

Right Apical, Biventricular and Right High Septal Ventricular Pacing: A Comparison of Procedural Burden and Long Term Electrical Performance

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Abstract

Background/Aims: It has previously been shown that permanent right ventricular (RV) apical pacing may lead to worsening of cardiac function due to associated electrical and mechanical dyssynchrony. Cardiac resynchronization therapy (CRT) or high septal RV pacing could be beneficial to prevent patients from these negative effects.

Methods/Results: In this single center clinical study 164 patients with permanent ventricular pacing indication, but without CRT indication, were assigned to three groups based on pacing location: RV apical pacing (RV apical; n=62), biventricular pacing (BiV; n=60) and RV high septal pacing (RV septal; n=42). Study objectives were procedural burden (procedure and fluoroscopy time) and electrical lead performance over two years follow up.

The BiV-group had the longest implant duration (64.9 ± 0.3 min) and fluoroscopy time (13.8 ± 10.9 min; $p < 0.05$ to RV apical and RV septal). The implant duration was similar ($p = ns$) in RV apical (36.0 ± 10.1 min.) and RV septal group (40.1 ± 19.1 min.) as well as fluoroscopy time (4.3 ± 5.5 min vs 4.0 ± 3.6 min; $p = ns$).

Acute RV septal sensing was lower [7.8 ± 3.4 mV vs 17.5 ± 20.8 mV (RV apical) and 14.2 ± 7.1 mV (BiV), $p < 0.05$], RV-pacing thresholds were higher (0.7 ± 0.3 V/0.5 ms vs 0.5 ± 0.2 V/0.5 ms and 0.4 ± 0.1 V/0.5 ms, $p < 0.05$) and pacing impedance was lower ($555 \pm 73 \Omega$ vs $774 \pm 169 \Omega$ and $821 \pm 178 \Omega$, $p < 0.05$). This difference maintains during long-term follow-up.

Conclusions: High septal placement of RV pacing leads creates no additional procedural burden for patients and despite slightly worse electrical performance overall, maintains acceptable performance over the long term. Considering the potential for adverse outcomes from RV apical pacing and the risks associated with CRT, we suggest that RV septal placement may be considered for patients with permanent ventricular pacing requirement.

Keywords: Right ventricular high septal pacing, Right ventricular apical pacing, Pacing induced dyssynchrony, Cardiac resynchronization therapy, Selected site pacing

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Introduction

Independent of permanent pacing indication, a ventricular pacing lead is currently included in 99.5% of all pacemaker implantations [1]. Published data from the DANPACE trial [2] and

technical advancements in device algorithms designed to prevent unnecessary ventricular pacing, are likely the major reasons for this. The right ventricular (RV) apex remains the preferred implant site for endocardial transvenous ventricular leads due to ease of placement, electrical stability, reliability, and lead design. It has

been documented however that RV apical pacing can induce non physiologic ventricular activation patterns [3] resulting in dyssynchrony. Prolonged dyssynchrony has a negative impact on systolic and diastolic function, resulting in a higher risk for heart failure hospitalization and a negative impact on long term outcome [3,4]. In patients requiring ventricular pacing, alternative RV pacing sites (e.g. RV outflow tract [5], ventricular septum [6] and HIS-Bundle [7]), biventricular (BiV) pacing modes [8,9] and isolated left ventricular (LV) pacing [10,11] have been investigated in an attempt to reduce pacing-induced dyssynchrony. High septal ventricular pacing appears to be the most promising configuration of these alternative pacing sites [11]. This study was designed to investigate the procedural burden, implant feasibility and acute and chronic electrical performance of high septal pacing when compared to standard RV apical and BiV pacing.

Methods

Patient cohorts

The study was a single center clinical study designed to evaluate patient outcome over two years of follow up (including procedure, hospital discharge, 6-, 12- and 24 month follow ups). It investigated the procedural burden (defined as average implant procedure and fluoroscopy times) and feasibility (defined as implant success) of three different ventricular lead pacing sites- RV apical pacing (RV apical), biventricular pacing (BiV) and high septal pacing (RV septal). Eligible patients were those with a permanent pacemaker indication anticipated to require a high rate of RV pacing, but without an indication for CRT. The study was approved by the Institutional Ethics Committee and patients were enrolled to the study after written informed consent has been provided.

RV apical and BiV patients were prospectively randomized to their pacing modes via their participation in the BIOPACE trial [8]. Following the completion of the BIOPACE trial, a third, consecutive patient cohort meeting the same inclusion criteria and following the same follow-up schedule, was enrolled and included as the RV septal group. Patients were included over a period of 5.5 years.

Implant procedure

In patients with long lasting persistent atrial fibrillation a pacemaker without an atrial lead was implanted (bradyarrhythmia, **Table 1**). For all other patients a dual chamber or CRT pacemaker was implanted depending on randomization. The Identity ADx; Victory, Frontier I and II pacemaker models were implanted (St. Jude Medical, St. Paul, Minnesota, USA) with either an active fixation RV pacing lead in the RV septal group (Tendril, St Jude Medical), a passive fixation lead in the RV apical and BiV group (Isoflex, St Jude Medical) and a coronary sinus (CS) lead for the BiV group (Quicksite, St Jude Medical).

If needed, a steerable stylet (Locator, St. Jude Medical) was utilized to reach the parahisian ventricular septum in selected cases. Correct high septal lead placement in the RV septal group was confirmed by fluoroscopy in an angulated projection (left anterior oblique, **Figure 1**) in combination with standard electrocardiogram (ECG) configuration testing [12]. A similar

method was used to ensure a posterolateral CS lead position in the BiV group.

Study endpoints

The primary objective of this study was to evaluate the procedural burden associated with ventricular lead implantation for the three groups. Burden was defined as average implant duration (including implantation of all system-required leads and the pacemaker) and total fluoroscopy time required for successful implantation. The secondary endpoints were feasibility (defined as implant success) and acute and chronic electrical performance of the RV leads (average pacing and sensing thresholds and pacing impedance).

Statistics

Categorical variables are presented as absolute numbers and percentages and are compared by Chi Square test. Continuous variables are expressed as means \pm standard deviation or medians with interquartile ranges and are compared using a Kruskal-Wallis test or Wilcoxon test. In the case of multiple pair comparisons, Bonferroni correction was performed.

Results

Baseline characteristics

During a period of 5.5 years, 164 patients with a preserved ejection fraction (mean $56 \pm 13\%$) and a permanent pacemaker but without CRT indication were included in the study (**Table 1**). 68.9% of the patients were male ($n=113$) with a mean age of 74 ± 9.3 years. Randomization procedure assigned 62 patients to the RV apical group (38%) and 60 to the BiV group (37%). In addition 42 consecutive patients were subsequently enrolled to the RV septal group (26%). Baseline characteristics were similar between groups and there were no significant differences in comorbidities (**Table 1**).

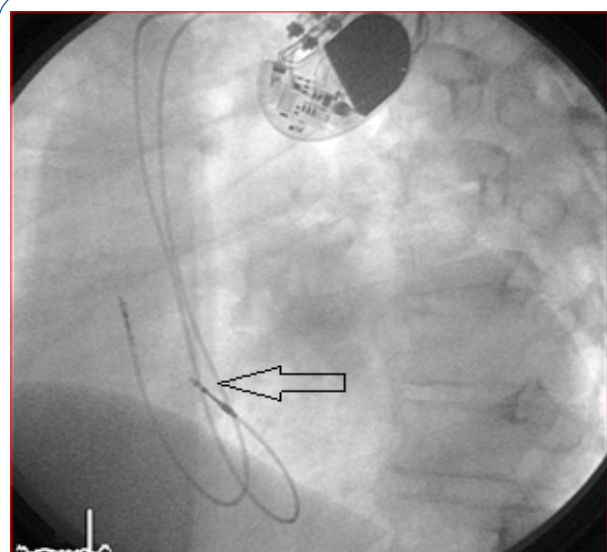


Figure 1 Implantation of the RV septal lead. Fluoroscopy during implantation (LAO 60°): high septal ventricular lead (black arrow).

Acute procedural implant data

All enrolled patients were successfully implanted with the appropriate pacing system according to allocated groups leading to 100% implant success (feasibility).

Mean implant duration for the BiV group was significantly longer than for both the RV apical group and RV septal group ($p < 0.001$). The mean implantation duration for the BiV pacing system was 65 ± 30 minutes [(min), median 50 min.] compared to 40 ± 19 min (median 38 min) for the conventional pacemaker system implantation in the RV apical group and 36 ± 10 min (median 35 min) for the RV septal pacemaker implant.

Similar to the implant duration results, the average total fluoroscopy exposure during implantation was significantly shorter in the RV apical group (4.3 ± 5.5 min; median 2.5 min) and the RV septal group (4.0 ± 3.6 min; median 3.4 min) than in the BiV group (13.8 ± 10.9 min; median 10.2 min, $p = 0.05$). Importantly, the overall procedure burden (implantation duration and fluoroscopy exposure) was not different for the placement of an RV septal lead vs an RV apical lead ($p = ns$).

Table 1 Pacing indications and comorbidities.

	RVapical group	BiV group	RVseptal group
Pacing Indication			
Bradyarrhythmia	n=9 (15%)	n=11 (18%)	n=0 (0%)
Binodal disease	n=20 (32%)	n=10 (17%)	n=5 (12%)
AV-Block II°	n=11 (18%)	n=14 (23%)	n=29 (69%)
AV-Block III°	n=22 (35%)	n=25 (42%)	n=8 (19%)
Comorbidities			
Coronary artery disease	n=10 (16%)	n=18 (30%)	n=12 (29%)
Dilated cardiomyopathy	n=7 (11%)	n=5 (8%)	n=2 (5%)
Valvulopathy	n=3 (5%)	n=3 (5%)	n=2 (5%)
Hypertension	n=57 (92%)	n=55 (92%)	n=38 (91%)
Renal Disease	n=11 (18%)	n=10 (17%)	n=5 (12%)
Diabetes Mellitus	n=18 (29%)	n=14 (23%)	n=11 (26%)
Stroke	n=0 (0%)	n=2 (3%)	n=3 (7%)

Acute electrical performance

At implantation, the acute electrical performance of sensing, pacing and impedance parameters were acceptable for all three RV leads (**Table 2**) however, there were some minor differences documented between groups. In general, the RV septal leads had significantly lower ventricular sensing than both the RV apical and BiV leads (7.8 ± 3.4 mV vs 17.5 ± 20.8 mV and 14.2 ± 7.1 mV respectively, $p < 0.05$) and higher pacing thresholds (0.7 ± 0.3 V/0.5 ms vs 0.5 ± 0.2 V/0.5 ms and 0.4 ± 0.1 V/0.5 ms respectively $p < 0.05$). In addition, average pacing impedance was lower ($555 \pm 73 \Omega$ vs $774 \pm 169 \Omega$ and $821 \pm 178 \Omega$ $p < 0.05$).

Chronic electrical performance

Electrical performance was tested every 6-months following implantation over a total follow up period of two years (24 ± 1 months). **Table 2** and **Figures 2-4** documents the values recorded at each follow-up over this time for RV leads of each group. In general, electrical performance remained stable for RV apical or RV septal lead location. However, the significant differences in performance of RV leads documented acutely between the RV septal group and the RV apical and BiV groups, persisted.

Clinical outcome

Figure 5 documents the major clinical complications recorded throughout the duration of the trial. A total of 29 major clinical events were documented from 29 individual patients (17.7%). Of these, ten events were device or procedure-related events (6.4%); two in the RV apical group (3.2%); five in the BiV group (8.3%) and three in the RV septal group (7.1%). Only one RV lead related event was observed: Exit block with lead revision in one patient of the septal group.

The majority of other major clinical events were related to atrial fibrillation ($n = 13$) either new onset or chronic, including two patients who required isthmus ablations (one in the BiV group and one in the RV septal group). Two patients were hospitalized for heart failure in the RV apical group (one requiring upgrade

Table 2 Acute and chronic electrical performance (mean \pm standard deviation) for each type of RV lead during follow up (6mFU: 6 month follow up, 12mFU: 12 month follow up; 24mFU: 24 month follow up).

	RV Sensing in mV				
	Implantation	Discharge	6mFU	12mFU	24mFU
RV apical group	17.5 ± 20.8	9.2 ± 3.4	10.2 ± 3.2	10.6 ± 2.9	9.9 ± 3.0
BiV group $p = ns$	14.2 ± 7.1	8.8 ± 3.8	10.0 ± 3.3	9.9 ± 3.7	9.9 ± 3.3
RV septal group	7.8 ± 3.4	6.3 ± 2.8	6.4 ± 3.0	6.7 ± 3.0	6.8 ± 2.8
	RV Pacing Threshold in V/0.5ms				
	Implantation	Discharge	6mFU	12mFU	24mFU
RV apical group	0.5 ± 0.2	0.5 ± 0.3	0.7 ± 0.3	0.6 ± 0.3	0.7 ± 0.3
BiV group $p = ns$	0.4 ± 0.1	0.5 ± 0.3	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.3
RV septal group	0.7 ± 0.3	0.6 ± 0.2	0.9 ± 0.5	0.9 ± 0.4	1.0 ± 0.4
	RV Impedance in Ω				
	Implantation	Discharge	6mFU	12mFU	24mFU
RV apical group	774 ± 169	520 ± 96	495 ± 100	474 ± 101	466 ± 80
BiV group $p = ns$	821 ± 178	580 ± 178	531 ± 136	519 ± 137	510 ± 141
RV septal group	555 ± 73	413 ± 95	383 ± 74	377 ± 70	385 ± 72

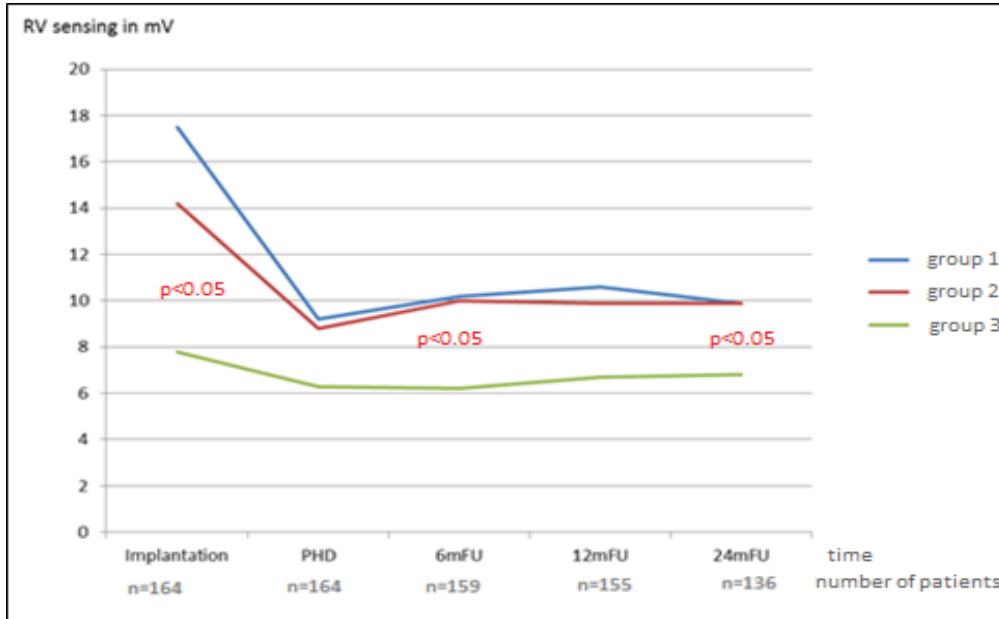


Figure 2 Sensing values of RV lead over the time (PHD: pre home discharge, 6mFu: 6 month follow up, 12mFU: 12 month follow up; 24mFU: 24 month follow up).

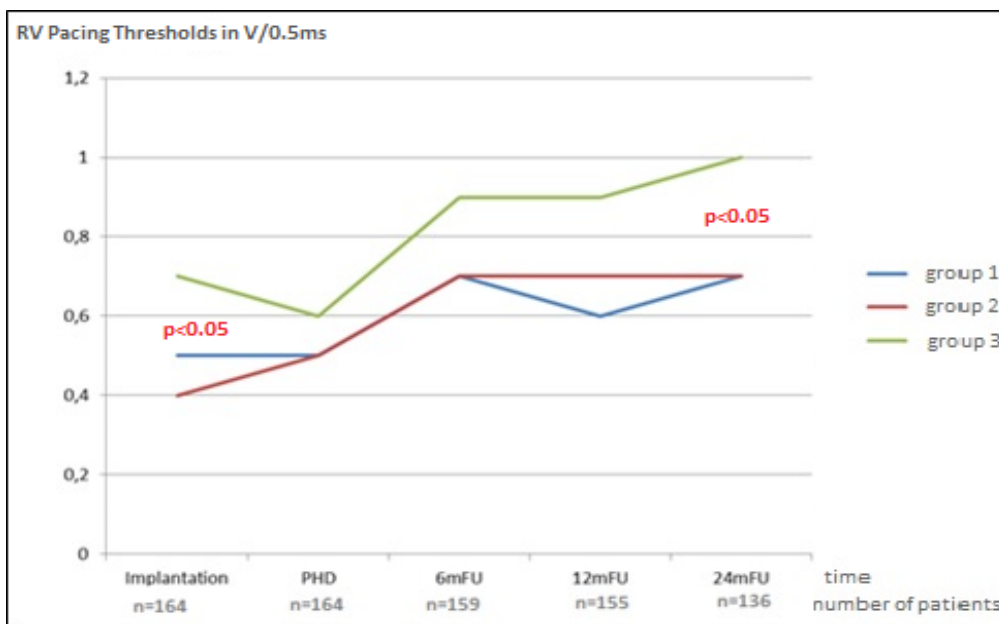


Figure 3 Pacing Thresholds of RV lead over the time (PHD: pre home discharge, 6mFu: 6 month follow up, 12mFU: 12 month follow up; 24mFU: 24 month follow up).

to BiV ICD) while one patient was hospitalized for COPD in the BiV group. One patient in the RV septal group required a valve replacement during follow-up.

A total of nine deaths occurred during follow-up (5.5%) none of which were deemed procedure or device-related. Of the six patients that died in the RV apical group (9.8%) two deaths were attributed to heart failure and four to non-cardiac causes. The remaining three deaths were in the BiV group (5%), one death was related to worsening of chronic heart failure and two to non-cardiac causes.

Discussion

RV apical pacing is known to cause desynchronization of ventricular contraction through the creation of a left bundle branch block-like morphology due to the change in activation of both ventricles. This may lead to impairment of LV function, induction of heart failure [12] and can also induce histological changes [13]. In contrast, CRT therapy with BiV pacing has become the gold standard in patients with heart failure, reduced LV function and left bundle branch block and data suggests that

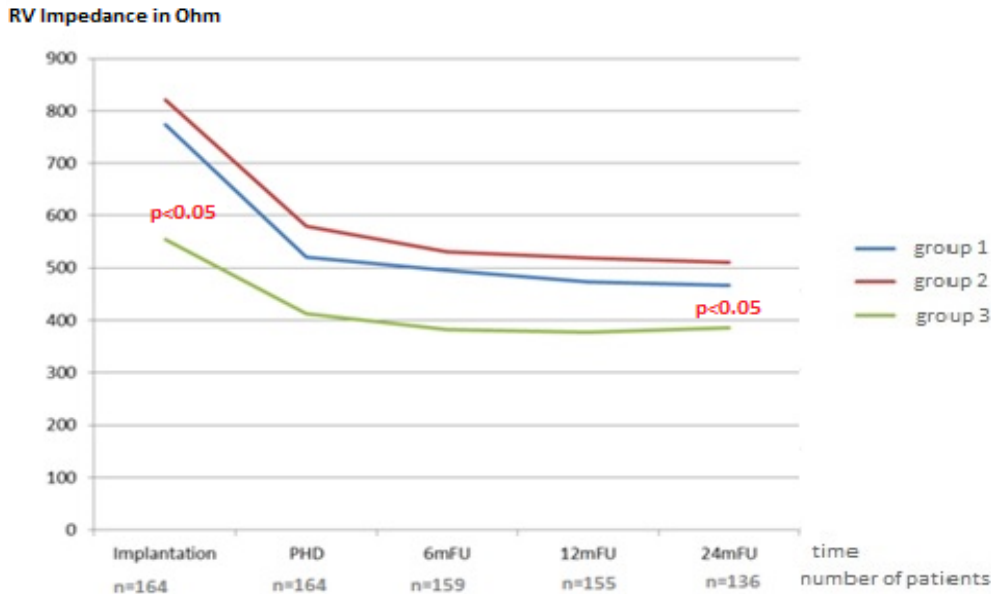


Figure 4 Pacing Impedance of RV lead over the time (PHD: pre home discharge, 6mFu: 6 month follow up, 12mFU: 12 month follow up; 24mFU: 24 month follow up).

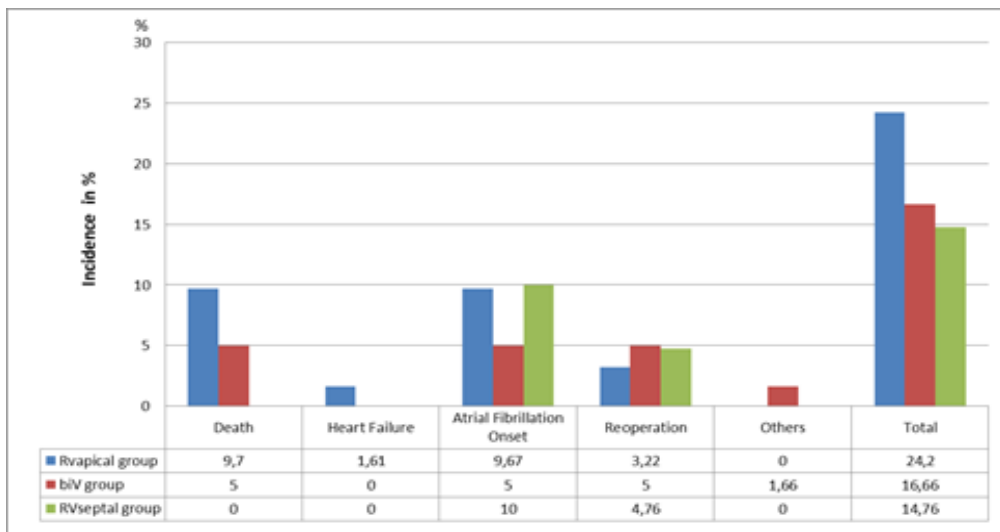


Figure 5 Adverse events during 2 year follow up (% of occurrence).

the wider the bundle branch block the better the response may be to CRT [14]. In patients with atrial fibrillation, it has also been shown that CRT can be beneficial as long as BiV stimulation is delivered sufficiently [14].

The protective effect of CRT on hemodynamic changes remains controversial, especially in patients with preserved LV ejection fraction. Some studies have not demonstrated any benefit of CRT in the prevention of the development of heart failure (PREVENT HF trial; 9) during short term follow up. The superiority of CRT over RV apical pacing in the prevention of the onset of heart failure after two years follow-up has been shown in the Block HF-trial [15]. However, the trial also demonstrated the complexity

associated with implantation of an additional CS lead. In total more than 6% of patients in Block HF could not be successfully implanted with a CS lead, mainly because of difficulties related to CS access. In addition to the implant failure rate, 10.3% of successfully implanted patients had significant problems with the CRT system during follow-up resulting in the need for subsequent system revisions. Over two years of follow up we have also observed that the incidence of system related issues with CRT devices is approximately 15% and even in the BIOPACE trial [8], an implant failure rate of 14.8% was observed for the BiV group. In addition to the high failure to implant rate, for those patients who have a successful implantation, there often is a significantly longer implant duration and higher exposure to

fluoroscopy, increasing risks for both patients and implanters. Finally, in addition to overall increased burden associated with implantation of a CRT system, the costs are substantially higher when compared to conventional systems.

As long as the advantage of CRT in patients with preserved LV function requiring ventricular pacing is not clearly shown, alternatives right ventricular sites should be considered. For these reasons, the current study was designed to evaluate whether RV septal pacing was a feasible alternative to RV apical pacing.

The data demonstrate that high RV septal pacing is feasible and comparable to RV apical pacing with respect to implantation burden when evaluated by average implantation time and fluoroscopy exposure. These similarities also translate into a comparable cost since you are using the same devices and leads and the same implantation effort is needed. While there was a statistically significant difference in both acute and chronic parameters of electrical performance for the RV septal leads when compared to a traditional apical position, it should be remembered that all measured values were in the normal and acceptable range, providing safe and effective ventricular stimulation from a clinical point of view. This is comparable with data using leads with passive fixation mechanism [16]. In addition, the incidence of lead related events was not significantly higher in the RV septal group vs RV apical.

Our findings are generally in line with the Protect Pace study [6], which shows similar results over long term follow up. In contrast to our observation of no difference in implantation burden, the Protect Pace authors did report a significant difference in implant duration and fluoroscopy time between septal and apical RV pacing. In the Protect Pace study, the location of RV septal lead is discussed extensively which likely resulted in the additional implant time. It is our belief that minor variations in septal lead location are not really critical, due to programming the ventricular output twice of the pacing threshold parahisian stimulation will result [7]. Pacing in the RV outflow tract can be avoided through ECG identification and LAO angulated fluoroscopy.

Some studies with longer observation have shown a continuous improvement in LV function [17,18] in RV septal paced patients.

In addition, the processes of remodeling and reverse remodeling are very dynamic and could be observed echocardiographically. RV septal pacing has been shown to induce a change in activation time (strain analysis) but without the appearance of dyssynchrony in contrast to RV apical pacing, where tissue velocity imaging may also document dyssynchrony. An echocardiographic sub-analysis (LV ejection fraction) of the Protect Pace patients demonstrated a worsening in all patients without any overall group effect, the strain analysis showed greater dyssynchrony in the RV apical group [19,20].

However, the time period of two years in our study might be too short to show hemodynamic benefits.

Limitations

One limitation of the study is that the RV septal pacing group was not enrolled at the same time as the RV apical and BiV groups which were included in the BIOPACE study. This could lead to potential differences in patient population however that was limited by using the same inclusion criteria and follow-up protocol. The absence of clinical and echocardiographic data is also a limitation since it could provide additional support to the hypothesis that LV function can be preserved by high septal RV stimulation rather than RV apical stimulation. Due to a short observational time period of two years hemodynamic outcome of this patients could not be measured.

Conclusion

There appears to be no additional implantation burden associated with high septal placement of RV leads and acute and chronic performance is acceptable. Since the disadvantages of RV apical pacing and the risks associated with BiV pacing are well known, we believe that it may be considered to placing the RV leads into the high RV septum in pacemaker dependent patients. Further hemodynamic data is needed to support this statement, particularly in patients with reduced ejection fraction and narrow native QRS complex.

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