



Correlation of pacing site in right ventricle with paced QRS complex duration

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ARTICLE INFO

Article history:

Received 9 March 2018

Received in revised form

4 August 2018

Accepted 14 August 2018

Available online 17 August 2018

ABSTRACT

Background: Pacing from RV mid septum and outflow tract septum has been proposed as a more physiological site of pacing and narrower paced QRS complex duration. The paced QRS morphology and duration in different RV pacing sites is under continued discussion. Hence, this study was designed to address the correlation of pacing sites in right ventricle with paced QRS complex duration.

Methods: Two hundred fifty-two consecutive patients who underwent pacemaker implantation were enrolled. Baseline clinical characteristics were recorded for each patient. All patient underwent fluoroscopy, electrocardiogram and echocardiography post pacemaker implantation. Paced QRS duration was calculated from the leads with maximum QRS duration.

Results: Mean paced QRS (pQRS) duration was significantly higher in apical septum group with a mean of 148.9 ± 14.8 ms compared to mid septum (139.6 ± 19.9 ms; p-value 0.003) and RVOT septum (139.6 ± 14.8 ms; p-value 0.002) groups, respectively. There was no significant difference between mid-septal and RVOT septal pQRS duration. On multivariate analysis, female gender, baseline QRS duration and RVOT septal pacing were the only predictors for narrow pQRS duration (<150 msec).

Conclusion: RV mid-septal and RVOT septal pacing were associated with significantly lower pQRS duration as compared with apical pacing. Based on multivariate analysis RVOT septal pacing appears to be preferred and more physiological pacing site.

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1. Introduction

Permanent ventricular pacing for symptomatic bradycardia has proven benefits. However, possible disadvantageous effects on cardiac function have only recently been recognized. Among possible ventricular pacing sites, right ventricular apex (RVA) has been selected as the conventional site. RVA site is easily accessible, allow safe and stable long-term pacing, despite its important advantages, long term RVA pacing causes left ventricular dyssynchrony, hemodynamic impairment, LV dysfunction with or without heart failure, especially in pacing dependent patients [1]. An increasingly recognized goal in cardiac pacing is to achieve a less eccentric, more physiological ventricular activation and timing patterns. In order to maintain normal cardiac function in patients

with permanent ventricular pacing, other alternative pacing site might be superior to RVA [2]. Septal RV pacing might be an alternative site because it is associated with shorter QRS duration and thus lesser dyssynchrony than anywhere else in the RV [3].

Thus different pacing sites of interventricular septum (IVS) may be more physiological and may provide better hemodynamics. Studies have revealed that the mean QRS duration is significantly longer during RVA than mid-septal pacing [4]. Paced QRS complex duration (pQRSd) reflects homogenization of contraction and is a surrogate marker of dyssynchrony of LV contraction. The relationships between pQRSd and various sites of right ventricular pacing have not yet been studied in detail in a large cohort of patients. Therefore, this study was designed to address this clinical question for correlation of pacing sites in right ventricle with pQRSd.

2. Materials and methods

The study was a prospective observational study, 252 consecutive patients with a ventricular pacemaker implanted for standard

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Peer review under responsibility of Indian Heart Rhythm Society.

indications were recruited from September 2014 to December 2015. The protocol was submitted to Ethics Committee and approval was taken. Written informed consent was taken from patients prior to inclusion of study. The protocol was submitted to Ethics Committee and approval was taken. Patients with a pacemaker implanted for standard indications and age >18 years were included. Patients with single chamber pacemaker implantation in AAI or AAIR pacing mode were excluded.

2.1. Pacemaker implantation

All patients were implanted with dual-chamber or single chamber pacemakers in a sterile manner with a conscious state under local anaesthesia by an experienced operator. All leads were transvenously inserted from the left or right axillary/subclavian vein. The site of ventricle lead implantation was as per the operator's discretion. All patients underwent CXR posteroanterior (PA) and lateral view to look for lead position. Electrocardiogram (ECG) was done to calculate QRS duration in the lead which was having maximum paced QRS duration (pQRSd). We divided patient into two groups based on pQRS duration. Group I with pQRS Duration less than 150 msec and group II with pQRS duration more than 150 msec. We also subdivided the group I with pQRS duration less than 150 msec into two groups. One group with pQRS duration less than 120 msec (Group 1a) and other between 120 to 150 msec (Group 1b). This arbitrarily cut off was taken from the ESC guidelines which recommend LBBB with QRS duration more than 150 msec as Class I recommendation for Biventricular pacing [5]. QRS axis was also calculated. ECG was digitized and measurements were done with digital calipers. Automatically acquired pQRS duration by ECG machine was also noted. If manually calculated pQRS duration does not matched automated acquired pQRS duration, only manually calculated pQRS duration was used in analysis.

Fluoroscopy was done to look for optimal lead position in anteroposterior (AP), left anterior oblique (LAO) 40°, right anterior oblique (RAO) 30° and lateral position. Fluoroscopic images were available in all except ten patients. Pacemaker lead tip was divided into three septal positions based on fluoroscopic findings (i) mid septal, (ii) high septal or right ventricular outflow tract (RVOT) septum and (iii) RV apical septum. Lead tip at any site other than mentioned above was kept in others. Final lead position assessment was done independently by one of the investigator. All patients underwent post procedure echocardiogram. Lateral fluoroscopic view was considered the best view for lead localization. Echocardiography was used as a supplemental tool whenever there was an ambiguity in determining the lead position.

The LV ejection fraction (EF) was calculated using Simpson's rule from apical four chamber and apical two chamber views. Ventricular dyssynchrony was assessed post implantation by echocardiography. Criteria for dyssynchrony were septal to posterior wall motion delay of >130 msec and interventricular mechanical delay of >40 msec. Patients with intermittent pacing requirements were studied by temporarily setting the pacing rate at higher than baseline rhythm. Patient with potential fusion/native rhythm were paced at a higher rate to get a pure paced complex for measurement purpose.

2.2. Statistical analysis

Quantitative variables like age, LV function, QRS duration were summarized as mean \pm SD. Qualitative variables such as gender, site of pacemaker etc were summarized as proportions. Continuous variables were compared among the group by one way analysis of variance (ANOVA) followed by post hoc comparison using bonferroni test. Categorical variables were analyzed by chi square or fisher exact *t*-test. Correlation between two continuous variables

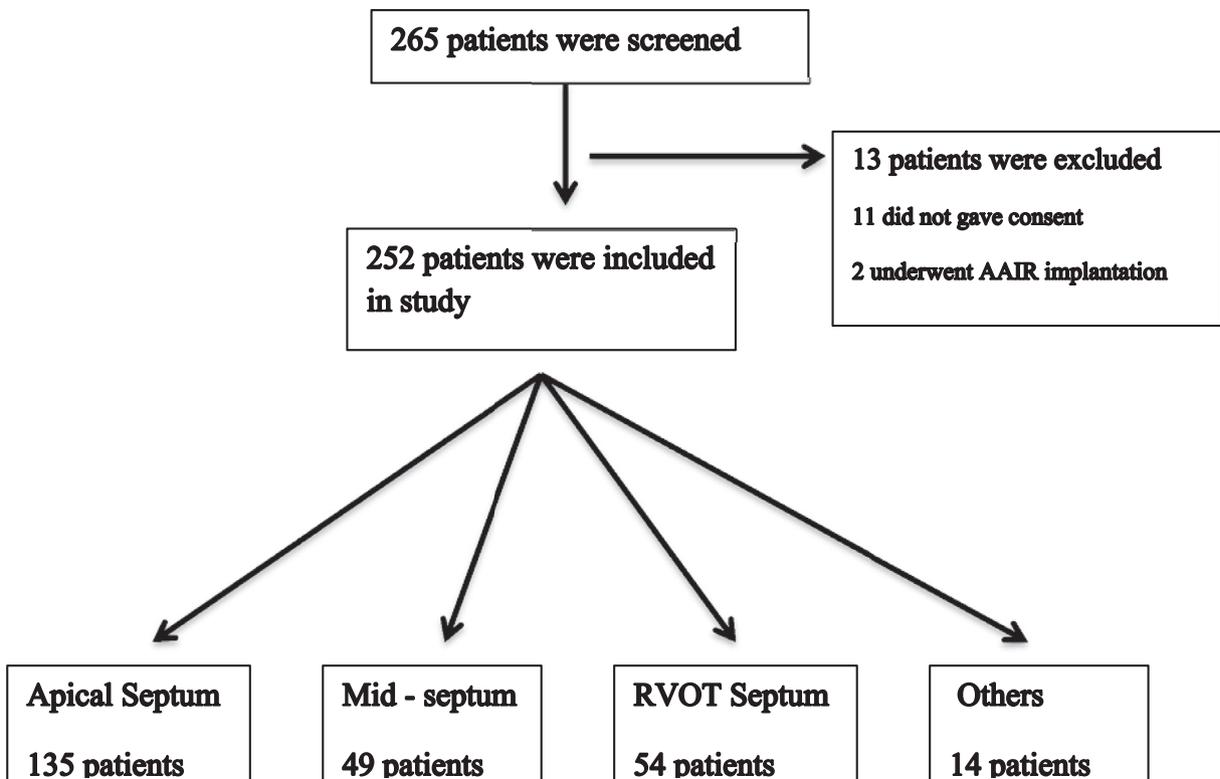


Fig. 1. Study flow chart.

Table 1
Baseline characteristics of patients according to pQRS duration.

		pQRS <150 msec	pQRS ≥150 msec	p value
Total (n)	252	159 (63.1%)	93 (36.9%)	NS
Age (Mean ± SD)	60 ± 15	59 ± 15	61 ± 12	0.02
Males	162 (64.3%)	89 (55.9%)	73 (78.4%)	<0.001
Pacing site				
Apical	135	73 (54%)	62 (46%)	
Mid Septal	49	36 (73.5%)	13 (26.5%)	<0.0001
RVOT Septal	54	46 (85.2%)	8 (14.8%)	
Others	14	6 (42.9%)	8 (57.1%)	
CAD	40 (15.8%)	21 (13.2%)	19 (20.4%)	NS
DM	46 (18.2%)	26 (16.3%)	20 (21.5%)	NS
HTN	86 (34.1%)	47 (29.5%)	39 (41.9%)	NS
Postoperative	18 (7.1%)	9 (5.6%)	9 (9.6%)	NS
LV Function (Mean ± SD)	57.8 ± 10.2%	59.4 ± 9.0	54.8 ± 11.3	<0.001
Baseline prepacing QRS Duration (Mean ± SD)	118.4 ± 23.4	113.2 ± 22.2	127.5 ± 22.3	<0.001
RBBB/Bifascicular block	60 (23.8%)	35 (22.0%)	25 (26.8%)	NS
Complete LBBB	49 (19.4%)	25 (15.7%)	24 (25.8%)	NS
Single chamber pacemaker	124 (49.2%)	83 (52.2%)	41 (44.0%)	NS
Interventricular dyssynchrony ¹	15 (5.9%)			
Intraventricular Dysynchrony ²	5 (1.9%)			

CAD: coronary artery disease; DM: diabetes Melitus; HTN: hypertension; LV - left ventricular; RBBB: right bundle branch block; LBBB: left bundle branch block. 1 Defined as difference between RV and LV ejection time of more than 40 msec 2 Defined as septal wall to posterior wall motion delay of more than 130 msec on post procedure echocardiography.

was assessed by Karl Pearson correlation coefficient. All analysis was implemented on STATA software 11.2. P value of less than 0.05 was taken as statistically significant.

3. Results

Two hundred sixty-five patients who underwent pacemaker implantation during the study period were screened. Thirteen patients were excluded (11 did not give consent, two patients underwent single-chamber pacemaker in AAIR pacing mode (Fig. 1). Two hundred fifty-two patients constituted the study cohort. Baseline characteristics of study group are shown in Table 1. 162 patients (64.3%) were males. Mean age of the patients was 60 years with range of 18–90 years. Eighteen (7.1%) patients were post-operative, five patients had undergone coronary artery bypass grafting (CABG) in past, eleven patients had undergone valve replacement, one patient had undergone ruptured sinus of valsalva (RSOV) repair and one patient developed complete heart block after myectomy for hypertrophic cardiomyopathy. Table 1 shows that there was no significant difference in baseline characteristics between two groups I and II except age and gender. Table 2 depicts

baseline characteristics and ventricular dyssynchrony parameters according to pacing site. Group 1a (pQRS < 120 msec) had 12 patients, seven were in mid septal, four were in RVOT septal and one was at apical septum (Table 3).

Most common indication of pacemaker implantation was

Table 3
Different sites of pacing on basis of different pQRS duration.

	pQRS duration	Patients (n)	Site
Group Ia	≤120 msec	12 (4.7%)	Apical - 1 Mid Septum - 7 RVOT - 4 Others - 0
Group Ib	121–149 msec	147 (63.5%)	Apical - 78 Mid Septum - 31 RVOT - 43 Others - 8
Group II	≥150 msec	93 (31.7%)	Apical - 56 Mid Septum - 11 RVOT - 7 Others - 6

RVOT: right ventricular outflow tract.

Table 2
Baseline characteristics of patients according to pacing site.

	Apical Pacing	Mid septal Pacing	RVOT septal pacing	Others	Overall P value
Total (n)	135 (53.5%)	49 (19.4%)	54 (21.4%)	14 (5.5%)	
Age (Mean ± SD)	63.2 ± 11.7	58.0 ± 17.6	54.1 ± 16.6	58.7 ± 19.8	<0.001
Males	93 (68.8%)	32 (65.3%)	30 (55.5%)	7 (50%)	NS
Females	42 (31.1%)	17 (34.7%)	24 (44.4%)	7 (50%)	
CAD	24 (17.7%)	9 (18.3%)	4 (7.4%)	3 (21.4%)	NS
DM	31 (22.9%)	7 (14.2%)	5 (9.2%)	3 (21.4%)	NS
HTN	50 (37.0%)	11 (22.4%)	18 (33.3%)	7 (50%)	NS
Postoperative	4 (2.9%)	6 (12.2%)	8 (14.8%)	0	<0.05
LV Function (Mean ± SD)	57.1 ± 10.0	59.0 ± 10.0	58.8 ± 10.2	56.5 ± 11.5	NS
Baseline prepacing QRS Duration (Mean ± SD)	123.6 ± 23.0	114 ± 20.9	108.6 ± 21.9	122.4 ± 27.5	NS
RBBB/Bifascicular block	35 (25.9%)	9 (18.3%)	11 (20.3%)	5 (35.7%)	NS
Complete LBBB	31 (22.9%)	12 (24.4%)	4 (7.4%)	2 (14.2%)	0.04
Interventricular dyssynchrony ^a	10 (7.4%)	3 (6.1%)	2 (3.7%)	0	NS
Intraventricular Dysynchrony ^b	4 (2.9%)	1 (2.0%)	0	0	NS

CAD: coronary artery disease; DM: diabetes Melitus; HTN: hypertension; LV - left ventricular; RBBB: right bundle branch block; LBBB: left bundle branch block.

^a Defined as difference between RV and LV ejection time of more than 40 msec.

^b Defined as septal wall to posterior wall motion delay of more than 130 msec on post procedure echocardiography.

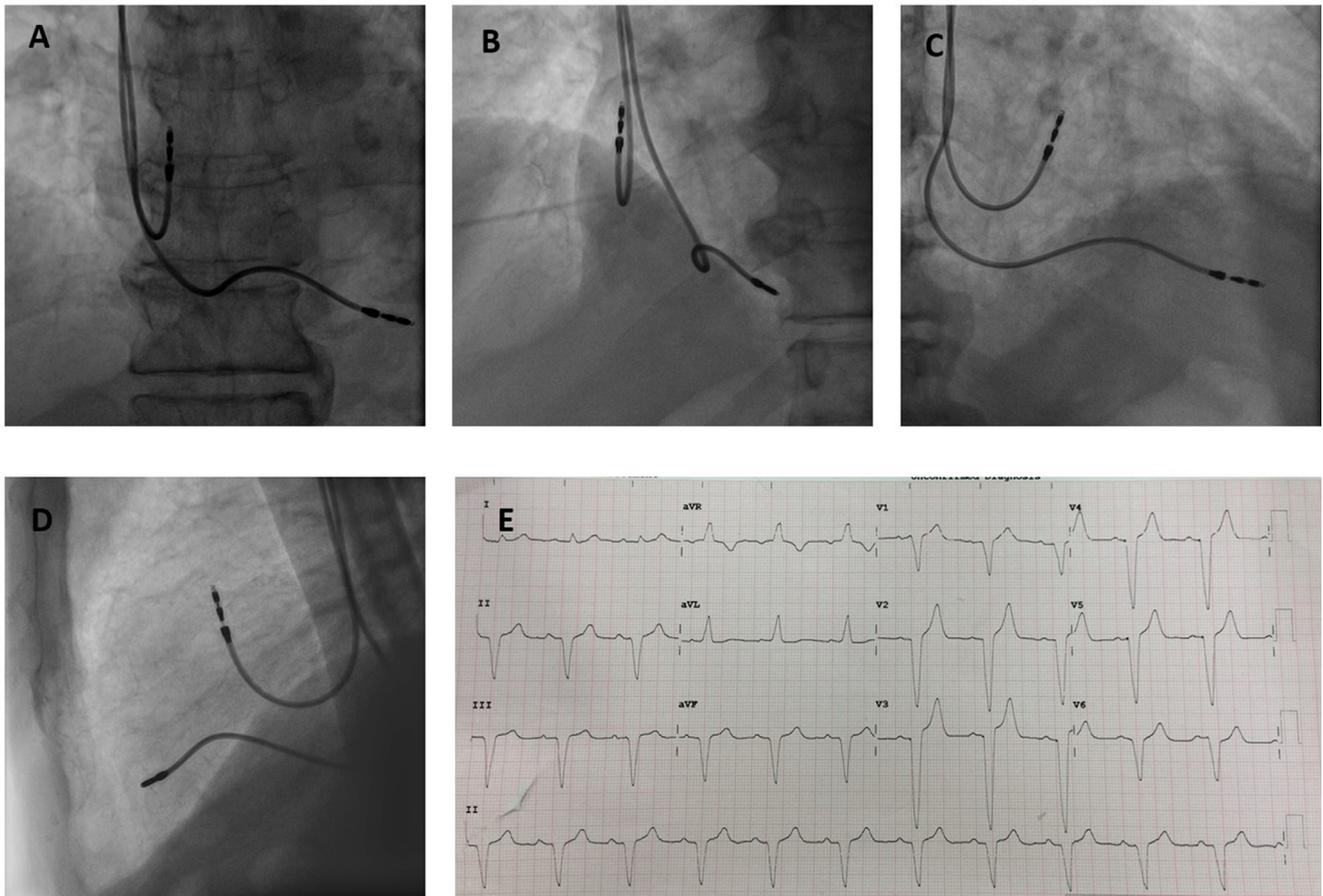


Fig. 2. Anteroposterior (A), 40° Left anterior oblique (B), 30° RAO (C) and left lateral (D) fluoroscopic images showing right ventricular lead tip at apical septum in a patient with dual chamber pacemaker. Twelve lead electrocardiogram of RV apical pacing, ECG showing superior axis with broad pQRS duration of 155 msec (E).

complete heart block (CHB) in 202 patients (80.1%) followed by sick sinus syndrome (SSS) in 16 (6.3%) patients. Type 2 AV Block was present in 13 (5.1%) patients. Other causes were symptomatic (history of syncope or presyncope) bifascicular or trifascicular block or left bundle branch block. Four patients had congenital complete heart block. Two patients had underlying sarcoidosis as the cause of CHB while remaining all were sclerodegenerative CHB. Most common clinical symptom at presentation was syncope in 160 (66.1%) patients.

Pacemaker lead tip was most commonly implanted at apical septum in 135 patients (Fig. 2, Supplementary video 1), followed by high septal or right ventricular outflow septum in 54 patients. (Fig. 3, Supplementary video 2). Forty-nine patients had lead tip at RV mid septum. (Fig. 4, Supplementary video 3). Lateral view plays a significant role in confirming true septal pacing at RVOT. Fourteen patients were in others group which included RV inferior wall, free wall, (Supplementary video 4), coronary sinus (2 patients) and RVOT free wall. Mean pQRS duration was significantly higher in apical septum with a mean of 148.9 ± 14.8 ms compared to mid septal (p-value 0.003) and RVOT septum (p-value 0.002) group, respectively. There was no difference between mid septal and RVOT septal with pQRS duration of 139.6 ± 19.9 ms and 139.6 ± 14.8 ms, respectively (Table 4). Female gender [OR 2.44 (1.22–4.76)], baseline QRS duration [OR 0.97 (0.96–0.99)] and RVOT septal pacing [5.89 (2.03–17.01)] predicted pQRS duration less than 150 msec in multivariate analysis (Table 5).

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.ipej.2018.08.001>.

Single chamber pacemaker was implanted in 124 (49.2%) patients. Dual chamber pacemaker was implanted in the remaining 128 (50.8%) patients. Magnetic resonance imaging (MRI) compatible pacemaker was implanted in 86 (34.1%) patients. There were three deaths in study cohort which occurred within 30 days of pacemaker implantation. Two patients died in hospital of ventricular fibrillation and one patient died of sepsis. Three patients developed pericardial effusion and one developed pericardial tamponade requiring pigtail drainage. All of these patients had lead in apical position. One patient developed pneumothorax requiring intercostal chest drain insertion. There was no incidence of pacemaker lead dislodgement.

4. Discussion

The problem with conventional RV apex pacing is that the impulse is conducted from the apex to the base of the heart and from the right to the left ventricle and hence the time for the conduction in the ventricles is prolonged. Earlier tying leads were available, which can be placed at RV apex only but now with the advent of screw in leads, alternate pacing sites are an option besides the routine apical pacing site. Apical pacing causes increased dyssynchrony [6] and hence the risk of ventricular dysfunction and atrial fibrillation [7]. The septal areas, mid-right ventricular (RV) septum and RV outflow tract (RVOT), have been proposed as alternative pacing sites to RV apical pacing, theoretically leading to a more physiologic electrical conduction to the left ventricle (LV) and therefore to a more physiologic contraction. Frequent problem

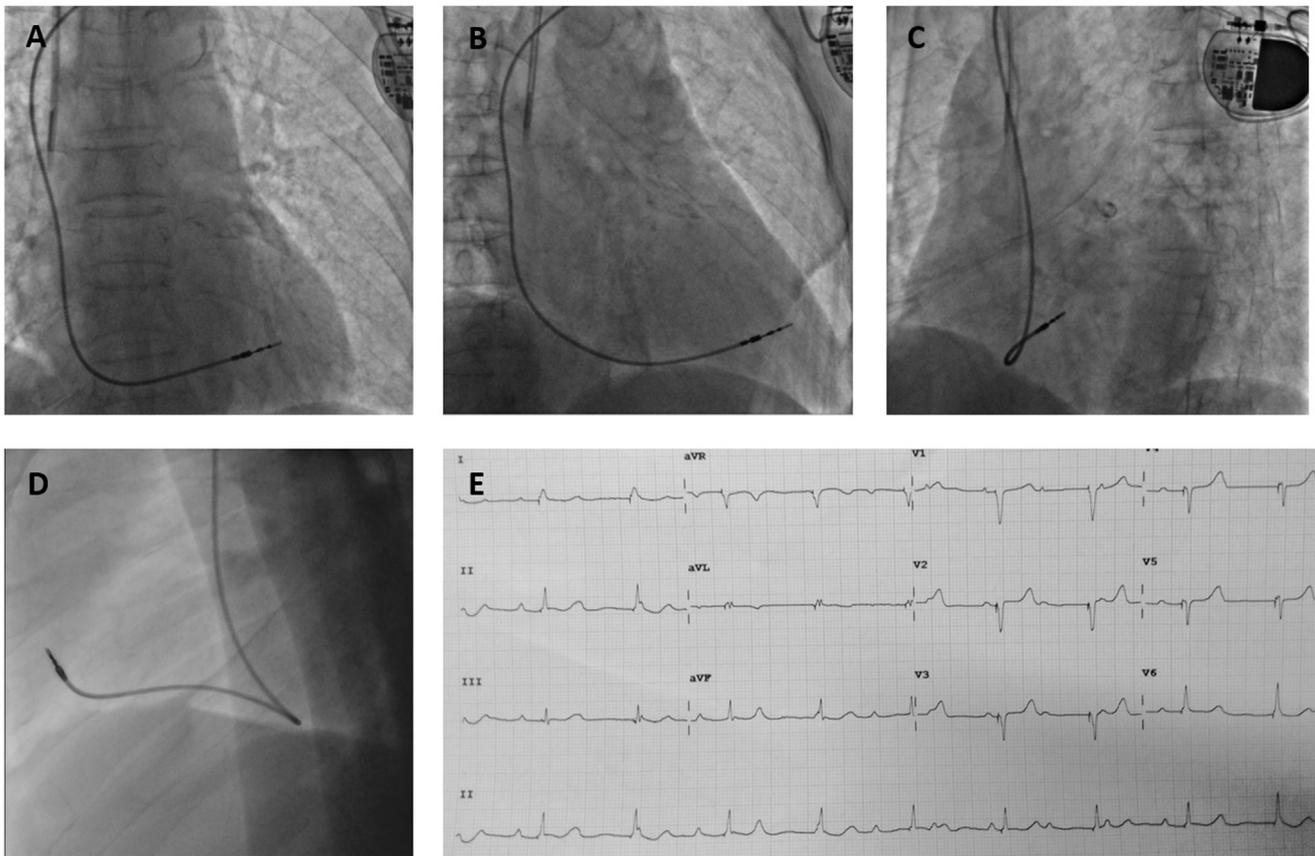


Fig. 3. Anteroposterior (A), 40° left anterior oblique (B), 30° RAO (C) and left lateral (D) fluoroscopic images showing right ventricular lead tip at mid septum in a patient with single chamber pacemaker. Twelve lead electrocardiogram of mid septal pacing showing narrow pQRS duration of 94 msec and normal axis (E).

encountered during placement of lead at mid and RVOT septum is the placement of lead at RV anterior wall and RVOT free wall which is difficult to diagnose on basis of standard fluoroscopic and chest X rays.

Data from various large resynchronization therapy studies [8] proves that QRS duration is the most important marker of dyssynchrony. Paced QRS duration, a good marker of ventricular dyssynchrony while pacing, has been accepted as a valuable predictor of this adverse effect. Paced QRS duration reflects homogenization of contraction and is a surrogate marker of dyssynchrony of LV contraction.

Most commonly pacemaker tip was implanted in apical group in our study group constituting more than half (53.5%) of patients. It shows that apical septum is still a preferable pacemaker implantation site. Possible causes being difficulty to put pacing lead in true septal position in mid septum or RVOT septum, ease of lead implantation at apex and lead stability achieved at apex. Poor threshold at non-apical sites and physician's expertise are other factors for preferring apical pacing. RVOT and mid septum were next common sites. Fourteen patients did not have pacemaker implanted at septal position on basis of fluoroscopic images. Lead tip was in RV anterior wall or RVOT free wall or coronary sinus tributaries in these patients. These patients had broader pQRS duration of 146.7 ± 12.3 msec. Implantation at these sites is risky due to increased risk of tamponade [9], damage to left anterior descending artery [10] and poor pacing parameters on long term follow up. Hence all four recommended views should be done during implantation to avoid pacing at other than true septal position. However, in a recently published study Matthew Rowe et al.

showed in a small number of patients that surface ECG and fluoroscopy are not predictive of right ventricular septal lead position compared to cardiac computed tomography [11].

In our study, pQRS duration was statistically significantly higher (148.9 ± 14.8 msec) in apical group versus mid septal (139.6 ± 19.9 msec) or RVOT (139.6 ± 14.8 msec) site. There was no significant difference in pQRS duration between RVOT septum and mid septum group in our study. Short-term studies have found significant differences in hemodynamic parameters in favor of the RVOT [12]. One study, however, reported only insignificant positive hemodynamic changes [13] and other showed insignificant differences in functional performance in favor of the RVOT [14]. Recent few studies have shown mid septal as the site with narrowest QRS duration. In a study done by Satoru Yusu et al. [4], the mean QRS duration was significantly lower in selective site pacing from the RV mid septum compared to RV apical pacing (123 ± 16 msec versus $150 \pm$ msec, $P < 0.0001$). It was found that selective site pacing from RV mid – septum was feasible and results in less conduction delay compared to conventional RV apical pacing. In a recent study, RVOT pacing when compared to apical pacing is associated with shorter pQRS duration and preservation of left ventricular function on follow up at 12 months [15]. Optimization of the pacing site on the RV septum by achieving maximum shortening of the original duration of paced QRS from the RVA led to improved LV function. The positive effect correlated with reduction of the duration of the QRS complex [3]. In contrast, prolonged paced QRS duration in RVA pacing predicted the development of heart failure [16]. There are few studies which have compared RV mid septal pacing versus RVOT pacing. In a small study of seventeen patients, there were no

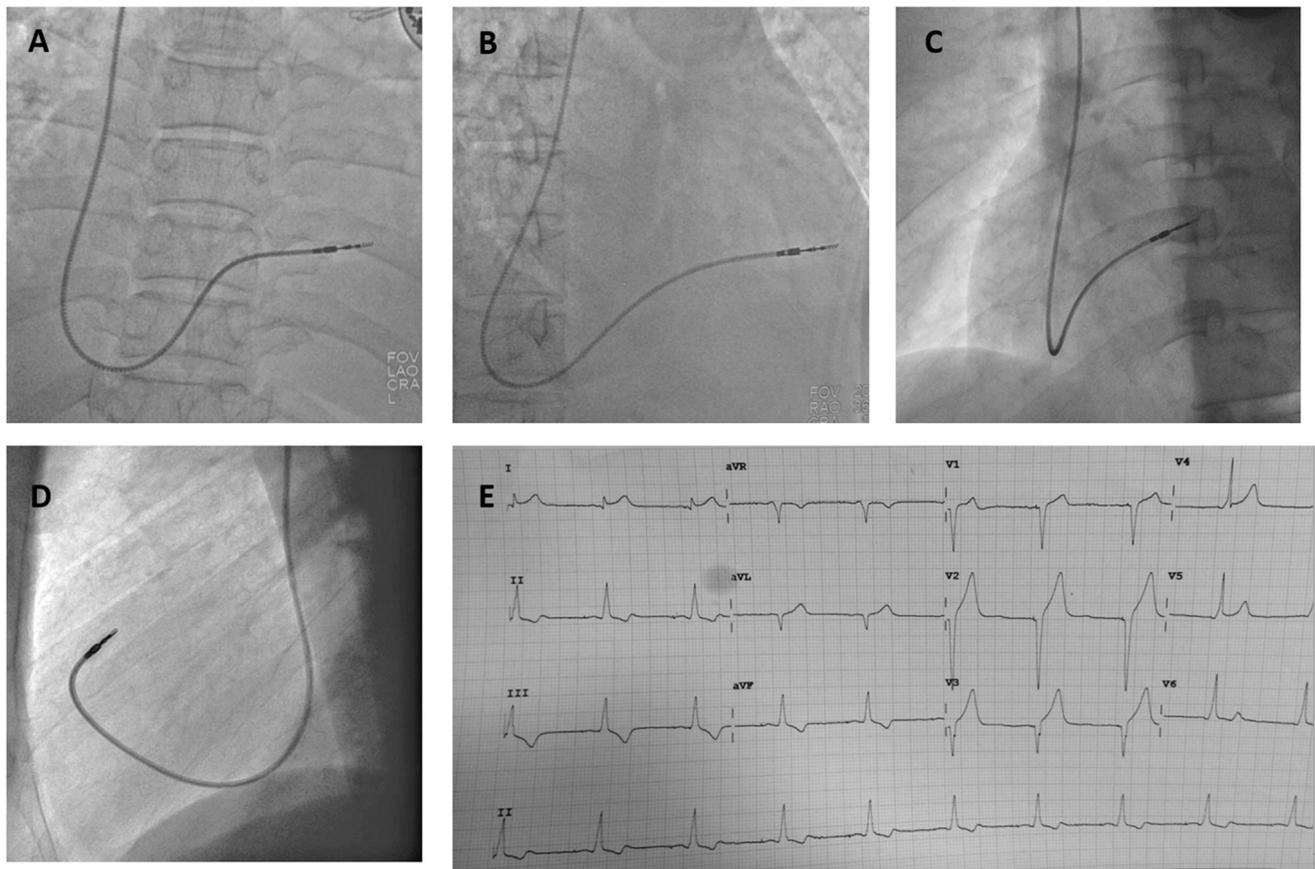


Fig. 4. Anteroposterior (A), 40° Left anterior oblique (B), 30° RAO (C) and left lateral (D) fluoroscopic images showing lead tip at RVOT septum in a patient with single chamber pacemaker. In left lateral position lead tip is being seen at posterior orientation confirmed it to be on the true RVOT septum. Twelve lead electrocardiogram of RVOT pacing showing inferior axis with narrow pQRS duration of 102 msec (E).

Table 4
Mean Paced QRS duration post implantation according to site.

Group	Number of Patients n (%)	pQRS duration (sec) Mean \pm SD	p value	p value	p value
1. Apical septum	135 (53.5%)	148.9 \pm 14.8	Gr 1 vs Gr2 0.003	Gr 1 vs Gr3 0.002	Gr 1 vs Gr4 1
2. Mid septum ¹	49 (19.4%)	139.6 \pm 19.9		Gr 2 vs Gr 3 1.0	Gr 2 vs Gr4 0.8
3. RVOT septum ¹	54 (21.4%)	139.6 \pm 14.8			Gr 3 vs Gr4 0.8
4. Others	14 (5.5%)	146.7 \pm 12.3			

RVOT: right ventricular outflow tract; 1 Group 1 vs Group 2 and 3 (combined) had p value < 0.001.

Table 5
Predictors of paced QRS duration <150 msec using multivariate logistic regression model.

Variables	Odds ration (95% CI)	p value
Female gender	2.4 (1.24–4.76)	0.006
LV Function	1.02 (0.99–1.05)	0.06
Baseline QRS duration	0.97 (0.96–0.99)	0.001
RVOT Septal pacing	5.89 (2.03–17.01)	0.04

RVOT: right ventricular outflow tract.

significant differences in mean pQRS duration between the two sites [17]. The QRS duration in the RVOT septum was 151 \pm 14 msec and in the mid-RV septum 145 \pm 13 msec (P = 0.150). In another study of 50 patients, the right ventricle was arbitrarily divided into 5 sites, high and low right ventricular outflow tract, mid septum, low septum, and apex. pQRS duration was 162 \pm 20 ms during high

right ventricular outflow tract pacing, 143 \pm 17 ms during low right ventricular outflow tract pacing, 151 \pm 20 msec during mid-septal pacing [18]. In our study both mid septal and RVOT septum had similar pQRS duration, which were lesser than other published studies in literature. The factors responsible for a narrower pQRS duration were female gender, baseline QRS duration and RVOT septal pacing. Hence, authors would suggest RVOT septal pacing as the preferred site for pacing during pacemaker implantation. Achievement of narrower pQRS duration becomes more significant in patients with known LV dysfunction prior as these patients are more likely to develop LV dysfunction on long term follow up.

We divided the study cohort into two groups on basis of pQRS duration of more than 150 and less than 150 msec as described in methods. Baseline characteristics were similar between the two groups with respect to the presence of predisposing cardiac disease like hypertension, coronary artery disease, diabetes mellitus,

baseline QRS duration and LV function. Narrower pQRS duration (<150 msec) was associated with female gender, younger age, baseline LV function and baseline QRS duration in univariate analysis. However, in multivariate analysis, only female gender and baseline QRS duration predicted narrower pQRS duration (<150 msec). Male gender as a predictor of higher pQRS duration was also shown by Qiao Q et al. [19] in a cohort of 170 patients who had undergone apical pacing only. In the same study, preimplant left ventricular end-diastolic dimension (LVEDD) and body weight were found to be independently associated with the paced QRS duration. Similarly, in a study of heart failure patients, male gender was predictor of higher QRS duration [20].

We subdivided the pQRS duration <150 msec in two groups with pQRS duration less than 120 msec as one group. pQRS duration ≤120 msec was seen in 12 patients. Seven patients were in mid septal group, 4 were in RVOT septum and one patient was in apical group. However, it was not statistically different between RVOT septal vs mid septal pacing ($p = 0.53$). His bundle pacing is rapidly emerging as the most physiological mode of pacing and has shown to be superior in a recent metaanalysis [21]. However, higher pacing thresholds, operator expertise, increased fluoroscopic time and potential for lead dislocation are the problem area with this mode of pacing.

This study had few limitations. Firstly, no data was kept of pacing parameters such as pacing threshold, impedance and sensitivity. Secondly, patients having postoperative CHB were included in the study cohort. These patients are more likely to be having LV dysfunction in the perioperative period and prolonged pQRS duration. Thirdly, patients of sarcoidosis and HCM were also included. These diseases can itself affect QRS duration and axis. Fourthly, as the pacing site during implantation was left on operator discretion, there were more patients in the apical group compared to other two groups. Finally, long-term outcomes such as QRS duration and LVEF over time were not studied.

5. Conclusion

Female gender, baseline QRS duration and RVOT septal pacing were the only predictor for a narrow pQRS duration (<150 msec). Both RV mid septal and RVOT septal pacing are associated with lower pQRS duration as compared with apical pacing. Follow up studies are needed to determine the best pacing site and importance of paced QRS duration.

Author contributions

NP and AG had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. They also contributed to study conception and design, analysis and interpretation of data. RB contributed to study conception and design, analysis and interpretation of data. SKV, AR, GS, RY, NN and VKB contributed to study conception and design. RJ contributed to study conception and design, analysis and interpretation of data. All authors participated in writing the paper and all approved the final manuscript.

Conflicts of interest

None to declare.

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