

EFFECT OF LEFT BUNDLE BRANCH AREA PACING ON INDICES OF REPOLARIZATION: AN OBSERVATIONAL STUDY

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Post Doctoral fellowship in cardiac electrophysiology

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**SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM**

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**EFFECT OF LEFT BUNDLE BRANCH AREA PACING ON INDICES OF
REPOLARIZATION: AN OBSERVATIONAL STUDY**

A RESEARCH PROJECT SUBMITTED BY

DR.JYOTHI VIJAY M.S

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

POST DOCTORAL FELLOWSHIP IN CARDIAC ELECTROPHYSIOLOGY

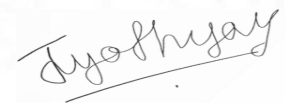
2022

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CERTIFICATE

I, **DR. JYOTHI VIJAY M.S** hereby certify that I had personally carried out the work depicted in the thesis titled, “**EFFECT OF LEFT BUNDLE BRANCH AREA PACING ON INDICES OF REPOLARIZATION: AN OBSERVATIONAL STUDY.**”

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.



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25/11/2022



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was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

*Clearance was obtained from the Institutional Ethics Committee / Institutional Animal Ethics / Institutional Committee for Stem Cell Research / Other appropriate committees (if any, specify) for carrying out the study.

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Dr Jyothi Vijay MS

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SYNOPSIS

**“EFFECT OF LEFT BUNDLE BRANCH AREA PACING ON INDICES
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SYNOPSIS

BY

DR. JYOTHI VIJAY M.S

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SYNOPSIS

Conduction system pacing is the newer method of cardiac pacing where cardiac conduction system is captured instead of plain myocardial capture. Though first attempts in feasibility conduction system pacing came in 1970's, its benefits have been increasingly recognised in the last hemi decade. Initial attempts on conduction system pacing was bundle of His pacing. But due to inherent drawbacks of permanent His bundle pacing there have been introduction of left bundle branch area pacing.

There have been wider applicability of left bundle branch area pacing the last few years. But there is meagre data on this subject from our country. Also, the impact of the left bundle pacing on parameters on indices of cardiac repolarisation is also unknown. This was an observational study primarily on a single centre experience on left bundle pacing and its short term and long-term outcomes. Effect of left bundle branch area of pacing on repolarisation parameters were also looked into.

Of total 70 subjects ,67 who underwent successful left bundle pacing were enrolled in the study.49 patients underwent a left bundle branch area optimized pacemaker compared with 18 cases who underwent a left bundle branch area optimized cardiac resynchronization therapy (LOT CRT). Both left bundle pacing group and LOT-CRT were comparable in terms of age distribution gender, comorbidities, or type of pacing lead used.($p \geq 0.05$)

Comparison of presence and severity of left ventricular dysfunction of subjects according to the type of procedure showed significant difference in cases requiring permanent pacemaker and LOT CRT as more severe cases of LV dysfunction has received CRT.

Mean left bundle capture threshold at implant was 0.7 ± 0.3 volts for LBP group and 0.7 ± 0.2 volts for LOT CRT group. Mean R wave amplitude in millivolts was 11.2 ± 4.3 for LBP and 11.9 ± 5.7 millivolts for LOT CRT group. Mean LV activation time in milliseconds was 67 ± 13.6 milliseconds for LBP group and 79.2 ± 11.9 milliseconds for LOT CRT group.

There was no difference in final paced QRS duration at implant LOT CRT group that LBP group. 116 vs 110.2 milliseconds. There was significant reduction in QT interval both corrected and uncorrected post procedure in comparison to pre procedure values.

Maximum follow up period was 10.7 +/- 8.3 months. LBP maximum follow up period available was 11.2 +/- 8.6 months and LOT CRT was 9.3 +/- 7.3 months.

Correlation of outcomes based on grade of LV dysfunction indicated that stable left bundle capture is more likely preserved long term at maximum follow up in those without LV dysfunction than those with severe LV dysfunction. Those with more severe LV dysfunction got more QRS duration reduction compared to baseline. Selective LB pacing was associated with a lower paced QRS duration at implant. (108.9 vs 120.88 milliseconds)

Conclusion: Left bundle branch area pacing provided narrow QRS which is sustained on short term and long term follow up. It also improves parameters of repolarisation. Short term and long-term pacing outcomes of left bundle branch area pacing from this single centre study appears promising and comparable to results previously reported in literature.

INTRODUCTION

Synchronous contraction of various cardiac chambers are mediated by the propagation of electrical impulse over the cardiac conduction system. Impaired sinus node function and degeneration of the atrioventricular conduction system axis are the major reasons for bradyarrhythmia. This can occur as congenital or in any age. Cardiac pacing has become the procedure of choice for all irreversible and hemodynamically significant bradyarrhythmia. But it has been shown that chronic right ventricular pacing is not physiological nevertheless it has helped save many patients from life-threatening heart blocks

Conduction system pacing is the newer method of cardiac pacing where cardiac conduction system is captured instead of plain myocardial capture. Though first attempts in feasibility conduction system pacing came in 1970's, its benefits have been increasingly recognised in the last hemi decade. Initial attempts on conduction system pacing was bundle of His pacing. But due to inherent drawbacks of permanent His bundle pacing there have been introduction of left bundle branch area pacing.

There have been wider applicability of left bundle branch area pacing the last few years. But there is meagre data on this subject from our country. Also, the impact of the left bundle pacing on parameters on indices of cardiac repolarisation is also unknown.

In this study we plan to make an attempt to identify the various clinical, echocardiographic, electrocardiographic and electrophysiological parameters of patients who undergo left bundle pacing alone or CRT.

LITERATURE REVIEW

Below an attempt is made to briefly review basics and development of conduction system pacing

Anatomy of cardiac conduction system

“Anatomy is to physiology as geography is to history; it describes the theatre of events” - Jean François Fernel (1497-1558)(1)

For understanding any biological process it is imperative to appreciate the structural anatomy with functional architecture.

SA NODE

Sinoatrial(SA) node is the primary pacemaker of the heart. Initially discovered by Keith and Flack(2), sinoatrial node continues to be enigma.

SA node is connected to atrioventricular(AV) node by internodal tracts within the atrial musculature. Right atrium is electrically connected to the lefty atrium by Bachmann bundle enabling interatrial synchrony. Muscular connections at the level of coronary sinus also contribute in interatrial coupling while activation across fossa ovalis is rare.(3)

SA node receives blood supply from the sinus nodal artery which usually travels retro cavally and which originates from the right coronary artery in 68 % of the patients (4)

AV node

After pioneering discovery of sunao Tawara (5)in his monograph "Das Reizleitungssystem des Säugetierherzens" (English: "The Conduction System of the Mammalian Heart") published in 1906,there have been significant growth in our understanding of atrioventricular conduction axis. (6)Tawara compared this arrangement of AV axis to a tree, with its roots in the base of the atrial septum, and its branches straddling the crest of the muscular ventricular septum. (7)This atrioventricular nodal axis is the primary electrical connection of atria and ventricles in the absence of an accessory pathway. Atrioventricular nodal axis consists of atrioventricular node,bundle of his and bundle branches.

The compact AV node is situated in the *triangle of Koch*. It is situated in the lower right atrial septum.

His Bundle penetrates on the atrial aspect of the hinge of the septal leaflet of the tricuspid valve in about half of cases on histological studies.(8) There can be variability in the depth of His bundle from right sided atrial endocardial surface. His bundle consists mainly of Purkinje cell containing few myofibrils and a large perinuclear clear zone.

The theory of longitudinal dissociation in cardiac conduction system was initially proposed by Kaufman. The cells, their orientation and their histologic connections vary across the longitudinal conduction system axis. Inside the His bundle conduction is stratified across the Purkinjean strands separated by collagen. (9) This anatomical separation accounts for the longitudinal separation of conduction in bundle of His.

The term "*sinoventricular conduction*" implies that the individual components of the activation wavefront leaving the sinus node, atrium and A-V node are predestined for specific areas of ventricular myocardium.(10)

The **bundle of His** is composed by two segments: the penetrating and branching portions. In anatomical studies comparing left bundle branch (LBB) of humans with other mammals, humans never exhibited a true bifurcation of bundle of His. LBB originates in the branching portion located underneath the membranous septum.(11)

Proximal LBB anatomy was extremely variable, demonstrating multiple fibre groups which fanned out over the entire left septal surface. Studies have shown that left bundle has three rather than two divisions. Left anterior fascicle is thin and long. Septal fascicle often originates from posterior fascicles.(12)

The terms anterior and posterior hemiblock may be a misnomer as rather than a true anatomical block in condition it represents the relative delay in activation of anterior and posterior left ventricular muscle activation.

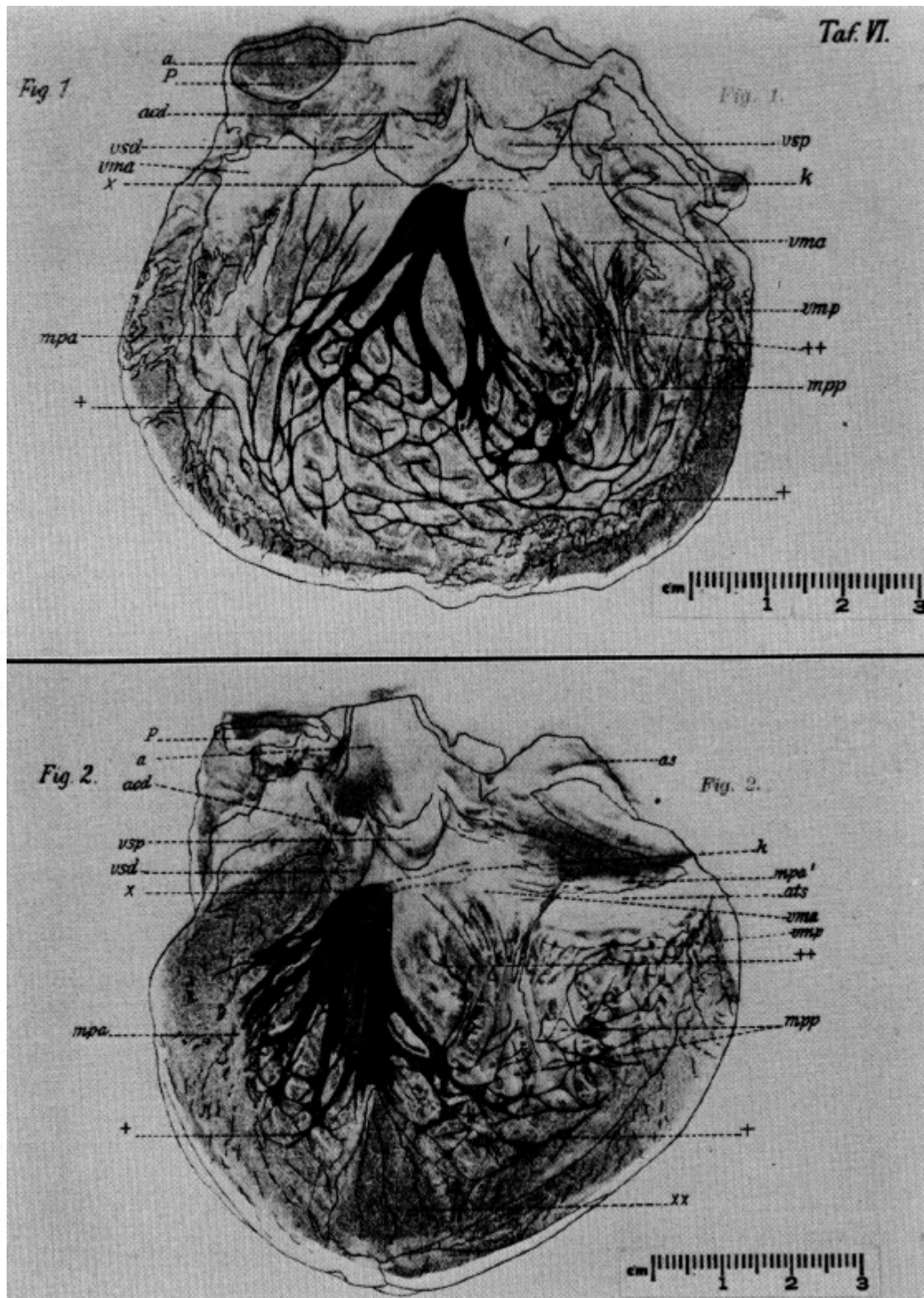


Figure 1: Anatomy of left bundle branch as depicted by sunao Tawara. (5, 12)

Left bundle branch also shows a similar pattern of longitudinal dissociation like His bundle for the initial few millimetres however there are more crossovers and

interconnections distally. Whereas right bundle branch is a thin sheet of interconnecting cells and does not elicit longitudinal dissociation.(13) This effective partition of longitudinal conduction of His and left bundle is not there in right bundle. Focal lesions of his results only in focal lesion of LV electrical activity. It also implies that these lesions remain focal and helps recruiting other fibres for pacing

Right bundle branch is thin chord like structure after exiting from septum near base of right medical papillary muscle and courses in the moderator band to further arborise as Purkinje fibres in the right ventricle.

Conduction system pacing; Historical perspectives

A new signal and a new classification!

Onkar S Narula(14) in his landmark paper provide evidence for longitudinal dissociation of fibres in His. This implies that a focal lesion in bundle of His can result in bundle branch block pattern and/or axis deviation. BH stimulation distal to the lesion due to synchronous impulse conduction to both the bundle branches resulted in narrow QRS complexes. In this 1977 paper only it was demonstrated that pacing distally in his can produce narrower QRS complexes during electrophysiological study providing very early evidence of his bundle pacing. Earlier in 1971 landmark paper from OS Narula, importance of His bundle recording and a new system classifying AV block has been proposed. This helped in our understanding of atrioventricular blocks beyond surface electrogram.(15)

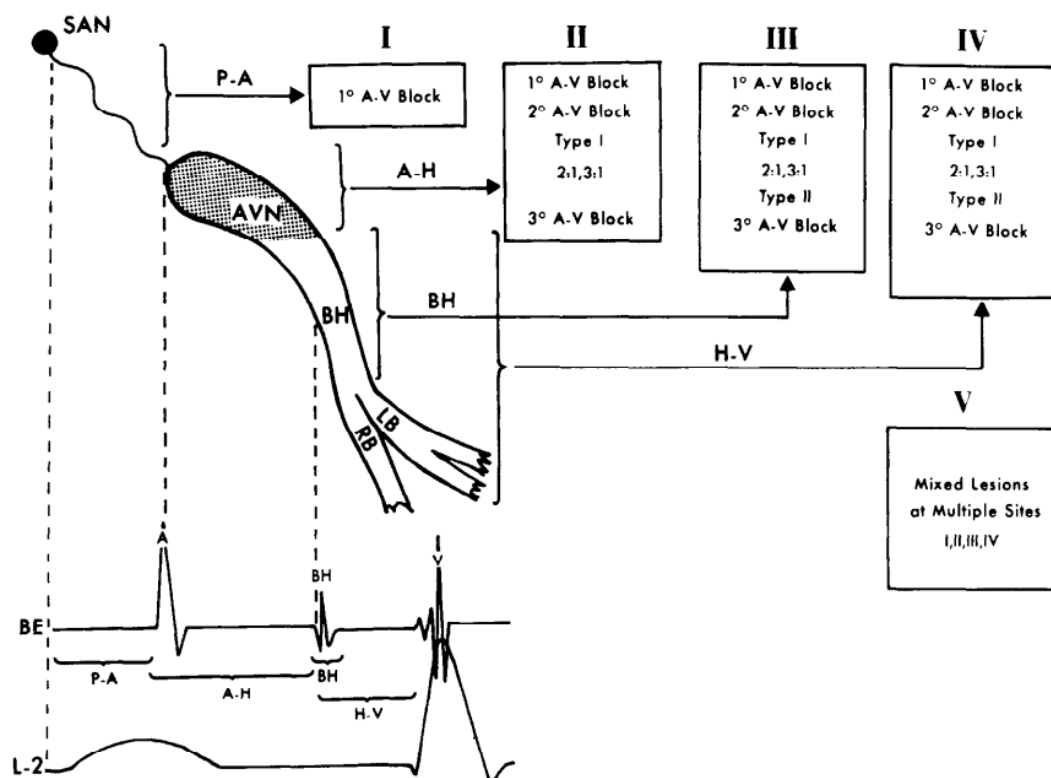


Figure 2: Diagrammatic representation from the landmark paper of OS Narula(1971) regarding importance of His recordings in understanding of AV conduction system(15)

Identifying shortcomings of RV apical pacing

Earlier in 1925, Wigger has shown that artificial pacing stimulus applied to ventricular musculature produce asynchronous activation of ventricles compared to synchronous activation over the cardiac conduction system.(16)

In canine experiments end-diastolic volume varied significantly among pacing sites tested, with right ventricular apical pacing producing the smallest end-diastolic and stroke volume.(17) Chronic RV apical pacing can cause histologic changes as well. In a study of 12 canine hearts, after 3 months of pacing of RV apex at 70 bpm, myofibrillar disarray was observed in 9 out of 12 hearts.

A study comparing left ventricular performance in young hearts during pacing from various sites showed better performance with septal pacing compared to RV apical pacing. Acute alterations in cardiac index, LV pressure, and contraction indices were measured at rest and exercise in young and a significant decrease in contraction indices and increase in LV end-diastolic pressure was noted with apical pacing.

Septal pacing in spite of loss of any atrial contribution to ventricular filling, maintained LV performance indices(18).

In a randomized comparison of permanent septal versus apical right ventricular pacing, In contrast to RV apical pacing, chronic RV septal pacing preserved LVEF in patients with baseline LVEF $\leq 45\%$.(19)

Initial Attempts at conduction system pacing

Pramod Deshmukh et al (20) demonstrated the feasibility of permanent direct his bundle pacing using an active fixation lead in selected patients with chronic atrial fibrillation and dilated cardiomyopathy. There was improvement in dimensions and heart failure on follow up.

His Bundle Pacing

Moving forward from the initial terminology like Hisian and parahisian pacing, terms selective and non-selective HBP (S- and NS-HBP, respectively) are preferred nowadays. S HBP results in capture of the His bundle alone while NS-HBP has capture of surrounding myocardium also.(21)

After obtaining a suitable His signal, appropriate EGM and ECG characteristics during pacing can confirm the suitability of the location for fixation. The C315 His sheath has got a primary curve that direct leads towards tricuspid annulus anteriorly and a secondary curve to reach the interventricular septum Then lead is slowly manually rotated (typically five). The screw penetrates the fibrous capsule of the His bundle, the conduction system fibres within the His bundle can be captured at relatively low thresholds. (21)His bundle pacing has drawbacks of higher threshold, concerns of battery life, higher learning curve led to more ubiquitous left bundle branch area pacing

Left bundle area pacing current concepts and evidence

In 2017 Huang demonstrated for the first time feasibility of pacing the left bundle branch (LBB) immediately beyond the conduction block to achieve a narrow QRS and improve heart failure symptoms. (22)

LBBP requires multiple rapid rotations of the lead through the IVS. Close watch for template beats, M beats should be taken. Periodic checking of the paced QRS characteristics and of lead impedance should be performed intermittently to confirm LBB capture.(21)

Jastrzębski et al(23) published a novel technique for confirming left bundle capture in patients undergoing pacemaker implantation by programmed stimulation delivered from the lead implanted in a deep septal position. In this article responses were categorised as observed during LB stimulation as follows

Table 1 Types of response by programmed stimulation

Type of response	Description
Type 1 ("myocardial,")	change of paced QRS into a morphology of myocardial-only paced QRS, broader, often slur/notch/plateau and/or with obvious change in amplitude/polarity in several leads.
Type 2 (Selective LBB)	selective QRS of RBBB morphology preceded by a latency interval
Nondiagnostic response	progressive QRS prolongation and only minor amplitude change

Continuous pace mapping while screwing-in can help in the identification of the QRS transition from a myocardial septal pacing to a ns-LBB QRS to selective .(24)

Fixation beats or premature ventricular beats (template beat)-guided lead deployment can further aid identifying the capture of LBB. These beats are thought to be generated from the Purkinje fibers due to mechanical trauma by the pacing lead as it rotates rapidly into the left bundle area.(25, 26)

Huang and colleagues demonstrated 97% success rate in LBBP for nonischemic cardiomyopathy and LBBB along with significant improvement in LV ejection fraction at 1 year. In their study LVEF had normalized ($\geq 50\%$) in 75% of patients at 1 year.(27)

There are case reports of Significant reduction in fluoroscopy time and radiation dose was achieved by electroanatomic mapping guided LBBP.(28)

AIMS AND OBJECTIVES

Hypothesis

Left bundle pacing improves parameter of repolarisation in electrocardiogram post implant compared to pre implantation.

Primary objective

- To evaluate the indices of repolarisation in electrocardiogram post implantation compared to preimplant in patients with conduction system pacing

Secondary objectives

1. To evaluate various clinical, echocardiographic, electrocardiographic and electrophysiological parameters of patients who undergo left bundle pacing alone or left bundle optimised CRT (LOT CRT)
2. To assess stability of pacing parameters on follow up CRT LBB pacing (LOT CRT versus LBB pacing) and to identify any predictors of final pacing parameters outcome.

MATERIALS AND METHODS

Left bundle branch area pacing procedures have been started in SCTIMST from 2019 onwards in line with availability of global evidence. Globally the procedure was started from 2017.

Study Design: Ambispective observational study

Study subjects

Patients who are undergoing the procedure for a clinical indication of left bundle were be taken into this observational study. Consecutive patients who are taken up for conduction system pacing (Left bundle branch area pacing) based on their clinical considerations were enrolled for the study. Data was obtained retrospectively from medical records.

Patients who are undergoing the procedure for a clinical indication of left bundle were be taken into this observational study. No procedure was done for study purpose. Design will be ambispective consisting of patients undergone this procedure from June 1 2019. (Because our institute started doing these procedures from 2019). This is to ensure maximum useful information was obtained from the study regarding the “Chitra experience” and outcomes of the patients in left bundle area pacing.

Data collection procedures

Patient records will be reviewed from the medical records. Baseline patient characteristics (including ECG, echo parameters, functional class) and indication for pacing shall be collected at enrolment. Pacing characteristics (pacing threshold, lead impedance and R wave amplitude, paced ECG pattern, intracardiac EGM

pattern, paced QRS duration, LV activation time, interval from the pacing spike to the beginning of the ECG QRS complex, total procedure time and fluoroscopy time) shall be recorded during implantation. Patients will be reviewed before discharge, at 1 month (usual follow up period of pacemakers in our institute) and 1 year of follow up. Clinical parameters (including ECG, echo parameters, functional class), pacing parameters and complications shall be recorded during follow up. Principal investigator collected the data under the guidance of co-principal investigators using a standard n proforma.

Statistical analysis

Data were entered in MS-Excel and analysed in SPSS V25. Descriptive statistics were represented with percentages for qualitative data, Mean with SD or Median with IQR for quantitative data. Shapiro wilk test was applied to find normality. Chi-square test, Fisher Exact test were applied for comparison of proportions.

Independent t-test, Man-whitney U test were applied for comparison between means and medians, Paired t-test, Wilcoxon test were calculated to compare paired samples. Karl pearson correlation and spearman correlation were applied. $P < 0.05$ was considered as statistically significant.

RESULTS

Following are the results in this study.

There were 70 cases during this time period where left bundle pacing/LOT CRT was attempted. Of the total 67 patients who underwent successful left bundle pacing were enrolled in the study, 49 patients underwent a left bundle branch area optimized pacemaker compared with 18 cases who underwent a left bundle branch area optimized cardiac resynchronization therapy (LOT CRT).

Table 2 : Distribution of subjects according to the type of procedure

Group	Number of subjects	%
LBP	49	73.1
LOT CRT	18	26.9
Total	67	100.0

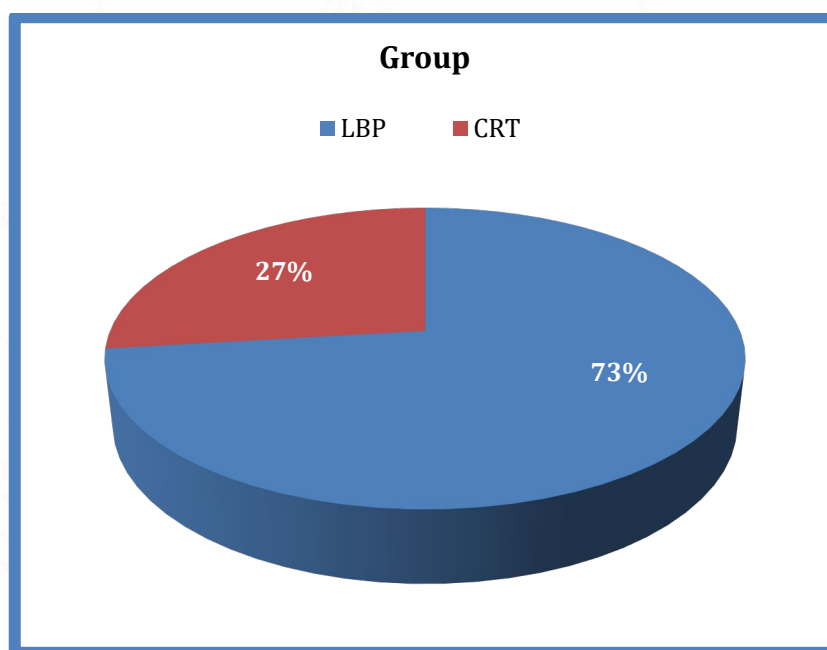


Figure 3: Distribution of subjects according to the type of procedure

There were 3 cases during this time period who underwent conventional RV lead placement due to unsuccessful lead placement after multiple attempts in getting a good

left bundle capture. Diagnosis in these unsuccessful cases were cardiac sarcoidosis with dilated cardiomyopathy and significant septal scarring, LVH due to severe AS and thin septum in a case of DCMP leading to recurrent septal perforation.

Table 3 :Age distribution of subjects

Age	Number	%
10-20	5	7.5
20-40	9	13.4
40-60	17	25.4
>60	36	53.7
Total	67	100.0

Predominant proportion of cases were more than 60 years. There was no significant difference in Left bundle pacing group and LOT CRT group in age distribution.

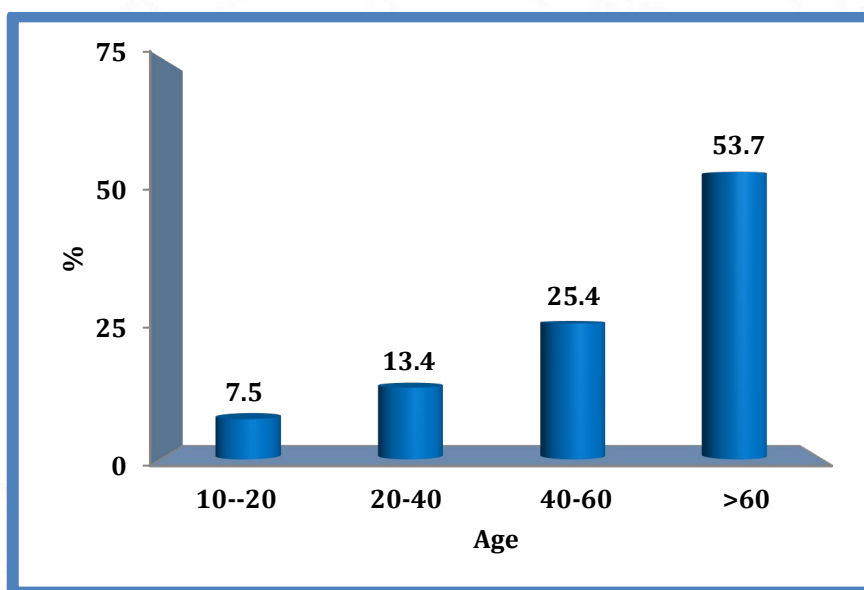


Figure 4: Distribution of subjects according to age

Table 4:Age distribution of subjects according to the type of procedure

Age	LBP		LOT CRT	
	Number	%	Number	%
10-20	5	10.2%	0	0%
20-40	7	14.3%	2	11.1%

40-60	11	22.4%	6	33.3%
>60	26	53.1%	10	55.6%
Total	49	100.0%	18	100.0%
P=0.46				

Table 5: Comparison of age distribution of subjects according to the type of procedure

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Age	LBP	10.0	85.0	53.0	20.2	61.0	32.0	0.28
	CRT	36.0	81.0	61.1	12.3	61.5	18.0	

Comparison of age distribution of subjects according to the type of procedure shows no significant difference in age distribution of cases requiring permanent pacemaker and LOT CRT.

Table 6: Gender distribution of subjects according to the type of procedure

Sex	LBP		LOT CRT	
	Number	%	Number	%
Male	15	30.6%	9	50.0%
Female	34	69.4%	9	50.0%
Total	49	100.0%	18	100.0%
P=0.16				

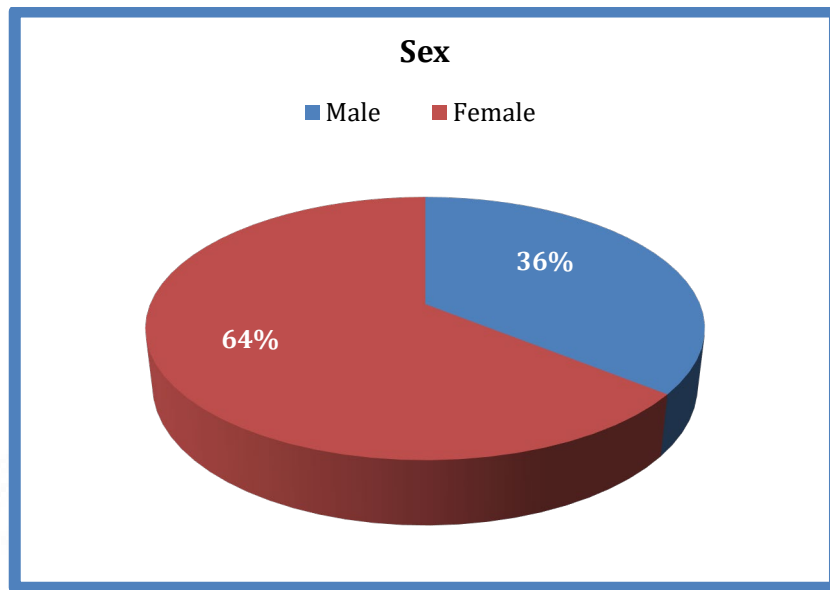


Figure 5: Gender distribution of subjects

Comparison of gender distribution of subjects according to the type of procedure shows no significant differences in distribution of cases requiring permanent pacemaker and LOT CRT.

Table 7: distribution of subjects according to the type of lead used

Type of lead	Frequency	%
Lumenless	50	74.6
Stylet driven	17	25.4
Total	67	100.0

Lumenless lead used was Medtronic 3830 lead and stylet driven was solia lead (Biotronik)

Table 8: Comparison of distribution of subjects according to the type of procedure and type of lead

Type of lead	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Lumenless	35	71.4%	15	83.3%
Stylet driven	14	28.6%	3	16.7%
Total	49	100.0%	18	100.0%

P=0.53

There was no significant difference in Left bundle pacing group and LOT CRT group in type of lead used.

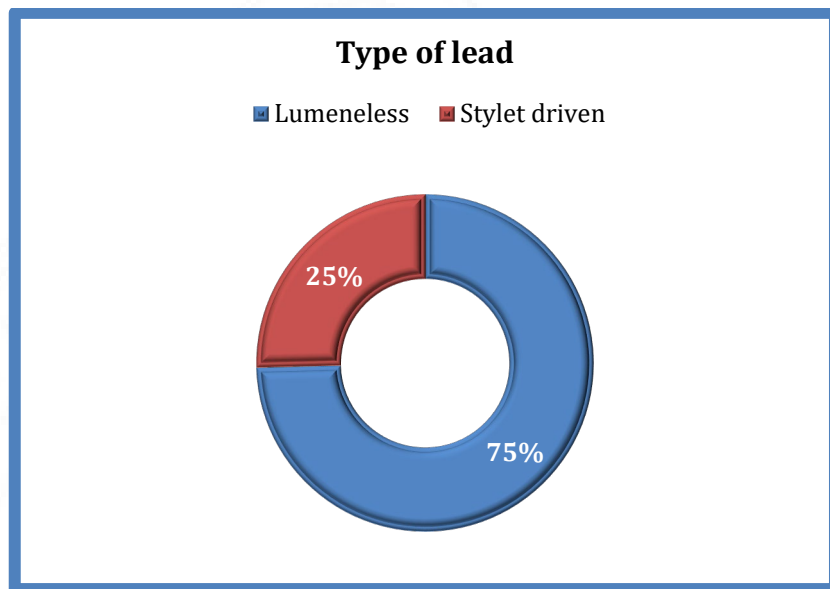


Figure 6: Distribution of subjects according to the type of lead

Table 9: Distribution of subjects according to the comorbidities and type of procedure

A

Diabetes	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	11	22.4%	8	44.4%
No	38	77.6%	10	55.6%
Total	49	100.0%	18	100.0%
P=0.12				

B

Hypertension	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%

Yes	18	36.7%	6	33.3%
No	31	63.3%	12	66.7%
Total	49	100.0%	18	100.0%
P=1				

C

CAD	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	6	12.2%	1	5.6%
No	43	87.8%	17	94.4%
Total	49	100.0%	18	100.0%
P=0.67				

Comparison of according to the type of procedure and comorbidities shows no significant difference in distribution of cases requiring permanent pacemaker and LOT CRT.

Table 10: Distribution of subjects according to the presence and severity of left ventricular dysfunction

LV Dysfunction	Frequency	%
No	44	65.7
Mild	5	7.5
Moderate	1	1.5
Severe	17	25.4
Total	67	100.0

65.7 % cases had normal LV systolic function while 25.4 % had severe LV systolic dysfunction (LVEF <30%)

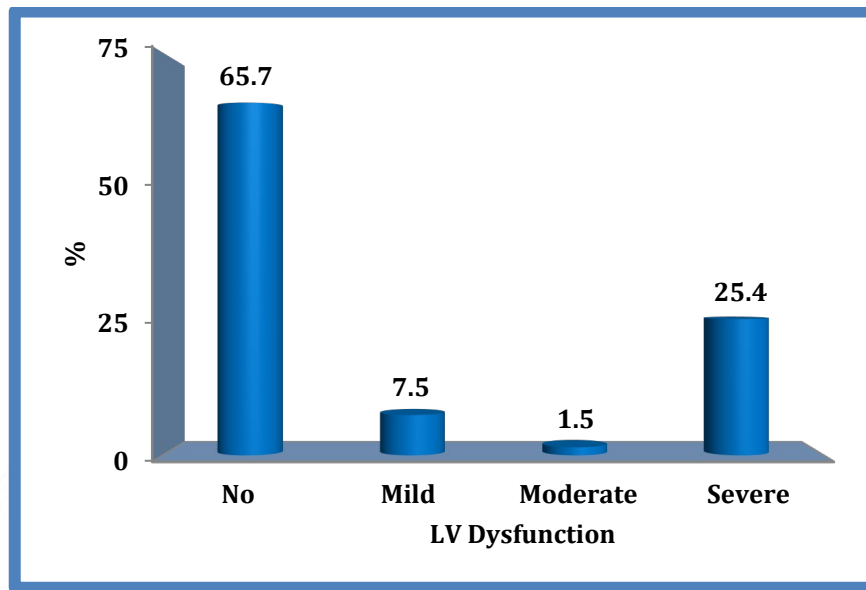


Figure 7: Distribution of subjects according to the presence and severity of left ventricular dysfunction

Table 11: Distribution of subjects according to the presence and severity of left ventricular dysfunction and type of procedure

LV Dysfunction Presence and severity	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
No LV dysfunction	42	85.7%	2	11.1%
Mild LV dysfunction	2	4.1%	3	16.7%
Moderate LV dysfunction	0	0%	1	5.6%
Severe LV dysfunction	5	10.2%	12	66.7%
Total	49	100.0%	18	100.0%
P<0.001				

Comparison of presence and severity of left ventricular dysfunction of subjects according to the type of procedure shows significant difference in cases requiring permanent pacemaker and LOT CRT. ($P<0.001$)

Table 12 : Distribution of subjects according to the presence of structural heart disease and type of procedure

Structural heart disease other than DCMP,ICMP	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	11	22.4%	7	38.9%
No	38	77.6%	11	61.1%
Total	49	100.0%	18	100.0%
P=0.22				

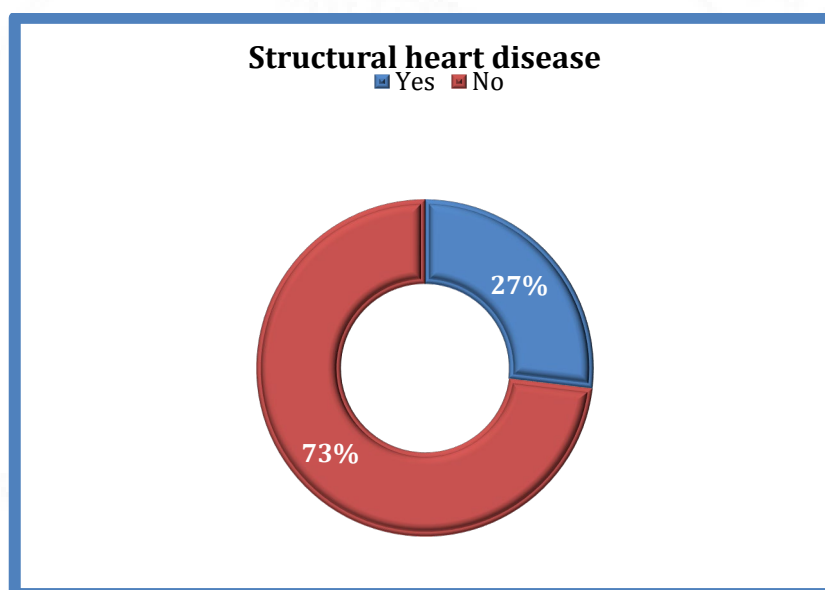


Figure 8 : Distribution of subjects according to the presence of structural heart disease

There was no significant difference in Left bundle pacing group and LOT CRT group in the presence of structural heart disease.

Table 13: Distribution of subjects according to the presence of atrial fibrillation

Atrial fibrillation was significantly more in LOT CRT group that LBP group(**P=0.042**)

AF	LBP	LOT CRT
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	Number of subjects	%	Number of subjects	%
Yes	7	14.3%	7	38.9%
No	42	85.7%	11	61.1%
Total	49	100.0%	18	100.0%
P=0.042				

Table 14: Distribution of subjects according to the NYHA Functional class

Functional class	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
1	9	18.4%	1	5.6%
2	33	67.3%	4	22.2%
3	7	14.3%	11	61.1%
4	0	0%	2	11.1%
Total	49	100.0%	18	100.0%
P<0.001				

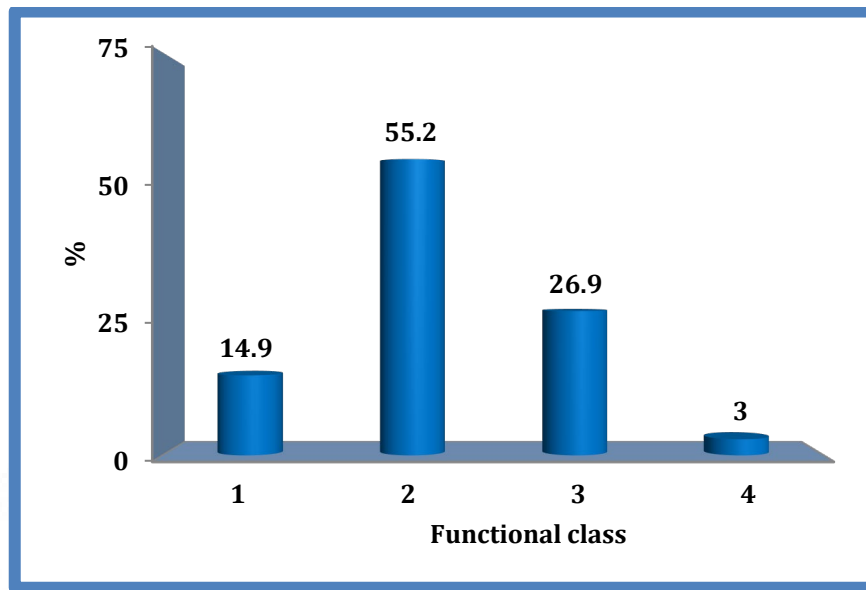


Figure 9: Distribution of subjects according to the NYHA Functional class

LOT CRT subgroup had significantly more cases in 3 and 4 NYHA functional class than LBP ($P < 0.001$).

Table 15: Distribution of subjects according to the indication for Device implantation

Indication for Device implantation	Frequency	%
AV BLOCK	45	67.2
SINUS NODE DYSFUNCTION	7	10.4
HF	15	22.4
Total	67	100.0

In our study 67.2 % AV block was the indication for pacing. Heartfailure was the second common indication in 22.4 % of patients

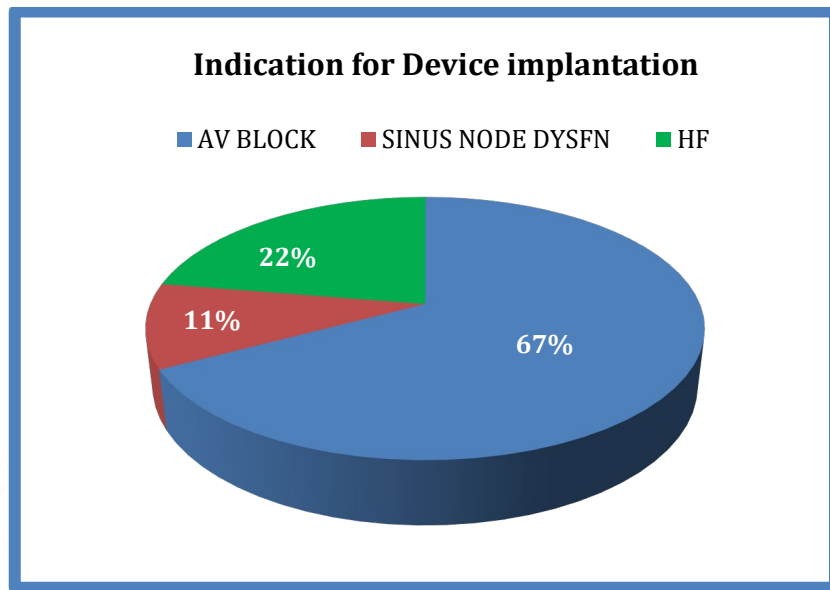


Figure 10: Distribution of subjects according to the indication for Device implantation

Table 16 : Comparison of ECG QRS duration at various time frames

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Base line ECG QRS duration	LBP	70.0	190.0	131.5	32.5	130.0	60.0	<0.001
	LOT CRT	100.0	220.0	168.6	32.4	180.0	34.0	
Discharge ECG QRS duration	LBP	90.0	140.0	109.4	11.4	110.0	20.0	0.009
	LOT CRT	96.0	140.0	118.6	12.2	119.0	20.0	
One month ECG QRS duration	LBP	89.0	144.0	112.6	12.6	110.0	18.0	0.26
	LOT CRT	90.0	140.0	117.1	14.6	117.0	19.5	
Six months ECG QRS duration	LBP	96.0	170.0	118.2	16.2	120.0	27.0	0.36
	LOT CRT	100.0	152.0	123.6	16.1	120.0	32.0	
One year ECG QRS duration	LBP	100.0	170.0	122.1	18.4	120.0	20.0	0.33
	LOT CRT	110.0	170.0	129.0	19.4	126.0	25.0	

Baseline ECG QRS duration was significantly more in those under went LOT CRT versus LBP(168.6 versus 131.5 milliseconds). Initial QRS after pacing was narrower in LBP group compared to LOT CRT group (109.4 milliseconds versus 118.6 milliseconds).

There was no significant difference in 1 month,6 month and 1 year ECG QRS duration among those with left bundle optimized permanent pacemaker and LOT CRT.

Table 17 : Comparison of various echocardiographic parameters(The term CRT here implies left bundle optimised CRT group here)

A

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Base line echo LVIDD	LBP	32.0	72.0	46.1	8.5	46.0	11.5	<0.001
	CRT	36.0	70.0	56.8	8.1	57.0	11.5	
Base line echo LVIDS	LBP	2.0	61.0	30.8	9.7	29.0	8.0	<0.001
	CRT	27.0	57.0	44.5	8.3	44.5	12.0	
Base line echo IVS	LBP	6.0	14.0	8.9	1.5	9.0	2.0	0.99
	CRT	6.0	14.0	8.9	1.8	8.5	2.0	
Base line echo EF in %	LBP	19.0	77.0	59.6	12.2	60.0	11.5	<0.001
	CRT	15.0	65.0	33.8	14.8	30.0	21.8	
Base line LA IN MM	LBP	23.0	43.0	32.7	4.9	32.0	7.0	<0.001
	CRT	35.0	55.0	42.3	4.8	40.5	7.0	
EDV ML/M2	LBP	71.0	204.0	126.8	47.4	125.0	76.8	0.89
	CRT	58.0	244.0	138.1	63.5	128.0	107.0	
ESV ML/M2	LBP	35.0	167.0	83.8	45.9	70.5	63.0	0.32
	CRT	35.0	208.0	107.6	56.5	105.0	82.0	
Stroke Volume ML/M2	LBP	29.0	82.0	42.8	19.4	36.5	15.5	0.053
	CRT	23.0	50.0	30.3	9.7	26.0	12.5	
LVEF in MRI	LBP	19.0	56.0	36.9	15.4	31.8	30.7	0.09
	CRT	14.0	40.0	25.2	7.3	25.0	8.8	
RVEF	LBP	43.0	71.0	53.1	10.5	49.0	17.0	0.15
	CRT	26.0	64.0	40.8	15.8	35.5	30.7	

B

Base line echo MR	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
NO	41	83.7%	8	44.4%
MODERATE	6	12.2%	5	27.8%

SEVERE	1	2.0%	5	27.8%
4	1	2.0%	0	0%
Total	49	100.0%	18	100.0%
P=0.002				

C

Base line echo TR	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
NO	45	91.8%	10	55.6%
MODERATE	4	8.2%	7	38.9%
SEVERE	0	0%	1	5.6%
Total	49	100.0%	18	100.0%
P=0.002				

D

Base line echo RVSP	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
NO PH	47	95.9%	12	66.7%
MILD	2	4.1%	4	22.2%
MODERATE	0	0%	2	11.1%
Total	49	100.0%	18	100.0%
P=0.003				

E

	LBP	lotCRT
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Base line RV dysfunction	Number of subjects	%	Number of subjects	%
Yes	3	6.1%	12	66.7%
No	46	93.9%	6	33.3%
Total	49	100.0%	18	100.0%
P<0.001				

Analysis of baseline echo parameters showed significantly larger LV diastolic dimensions, lower mean LVEF(33.8% VS 59.6%), higher mean left atrial anteroposterior dimensions (42.3 mm vs 32.7 mm) (P<0.001).

MR,TR,RV dysfunction were more with LOT CRT group compared to LBP group

Table 18: Distribution of subjects according to cardiac MRI report

Cardiac MRI	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	6	12.2%	11	61.1%
No	43	87.8%	7	38.9%
Total	49	100.0%	18	100.0%
P<0.001				

Evaluation by Cardiac MRI was often available with those underwent LOT CRT.

Table 19: Distribution of subjects according to cardiac MRI diagnosis

MRI diagnosis	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
DCM	3	50.0%	7	70.0%
OTHERS	3	50.0%	3	30.0%

Total	6	100.0%	10	100.0%
P=0.61				

Table 20: Distribution of subjects according to presence of LGE in cardiac MRI

LGE in mri	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
1	3	50.0%	4	40.0%
2	3	50.0%	6	60.0%
Total	6	100.0%	10	100.0%
P=1				

Parameters at implant

Table 21: Distribution of subjects according to left bundle capture threshold and R wave at time of implant

LB capture thresholds in volts at time of implant (Bipolar?)	LBP	0.3	2.1	0.7	0.3	0.7	0.4	0.89
	LOT CRT	0.3	1.2	0.7	0.2	0.7	0.2	
R wave amplitude in millivolts	LBP	5.0	20.0	11.2	4.3	10.0	6.0	0.99
	LOT CRT	5.0	23.0	11.9	5.7	10.4	9.3	

Table 22: Distribution of subjects according to presence of left bundle potential

Left bundle potentialL	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Present	15	30.6%	5	27.8%
Absent	34	69.4%	13	72.2%
Total	49	100.0%	18	100.0%
P=1				

30.6 % of LBP cases and 27.8 % of LOT CRT cases left bundle potential was noted during time of implant.

Table 23: Distribution of subjects according to type of LB pacing at implant

A

Type of LB pacing at implant	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Selective	40	81.6%	11	61.1%
Non selective	9	18.4%	7	38.9%
Total	49	100.0%	18	100.0%
P=0.11				

Type of LB pacing at implant, selective versus non selective there was no significant difference between groups.

B

Type of LB pacing at implant	Frequency	%
Selective	51	76.1
Non selective	16	23.9
Total	67	100.0

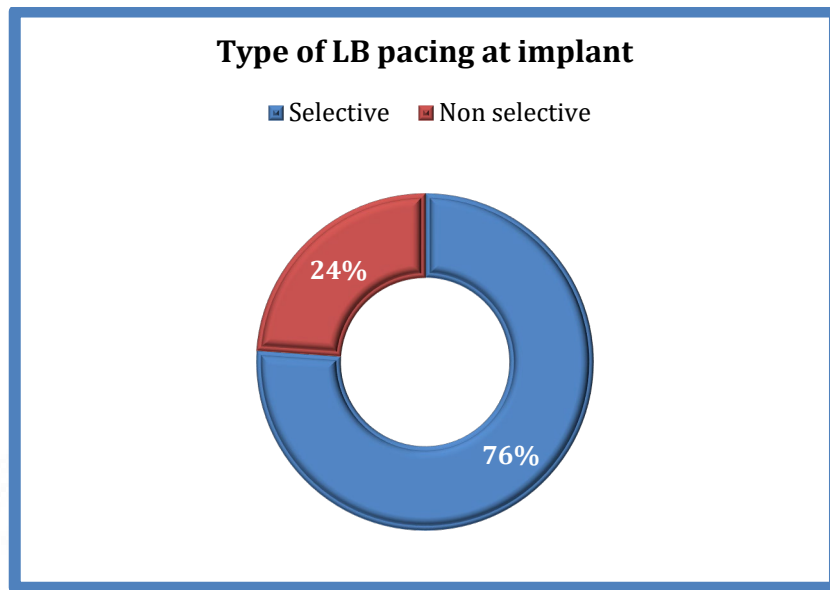


Figure 11 : Distribution of subjects according to type of LB pacing at implant

Table 24: Distribution of subjects according to LVAT and final paced QRS

A

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
LVAT in milliseconds	LBP	38.0	95.0	67.0	13.6	68.0	20.0	0.002
	LOT CRT	56.0	100.0	79.2	11.9	75.0	18.0	
Paced QRS duration in milliseconds	LBP	85.0	148.0	110.2	11.5	110.0	18.0	0.17
	LOT CRT	90.0	144.0	116.0	15.5	110.0	22.0	

B

Variable	Min.	Max.	Mean	SD	Median	IQR
LVAT in milliseconds	38.0	100.0	70.3	14.2	72.0	18.0
Paced QRS duration in milliseconds	85.0	148.0	111.8	12.8	110.0	18.0

Mean LV activation time in milliseconds was 67+/- 13.6 milliseconds for LBP group and 79.2 +/-11.9 milliseconds for LOT CRT group.p=**0.002**

There was no difference in final paced QRS duration at implant LOT CRT group that LBP group

Table 25: Distribution of subjects according to paced ECG QRS duration at implant

A

Paced QRS duration in milliseconds	Frequency	Percent
<100	8	11.9
100-120	46	68.7
120-140	11	16.4
>140	2	3.0
Total	67	100.0

B

Paced QRS duration in milliseconds	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
<100	6	12.2%	2	11.1%
100-120	37	75.5%	9	50.0%
120-140	5	10.2%	6	33.3%
>140	1	2.0%	1	5.6%
Total	49	100.0%	18	100.0%
P=0.11				

Table 26: Distribution of subjects according to paced ECG QRS morphology at implant

QR pattern	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	40	81.6%	14	77.8%
No	9	18.4%	4	22.2%
Total	49	100.0%	18	100.0%
P=0.74				

Most cases had a qR pattern at implant ECG

Table 27: Distribution of subjects according to parameters of repolarisation

A

Variable	Min.	Max.	Mean	SD	Median	IQR	P-value
QT interval Basal	370.0	678.0	486.6	68.2	480.0	104.0	<0.001
QT interval post	120.0	492.0	392.7	60.5	404.0	54.0	

Table: Distribution of subjects according to parameters of repolarisation

B

Variable	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal QTc	372.0	678.0	473.3	61.0	465.0	85.0	<0.001
Post QTc	260.0	528.0	432.6	38.2	435.0	37.0	

C

Variable	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal QT dispersion	4.0	137.0	72.3	26.9	70.0	30.0	<0.001
Post QT dispersion	20.0	110.0	44.9	16.8	40.0	10.0	

D

Variable	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal Tp-Te interval	20.0	160.0	97.5	30.2	100.0	40.0	<0.001
Post Tp-Te interval	30.0	120.0	58.6	19.4	60.0	32.0	

E

Variable	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal Frontal QRS T angle in degrees	2.0	234.0	106.9	60.9	108.0	108.0	0.27
Post Frontal QRS T angle	2.0	329.0	100.6	66.3	105.0	101.0	

Table 28: Distribution of subjects according to parameters of repolarisation and type of procedure

A

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
QT interval Basal	LBP	370.0	678.0	481.6	71.9	470.0	116.5	0.22
	LOT CRT	414.0	612.0	500.0	56.6	488.0	71.5	
QT interval post	LBP	120.0	462.0	389.3	54.0	400.0	58.0	0.07
	LOT CRT	120.0	492.0	401.9	76.5	416.0	31.0	

There was no significant difference in Left bundle pacing group and LOT CRT group

B

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal QTc	LBP	372.0	678.0	461.6	62.7	449.0	77.0	0.001
	LOT CRT	423.0	581.0	505.0	43.6	511.5	58.3	
Post QTc	LBP	260.0	506.0	428.6	37.6	431.0	32.5	0.17
	LOT CRT	377.0	528.0	443.3	38.7	439.0	41.8	

C

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal QT dispersion	LBP	4.0	130.0	74.2	25.7	70.0	30.0	0.11
	LOT CRT	40.0	137.0	67.1	30.0	60.0	45.0	
Post QT dispersion	LBP	20.0	110.0	46.8	18.0	40.0	15.0	0.12
	LOT CRT	20.0	60.0	39.8	11.9	40.0	12.5	

There was no significant difference in Left bundle pacing group and LOT CRT group

D

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal Tp-Te interval	LBP	20.0	160.0	99.8	32.2	100.0	40.0	0.23
	LOT CRT	50.0	120.0	91.1	23.6	95.0	35.5	

Post Tp-Te interval	LBP	30.0	120.0	58.1	19.7	50.0	31.0	0.58
	LOT CRT	30.0	90.0	60.0	18.8	60.0	40.0	

There was no significant difference in Left bundle pacing group and LOT CRT group

E

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Basal Frontal QRS T angle in degrees	LBP	2.0	234.0	96.8	61.2	104.0	92.5	0.03
	LOT CRT	40.0	224.0	134.3	52.6	152.5	81.8	
Post Frontal QRS T angle	LBP	2.0	329.0	94.7	64.4	93.0	98.5	0.17
	LOT CRT	7.0	270.0	116.4	70.8	122.5	112.5	

F

Basal Presence of macroT wave alternans	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	1	2.0%	0	0%
No	48	98.0%	18	100.0%
Total	49	100.0%	18	100.0%
P=1				

There was no significant difference in Left bundle pacing group and LOT CRT group

G

Post Presence of macroT wave alternans	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
No	49	100.0%	18	100.0%
Total	49	100.0%	18	100.0%

There was no significant difference in Left bundle pacing group and LOT CRT group

H

	LBP	LOT CRT
--	-----	---------

Basal QRS Fragmentation	Number of subjects	%	Number of subjects	%
Yes	20	40.8%	11	61.1%
No	29	59.2%	7	38.9%
Total	49	100.0%	18	100.0%
P=0.17				

There was no significant difference in Left bundle pacing group and LOT CRT group

I

Post QRS Fragmentation	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	10	20.4%	3	16.7%
No	39	79.6%	15	83.3%
Total	49	100.0%	18	100.0%
P=1				

There was no significant difference in Left bundle pacing group and LOT CRT group

J

Basal J waves/ERP	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
Yes	0	0%	2	11.1%
No	49	100.0%	16	88.9%
Total	49	100.0%	18	100.0%
P=0.07				

There was no significant difference in Left bundle pacing group and LOT CRT group

K

Post J waves/ERP	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
No	48	100.0%	18	100.0%

Total	48	100.0%	18	100.0%
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There was no significant difference in Left bundle pacing group and LOT CRT group

Table 29: Distribution of subjects according to pacing impedance at various time frames

Variable	Group	Min.	Max.	Mean	SD	Median	IQR
Impedance at implant ohms	LBP	495	998	723.2	147.0	685.0	216
	LOT CRT	540	1046	742.8	160.6	709.5	234
Lead impedance at 1 month ohms	LBP	130.0	790.0	602.9	123.1	618.5	116.5
	LOT CRT	456.0	690.0	582.2	78.8	586.0	158.0
Lead Impedance 6 months ohms	LBP	480.0	714.0	602.4	69.5	604.0	124.0
	LOT CRT	475.0	608.0	532.6	50.1	523.0	99.0
Lead Impedance 1 year in ohms	LBP	1.3	690.0	559.7	134.8	575.0	120.3
	LOT CRT	470.0	627.0	528.8	52.4	513.5	80.5

There was no significant difference in Left bundle pacing group and LOT CRT group

Table 30: Distribution of subjects according to pacing threshold on follow up

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Pacing threshold at 1 month	LBP	0.5	2.0	0.8	0.3	0.8	0.1	0.49
	LOT CRT	0.7	1.3	0.8	0.2	0.8	0.2	
Pacing threshold 6 months	LBP	0.5	1.5	0.8	0.2	0.8	0.3	0.97
	LOT CRT	0.5	1.5	0.9	0.3	0.8	0.3	
Pacing threshold 1 year	LBP	0.7	1.5	0.9	0.3	0.8	0.3	0.79
	LOT CRT	0.7	1.5	0.9	0.3	0.9	0.3	

There was no significant difference in Left bundle pacing group and LOT CRT group

Table 31: Distribution of subjects according to stable lead parameters on follow up

A

	LBP	LOT CRT
--	-----	---------

Stable parameters at longest follow up?	Number of subjects	%	Number of subjects	%
Yes	45	91.8%	17	94.4%
No	4	8.2%	1	5.6%
Total	49	100.0%	18	100.0%
P=1				

There was no significant difference in Left bundle pacing group and LOT CRT group

B

Stable parameters at longest follow up?	Frequency	%
Yes	62	92.5
No	5	7.5
Total	67	100.0

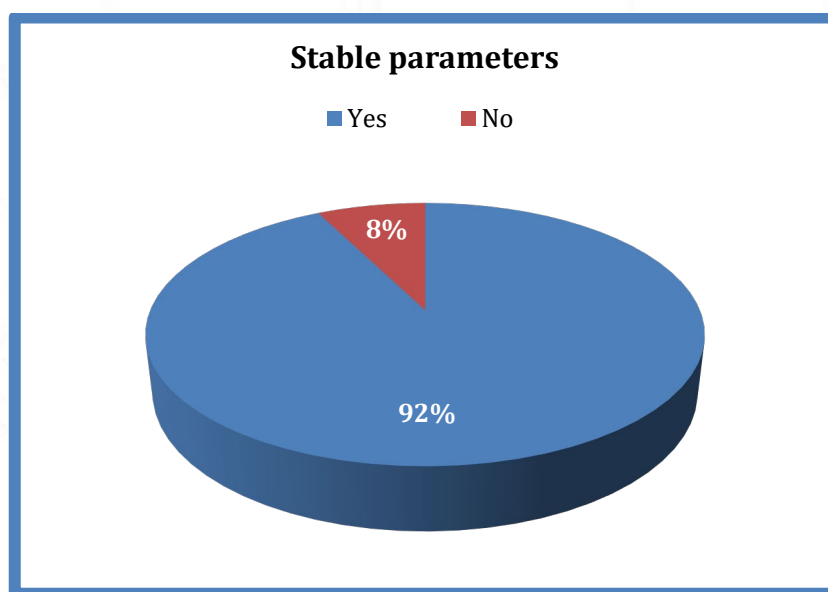


Figure 12: Distribution of subjects according to stable lead parameters on follow up

Table 32: Distribution of subjects according to Stable left bundle capture at longest follow up

A

Stable left bundle capture at longest follow up	Frequency	%
Yes	61	91.0
No	6	9.0
Total	67	100.0

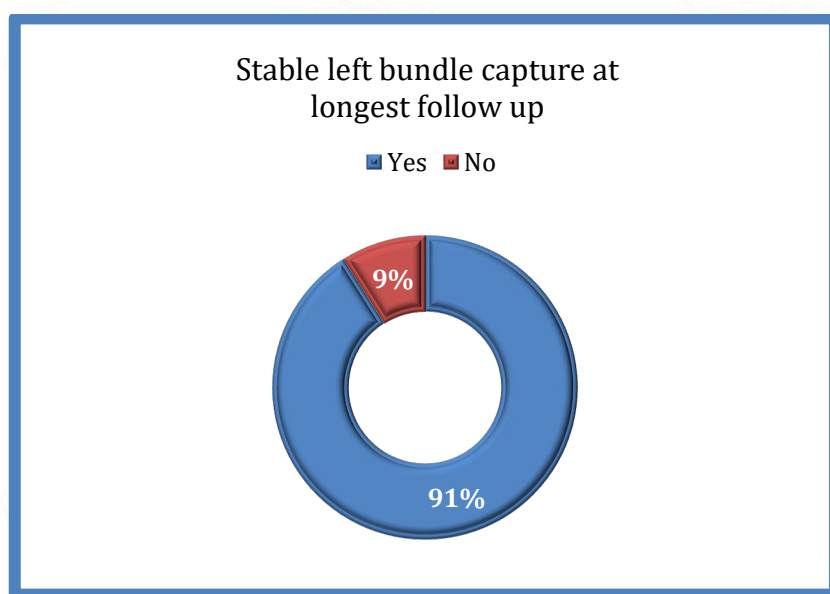


Figure 13 : Distribution of subjects according to Stable left bundle capture

B

Stable left bundle capture at longest follow up	LBP		LOT CRT	
	Number of subjects	%	Number of subjects	%
1	44	89.8%	17	94.4%
2	5	10.2%	1	5.6%
Total	49	100.0%	18	100.0%

P=1

There was no significant difference in Left bundle pacing group and LOT CRT group

Table 33: Distribution of subjects according to Mean hospital stay (days)

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Mean hospital stay days	LBP	2.0	11.0	3.8	1.7	3.0	1.0	0.002
	LOT CRT	3.0	13.0	5.8	3.3	5.0	4.0	
Mean hospital stay days after implant	LBP	1.0	7.0	2.3	0.9	2.0	0.5	0.002
	LOT CRT	2.0	11.0	3.8	2.7	3.0	2.0	

Table 34: Distribution of subjects according to maximum available follow up period in months

Variable	Group	Min.	Max.	Mean	SD	Median	IQR	P-value
Maximum available follow up period in months	LBP	0.2	36.0	11.2	8.6	10.0	10.0	0.51
	LOT CRT	0.5	26.0	9.3	7.3	9.5	11.5	

There was no significant difference in Left bundle pacing group and LOT CRT group

Table 35: Distribution of subjects according to complications in the left bundle pacemaker group

Complications	LBP	
	Number of subjects	%
No complication	44	93.8%
Pocket hematoma	1	2.1%
Pneumothorax	0	0%
Loss of left bundle capture	2	4.2%
Rise in threshold	1	2.1%
Pericardial Effusion	0	0%
Total	48	100.0%

Note 1 case is common with both rise in threshold and loss of capture

Major and minor complications occurred in 6.2 % in LBP group. one case had self-resolving mild pericardial effusion and one case had iatrogenic right bundle injury which was transient.

Table 36: Correlation of outcomes based on type of lead

A

Variable	Category	Type of lead				P- value
		Lumeneless		Stylet driven		
		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	47	94.0%	15	88.2%	0.6
	No	3	6.0%	2	11.8%	
Stable left bundle capture at longest follow up	1	46	92.0%	15	88.2%	0.6
	2	4	8.0%	2	11.8%	
Complications	no complication	43	86.0%	14	87.5%	0.4
	Pocket hematoma	1	2.0%	0	0.0%	
	Pneumothorax	2	4.0%	1	6.3%	
	Loss of left bundle capture	3	6.0%	0	0.0%	
	Rise in threshold	0	0.0%	1	6.3%	
	Pericardial Effusion	1	2.0%	0	0.0%	

There was no significant difference in Left bundle pacing group and LOT CRT group with type of lead.

B

Variable	Type of lead	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	Lumenless	-94.00	40.00	-32.08	34.05	-30.00	60.00	0.33
	Stylet driven	-68.00	44.00	-22.12	30.05	-20.00	40.00	
Paced QRS duration in milliseconds	Lumen less	85.00	148.00	112.80	12.78	110.00	15.25	0.29
	Stylet driven	90.00	132.00	108.71	12.79	104.00	20.00	

There was no significant difference in Left bundle pacing group and LOT CRT group

Table 37: Correlation of outcomes based on grade of LV dysfunction

A

Variable	Category	LV Dysfunction Presence and severity								P- value
		No LV dysfunction		Mild LV dysfunction		Moderate LV dysfunction		Severe LV dysfunction		
		Number of subjects	%	Number of subjects	%	Number of subjects	%	Count	%	
Stable parameters at longest follow up?	Yes	40	90.9%	5	100.0%	1	100.0%	16	94.1%	0.87
	No	4	9.1%	0	0.0%	0	0.0%	1	5.9%	
Total		44	100.0%	5	100.0%	1	100.0%	17	100.0%	
Stable left bundle capture at longest follow up	1	40	90.9%	5	100.0%	0	0.0%	16	94.1%	0.01
	2	4	9.1%	0	0.0%	1	100.0%	1	5.9%	
Total		44	100.0%	5	100.0%	1	100.0%	17	100.0%	
Complications	no complication	40	93.0%	4	80.0%	1	100.0%	12	70.6%	0.53
	Pocket hematoma	0	0.0%	0	0.0%	0	0.0%	1	5.9%	
	Pneumothorax	0	0.0%	1	20.0%	0	0.0%	2	11.8%	
	Loss of left bundle capture	2	4.7%	0	0.0%	0	0.0%	1	5.9%	
	Rise in threshold	1	2.3%	0	0.0%	0	0.0%	0	0.0%	
	Pericardial Effusion	0	0.0%	0	0.0%	0	0.0%	1	5.9%	
Total		43	100.0%	5	100.0%	1	100.0%	17	100.0%	

B

Variable	LV Dysfunction	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	No LV dysfunction	-88.00	44.00	-19.00	30.52	-19.00	43.00	0.001
	Mild LV dysfunction	-50.00	2.00	-27.60	18.68	-30.00	26.00	

	Severe LV dysfunction	-90.00	10.00	-53.65	27.55	-60.00	30.00	
Paced QRS duration in milliseconds	No LV dysfunction	85.00	148.00	109.30	11.60	110.00	16.00	0.14
	Mild LV dysfunction	92.00	140.00	113.40	17.26	110.00	26.50	
	Severe LV dysfunction	90.00	144.00	117.76	13.58	120.00	19.00	

Those with more severe LV dysfunction got more QRS duration reduction compared to baseline. **P<0.001**

Table 38: Correlation of outcomes based on presence of structural heart disease

A

Variabe	Category	Structural heart disease other than DCMP,ICMP				P-value
		Yes		No		
		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	18	100.0%	44	89.8%	0.31
	No	0	0.0%	5	10.2%	
Total		18	100.0%	49	100.0%	
Stable left bundle capture at longest follow up	1	17	94.4%	44	89.8%	1
	2	1	5.6%	5	10.2%	
Total		18	100.0%	49	100.0%	
Complications	no complication	15	83.3%	42	87.5%	0.23
	Pocket hematoma	0	0.0%	1	2.1%	
	Pneumothorax	2	11.1%	1	2.1%	
	Loss of left bundle capture	0	0.0%	3	6.3%	
	Rise in threshold	0	0.0%	1	2.1%	
	Pericardial Effusion	1	5.6%	0	0.0%	
Total		18	100.0%	48	100.0%	

B

Variable	Structural heart disease other than DCMP,ICMP	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	Yes	-90.00	20.00	-34.33	31.62	-35.00	61.00	0.53
	No	-94.00	44.00	-27.80	33.84	-30.00	51.50	

Paced QRS duration in milliseconds	Yes	85.00	148.00	117.22	15.91	120.00	19.75	0.03
	No	90.00	144.00	109.76	10.98	110.00	16.00	

Presence of structural heart disease other than DCMP OR ICMP did not influence stability of lead parameters or left bundle capture at maximum follow up nor incidence of complications. But presence of structural heart disease other than DCMP OR ICMP is associated with a higher paced QRS duration at implant.(117.22 vs 10.9.76 milliseconds) **P=0.03**

Table 39: Correlation of Baseline RV dysfunction with outcomes

A

Variable	Category	Base line RV dysfunction				P-value
		Yes		No		
		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	14	93.3%	48	92.3%	1
	No	1	6.7%	4	7.7%	
Total		15	100.0%	52	100.0%	
Stable left bundle capture at longest follow up	1	14	93.3%	47	90.4%	1
	2	1	6.7%	5	9.6%	
Total		15	100.0%	52	100.0%	
Complications	no complication	12	80.0%	45	88.2%	0.49
	Pocket hematoma	0	0.0%	1	2.0%	
	Pneumothorax	1	6.7%	2	3.9%	
	Loss of left bundle capture	1	6.7%	2	3.9%	
	Rise in threshold	0	0.0%	1	2.0%	
	Pericardial Effusion	1	6.7%	0	0.0%	
Total		15	100.0%	51	100.0%	

B

Variable	Base line RV dysfunction	Min.	Max.	Mean	SD	Median	IQR	P-value
	Yes	-94.00	-4.00	-59.07	24.60	-60.00	38.00	<0.001

QRS_Difference Base_to_Discharge	No	-88.00	44.00	-21.04	30.43	-20.00	48.50	
Paced QRS duration in milliseconds	Yes	90.00	144.00	115.00	13.25	110.00	12.00	0.26
	No	85.00	148.00	110.83	12.65	110.00	19.50	

Table 40: Correlation of LGE in MRI with outcomes

Variable	Category	LGE in mr				P-value
		1		2		
		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	6	85.7%	9	100.0%	0.44
	No	1	14.3%	0	0.0%	
Total		7	100.0%	9	100.0%	
Stable left bundle capture at longest follow up	1	6	85.7%	9	100.0%	0.44
	2	1	14.3%	0	0.0%	
Total		7	100.0%	9	100.0%	
Complications	no complication	5	71.4%	9	100.0%	0.23
	Pneumothorax	1	14.3%	0	0.0%	
	Loss of left bundle capture	1	14.3%	0	0.0%	
Total		7	100.0%	9	100.0%	

Variable	LGE in mr	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	1	-90.00	10.00	-56.00	31.60	-62.00	20.00	0.92
	2	-88.00	-30.00	-61.11	20.55	-58.00	37.00	
Paced QRS duration in milliseconds	1	120.00	148.00	131.43	10.63	128.00	22.00	0.001
	2	90.00	130.00	107.78	10.74	110.00	9.00	

Table 41: Correlation of presence of Left bundle potential and outcomes

A

Variable	Category	Left bundle potential		P-value
		Present	Absent	

		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	19	95.0%	43	91.5%	1
	No	1	5.0%	4	8.5%	
Total		20	100.0%	47	100.0%	
Stable left bundle capture at longest follow up	1	18	90.0%	43	91.5%	1
	2	2	10.0%	4	8.5%	
Total		20	100.0%	47	100.0%	
Complications	no complication	18	90.0%	39	84.8%	0.93
	Pocket hematoma	0	0.0%	1	2.2%	
	Pneumothorax	1	5.0%	2	4.3%	
	Loss of left bundle capture	1	5.0%	2	4.3%	
	Rise in threshold	0	0.0%	1	2.2%	
	Pericardial Effusion	0	0.0%	1	2.2%	
Total		20	100.0%	46	100.0%	

B

Variable	Left bundle potential	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	Present	-88.00	40.00	-18.05	31.97	-4.50	44.00	0.06
	Absent	-94.00	44.00	-34.45	32.75	-40.00	50.00	
Paced QRS duration in milliseconds	Present	85.00	148.00	107.05	13.89	105.50	14.50	0.02
	Absent	90.00	144.00	113.77	11.91	112.00	16.00	

Table 42: Correlation of Type of LB pacing at implant and outcomes

A

Variable	Category	Type of LB pacing at implant				P-value
		Selective		Non selective		
		Number of subjects	%	Number of subjects	%	
Stable parameters at longest follow up?	Yes	48	94.1%	14	87.5%	0.59
	No	3	5.9%	2	12.5%	

Total		51	100.0%	16	100.0%	
Stable left bundle capture at longest follow up	1	47	92.2%	14	87.5%	0.62
	2	4	7.8%	2	12.5%	
Total		51	100.0%	16	100.0%	
Complications	no complication	47	94.0%	10	62.5%	0.02
	Pocket hematoma	0	0.0%	1	6.3%	
	Pneumothorax	1	2.0%	2	12.5%	
	Loss of left bundle capture	1	2.0%	2	12.5%	
	Rise in threshold	1	2.0%	0	0.0%	
	Pericardial Effusion	0	0.0%	1	6.3%	
Total		50	100.0%	16	100.0%	

B

Variable	Type of LB pacing at implant	Min.	Max.	Mean	SD	Median	IQR	P-value
QRS_Difference Base_to_Discharge	Selective	-94.00	44.00	-25.92	32.03	-30.00	50.00	0.13
	Non selective	-90.00	22.00	-41.13	35.04	-47.00	61.00	
Paced QRS duration in milliseconds	Selective	85.00	148.00	108.90	11.68	110.00	16.00	0.002
	Non selective	100.00	144.00	120.88	12.26	120.00	18.25	

DISCUSSION

Of total 70 subjects ,67 who underwent successful left bundle pacing were enrolled in the study.49 patients underwent a left bundle branch area optimized pacemaker compared with 18 cases who underwent a left bundle branch area optimized cardiac resynchronization therapy (LOT CRT).

Vijayaraman et al (29)and Padala, S. K., et al. (30)had acute success of 93 % and 89% respectively in their series of left bundle area pacing.

Diagnosis in our unsuccessful cases were cardiac sarcoidosis with dilated cardiomyopathy and significant septal scarring, LVH due to severe AS and thin septum in a case of DCMP leading to recurrent septal perforation. These cases were tried with non stylet driven lead which was available at that time (3830 lead). Whether use of a stylet driven lead improves septal penetration and procedural success in these cases is unknown.

Comparison of presence and severity of left ventricular dysfunction of subjects according to the type of procedure showed significant difference in cases requiring permanent pacemaker and LOT CRT as more severe cases of LV dysfunction have received CRT. This difference in baseline may be related to selection bias as more severe Dysfunction cases were given an option of proven therapy of LOT CRT first as a therapy with more stronger evidence base.

Atrial fibrillation was significantly more in LOT CRT group than LBP group as higher left atrial dimensions and advanced left ventricular dysfunction may have promoted development of atrial fibrillation in those who underwent LOT CRT.

In our study 67.2 % AV block was the indication for pacing. Heart failure was the second common indication in 22.4 % of patients. HF was the predominant indication for a LOT-CRT procedure while AV block was the predominant indication for device implantation in those who underwent LBP. In a similar study by Vijayaraman et al (29) where 54% had AV block. In study by Ponnusamy et al (31) indication for pacing included atrioventricular (AV) block 43%, cardiac resynchronization therapy 44%, and AV node ablation 4%.

Ponnusamy et al reported presence of LB potential in 40 % of their subjects while in our study 30.6 % of LBP cases and 27.8 % of LOT CRT cases left bundle potential was noted during time of implant.(31)

Mean peak LV activation time in milliseconds was 67 ± 13.6 milliseconds for LBP group and 79.2 ± 11.9 milliseconds for LOT CRT group.

Peak LV activation time is a surrogate for local depolarization of ventricular myocardium beneath chest electrodes. The peak LVAT was relatively short and

remained constant at low and high outputs when the LBB was captured as reported in previous literature.

In our study, mean QRS duration after implantation in LBP group 110.2 ± 11.5 milliseconds. Vijayaraman et al.(29) demonstrated successful left bundle pacing in 93 % patients including AV nodal block, left bundle branch block, right bundle branch block, and intraventricular conduction defect.(29)The average paced QRS duration post implant was 136 ± 17 ms and the average peak LVAT was 75 ± 16 ms. Pacing lead threshold was $0.6 \text{ V} \pm 0.4 \text{ V}$ at 0.5 ms and R wave $10 \pm 6 \text{ mV}$ and remained stable during median follow-up period of 3 months. Selective LB pacing was associated with a lower paced QRS duration at implant.(108.9 vs 120.88 milliseconds)

There was no significant difference in pre and post QT interval or QT dispersion in both groups. But basal QTc was significantly higher with LOT CRT group.

There was significant reduction in QT interval both corrected and uncorrected, QT dispersion(QTD), Tp-Te interval and presence of QRS fragmentation post procedure in comparison to pre procedure values.

In a study by Wang et al (32)left bundle area pacing achieved a shorter QT interval and QTc interval, lower QTD and shorter TpTe interval than right ventricular septal pacing.

Maximum follow up period was 10.7 ± 8.3 months. LBP maximum follow up period available was 11.2 ± 8.6 months and LOT CRT was 9.3 ± 7.3 months. The difference among groups were not significant.

The Lead dislodgement rates were less compared to lead dislodgement rate of about 1% with traditional RV pacing leads.(33) Presence of LGE in cardiac MRI predicted higher final paced QRS duration.

Table 43: Comparison of current study with recent studies on left bundle pacing in literature

Author(published year)	Number of cases	Acute success %	Paced QRS duration	LVAT	LB potential %	Follow up duration	Stable parameters
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						(Months)	on follow up
Vijayaraman P et al(2019)(29)	93	93	136 ±17 ms	75 ± 16 ms	63	3 months	yes
Ponnusamy et al(2020)(31)	93	94	110.8 ± 12.4 ms	72.5 ± 10.8 ms	40	4.8	Yes
Padala, S. K., et al. (2020).(30)	305	89	112 ± 11.7 ms	74.7 ± 11 ms	41	3 months	Yes
Current study(2022)	67	95.7	111.8 ±12.8 ms	70.3±14.2ms	30.6	10.7±8.3	Yes

SUMMARY

- Of total 70 subjects ,67 who underwent successful left bundle pacing were enrolled in the study.49 patients underwent a left bundle branch area optimized pacemaker compared with 18 cases who underwent a left bundle branch area optimized cardiac resynchronization therapy (LOT CRT).

Baseline parameters

- Both left bundle pacing group and LOT-CRT were comparable in terms of age distribution gender, comorbidities, or type of pacing lead used.($p>0.05$)
- Comparison of presence and severity of left ventricular dysfunction of subjects according to the type of procedure showed significant difference in cases requiring permanent pacemaker and LOT CRT as more severe cases of LV dysfunction has received CRT.($P<0.001$)
- Distribution of subjects according to the presence of structural heart disease other than DCMP and ICMP and type of procedure showed no significant difference in cases requiring permanent pacemaker and LOT CRT
- Atrial fibrillation was significantly more in LOT CRT group than LBP group($P=0.042$)
- LOT CRT subgroup had significantly more cases in 3 and 4 NYHA functional class than LBP ($P<0.001$).
- HF was the predominant indication for a LOT-CRT procedure while AV block was the predominant indication for device implantation in those underwent LBP.
- Baseline ECG QRS duration was significantly more in those under went LOT CRT versus LBP(168.6 versus 131.5 milliseconds)($P<0.001$).
- Initial QRS after pacing was narrower in LBP group compared to CRT group (109.4 milliseconds versus 118.6 milliseconds)(P value-0.009). There was no significant difference in 1 month,6 month and 1 year ECG QRS duration among those with left bundle optimised permanent pacemaker and LOT CRT.
- Underlying LBBB was more common with LOT CRT while RBBB at baseline was more common with LBP.($P<0.001$).
- Analysis of baseline echo parameters showed significantly larger LV diastolic dimensions, lower mean LVEF(33.8% VS 59.6%), higher mean left atrial anteroposterior dimensions (42.3 mm vs 32.7 mm) ($P<0.001$) for LOT CRT group.

Left bundle implant parameters

- Mean left bundle capture threshold at implant was 0.7 +/- 0.3 volts for LBP group and 0.7 +/- 0.2 volts for LOT CRT group. Mean R wave amplitude in millivolts was 11.2 +/- 4.3 for LBP and 11.9 +/- 5.7 millivolts for LOT CRT group.
- 30.6 % of LBP cases and 27.8 % of LOT CRT cases left bundle potential was noted during time of implant.
- In analysis of type of LB pacing at implant, selective versus non selective there was no significant difference between groups.

- Mean LV activation time in milliseconds was 67+/- 13.6 milliseconds for LBP group and 79.2 +/-11.9 milliseconds for LOT CRT group.**p=0.002**
- There was no difference in mean final paced QRS duration at implant for LOT CRT group that LBP group.116 vs 110.2 milliseconds.**p=0.17**

Parameters of repolarisation

- There was no significant difference in pre and post QT interval or QT dispersion in both groups. But basal Qtc was significantly higher with CRT group.
- There was no significant difference in Left bundle pacing group and LOT CRT group with respect to basal and post T peak-T end interval, basal and post QRS fragmentation, presence of macro T wave alternans waves/ERP pattern
- Basal Frontal QRS T angle was higher in those underwent CRT compared to LBP.
- There was significant reduction in QT interval both corrected and uncorrected post procedure in comparison to pre procedure values. **P<0.001**
- There was significant reduction in QT dispersion post procedure in comparison to pre procedure values. **P<0.001**
- There was significant reduction in Tp-Te interval post procedure in comparison to pre procedure values. **P<0.001**
- Frontal QRS-T angle did not differ pre and post procedure.

Outcome measures on follow up

- Maximum follow up period was 10.7 +/-8.3 months. LBP maximum follow up period available was 11.2 +/- 8.6 months and LOT CRT was 9.3 +/-7.3 months. The difference among groups were not significant
- Stable lead parameters and stable left bundle capture was preserved in most patients with LOT CRT and LBP group and there was no significant difference in 1 month,6 month and 1 year follow up.
- Median hospital stay was 3 days and 5 days respectively for LBP and CRT. In comparison median hospital stay after implant procedure was 2 days and 3 days respectively for LBP and CRT.
- Major and minor complications occurred in 6.2 % in LBP group. Pneumothorax was significantly more seen with CRT none with LBP.one case had self-resolving mild pericardial effusion and one case had iatrogenic right bundle injury which was transient.

Subgroup analysis and predictors of final outcome

- Correlation of outcomes based on type of lead showed there was no significant difference in Left bundle pacing group and LOT CRT group with type of lead.(P value>0.2)
- Correlation of outcomes based on grade of LV dysfunction indicated that stable left bundle capture is more likely preserved long term at maximum follow up in those without LV dysfunction that those with severe LV dysfunction. **P=0.01**

- Those with more severe LV dysfunction got more QRS duration reduction compared to baseline. **P<0.001**
- Presence of structural heart disease other than DCMP OR ICMP did not influence stability of lead parameters or left bundle capture at maximum follow up nor incidence of complications. But presence of structural heart disease other than DCMP OR ICMP is associated with a higher paced QRS duration at implant.(117.22 vs 109.76 milliseconds) **P=0.03**
- Maximum reduction in baseline to post left bundle pacing QRS duration occurred in group with baseline LBBB followed by those with undetermined BBB followed by those with RBBB (50.5 VS 41.6 VS 28.9 milliseconds) **P<0.001**
- Presence of RV dysfunction did not influence stability and preservation of parameters at follow up or complications
- Presence of LGE in cardiac MRI predicted higher paced QRS duration(131.43 milliseconds versus 107.78 milliseconds). **P<0.001**
- Presence of left bundle potential did not influence stability of lead parameters or left bundle capture at maximum follow up nor incidence of complications. But presence of Left bundle potential is associated with a lower paced QRS duration at implant.(107.05 vs 113.77 milliseconds) **P=0.02**
- Selective LB pacing was associated with a lower paced QRS duration at implant.(108.9 vs 120.88 milliseconds) **P=0.002**
- incidence of procedural complications were more common with lot crt than left bundle pacemaker. **P=0.03**

STUDY LIMITATIONS

- This was a single centre non randomised observational study
- Routine echocardiogram on periodic follow up was not available for all patients.
- Techniques like programmed deep septal stimulation were not routinely used to identify left bundle capture
- Longer duration studies are needed to identify long term effects on left bundle capture

CONCLUSION

Left bundle branch area pacing provided narrow QRS which is sustained on short term and long term follow up. Pacing impedance and pacing threshold of patients also remain stable on long-term follow up. There was no significant difference among left bundle pacing group and left bundle CRT group. It also improves parameters of repolarisation post implant compared to pre implant. This may have implications on reducing arrhythmia risk and improving survival.

Short term and long-term outcomes of left bundle branch area pacing from this single centre study appears promising and comparable to results previously reported literature.

Left bundle branch area pacing has potential to come up as the major technique for cardiac pacing in future. Long term randomised multicentric studies in conduction system pacing are the need of the hour.

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