Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: June 30, 2024

Citation: Mahmud R, Anderson RH, et al., 2024. Transfiguration of Human Atrioventricular Conduction Axis with His bundle Pacing: Effect on Underlying Bundle Branch Block, Medical Research Archives, [online] 12(6). https://doi.org/10.18103/mra.v12i6.5373

DOI
https://doi.org/10.18103/mra.v12i6.5373

ISSN: 2375-1924

RESEARCH ARTICLE

Transfiguration of Human Atrioventricular Conduction Axis with His bundle Pacing: Effect on Underlying Bundle Branch Block

Rehan Mahmud*[1], Robert H Anderson[2], Damian Sanchez-Quintana[3], Eduardo Sternick.[4]

[1]College of Medicine, Central Michigan University, Mt. Pleasant, MI, USA
[2]Biosciences Institute, Newcastle University, Newcastle-upon-Tyne, United Kingdom
[3]Department of Human Anatomy and Cell Biology, Faculty of Medicine, University of Extremadura, Badajoz, Spain
[4]Arrhythmia and Electrophysiology Department, Biocor Institute, Nova Lima, Brazil

***Corresponding author:** Rehan drmahmud@msn.com

ABSTRACT
His bundle pacing comes with the expectation of avoiding morbidity and mortality associated with pacing the ventricular myocardium. The His bundle paced complex typically exhibits a delta wave and resembles the relatively normal QRS complex of fasciculoventricular preexcitation, which we now believe is caused by activation of dormant septal connections found in most adult hearts. In patients with bundle branch block, His bundle pacing 'corrects' both right and left bundle branch block, but the mechanism of correction remains unclear. We selected 51 consecutive patients with normal QRS complex, 35 patients with right bundle branch block and 41 patients with left bundle branch block who underwent His bundle pacing pacing for guideline-based indications, and analyzed the changes in the paced QRS complex. In all patients His bundle pacing caused a decrease in ventricular activation time, an increase in lead 1 voltage, an inferior shift in the frontal QRS axis, and a rightward shift in of the R wave transition in the precordial leads. In patients with normal QRS complexes, despite these changes, the paced complex remained in normal range. In left bundle branch block, these changes resulted in decrease of prolonged ventricular activation time, increased lead 1 voltage, with normalization of the delayed R wave transition in the precordial leads. The correction of right bundle branch block suggested that the right ventricular free wall was being activated earlier. This was consistent with early rightward transition of the precordial R waves, the inferior QRS axis, and the known base-to-apex activation of the right ventricular wall in fasciculo-ventricular preexcitation. We conclude that the His bundle paced complex, like that seen in fasciculo-ventricular preexcitation, is caused by rapidly conducting, base-to-apex, and septum-to-lateral wall activation in both left and right ventricles. This would explain the correction of left axis deviation, and the reversal of the delayed activation of the lateral walls in both right and left bundle branch block.
Keywords: His bundle pacing. Fasciculo-ventricular connections.

Introduction

The atrioventricular conduction axis of the human heart controls the optimal timing between the atrial and the ventricular contractions. The normally conducting bundle branches initiate myocardial activation from the mid-septum and paraseptal regions in an apex-to-base direction. Decades of research has established that pacing the ventricular myocardium increases cardiac morbidity and mortality.[1,2] What is less well known is that the avoidance of ventricular pacing by preferring atrial pacing disrupts the atrioventricular timing, with outcomes comparable to those associated with the high burden of ventricular pacing.[3-7] Pacing the conduction axis comes with the promise of normal myocardial activation and preservation of normal atrioventricular conduction delay. In patients requiring permanent pacing, the conduction axis and its ramifications are often diffusely diseased. This makes it unlikely that selectively pacing the diseased axis would 'correct' the conduction block.[8] We have recently reported that His bundle pacing results in activation of the dormant connections known to exist, in most adult hearts, between the His bundle and the crest of the muscular ventricular septum. [9,10] When activating these superior septal pathways, the His bundle paced complex is no different than observed in individuals with overt fasciculo-ventricular preexcitation.[10] In this study, we have analyzed the electrocardiographic changes of fasciculo-ventricular preexcitation in His bundle pacing, aiming to assess possible mechanisms by which activation of the septal connections might lead to the observed 'correction' of both right and left bundle branch block.

Methods

Informed consent, following the guidelines established by the Helsinki declaration, was obtained in all patients. In our institution, all patients undergoing permanent pacing for guideline-based indications received a His bundle pacing lead. We selected 51consecutive patients with normal QRS complexes, 35 consecutive patients having right bundle branch block and left axis deviation, and 41 consecutive patients with left bundle branch block. We made a detailed analysis of the changes noted in the paced QRS complex. For His bundle pacing, we used a steerable Medtronic C-304 guide catheter to deploy a Medtronic 3830 lead. A distal His bundle electrogram was recorded, and a pacing threshold was obtained. Sites were accepted for permanent pacing only when the paced QRS complex remained in normal range. His bundle pacing was done at a pulse width of 1.0 msec. Pacing was started at 5 volts, and decreased to 0.25 volts. Ventricular activation times were measured from the pacing stimulus to the peak of the R-wave in lead I. As the voltage was lowered, the paced QRS was examined for prolongation of the ventricular activation times, the presence or absence of the delta wave, and changes in the QRS axis. For statistical analysis, we have presented continuous variables as means with standard deviation, and categorical variables as totals with percentages. All tests were 2-sided, with P values less than 0.05 indicating statistical significance.

Results

Only one individual who underwent His bundle pacing for sinus nodal dysfunction had overt intermittent fasciculo-ventricular preexcitation. In this patient, pacing at the site of the His bundle electrogram resulted in a paced complex comparable to the pre-excited complex observed during sinus rhythm. When pacing at lower voltage, the fasciculo-ventricular connection was no longer activated, with activation exclusively via the His bundle. The paced QRS complex then resembled a normally conducted sinus beat.

In all 51 patients with normal QRS complex, the paced complex showed a delta wave. The ventricular activation time of the paced complex decreased from 92 msec in sinus rhythm, to 87 msec with His bundle pacing ($p<0.01$). The lead I voltage increased significantly from 0.6 mv in sinus rhythm to 0.9 mv ($p<0.05$). The frontal QRS axis became more inferior but remained in normal range. We also noted an earlier transition of the R waves in the precordial leads from V4 to V3. (Figure 2)

His bundle pacing in a patient with intermittent fasciculoventricular pre-excitation.

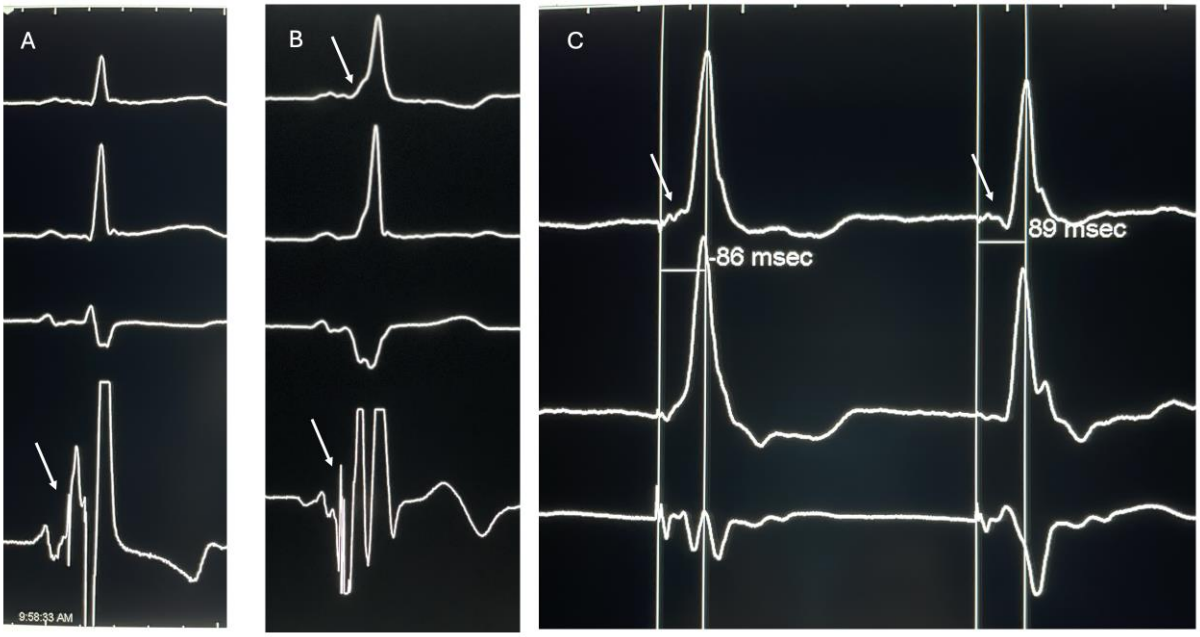

Figure 1. Panels A shows ECG leads 1, 2 and V1 and His bundle recording (arrow) in a normal sinus rhythm. Panel B shows fasciculoventricular preexcitation in same patient. Panel C shows His bundle pacing with and without a delta wave, compare with panels A and B.

Effect of His bundle pacing in patient with normal QRS complex

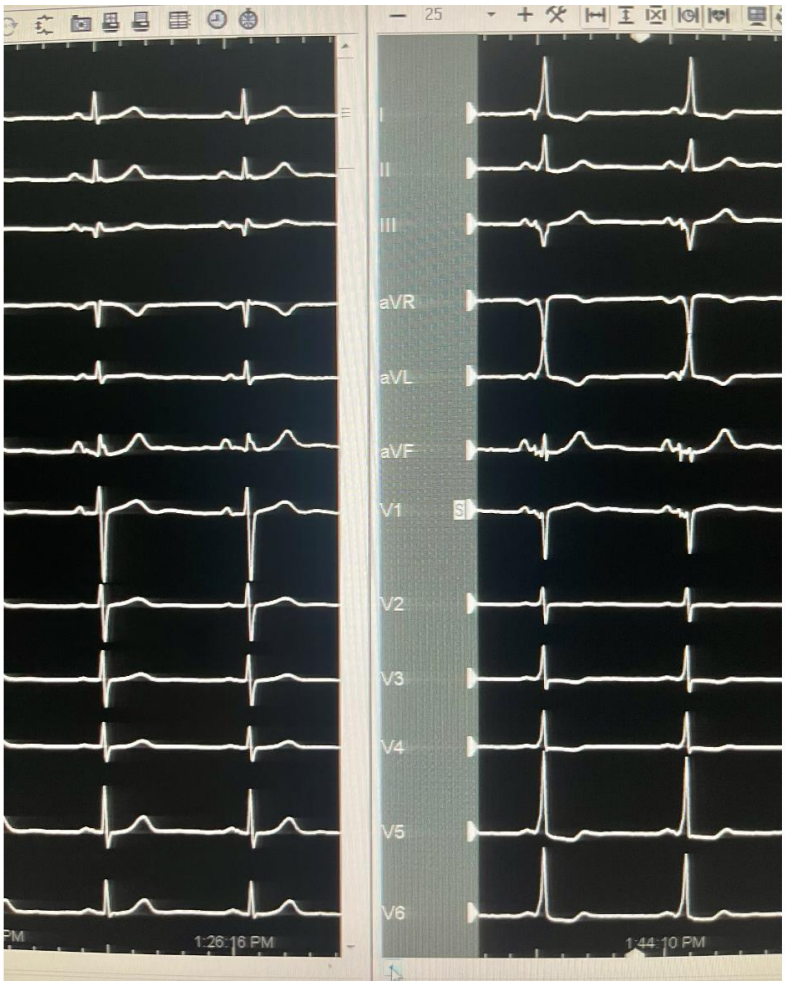

Figure 2: Left panel shows a 12-lead electrocardiogram of individual with normal QRS complex. Right panel shows typical changes with His bundle pacing. The paced complex remains in normal range and is no different from that in individuals with fasciculoventricular preexcitation. See text for details.

In the 35 patients with right bundle branch block, the abnormal changes were corrected only when a delta wave was observed in the paced complex (Figure 3). In 17 of these 35 patients, the delta wave was lost when pacing at lower voltages. Selective His bundle pacing was obtained with an isoelectric stimulus to QRS interval, and this was associated with abrupt recurrence of right bundle branch block (Figure 3, panel B).

Effect of His bundle pacing on right bundle branch block

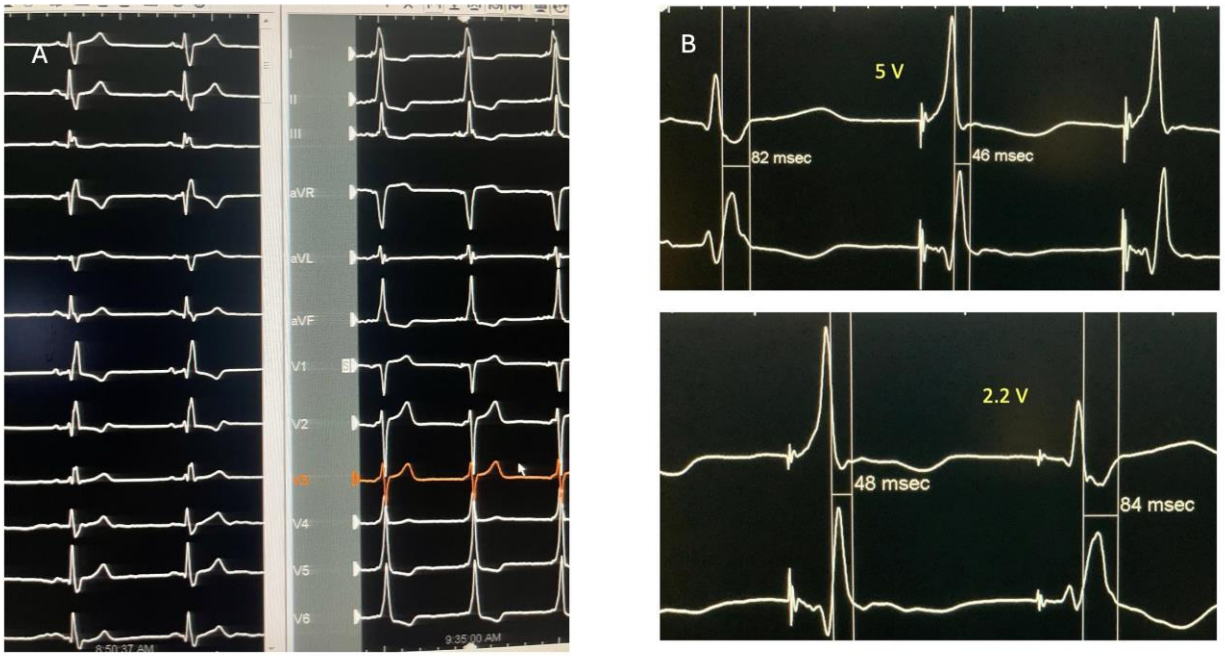

Figure 3. Panel A shows a 12-lead ECG of right bundle branch block and its 'correction' with His bundle pacing.

Panel B shows the characteristic feature of right bundle branch block (a broad S wave in lead 1) is corrected only when His bundle pacing causes a delta wave and recurs abruptly with His bundle pacing without preexcitation.

In 41 patients with left bundle branch block, the paced complex showed a delta wave, the left ventricular activation time decreased by 63msec from 188 msec to 125 msec ($p<0.01$), the lead1 voltage increased from 0.5 mv to 1.0 mv ($p<0.01$), the mid-QRS notch was resolved, the QRS axis remained in normal range, and left axis deviation was corrected (Figure 4). In 11 patients, as the pacing voltage was lowered the QRS complex widened, the lead 1 voltage decreased, the frontal QRS transitioned leftward, and the R wave transitioned leftward. These changes became more pronounced, with appearance of complete left bundle branch block, concomitant with abrupt loss of delta wave (Figure 3). In 16 patients with left axis deviation, the paced complex with a delta wave normalized the axis from -35° to +30° ($p<0.01$). In patients with left bundle branch block, the precordial R-wave transition occurred at lead V6. During His bundle pacing, however, the transition occurred between leads V3 and V4 ($p<0.01$).

Discussion

Our observations suggest that the superior septal connections between the His bundle and the basal crest of the muscular ventricular septum[9,10] have conduction properties comparable to those of the bundle branches. The main difference is that, unlike the bundle branches, the septal pathways remain dormant in sinus rhythm. Pacing at higher voltages is required to permit them to conduct rapidly. These pathways were first described as 'superior septal connections' by Mahaim in the 1930's.[9,10] They were later recognized by Hecht and colleagues as part of normal arrangement of the atrioventricular conduction axis.[10] Later labelled as fasciculo-ventricular pathways, their potential significance, being ubiquitous but electrically silent, has remained unrealized for decades. In this regard, it was accepted that normal cardiac activation is determined by conduction through the bundle branches, with the process starting from the distal septum and the paraseptal areas. The overall myocardial activation is then leftward and occurs from apex-to-base.[12,13]

The fasciculo-ventricular connections, however, can initiate myocardial activation from the septal crest. This shifts the QRS axis inferiorly in the frontal plane and increases the lead 1 voltage, reflecting the base-to-apex activation of the septum and the lateral ventricular walls.[13] The process is then seen as being rightward in the precordial leads, caused by early activation of the basal right ventricle,[14] with reversal of the normal 'apex-to-base' activation.[13] His bundle pacing in the setting, in essence, transfigures the conduction axis, which now includes fasciculo-ventricular preexcitation. This process is well represented in the changes observed in the normal 12-lead electrocardiogram, as well as in the electrocardiograms of individuals with right and left bundle branch block (Figure 2-4).

Effect of His bundle pacing in left bundle branch block

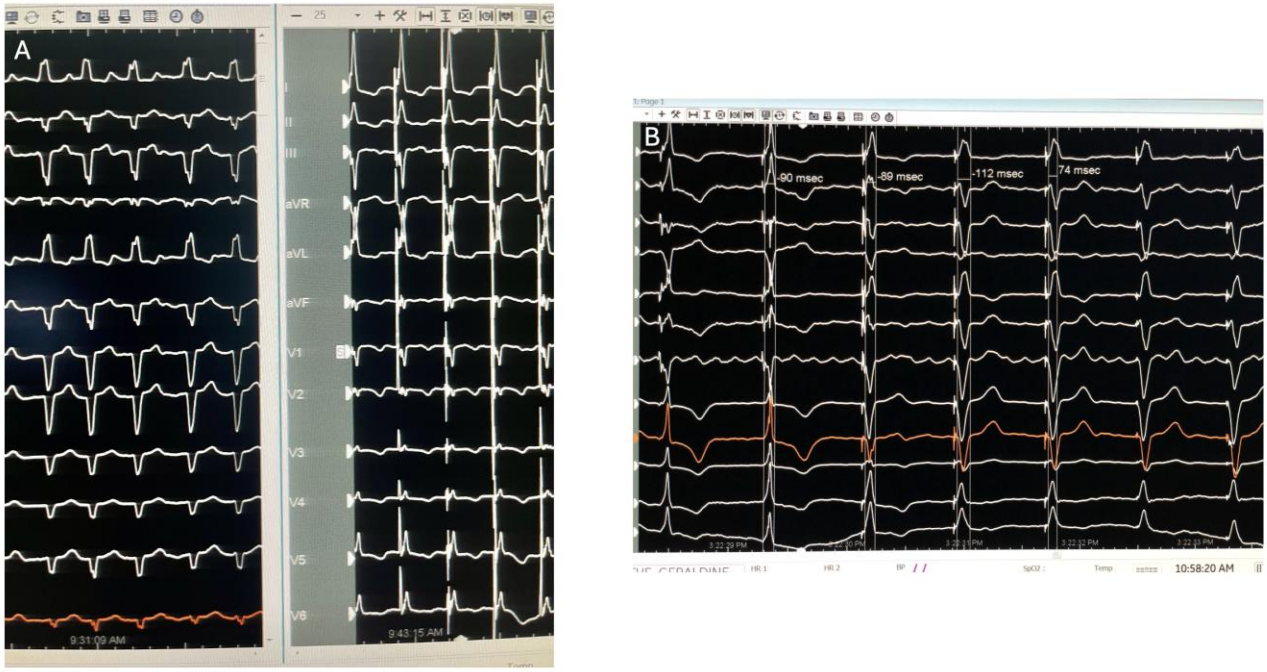

Figure 4. Panel A shows left bundle branch block and its correction with His bundle pacing. Panel B shows progressive transition to left bundle branch morphology as the pacing voltage is decreased. Note the widening of QRS, decrease in lead 1 voltage, the left axis and late precordial transition are reverse of chages caused by His bundle pacing.

The three-dimensional non-invasive activation map by Ghosh and colleagues, reproduced here with permission (Figure 5), allows a comparison to be made between the normal myocardial activation and the activation observed in individuals with fasciculo-ventricular pre-excitation.[13] This visual representation clarifies how widely separated regions of conduction delay caused by right and left bundle branch block and left superior fascicular block are 'corrected' by activation of the dormant septal pathways. The basal septal activation is quickly followed by activation of the left ventricular lateral wall in normal time (panels A-C).[13] The left superior fascicular block causes left axis deviation by delaying activation of the antero-superior paraseptal basal area of the left ventricle. This area, however, is activated early by the fasciculo-ventricular connections (Figure 5). This explains how the left axis deviation is nearly always corrected by His bundle pacing when a delta wave is present (Figure 4). As the activation continues to spread leftward anteriorly and posteriorly from the basal septum, it will activate early the left ventricular lateral wall, which is activated late in left bundle branch block, thus normalizing the characteristic notched and wide QRS complex. The right bundle branch block is caused by a delay in the activation of the right ventricular lateral wall. It is corrected when basal septal activation is followed by early activation of the basal right ventricular free wall in a base-to-apex direction (Figure 5 C).

Epicardial Maps in Normal Activation and in Fasciculoventricular Preexcitation

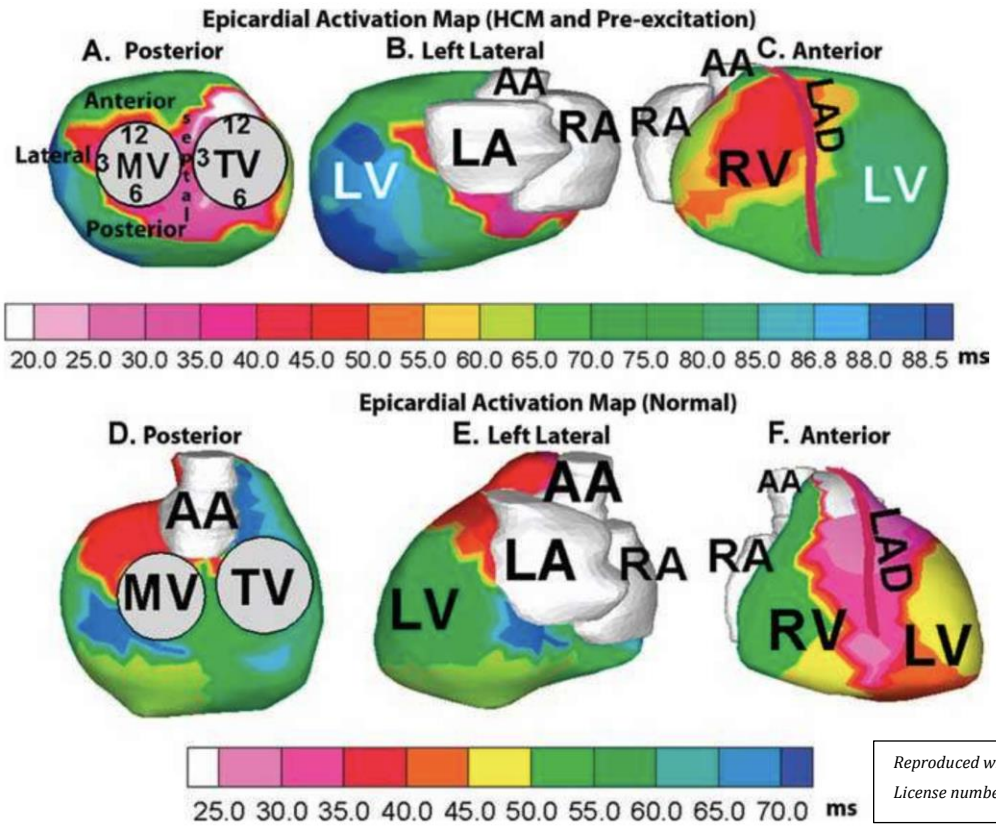

Figure 5. Myocardial activation times in fasciculoventricular preexcitation (A-C) is compared with normal activation (C-D). The normal apex-to-base activation of right ventricular free wall (F) changes to base-to-apex activation in fasciculoventricular preexcitation (C). The overall septum to left ventricular lateral wall activation times are similar.

Sharma and colleagues, also using non-invasive epicardial maps, showed that, when His bundle pacing corrected right bundle branch block, the base of the right ventricular wall was activated early.[14] In our own study of 'correction' of right and left bundle branch block with His bundle pacing, we found that the correction was more complete when we paced at higher voltages[16,17] (Figures 3 and 4). At lower voltages, the delta wave was prolonged. Slowing of conduction in the fasciculo-ventricular connection was then associated with progressively greater evidence of bundle branch block. At pacing voltages where conduction ceased in the fasciculo-ventricular connection, observed as a loss of the delta wave, there was abrupt recurrence of the underlying bundle branch block pattern (Figures 3 and 4). The conduction block in the septal connections is to be expected when pacing at lower voltage, as these connections do not conduct at the very low activation voltage of a sinus impulse. The voltage-dependent pacing phenomenon is unlikely to occur had the delta wave been the consequence of bystander activation of working septal myocardium.

Comparable superior septal connections have been described in mice by Lev and Thaemert, who recognized them as 'Mahaim fibers' between the branching His bundle and septum.[17] These findings are now further endorsed by our own observation in a single heart (Figure 6).

Fasciculoventricular connection in human and murine hearts

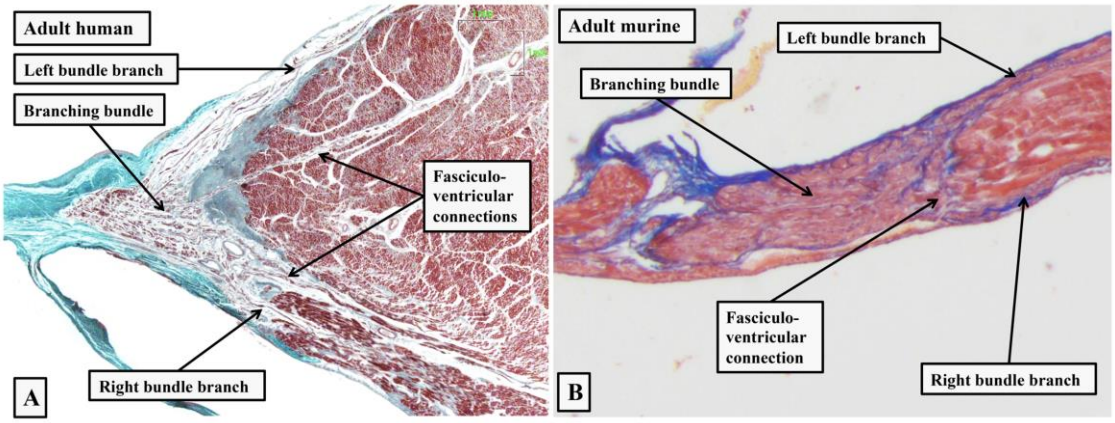

Figure 6. Panel A shows fasciculo-ventricular pathways, connecting the His bundle with the septum in human heart. Similar connections are present.in the murine heart (panel B).

In the murine heart, however, there is evidence that these connections conduct during normal sinus rhythm. In consequence, the overall cardiac activation has been described as occuring in base-to-apex fashion, comparable to that seen in human fasciculo-ventricular pre-excitation.[13,18] Thus, van Rijen and colleagues, when investigating the activation of the murine heart, showed that, in mutagenic animals with CX40 gap junction protein deficiency, conduction block could be observed in the smaller diameter right bundle branch, while conduction delay was present in the left bundle branch. The base-to-apex myocardial activation maps obtained in these CX40 deficient mice, nonetheless, remained unchanged when compared to their findings in the wild-type mice without bundle branch block.[18] These investigators suggested that electrical continuity between the common bundle and the septum prohibited comparison of mouse and human conduction axis, perhaps not taking into consideration findings of Mahaim and the common occurrence of fasciculoventricular preexcitation in man. Their results, nonetheless, are consistent with our explanation that, with His bundle pacing, it is the activation of the septal connections which masks the patterns of right and left bundle branch block. This interpretation, however, is contrary to the generally held belief that His bundle pacing corrects left bundle branch block because the lead tip is distal to a solitary culprit lesion in the atrioventricular conduction axis. In our experience, selectively pacing of the His bundle when a delta wave is not evident hardly ever 'corrects' either right or left bundle branch block.[15,16]

Conclusion

In this study, we have extended our previous work showing that His bundle pacing resulted in the excitation of dormant septal connections, producing a paced QRS that is no different than the pattern observed in individuals with fasciculo-ventricular preexcitation.[10] We have presented evidence that the electrocardiographic changes, which include a delta wave, an inferior frontal QRS axis, earlier precordial transition of the R waves, an increase in the lead 1 voltage, and a decrease in ventricular activation time, can also be observed in patients with bundle branch block. These changes reverse the widening of the QRS complex and the decrease in the lead 1 voltage observed with left bundle branch block. The left axis deviation is corrected by an inferior shift in the frontal QRS axis. The correction of the right bundle branch block is explained by earlier base-to-apex activation of the right ventricular free wall. Thus, His bundle pacing transfigures the atrioventricular conduction axis by activating dormant septal pathways. In patients with normally conducting bundle branches, the paced QRS complex remains in the normal range. In patients with bundle branch block, the septal activation mitigates the abnormal myocardial activation.

Conflict of interest: None

Funding sources: None

Acknowledgements: Yoram Rudy and colleagues for graciously allowing us the use of their illustration.

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