to the beginning of the systolic(S) wave in the tissue Doppler velocity tracing(time to peak S). This time represent the electromechanical delay in each wall.

Intra ventricular electromechanical delay (ms):

It was calculated by subtracting the shortest regional delay from the longest one. Intraventricular delay (IVD) = the longest regional delay – the shortest regional dela***y.***

Statistical analysis

All data were statistically described in terms of range, mean, standard deviation (±SD), median, frequencies (number of cases)and relative frequencies (percentage). Comparison between different groups in the present study was done using *paired-t* test for comparing continuous data when normally distributed and Mann Whitney *U* test when not normally distributed. A probability value (*p* value) less than 0.05 was considered significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical package for the Social Science; SPSS Inc., Chicago, IL, USA) Statistical program.

3. Results

Age and sex distribution:

Our study included 40 pts with a mean age of 54.0±7.22 years, 21 male pts. and 19 female pts with no statistically significant difference between both groups {P value= 0.932, 0.759 respectively} (Table.1).

Table (1): Age and sex distribution in both groups

Sex	Apical pacing		Septal pacing		P value
	Male	female	male	Female	
No. of pts	11	9	10	10	0.759
Age	54.1	7.594	53.9	7.026	0.932

Clinical data

Out of the studied patients 24 were hypertensive; 17 were smoker; 11 were diabetic and 6 patients had ischemic heart disease distributed between both groups as shown in figure(1) revealing no statistically significant difference between both groups.

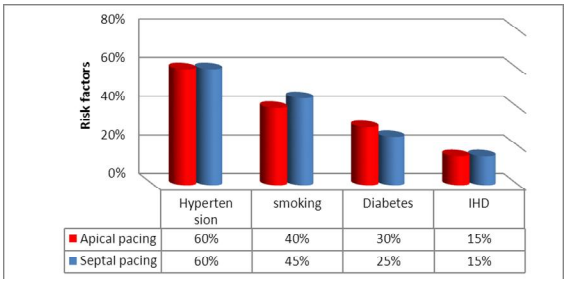

Figure (1): Risk factors distribution in both groups

Comparison between both groups regarding electrical parameters measured at implant:

In our study, in RV septal paced patients ***(Group II)*** compared to RV apical paced patients ***(Group I),*** there were no statistically significant difference regarding the fluoroscopic time (p=0.62), the bipolar mean stimulation threshold (p=0.858), the R-wave sensing (p=0.69), and the lead impedance (p=0.784) at implant. No lead dysfunction was noted or dislodgement occurred throughout the follow up duration (Table.2). QRS duration was significantly narrower in pts with septal pacing compared to RVA pacing (P < 0.001).

Table(2): Electrical parameters and Fluoroscopic time in both groups

Electrical parameters	Apical pacing(Group I)	Septal pacing(Group II)	P value
	Mean±SD	Mean±SD	
QRS width (ms)	162.1±5.9816	148.85±6.8998	<0.001
Threshold (V)	0.525±0.1618	0.515±0.1872	0.858
R wave (mV)	11.85±1.6631	11.65±1.5652	0.698
Impedance (ת)	624.5±88.762	632.5±94.3049	0.784
Fluoroscopic time (min)	12.4±1.9841	12.1±1.8325	0.622

Comparison between both groups regarding global LV systolic function

In our study, within one week following permanent implantation, in RV septal paced patients compared to RV apical paced patients there were no statistically significant difference regarding the LVEDD (p=0.54), LVESD (p=0.79), LVEF (p=0.76), CO (p=0.68) (Table 3).

Table (3): Assessment of Global LV systolic function in both groups within one week from permanent implantation.

Within One week	Apical pacing(Group I)	Septal pacing(Group II)	P value
	Mean±SD	Mean±SD	
LVEDD	4.72±0.65	4.60±0.54	0.54
LVESD	3.12±0.45	3.09±0.36	0.79
LVEF	67.60±7.33	68.30±7.29	0.76
Cardiac output	5.04±0.42	5.09±0.42	0.68

At six months follow up, in RV septal paced patients compared to RV apical paced patients, there were no statistically significant difference regarding the LVEDD (p=0.27), while LVESD was statistically significantly lower (p=0.004), LVEF was statistically significantly higher (p=0.006) and CO was statistically significantly higher (p=0.019) (Table 4).

Table (4): Assessment of Global LV systolic function in both groups Six months later from permanent implantation

Six months later	Apical pacing(Group I)	Septal pacing(Group II)	P value
	Mean±SD	Mean±SD	
LVEDD	4.94±0.61	4.73±0.59	0.27
LVESD	3.42±0.45	3.02±0.37	0.004*
LVEF	61.60±6.89	68.60±8.39	0.006*
Cardiac output	4.50±0.62	4.88±0.29	0.019*

Comparison between both groups regarding left ventricular intraventricular delay.

There was no statistically significant difference between both groups regarding lateral to septal delay while they are on temporary RV apical pacing at the baseline assessment {*P value*=0.294} and but it was statistically significantly lower within one week later {*P value*=0.002} and six months following permanent implantation in RV septal paced patients compared to RV apical paced patients {*P value* <0.001} (Table.5).

Table (5): Assessment of Intraventricular Delay in both groups

Lateral to septal delay	Apical pacing (GroupI)	Septal pacing (Group II)	P value
	Mean±SD	Mean±SD	
Baseline on Temporary pacing	75.7±7.7058	78.5±8.8823	0.294
Within One week	77.45±7.9105	70.55±4.8393	0.002*
Six months later	83.95±6.5572	72.2±5.1972	<0.001*

Follow up data regarding global LV systolic function and intra-ventricular delay within each group throughout the study duration:

On following up data regarding global LV systolic function and intraventricular mechanical delay within each group throughout the study duration, in RV septal paced patients there were no statistically significant changes ,while in RV apical paced patients there was statistically significant decrease in LVEF {*P-value*=0.01} ,and statistically significant decrease CO {*P-value*=0.003}and statistically significant increase in lateral to septal delay {*P-value*=0.007} (Tables 6,7). Other parameters including LVEDD and LVESD did not show any statistically significant difference.

Table (6): Follow up data regarding global LV systolic function and intraventricular delay within Group I.

Apical pacing(GroupI)	*Within week*	*Six months later*	*P value*
LVEDD	4.71±0.64	4.94±0.61	0.226
LVESD	3.1±0.45	3.4±0.45	0.058
LVEF	67.6±7.3	61.6±6.88	0.01*
CO	5.04±0.42	4.5±0.62	0.003*
Lateral to septal delay	77.45±7.9	83.9±6.55	0.007*

Table (7): Follow up data regarding global LV systolic function and intraventricular delay within Group II.

Septal pacing(GroupII)	Within week	Six months later	P value
LVEDD	4.6±0.53	4.7±0.6	0.48
LVESD	3.08±0.36	3.01±0.36	0.5
LVEF	68.3±7.29	68.6±8.3	0.9
CO	4.87±0.22	4.8±0.29	0.9
Lateral to septal delay	70.5±4.8	72.2±5.19	0.3

4. Discussion

Since the dawn of transvenous cardiac pacing, almost 50 years ago[10], the right ventricular (RV) apex has been the default site for endocardial transvenous ventricular lead implantation due to the ease of placement, stability, and lead design. However, prolonged pacing from the RV apex has recently been shown to result in progressive left ventricular (LV) dysfunction[1-2,11-13] due to a remodeling process consequent to abnormal ventricular activation and contraction [3,4,8,14-20] . This deleterious effect has prompted an interest in alternate ventricular pacing sites with a more favorable hemodynamic profile. Among the different sites for RV pacing, the septal areas are theoretically associated with a more physiological ventricular activation resembling that of normal atrio-ventricular (AV) conduction from base to apex.

True RV septal pacing has until recently been difficult to consistently achieve. Some of these difficulties relate to the lack of suitable lead technology, the non-standardized nomenclature, and the inability to consistently and accurately position the pacing leads onto the septum because of its posterior orientation within the RV chamber. We now have a much clearer understanding of the relationship between the anatomy of the RV chamber and the fluoroscopic appearances and electrocardiographic patterns, which in turn has allowed successful development of tools to reliably direct active-fixation leads onto the true RV septum[10].

This study was aimed to evaluate feasibility, real ability and efficacy of RV septal pacing and to evaluate the effects of RV apical vs RV septal pacing on LV Global Systolic Function and Synchrony.

In our study QRS duration was significantly narrower in pts with septal pacing compared to RV apical pacing and these findings are consistent with those reported by Schwaab et al. [21] who tested the feasibility of RV septal lead implantation technique guided by surface ECG and the degree to which this technique reduces paced QRS duration compared to RV apical stimulation In 120 consecutive patients with standard pacing indications and found that QRS was significantly shorter during septal pacing compared with apical pacing (151 ± 20 vs 162 ± 23 ms, $P < 0.001$). There was a tendency towards greatest QRS reduction when the high septum was stimulated (22 ± 11 ms reduction) as compared with mid- (18 ± 11 ms) or apical parts of the RV septum (16 ± 10 ms). QRS reduction was most likely if apical QRS width was > 170 ms ($P = 0.0002$), and there was an inverse correlation between apical QRS and Δ QRS ($r = 0.53$ $P < 10^7$) [21].

In the study of Buckingham et al., the QRS duration was identical in RVA and RVOT pacing. Only dual site synchronous pacing (i.e., simultaneous RVA and RVOT pacing), provided thinner QRS complexes [22].

In contrast to the study of Yoon et al., conducted on 30 patients with the pacing in the RV apex (RVA), RV septum (RVS), and RV outflow tract (RVOT) in a sequential manner ,QRS duration (148.1 +/- 12.8 ms) of RVA pacing was significantly shorter than that of RVS pacing (154.4 +/- 14.1 ms, $P < 0.01$) and RVOT pacing (160.6 +/- 15.7 ms, $P < 0.001$) and explaind that by heterogenous pacing sites detected later on by transthoracic echocardiography [23].

In our study, in RV septal paced patients compared to RV apical paced patients there were no statistically significant difference regarding the fluoroscopic time (p=0.62), the bipolar mean stimulation threshold (p=0.858), the R-wave sensing (p=0.69), and the lead impedance (p=0.784) at implant. No lead dysfunction was noted or dislodgement occurred throughout the follow up and this was consistent with study published by Vlay who reported that there was no difference in R wave sensing, pacing threshold and lead impedance between the two pacing sites. Late dislodgment of the RVOT lead occurred 6 days after the implantation in a patient with severe pulmonary hypertension. There were no increased thresholds requiring repositioning either acutely or chronically [24]. In addition to those studies, our present study with a mean follow-up period of 6 months provides important information about the safety and efficacy of RVOT pacing in the long-term. We were not able to detect any significant change in chronic pacing and sensing parameters within RVOT group as well as when compared with RVA pacing.

In our study, within one week following permanent implantation ,comparing RV septal paced patients to RV apical paced patients, there were no statistically significant difference regarding the LVEDD (p=0.54),LVESD (p=0.79), LVEF (p=0.76), CO (p=0.68) while lateral to septal delay was statistically significantly lower in RV septal paced patients compared to RV apical paced patients(p=0.002). At six months follow up, in RV septal

paced patients compared to RV apical paced patients. There were no statistically significant difference regarding the LVEDD(p=0.27),while LVESD was statistically significantly lower(p=0.004), LVEF was statistically significantly higher(p=0.006), CO was statistically significantly higher(p=0.019) and lateral to septal delay was statistically significant lower in RV septal paced patients compared to RV apical paced patients (p<0.001).

Of the acute studies, about 50% showed a physiologic preference for RVOT pacing [25-29] and because the negative remodeling effects of RV apical pacing may take years to manifest, it seems illogical to extrapolate acute physiologic conclusions, particularly with normal or near normal ventricles, to chronic RV pacing sites.

Our findings are consistent with those reported by Lewicka-Nowak E et al., who compared long-term effects of RVOT versus RVA pacing on clinical status and left ventricular (LV) function in 27 patients(14 RVOT Vs 13 RVA) and found that, in the RVA group significant LV ejection fraction decrease was observed (from 56+/-11% to 47+/-8%, p <0.05); in the RVOT group LV ejection fraction did not change (54+/-7% and 53+/-9%; NS) [30].

In the studies of Katsuji Inoue conducted on 103 patients with mean age (74±9 years) with symptomatic bradyarrhythmia and preserved LV ejection fraction, and 50 age-matched control subjects were studied. All patients received a permanent pacemaker and were randomly assigned into 2 groups (RVA: n=51, RVS: n=52). After insertion, patients underwent an echocardiographic study during RV pacing. LV dyssynchrony was analyzed using Color-coded tissue Doppler ehocardiograph. LVEF% showed a significant decrease in RV apical paced patients compared to the control group(65±5 vs 69±6%, p<0.05) while the lateral to septal delay showed a significant increase in RV apical paced patients compared to RV septal paced patients (62± 40 vs 32±30, p<0.001) [31].

Some investigators have proposed the idea of a hemodynamic "sweet spot," where each patient has a particular optimal pacing site [3, 27, 32].

The ideal ventricular pacing site should resemble the normal activation and synchronicity of ventricular activation observed with an undamaged conduction system. A pacing site that is in closer proximity with the proximal portion of His bundle at the RV septum should lead to a narrower QRS which in turn might reflect a lesser degree of activation delay compared with RVA pacing and less dyssynchrony, as demonstrated by multiple echocardiographic techniques (3,34- 38).

Study limitations

1- Evaluation of the pattern of electrical activation of the left ventricle by electroanatomical mapping was outside the scope of this study, but would provide insight into the complex nature of electromechanical coupling

2-Although RVOT Pacing Was Associated With Superior LV Systolic Function, Intra-LV And Interventricular Synchrony Than RV apical Pacing, The Causal Relationship Between LV Function And Cardiac Synchrony Could Not Be Established.

Bleeker et al., *in 2007* [39] have shown that restoration of cardiac synchrony is the most important predictor of response to cardiac resynchronization therapy. The results of this study are consistent with the corollary—that the development of greater dyssynchrony promotes greater decline in systolic LV function.

Conclusion

We may conclude that RV septal pacing site can be considered at least as safe and effective as the apical pacing site in terms of lead stability and pacing parameters associated with less adverse effects on LV function and synchrony rather than RV apical pacing probably due to RV apical pacing-induced delayed LV activation, prolonged QRS duration and LV dyssynchrony.

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