

Assessing Reduction in Left Ventricular Activation Time with His-Bundle Pacing Utilizing a Novel Left Lateral Accessory Pathway Model

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Abstract

Aims: Right ventricular pacing results in a prolongation of the left ventricular activation time, which is attributed to delayed activation of the left ventricular lateral wall. Left ventricular activation time has only been indirectly recorded in human subjects. The objective of this study was to model to directly measure left ventricular activation time utilizing a novel left lateral accessory pathway model and assess its shortening with His-bundle pacing, a proposed physiological pacing modality.

Materials and Methods: Consecutive adults with a pure retrograde conducting left lateral accessory pathway and both His-bundle as well as isolated myocardial capture were included. The interval from the pacing stimulus to the atrial activation in the left lateral region was measured as the left ventricular activation time, which was then compared during His-bundle versus myocardial pacing using paired t-test for means.

Results: A total of 50 subjects were found eligible for inclusion (Males=27; mean age=39±14). His-bundle pacing resulted in a significant reduction of left ventricular activation time when compared to myocardial pacing (122±15 vs 152±17; p<0.001).

Conclusion: Left ventricular activation time can be directly recorded in human subjects utilizing a pure-retrograde left lateral accessory pathway model and is significantly reduced with His-bundle pacing.

Keywords: Ventricular dyssynchrony; Para-Hisian; His-bundle; Optimal pacing; Left ventricular activation time

Abbreviations: LVAT: Left Ventricular activation time; LLAP: Left lateral accessory pathway; CS: Coronary sinus

Introduction

Ideally, ventricular pacing should be as physiological as possible to prevent dyssynchrony and consequent ventricular dysfunction. Non-physiological pacing modalities, such as right ventricular pacing, have many negative hemodynamic effects that have been attributed to delayed activation of the left ventricular free wall [1] and the resultant increase in left ventricular activation time (LVAT). Direct His-bundle [2,3] and para-His [4] pacing with His bundle capture have been suggested as strategies to preserve the normal activation sequence and maintain synchrony by reducing LVAT.

LVAT may be superior to surface ECG in the assessment of left ventricular synchrony and its accurate measurement may help predict response to physiological pacing modalities as well as cardiac resynchronization therapy. Several methods have been used to measure LVAT in humans, including experimental techniques [5] as well as indirect measurements using three-dimensional electroanatomic mapping [6] and ventricular electrograms recorded from the coronary sinus [7].

Hitherto, LVAT has not been directly recorded in human subjects. We utilized a novel left lateral accessory pathway (LLAP) model to directly measure LVAT in human subjects. Shortening of LVAT with His-bundle pacing as compared to direct myocardial pacing was assessed using this model.

Materials and Methods

This prospective study was conducted at a tertiary cardiac center over a three-year period (January 2007 to December 2009) and was approved by the director of Holy Family Hospital, Mumbai, India. Consecutive subjects undergoing electrophysiological testing for documented narrow QRS tachycardia (suspected atrioventricular re-entry tachycardia) were screened for inclusion. Eligibility criteria for inclusion were: (1) Age>18 yrs; (2) No prior known cardiac/arrhythmia history (apart from suspected atrioventricular re-entry tachycardia) (3) A normal echocardiogram including normal chamber dimensions, left ventricular ejection fraction and inflow pattern; (4) Normal QRS duration during sinus rhythm with absence of underlying bundle branch block; (5) Ability to introduce a decapolar catheter through the femoral route with the distal electrodes in the left lateral region; (6) Presence of a non-decremental LLAP; (7) Retrograde conduction solely via the LLAP during right ventricular stimulation at a cycle length of 400 ms; (8) Ability to obtain both His-bundle capture and isolated myocardial capture from the His-bundle region during para-His pacing.

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Electrophysiological study was performed with patients in a fasting state under local anesthesia with 2% Lidocaine. Drugs that could interfere with the electrophysiology study such as beta-blockers and calcium channel blockers were discontinued three to five days prior to the procedure. Mapping was performed using a 6 Fr, deflectable, decapolar catheter (Cordis-Webster), with a 2-mm inter-electrode distance within each pair and 5-mm of space between each electrode pair. The catheter was introduced via the femoral vein and advanced under fluoroscopic guidance such that the distal tip was in the left lateral region (Figure 1a and Figure 1b). A 6 Fr deflectable quadripolar catheter (Cordis-Webster) was positioned at the His-bundle region for pacing. A cycle length of 400 ms was chosen for pacing to prevent retrograde AV nodal conduction at higher cycle lengths. Initially bipolar pacing was performed with current strengths just above capture threshold; subsequently, current strength was increased to achieve His-bundle capture. His-bundle capture was confirmed using the following criteria: 1) Electrocardiographic concordance of QRS complexes and T

waves suggesting His-Purkinje mediated depolarization/repolarization; 2) Similarity of paced-ventricular and His-ventricular intervals.

Initially, we sought record a 'bracketing' pattern of the atrial electrograms in the coronary sinus (CS) electrodes during ventricular pacing, such that the electrograms in the distal and proximal CS electrodes occurred after the electrogram in the middle CS electrode. This would confirm that we had successfully recorded the earliest atrial activation. However, in several patients it was not possible to advance the CS electrode more distally due to the presence of a valve in the left lateral region. Hence, for the sake of uniformity, the CS electrode was placed in a position depicted in (Figure 1 and Figure 2). The interval from pacing the His-bundle region to earliest atrial activation in the left lateral region was measured as the LVAT. The QRS duration and LVAT were measured after both myocardial and His-bundle capture (Figure 2) for each subject. These measurements were performed by a single experienced reader using on-screen digital calipers (CardioCalipers 3.3 for Windows [Iconico, New York, New York; available at: <http://www.iconico.com>]) with a 1 ms resolution. The intra-reader variability evaluation was performed on a sub-set of 25 tracings for the reader. The mean intra-reader variability was 4 ± 3 ms for QRS duration and 5 ± 3 ms for LVAT.

Mean and standard deviation were calculated for QRS duration and LVAT. Values from myocardial and His-bundle pacing were compared using a paired Student's t-test. A p value < 0.05 was considered significant.

Results

A total of 50 patients were found eligible for inclusion with 27 males and 23 females. The mean age was 39 ± 14 years and atrioventricular re-entry tachycardia was inducible in all these patients during the electrophysiological study. The results are depicted in Figure 3. As

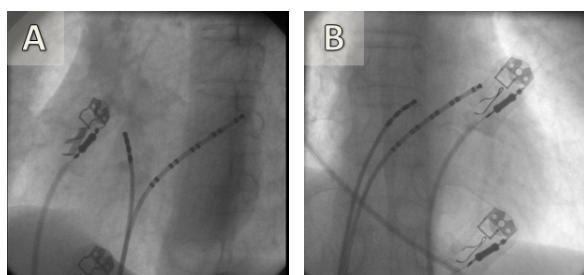


Figure 1: A- 40 degree left anterior oblique projection showing the position of the decapolar catheter in the coronary sinus; B- Anterior posterior projection showing the position of the decapolar catheter in the coronary sinus.

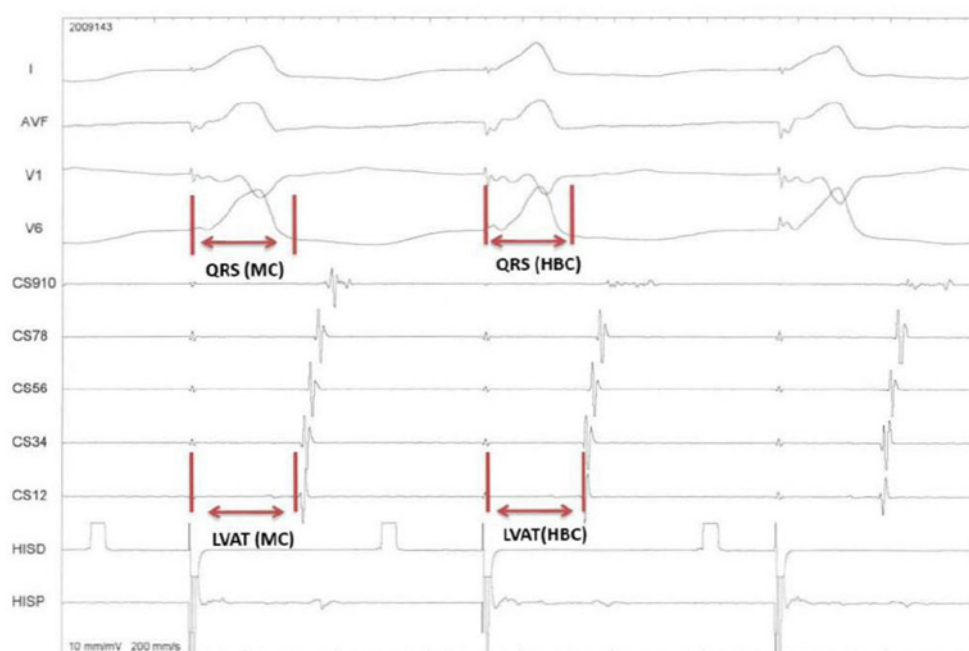
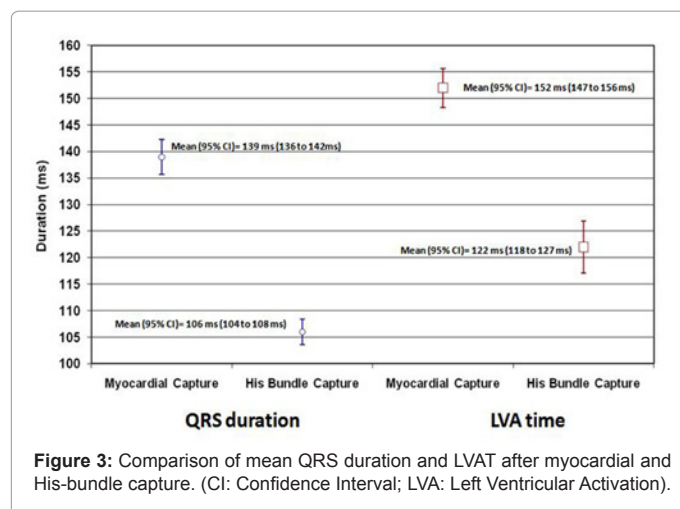


Figure 2: An example of recording the QRS duration and left ventricular activation time (LVAT) with isolated myocardial capture and His-bundle pacing. The interval from the pacing stimulus to the left lateral atrial electrogram was measured as the LVAT. (HBC: His-bundle capture; MC: Myocardial capture; LVAT: Total ventricular activation time)



expected, the QRS duration was reduced with His-bundle capture when compared to pure myocardial capture (106 ± 9 vs 139 ± 11 ; $p < 0.001$). The LVAT was also significantly lower with His-bundle capture than myocardial capture (122 ± 15 vs 152 ± 17 ; $p < 0.001$).

Discussion

We propose a novel LLAP model for directly measuring LVAT in humans. Utilizing this model, we have demonstrated a significant reduction in LVAT with His-bundle pacing when compared to myocardial pacing.

In animals, directly recorded unipolar electrograms have been used to accurately assess LVAT [8]. LVAT in human subjects was initially estimated from ECG recordings [9,10]. Over the years, it has been indirectly measured in humans using non-fluoroscopic three-dimensional endocardial mapping [6] and ventricular electrograms recorded from the coronary sinus [7]. A LLAP with pure retrograde conduction provides the unique opportunity to directly measure LVAT in humans from recording the earliest atrial electrogram in the CS electrode and assess its shortening by pacing at different sites. Comparison of data from this model with previous methods will be beneficial and should be pursued in future studies.

Using QRS duration [11] and epicardial maps [5], reduction in LVAT by proximal septal versus apical pacing has been demonstrated in animal experiments. However, using the surface QRS duration as a surrogate for LVAT may be misleading, especially in the setting of cardiomyopathy and right ventricular myocardial disease. To the best of our knowledge, this is the first report of shortening of LVAT as measured by His-bundle pacing that has been directly assessed in human subjects. Though a similar conclusion can be drawn from QRS shortening, the use of this model proves that the delay by non-physiological pacing is primarily due to late activation of the left ventricular lateral wall, which has only been shown in-vitro and in electro-anatomic models thus far. The late contraction of the left ventricular lateral wall against a relaxed septum during right ventricular pacing is thought to be responsible for reduction in systolic function, mitral insufficiency (from papillary muscle dysfunction) and diastolic failure [from increased ventricular systolic time] [1]. Accurately measured LVAT reduction may serve as a better predictor of response to cardiac resynchronization therapy than surface QRS shortening.

The benefits of physiological pacing cannot be overemphasized. Right ventricular apical pacing leads to electrical as well as mechanical ventricular asynchrony resulting in poor clinical outcomes [12]. Biventricular pacing has demonstrated significant improvement in cardiac function as well as quality of life in presence of LV dysfunction with left bundle branch block [13,14]. However, with preserved intraventricular conduction, His-bundle pacing would be expected to result in a more physiological activation of the ventricles. As such, permanent His-bundle pacing [2,3] as well as the technically easier para-Hisian pacing [4], have shown an improvement in hemodynamic function and clinical outcomes when intraventricular conduction is preserved. The result of this study provides further encouragement for refinement of such “physiological” pacing modalities.

Limitations of our study include the exclusion of other comorbidities and medications from the analysis, which may affect LVAT measurement. The LVAT is marginally overestimated as it includes the conduction time across the accessory pathway as well as atrial tissue between the accessory pathway insertion site and the CS pole; this may be especially pronounced with decremental accessory pathways (which were excluded in our study). The LLAPs that are slightly anterior in location are closer to the left anterior fascicle and will hence record shorter LVATs compared with the posterior LLAPs. Our method did not account for this and could cause variation in the measured LVATs as compared to the actual LVATs. Additionally, we could not advance the CS catheter to the desired position in all patients (see methods). However, each patient served as his/her own control in the study. Hence, the aforementioned limitations will not affect the primary objective of our study, which is assessing the reduction in LVAT with para-His pacing with His bundle capture, as compared with isolated myocardial pacing.

In conclusion, His-bundle pacing resulted in a significant reduction in LVAT as compared to myocardial pacing when measured by a novel LLAP model. Larger studies are needed to validate our findings.

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