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Echocardiographic Evaluation of His Bundle Pacing in Patients with Prolonged PR Intervals

Ethan Fry[1*], Karam Ayoub[2], Vincent L Sorrell[1], Joseph Souza[1], Aaron Hesselson[1], Steve Leung[1], Kristin Ellison[1]

Abstract

Background: Patients with PR intervals >240ms have atrio-ventricular (AV) dyssynchrony, which can increase risk of atrial fibrillation and all-cause mortality. When requiring pacing, long AV delays (AVDs) have been programmed to avoid ventricular dyssychrony. His bundle pacing (HBP) may provide improved AV synchrony in patients with prolonged PR.

Methods: 10 patients with sinus node dysfunction and prolonged PR who received HBP were studied. Real-time echocardiographic was performed with 3 pacemaker modes (RV septal, non-selective HBP, and selective HBP) using the following pacemaker settings: control (no ventricular pacing), pacing with AVD of 180ms, 150ms, 120ms, 100ms, and 70ms. Echocardiographic Doppler measurements: EA/RR, >40% = AV synchrony; E/e', <8 = normal left atrial pressure; pulmonic-to-aortic pre-ejection time difference, <40ms = interventricular synchrony; septal-to-lateral wall activation time difference, <56ms = intraventricular synchrony; and LVOT VTI. Unpaired T test was used to evaluate for significance. Exclusion criteria: persistent atrial fibrillation, second-degree AV block.

Results: Compared to control programming, HBP showed a 31.5% increase in EA/RR time, a decrease in E/e' of 26.9%, and an increase in the LVOT VTI of 21.3%. Compared to RV septal pacing, there was a similar increase in LVOT VTI. These findings met statistical significance and were considered optimal based on Doppler echocardiography findings primarily at AVDs of 150ms and 120ms. Comparisons between selective and non-selective pacing were not significantly different.

Conclusion: Compared to controls and RV septal pacing, physiologic His bundle pacing was shown to increase markers of AV synchrony and LV stroke volume while maintaining ventricular synchrony.

Keywords: Atrio-Ventricular Synchrony; Echocardiogram; His Bundle Pacing; Prolonged PR; Selective; Non-Selective

Introduction

Pacing techniques have advanced significantly over the past 20 years. Conventional pacing at the right ventricular (RV) apex results in ventricular dyssynchrony, impaired contractility, increased incidence of atrial fibrillation, and decline in ejection fraction [1-4]. Significant data has emerged regarding the benefits of physiologic conduction system pacing with either His bundle pacing (HBP) or left bundle branch pacing (LBBP) [5-7]. Both techniques utilize the intrinsic conduction system to activate the ventricle and can avoid pacemaker-induced dyssynchrony. Several studies have shown the feasibility

Affiliation:

[1]Department of Medicine, Division of Cardiovascular Medicine, Gill Heart and Vascular Institute, University of Kentucky, Lexington, KY, USA

[2]Department of Medicine, Division of Cardiovascular Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

Corresponding author:

Ethan Fry, Department of Medicine, Division of Cardiovascular Medicine, Gill Heart and Vascular Institute, University of Kentucky, Lexington, KY, USA.

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of conduction system pacing [5, 6], and a recent retrospective study has suggested mortality benefit with physiologic pacing compared to conventional RV pacing [7].

Patients with prolonged PR intervals (>200ms) are at risk for atrio-ventricular (AV) dyssynchrony, impaired diastolic and systolic ventricular function, atrial fibrillation and increased all-cause mortality [8-11]. Conversely, resynchronization with BiV pacing in patients with PR prolongation >230ms and non-LBBB resulted in a significant reduction in risk of death or heart failure, supporting the benefits of AV synchrony restoration [12]. In clinical practice, conventional dual chamber pacing utilizes long AV delays (AVDs) in an effort to avoid RV pacing and preserve ventricular synchrony. However, this programming adversely results in AV dyssynchrony. HBP, with either selective (activating only the His bundle) or non-selective (activating the His bundle and the surrounding RV tissue) settings, may result in improved AV synchrony without causing ventricular dyssynchrony.

In this pilot study, Doppler echocardiography was utilized to investigate the cumulative atrioventricular effects of HBP in patients with a prolonged PR interval.

Methods

Population

The protocol was approved by the institutional review board at the University of Kentucky. After appropriate informed consent was obtained, ten patients with sinus node dysfunction and PR >240ms who received physiologic His bundle pacemakers were recruited. Baseline electrocardiograms (ECG) at the time of device implantation were obtained. All patients received physician-guided serial echocardiographic evaluations during specific pacemaker settings: Control (native rhythm), AVD of 180ms, 150ms, 120ms, 100ms, and 70ms. These pacemaker settings were obtained during 3 separate pacemaker modes – 1) RV septal pacing only, 2) non-selective HBP, and 3) selective HBP. These pacing modes were achieved by adjusting the output on the His lead as previously described [5, 6] (Figure 1). Patients served as their own controls by comparing changes seen during pacing to their native rhythm. Patients were excluded if they had a history of persistent atrial fibrillation or Mobitz 1 second-degree AV block.

Echocardiography

Focused 2D and Doppler echocardiographic images were performed serially at baseline and at each pacemaker setting. Parasternal long axis (PLAX), apical 2, 3, and 4 chamber views were obtained. Pulsed-wave Doppler (PWD) of the mitral early (E) and late (A) filling and the right and left ventricular outflow tract (RVOT, LVOT) velocities and continuous wave Doppler (CWD) of the LVOT were recorded. Tissue Doppler of the tricuspid and mitral annular velocities were obtained. Multiple semi-quantitative measurements, time intervals, and ratios were obtained.

Markers of AV synchrony, left atrial pressure (LAP), intraventricular synchrony, and LV stroke volume were primary points of investigation. E wave to A wave time compared to the R-to-R interval (EA/RR) was the primary measure of AV synchrony and represents the relative time for left ventricular filling with values >40% considered synchronous [13,14]. Average E/e' was used as a marker of LAP with values <8 considered normal and values >14 considered elevated. Aortic to pulmonic pre-ejection time differences were used as a marker of inter-ventricular synchrony (<40ms considered normal). Septal to lateral wall activation time (AT) was used as a marker of intra-ventricular synchrony (<56ms considered normal) [15, 16]. LVOT VTI can be used to calculate stroke volume (SV) and cardiac output (CO) using the following formulas: SV = LVOT area (πr^2;2) * LVOT stroke distance (VTI; cm); CO = SV* HR. As patients served as their own controls (e.g. LVOT area is constant) and since patients were paced (e.g. HR was constant), LVOT VTI was used as an effective surrogate marker for stroke volume and by extension cardiac output (Table 1).

Echocardiographic measurements were performed blinded to the pacing mode (Figure 2). Selective, non-selective, and RV septal pacing modes were attempted in all 10 patients, but clinical and technical limitations resulted in collectable data for selective pacing in 6 of the patients, non-selective pacing in 6 of the patients, and RV septal pacing in 4 of the patients. A total of 83 comprehensive echo Doppler analyses were performed with more than 800 individual echo measurements and 400 echo calculations. Ten percent of these findings were randomly and independently verified with an expert echocardiographer to provide internal validity.

Statistical Analysis

Sample characteristics are presented using descriptive statistics. Frequencies and percentages are used to describe

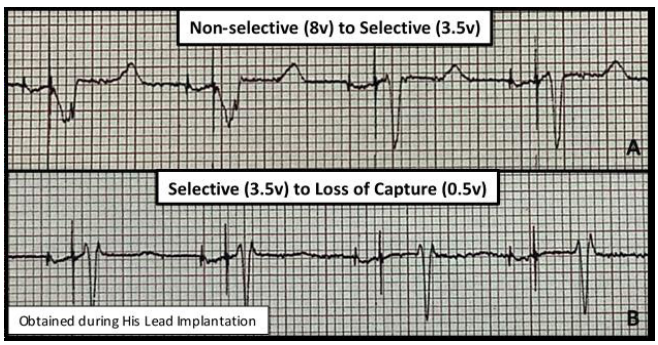

Figure 1: Panel A – Initial two beats demonstrate non-selective capture; subsequent two beats demonstrate selective capture. Panel B – initial two beats demonstrate selective capture; subsequent two beats demonstrate loss of capture.

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Table 1: Echocardiographic Parameters and Clinical Significance

	AV Synchrony	Left Atrial Pressure	Ventricular Synchrony		LV Stroke Volume
Measurement	EA/RR	E/e'	Septal to Lateral Activation Time	Aortic to Pulmonic Pre-Ejection time	LVOT VTI
Normal Value	>40%	<14	<56ms	<40ms	N/A
Clinical Significance	Normal AV Synchrony	Lower LAP	Intra-ventricular Synchrony	Inter-ventricular Synchrony	Higher values indicate increased LV stroke volume

Table 1: Echocardiographic measurements, normal values, and their clinical significance.

Figure 2: Echocardiographic Doppler Spectrum

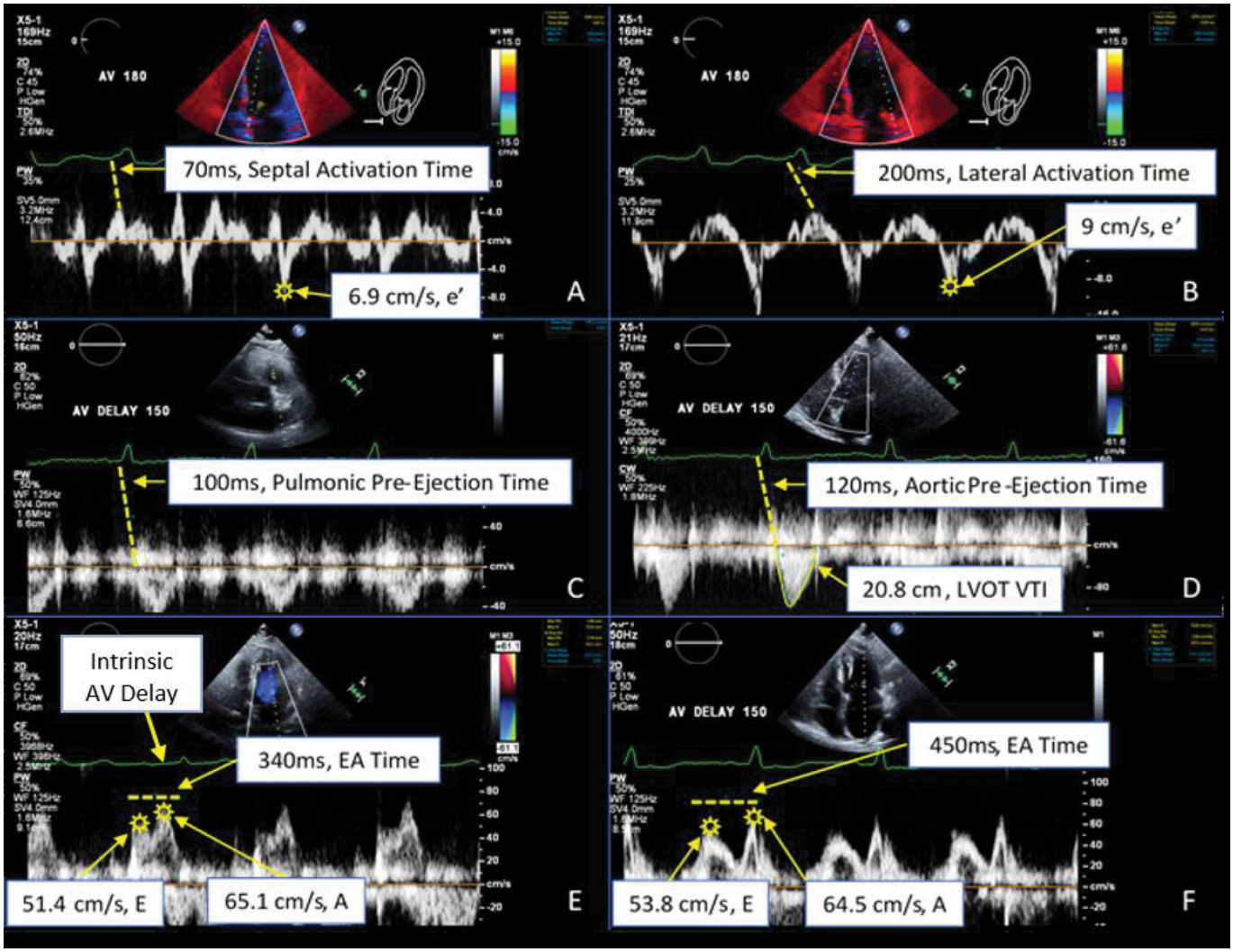

Figure 2: Doppler data acquisition. All measurements depicted were obtained at the various AVDs (180ms through 70ms), with several depicted here. (A) Tissue Doppler velocities of the septal (A) and lateral (B) mitral annulus demonstrating the e' and activation times (dashed line - beginning of QRS to peak mechanical activation). Pulsed-wave Doppler velocities from the pulmonic (C) and aortic (D) outflow tracts demonstrating the pre-ejection times (dashed line - beginning of QRS to initiation of flow) and VTI measures. Pulsed-wave Doppler velocities from the mitral inflow during baseline (control) prolonged AVD (E) and paced AVD 150ms (F) demonstrating the E and A wave velocities and E-A time (dashed line). Note the increased E/A separation and longer ventricular filling time during paced AVD setting of 150ms.

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Supplemental Tables: Results of unpaired T-test analysis for the echo parameters specified between multiple combinations consisting of 2 different pacing modalities. Activation Time SL = Activation time difference between the septal and lateral walls at the mitral annulus as measures by Doppler. Pre-ejection time PA = Pre-ejection time difference between pulmonary to aortic as measured by Doppler.

P-Values - Selective Compared to Non-Selective					
	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
EA/RR	0.3904	0.3767	0.4206	0.1944	0.1937
E/e'	0.4237	0.6886	0.6067	0.693	0.9767
Pre-ejection time PA	0.5871	0.3129	0.3975	0.0646	0.1
Activation Time SL	0.0922	0.0965	0.1438	0.1603	0.2209
LVOT VTI	0.1984	0.1545	0.1623	0.5373	0.0935
LVOT VTI % Change	0.6549	0.7653	0.8276	0.4386	0.3914
P-Values – Combined Selective/Non-selective Compared to Septal					
	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
EA/RR	0.2096	0.2408	0.2339	0.2259	0.2381
E/e'	0.5007	0.4462	0.087	0.1133	0.1855
Pre-ejection time PA	0.0822	0.1413	0.0442	0.0289	0.2444
Activation Time SL	0.0008	0.0643	0.0088	0.0057	0.0426
LVOT VTI	0.4307	0.418	0.4878	0.3171	0.3782
LVOT VTI % Change	0.0036	0.0029	0.0089	0.0079	0.0166
P-Values - Selective Compared to Septal					
	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
EA/RR	0.1367	0.0849	0.061	0.1981	0.1428
E/e'	0.02	0.0464	0.091	0.1323	0.126
Pre-ejection time PA	0.1075	0.0653	0.0494	0.0007	0.0171
Activation Time SL	<0.0001	0.0002	0.0121	<0.0001	<0.0001
LVOT VTI	0.8767	0.8938	0.9563	0.5135	0.7984
LVOT VTI % Change	0.0165	0.0158	0.0397	0.0309	0.0268
P values – Non-Selective Compared to Septal					
	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
LVOT VTI % Change	0.0353	0.0185	0.027	0.0097	0.0834
P Values - Combined Selective/Non-Selective Compared to Control					
	Control to AVD 180ms	Control to AVD 150ms	Control to AVD 120ms	Control to AVD 100ms	Control to AVD 70ms
EA/RR	0.0117	<0.0001	<0.0001	<0.0001	0.0002
E/e'	0.1019	0.0479	0.0642	0.2839	0.8185
LVOT VTI	0.2221	0.0682	0.0527	0.1421	0.4032
P Values - Combined Selective/Non-Selective AVD Comparisons					
	180ms to 150ms	180ms to 120ms	180ms to 100ms	180ms to 70ms	
EA/RR	0.0183	0.0041	0.0033	0.0273	
E/e'	0.4769	0.6558	0.4758	0.05	
LVOT VTI %	0.0628	0.0641	0.5127	0.0753	

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categorical variables. Means are used to describe continuous variables. An unpaired T test was utilized to test for associations in univariate comparisons of categorical data at a 95% confidence interval. See supplementary index for all p-value tables.

Results

The average age was 76 years old with primarily Caucasian (100%) men (80%). The average baseline PR interval was 304ms (SD = 74). 50% of patients had prolonged QRS >120ms. Most patients (80%) were prescribed beta blockers or anti-arrhythmic medications and 60% had a history of paroxysmal atrial fibrillation (Table 2).

Markers of AV synchrony were initially evaluated and compared. EA/RR time increased with HBP compared to controls with a maximal change seen at an AVD of 120ms (31.5%) (Table 3). The change in the EA/RR ratio when compared to controls was statistically significant at all AVD categories, though the largest difference was seen at AVDs of 150,120, and 100ms ($p<0.001$). Controls had 4 patients with EA/RR ratio <40%, which increased to >40% with HBP (Figure 3). E/e' showed peak reduction at an AVD of 120ms with a decrease in the E/e' ratio of 33.6% compared to controls (Figure 3). At shorter AVDs (100 and 70ms), the E/e' actually increased (Table 3). No control patient had normal LAP (E/e' <8) and 4 had elevated LAP (E/e' >14). With HBP, all patients achieved an E/e' <14 and 3 were able to achieve E/e' <8 (Figure 3). Reduction of the E/e' value was statistically significant when compared to control at an AVD of 150ms ($p=0.048$). To evaluate whether changes seen were due primarily to initiation of pacing as opposed to reduction in AV delay, changes between AVD 180ms and AVD 150-70ms were compared which showed significant increases in EA/RR time (at all AVDs) and trends of reduction in E/e' (at AVDs of 150 and 120ms) (Table 3).

To evaluate for potential benefit in patients that would normally qualify for standard dual chamber pacing, HBP was compared to conventional RV pacing which demonstrated an increase in the EA/RR ratio at all AVDs. The most prominent increase was seen when comparing selective HBP to RV pacing at an AVD of 120ms ($p = 0.06$) (Figure 4). E/e' values were decreased in the HBP group when compared to the conventional RV pacing group. Selective pacing at AVDs of 180ms and 150ms showed a significant decrease in E/e' ($p = 0.02$ and 0.046, respectively) when compared to RV pacing. There was no significant difference when comparing E/e' between selective and non-selective pacing at any AVDs, though selective HBP trended towards higher EA/RR and lower E/e' values (Figure 4).

HBP resulted in shorter Pulmonary/Aortic pre-ejection time differences compared to controls, with selective HBP demonstrating significant reductions when compared to conventional RV pacing at AVDs of 120ms, 100ms, and 70ms ($p = 0.049$, <0.001, and 0.017). Though no pacing groups had Pulmonary/Aortic pre-ejection time differences >40ms, which is the clinical mark of inter-

Table 2: Baseline Clinical and Electrocardiographic Characteristics

Patient	Age	Gender	Race	PR Interval	QRS interval	Baseline Conduction	Baseline EF (%)	Anti-arrhythmics	Comorbidities
1	72	M	Caucasian	288	154	RBBB, LAFB	61	sotalol	pAF, HTN
2	76	M	Caucasian	500	166	Atypical RBBB	60	sotalol	pAF, HTN, OSA
3	72	M	Caucasian	320	90	normal QRS	50	toprol	pAF, CABG, CKD, DM2, HTN
4	85	F	Caucasian	248	86	normal QRS	55	sotalol	pAF, CVA, HTN, Tremors
5	76	F	Caucasian	288	80	normal QRS	60	amiodarone, toprol	pAF, HFrEF, Breast Cancer, PVCs, HTN
6	76	M	Caucasian	312	140	RBBB	55	none	DM2, HTN, HLD, GERD
7	62	M	Caucasian	248	142	RBBB	30	toprol	HFrEF, Severe MR, CAD, CKD3, DM2
8	76	M	Caucasian	264	80	normal QRS	60	lopressor	CABG, Renal Txp, DM2, HTN
9	74	M	Caucasian	314	86	normal QRS	51	multaq, toprol	pAF, HFpEF, COPD, DM2, HTN
10	88	M	Caucasian	260	144	RBBB, LAFB	51	none	CAD, CKD, Prostate Cancer, PMR, CKD, OSA, HTN

Table 2: PR and QRS Intervals Obtained Prior to HBP. CAD- Coronary Artery Disease; CABG- Coronary Artery Bypass Graft; CKD- Chronic Kidney Disease; COPD- Chronic Obstructive Pulmonary Disease; CVA- Cerebrovascular Accident; DM2- Diabetes Mellitus; HFpEF- Heart Failure with Preserved Ejection Fraction; HFrEF- Heart Failure with Reduced Ejection Fraction; HTN- Hypertension; LAFB- Left Anterior Fascicular Block; MR- Mitral Regurgitation; OSA- Obstructive Sleep Apnea; pAF- Paroxysmal Atrial Fibrillation; PMR- Polymyalgia Rheumatic; RBBB- Right Bundle Branch Block; SND- Sinus Node Dysfunction; txp- Transplant.

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Figure 3: AV Synchrony and Left Sided Filling Pressures

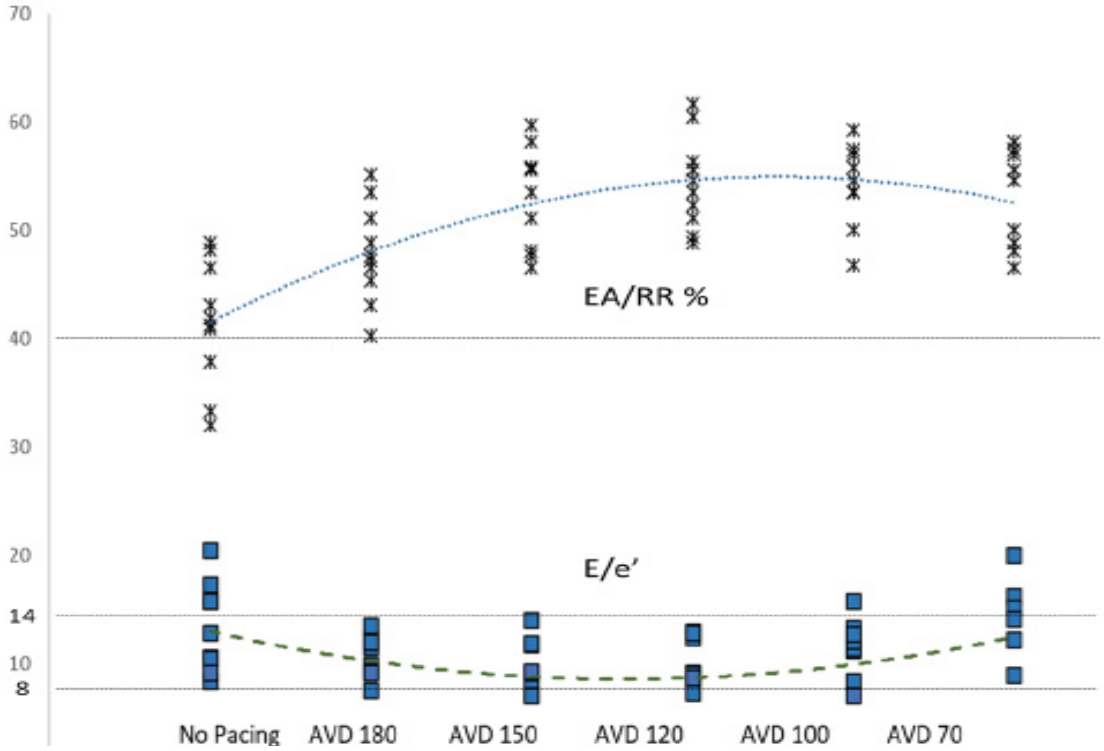

Figure 3: The superior portion of the graph details the EA/RR ratio in percentages. AVD values are displayed in milliseconds. A dotted line depicts the average value trends as you progress from control to AVD of 70. The inferior portion details the E/e' absolute values with a similar dashed line depicting average trend. Straight dotted lines are displayed at 40% EA/RR%, 14 E/e', and 8 E/e', which are the thresholds for AV synchrony (above line), elevated LAP (above line), and normal LAP (below line) respectively.

Table 3: Average Values of HBP Pacing Compared to Control

	Control	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
Average Absolute Values						
EA/RR	41.4 (5.7%)	47.9 (4.6%)	53.2 (4.6)	54.4 (4.3%)	54.1 (3.7%)	52.9 (4.5)
E/e'	13.41 (4.1)	10.62 (2)	9.79 (2.5)	10.13 (2.3)	11.50 (2.8)	13.87 (3.7)
LVOT VTI (cm)	20.51 (4)	23.36 (5.9)	24.81 (5.9)	24.88 (5.2)	23.82 (5.5)	22.14 (4.3)
Percentage Change in Values Compared to Control						
	Control	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
EA/RR		15.7%, p = 0.012	28.6%, p =<0.001	31.5%, p =<0.001	30.9%, p =<0.001	27.9%, p = 0.001
E/e'		-20.8%	-27%, p = 0.048	-24.4%	-14.3%	3.5%
LVOT VTI (cm)		13.9%	21%	21.3%, p = 0.053	16.1%	8%
Percentage Change in Values Compared to an AVD of 180ms						
	Control	AVD 180	AVD 150	AVD 120	AVD 100	AVD 70
EA/RR			11.1%, p = 0.018	13.6%, p = 0.004	13.1%, p = 0.003	10.5%, p = 0.027
E/e'			-7.8%	-4.6%	8.3%	30.7%, p = 0.050
LVOT VTI (cm)			6.2%	6.5%, p = 0.064	2%	-5.2%

Table 3: Divided into 3. The top section has the average values obtained for each category. Standard deviation displayed in (). The middle section displays the percentage change of the various pacing categories obtained in the top compared to controls. The bottom section displays the percentage change of these same pacing categories compared to what was obtained with an AVD of 180ms.

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Figure 4: Comparison of AV Synchrony Between Pacing Groups

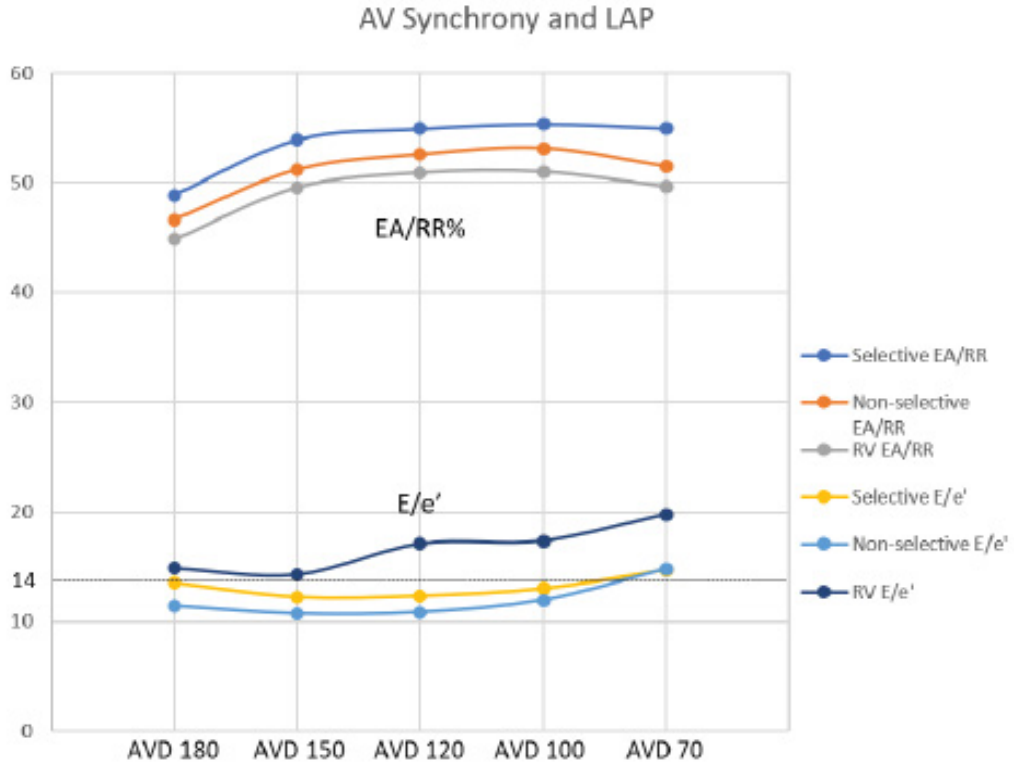

Figure 4: Measures of AV synchrony displayed with a straight dotted line detailing the clinical mark of 14, above which indicates elevated LAP. Dark blue line is selective EA/RR; Orange line is non-selective EA/RR; Gray line is right ventricular EA/RR; Yellow is selective HBP E/e'; Light blue is non-selective HBP E/e'; and Purple is right ventricular E/e'.

ventricular dyssynchrony. RV pacing was considered intra-ventricularly dyssynchronous, however, at all AVDs with pre-ejection times >56ms. HBP pacing with both selective and non-selective modes demonstrated more intra-ventricular synchrony (93% improvement) compared to conventional RV pacing ($p<0.001$). Selective pacing had shorter activation time differences compared to controls. (Figure 5b).

A mean increase in LVOT VTI was seen with HBP that peaked at an AVD of 120ms with an increase of 21.3% when compared to controls ($p = 0.053$) (Table 3, Figure 6a). Figure 6b details individual patient variation of LVOT VTI, showing a degree of patient variability at the various AVDs. The highest values were primarily seen at an AVD of 150ms or 120ms. The mean LVOT VTI worsened at an AV delay of 70ms when compared to the mean LVOT VTI at 180ms (Table 3).

HBP resulted in increased LVOT VTI at all AVDs when compared to RV pacing ($p = 0.01$) for non-selective and $p = 0.016$ for selective) (Figure 7), without significant differences between non-selective or selective. RV pacing was deleterious to LVOT VTI compared to control and was only able to achieve no difference between control and RV pacing at an AVD of 120ms.

In 2 cases, patient 1's QRS decreased from 166ms to 90ms while patient 7's QRS decreased from 142ms to 88ms (Figure 8) due to the capture of an atypical RBBB and RBBB respectively, below the level of the block.

Discussion

Physiologic pacing via the His bundle began clinical use in the early 2000s [17]. Recent data from experienced centers demonstrated >90% HBP lead placement success and similar fluoroscopy and procedural times in patients with a narrow QRS at baseline when compared to right ventricular pacing [18]. Biventricular pacing/cardiac resynchronization therapy (CRT) has proven to be very effective in improving LV global systolic function in patients with LBBB or widened QRS and need for pacing with reduced ejection fraction [19,20] and is considered a standard therapeutic approach for this patient population. HBP can also provide CRT when the His lead is able to capture the virtual electrode of pacing, distal to the site of block within the His bundle, recruiting the blocked bundles [21–23]. In patients in whom HBP was successfully achieved, echocardiographic outcomes were comparable or trended towards better for HBP-CRT relative to BiV-CRT [24, 25]. Of note, biventricular pacing is not indicated for patients with QRS <120ms or non LBBB morphologies [20], and may not achieve adequate resynchronization in patients with prolonged PR intervals [26].

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Figure 5: Comparison of Ventricular Synchrony Between Pacing Groups

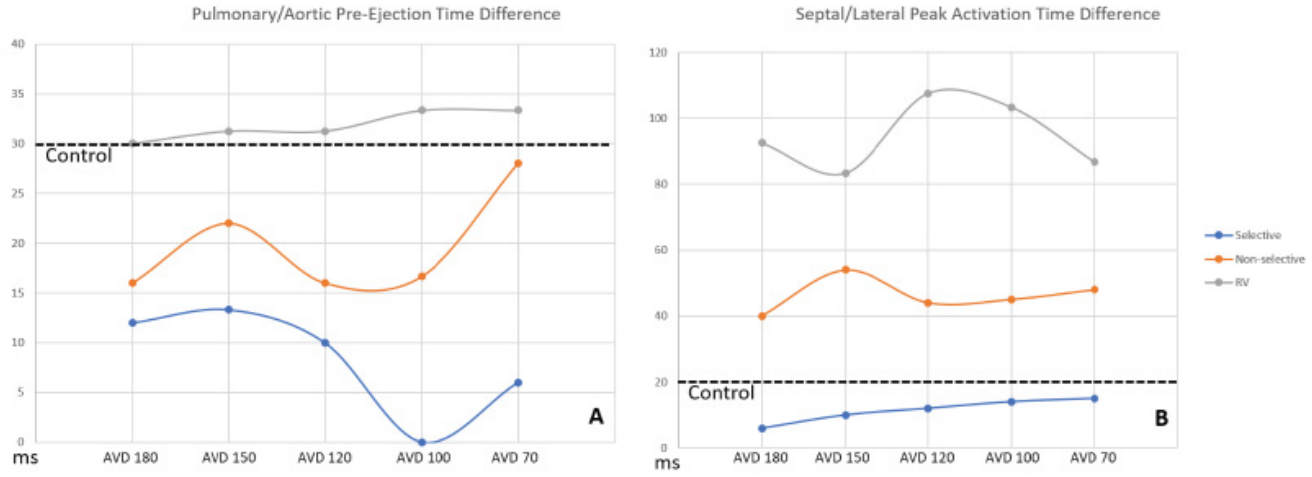

Figure 5: Measures of ventricular synchrony displayed with inter-ventricular synchrony in panel A, while intra-ventricular synchrony displayed in panel B. The average control pre-ejection/activation times for inter/intra ventricular synchrony are displayed with straight dotted lines. Blue line is selective HBP; Orange is non-selective HBP; Gray is right ventricular pacing.

Figure 6: Absolute and Percent Change of LVOT VTI

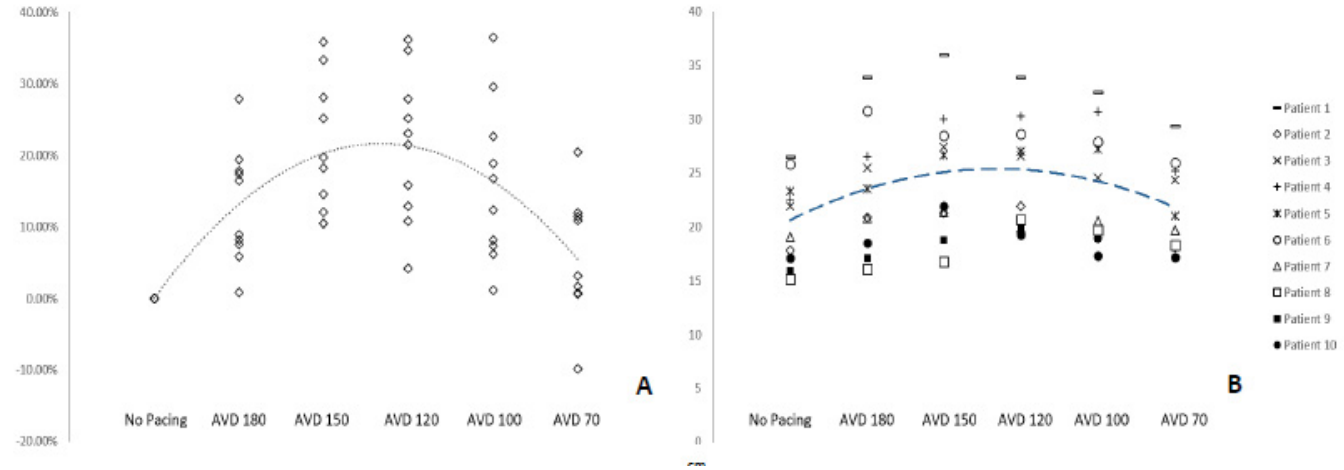

Figure 6: (A) The % change between the different AVD is displayed on the right with a dashed line depicting the average trend. (B) Individual patient absolute LVOT VTI (cm) trends. The dashed line depicts the average values trend.

With respect to individual components, HBP shows a noteworthy improvement in markers of AV synchrony when compared to controls. All patients with His bundle pacing were able to achieve >40% EA/RR and E/e' <14 compared to 60% of controls, and 30% achieving normal LAP pressures compared to 0% of controls. This is due to atrial lead sensing, which may allow for closer pairing of ventricular contractions with atrial activity. Though HBP trended towards higher markers of AV synchrony, improvement in these markers occurred in both HBP and RV pacing. However, HBP outperformed RV pacing in other ways, including LVOT VTI. This finding indicates that HBP may allow for more synchronized filling of the ventricle, independent of optimizing AVDs. While AV synchrony was optimized for most patients at an AVD of 150ms or 120ms it is important to note that two patients had optimum improvement with an AVD of 100ms. This highlights the individual nature of pacing optimization and that each patient is unique in their pacemaker needs. In addition, optimal AVDs may change over time for patients based on other factors, such as loading conditions, requiring additional optimization over time.

RV pacing resulted in marked intra-ventricular dyssynchrony (>56ms), while there was no evidence of His bundle pacing causing any degree of ventricular dyssynchrony. Improvement in intra-ventricular synchrony may be affected by correction or improvement of underlying

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Figure 7: LVOT VTI % Change Between Pacing Modes

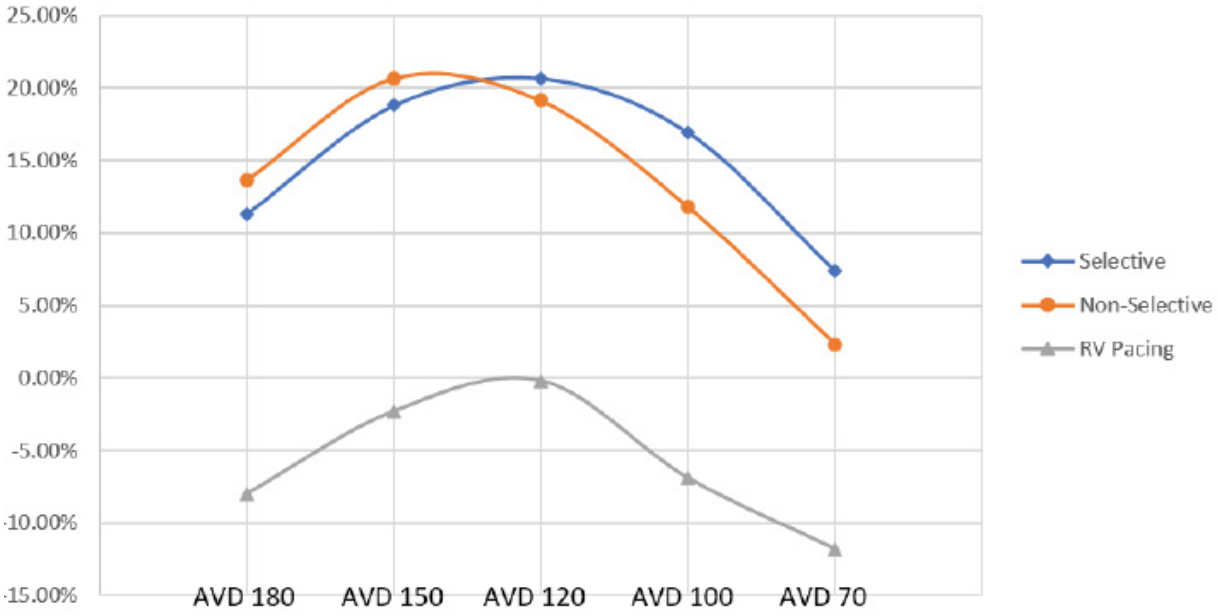

Figure 7: Comparison of LVOT VTI% change between selective, non-selective, and RV pacing. Blue line is selective HBP pacing; Orange is non-selective HBP; Gray is right ventricular pacing.

Figure 8: RBBB Capture

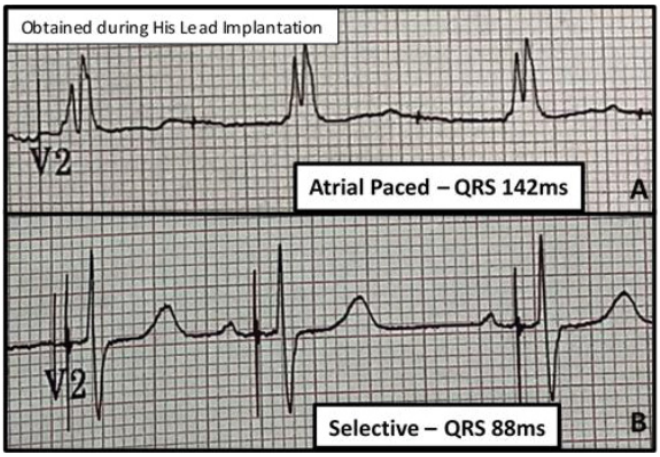

Figure 8: Example of HBP narrowing QRS by Right bundle recruitment.

conduction disease with HBP, which was most evident in 2 patients who had recruitment of the right bundles. This is emphasized by an average shortening of the QRS duration by 24ms with HBP in patients with underlying conduction disease, compared to controls. However, this degree of QRS narrowing did not meet markers of statistical significance and when evaluating the entire cohort, the average decrease in QRS was only 4ms.

Both AV and ventricular synchrony changes are likely secondary to utilization of the pre-existing conduction system. Being able to harness the native circuitry avoids ventricular dyssynchrony, as long as there is an absence of infra-Hissian conduction disease, or if the conduction system pacing captures beyond the level of the block. This, in turn, allows maintenance of ventricular synchrony at lower AVDs, which results in improved AV synchrony.

Improvement of LVOT VTI with HBP was significant with an average increase of >20% compared to controls which approached statistical significance ($p = 0.053$), without a notable difference between non-selective and selective HBP. The increased LVOT VTI is in part due to improved AV synchrony and subsequent LV filling, resulting in higher stroke volume. This is supported by simultaneous drops in AV synchrony and LVOT VTI at the shorter AVD of 70ms, despite ventricular synchrony being maintained. Furthermore, the highest LVOT VTIs and the most improved AV synchrony were seen at similar AVDs (150ms and 120ms). However, the degree of improvement in AV synchrony when comparing HBP to RV pacing (10.6%) was less than what was seen when comparing HBP to controls (31.5%). This would suggest that maintaining ventricular synchrony along with increased AV synchrony contributed to the increased LVOT VTI seen in HBP when compared to RV pacing. QRS narrowing when compared to baseline is unlikely to have contributed to the increase LVOT VTI, as there was only a minimal reduction in QRS on average, as previously noted. The increased LVOT VTI seen with HBP is a valuable physiologic finding as it serves as a marker of LV stroke volume. Accordingly, His bundle pacing at AVDs that maximize LVOT VTI may result in improved symptoms, and/or hemodynamics. In addition, very low LVOT VTI is predictive of adverse outcomes [27] and therefore, augmenting this value may improve prognosis.

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This is particularly important when considered RV pacing in patients with compromised LV function, as RV pacing was shown to be primarily deleterious to LVOT VTI.

These findings are applicable to not only patients with sinus node dysfunction and prolonged PR intervals, but theoretically may benefit patients with heart failure and prolonged PR intervals who would otherwise not qualify for resynchronization therapy, such has those without an underlying LBBB or IVCD. This echo study provides greater understanding of the physiologic and structural impacts of His bundle pacing in the setting of prolonged PR intervals, as well as providing insight into potential benefits of individual patient device programming.

Limitations

There are several limitations in this study. This is a single center, non-randomized study and the population is small, limiting generalizability. Interventricular synchrony was primarily shown via septal to lateral wall activation time and independent assessment of the right ventricular wall was not performed. LV stroke volume was not directly measured with the LVOT VTI being used as a surrogate marker. Lastly, there was an overall decrease in QRS duration which may have contributed to the Doppler findings, though this decrease was not statistically significant and is thought less likely to have impacted the results.

Conclusions

In this single center, observational study, patients with prolonged PR intervals >240ms were demonstrated by Doppler echocardiography to have improved markers of AV synchrony, LAP, and LV stroke volume using physiologic HBP compared to controls or conventional RV pacing, while maintaining ventricular synchrony. This benefit of HBP was noted with both selective and non-selective pacing modes. Doppler echocardiographic evaluation of other forms of conduction system pacing, such as left bundle branch or left bundle branch area pacing, would be beneficial. Larger prospectively designed studies are required to demonstrate if these imaging findings portend clinical benefits, especially in the heart failure population.

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