Retrograde slow pathway conduction in patients with atrioventricular nodal re-entrant tachycardia

Demosthenes G. Katritsis1*, Kenneth A. Ellenbogen2, Anton E. Becker3, and A. John Camm4

1 Department of Cardiology, Athens Euroclinic, 9 Athanassiodou St., Athens 11521, Greece; 2 Division of Cardiology, Medical College of Virginia, Richmond, VA, USA; 3 Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; and 4 Cardiac and Vascular Sciences, St George’s, University of London, London, UK

Received 22 February 2007; accepted after revision 21 March 2007; online publish-ahead-of-print 3 May 2007

Introduction

Little data exist describing the physiology of retrograde slow pathway conduction over the slow pathway in patients with typical (slow–fast) atrioventricular nodal re-entrant tachycardia (AVNRT) before and after ablation. Initial studies have demonstrated continuous ventriculo-atrial (VA) conduction curves with either fixed or minimal prolongation of the VA interval in patients with typical, slow–fast AVNRT.1–3 This has traditionally been explained by attributing all retrograde conduction jumps to the fast pathway.4 Decremental conduction or retrograde dual pathways, however, may also occur,5–8 although retrograde dual pathway conduction is demonstrated in only 4–23% of patients with slow–fast AVNRT.7 The role, therefore, of retrograde slow pathway conduction as the cause of decremental VA conduction is unknown. Retrograde conduction through the slow pathway is associated with a change in the retrograde atrial activation sequence, with a switch from earliest activation in the septal right atrium to earliest activation recorded at the coronary sinus (CS) ostium.6,9 However, although the atrioventricular (AV) node represents a true septal structure, no detailed mapping of the left septum has been performed during ventricular pacing.

We hypothesized that retrograde slow pathway conduction in patients with typical AVNRT can be mapped by analysis of the retrograde atrial activation pattern. We further hypothesized that if the slow pathway represents a distinct anatomical entity, ablation of the slow pathway in patients with AVNRT should result in a change in the retrograde VA conduction and the retrograde atrial activation sequence. The purpose of this study was to perform detailed characterization of retrograde slow pathway conduction in patients with AVNRT by means of right and left septal mapping before and after slow pathway ablation.

Methods

Patients

Nineteen patients with discontinuous AV nodal conduction curves and inducible typical slow–fast AVNRT were studied before and
after successful completion of the ablation procedure. Atrioventricular nodal re-entrant tachycardia was diagnosed according to standard criteria. Slow pathway ablation was accomplished by a combined anatomic and electrogram recording approach from the right side in all patients. Patients were studied in the post-absorptive state, under sedation with diazepam and diamorphine, and after all antiarrhythmic agents had been discontinued more than 5 days. No patient had received amiodarone for the preceding 3 months. The study received approval from our institutional review board, and all patients signed written, informed consent.

Electrophysiological study

Electrodes were introduced into the right atrium, across the tricuspid valve to record a right-sided His bundle electrogram, the CS, the right ventricular apex, and retrograde through the non-coronary cusp of the aortic valve to record a left-sided His bundle electrogram (Figure 1A–C) as described elsewhere. As retrograde positioning of the left septal catheter through the non-coronary cusp inevitably results in mapping of the anterior part of the septum, a trans-septal approach that should allow additional mapping of the left side of the septum was also attempted in 10 patients. Deflectable decapolar catheters with \( \frac{2}{5} \) mm interelectrode distance were positioned to record the His bundle electrogram on both the right and left sides of the septum. A deflectable decapolar catheter with \( \frac{2}{5} \) mm interelectrode separation was used for mapping the CS with the proximal pair of electrodes negotiating the ostium of the CS. Ventricular pacing was performed at a constant cycle length of 500 ms and stepwise decremented by 10 ms until AV nodal refractoriness was reached. Stimuli of 1 ms duration were delivered at twice the diastolic threshold. Care was taken to ensure catheter stability during recordings by means of continuous verification against stored fluoroscopic images and electrogram characteristics (Figure 2A and B).

Bipolar electrograms were filtered at 30–500 Hz, amplified at gains of 20–80 mm/mV, and displayed and acquired on a physiological recorder (Bard LabSystem Duo and Pro; Bard, Billerica, MA, USA), together with surface electrocardiograms. All measurements were accomplished at a speed of 200 mm/s using the on-line automated caliper system. Measurements were analysed by two different investigators at separate time intervals to assess inter-observer reproducibility. To assess temporal reproducibility, all measurements were made during repeated episodes of right ventricular pacing.

Definitions

Stimulus to atrium (St-A) intervals at constant pacing cycle lengths were measured from the stimulus artefact to the initial deflection of the atrial electrogram on the His bundle recording. Stimulus to atrium values obtained at retrograde VA maximal conduction decrement (St-A_{max}) were also recorded. Ventriculo-atrial conduction jumps or maximum decrement associated with change of retrograde atrial activation sequence were considered to indicate conduction via AV nodal inputs that engage fibres with slow pathway conduction properties (Figure 3). Retrograde conduction jumps were diagnosed using the criterion of an increase of at least 50 ms in the VA interval for a 10 ms decrease in the ventricular coupling interval. For comparative purposes, the difference (\( \Delta \)St-A) between St-A and St-A_{max} was also used as a measure of slow pathway conduction. Post-ablation, St-A values obtained at constant pacing and at maximal retrograde VA conduction decrement were measured.

Statistical analysis

Differences between St-A measured from the His bundle electrogram recorded from the right septum (R His) and the His bundle electrogram recorded from the left septum (TA His), and between St-A measured from R His and proximal coronary sinus electrode (pCS), were evaluated through the sign-rank test. This analysis was repeated for St-A_{max} and \( \Delta \)St-A. Intra-observer reproducibility of activation patterns was evaluated using the Bland–Altman method, which indicates the smallest detectable difference (i.e. the amount of detectable change above the random measurement error). The 95% confidence interval was estimated using the
method described by Shrout and Fleiss. Concordance between observers was assessed using the kappa coefficient. All reported P-values are based on two-sided tests and compared with a significant level of 5%. SPSS version 11.0 (SPSS Inc., USA) software was used for all statistical calculations.

Results

Electrophysiological study and ablation

Nineteen patients (11 men) with a median age of 41 years (range: 32–51) were studied before and after successful completion of the ablation procedure. All patients had normal left ventricular function, without evidence of underlying structural heart disease. Atrioventricular nodal conduction jumps and typical slow–fast AVNRT were reproducibly induced by atrial pacing in all patients. Ventricular pacing induced tachycardia in only two patients. Recording of a reproducible His bundle electrode from the trans-aortic approach was feasible in 18 patients. Recording of the His bundle electrogram from the trans-septal catheter was possible in only three out of the 10 patients in whom the technique was applied, despite prolonged mapping efforts. Comparisons between right and left His recordings, therefore, were mainly made by considering the left His recorded from the trans-aortic electrode. Slow pathway ablation was successfully accomplished in all patients, with elimination of inducibility of tachycardia and prevention of induction of echo beats. Continuous VA nodal conduction curves were documented in all patients after successful ablation.

Figure 2  (A and B) Verification of catheter position. Following the last ventricular extra-stimulus at 220 ms, there are both retrograde and anterograde (seen on sinus beat as well as following drive train) His bundle potentials on the right and left His catheters through the aorta. (A) No His can be seen on the trans-septal catheter. (B) No retrograde His is recorded, but anterograde His bundle potentials are seen in the following sinus beat on all three His-recording catheters. Recordings are at 100 mm/s. I, lead I of the surface ECG; II, lead II of the surface ECG; R His, right His bundle recording electrode; TA His, trans-aortic left His bundle recording; TS His, trans-septal left His bundle recording; CS, coronary sinus.
Slow pathway retrograde conduction

Pre-ablation

Pre-ablation, three patterns of retrograde conduction were noted. In eight patients (group 1), decremental retrograde VA conduction without jumps or discontinuities was recorded (Figure 4). In six patients (group 2), typical retrograde conduction jumps with a discontinuous conduction curve were demonstrated (Figure 5). In the remaining four patients (group 3), there was minimal prolongation of St-A times (Figure 6). Induction of tachycardia with ventricular pacing was possible in two patients from group 3. Stimulus to atrium and St-A\textsubscript{max} D intervals with ventricular extra-stimulation are presented in Tables 1–3. Considering DSt-A times, there were significantly longer DSt-A intervals on the right His compared with the left His (122 ± 25 ms vs. 110 ± 33 ms, \( P = 0.02 \), respectively) in group 1 and group 2 (140 ± 23 ms vs. 110 ± 35 ms, \( P = 0.03 \)), but not in group 3 (10 ± 4 ms vs. 13 ± 8 ms, \( P = 0.35 \)). No statistically significant differences were seen in DSt-A intervals on the right His.
compared with those on the pCS in group 1 (122 ± 25 vs. 118 ± 20 ms, \( P = 0.10 \)), group 2 (140 ± 23 vs. 115 ± 47 ms, \( P = 0.21 \)), and group 3 (10 ± 4 vs. 10 ± 4 ms, \( P = 0.72 \)).

**Post-ablation**

Post-ablation, all patients demonstrated decremental VA conduction without conduction jumps (Tables 1–3 and Figure 7). Considering \( \Delta \text{St-A} \) times, no significant differences between the right and left His were noted (77 ± 37 vs. 76 ± 33 ms, \( P = 0.53 \), respectively) in group 1, (100 ± 24 vs. 103 ± 21 ms, \( P = 0.35 \)) group 2, and (63 ± 32 vs. 66 ± 33 ms, \( P = 0.35 \)) group 3. Similarly, no significant differences were found between \( \Delta \text{St-A} \) times obtained from the right His and pCS (77 ± 37 vs.
Table 1  Group 1. Decremental retrograde conduction

<table>
<thead>
<tr>
<th></th>
<th>Pre-ablation</th>
<th>Post-ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>St-A</td>
<td>St-A_{max D}</td>
</tr>
<tr>
<td>R His</td>
<td>124 ± 12</td>
<td>246 ± 31</td>
</tr>
<tr>
<td>TA His</td>
<td>121 ± 9°</td>
<td>231 ± 38**</td>
</tr>
<tr>
<td>pCS</td>
<td>150 ± 10***</td>
<td>268 ± 28***</td>
</tr>
</tbody>
</table>

St-A intervals at constant pacing and at ventriculo-atrial conduction decrement (St-A_{max D}) during ventricular pacing; S₁–S₂ is the pacing interval at which maximum ventriculo-atrial conduction decrement was obtained. R His, His bundle electrogram recorded from the right septum; TA His, His bundle electrogram recorded from the trans-aortic catheter on the left septum; pCS, proximal coronary sinus. Values are expressed in ms as mean ± SD.

*P > 0.05 for the comparison between R His and TA His.
**P < 0.05 for the comparison between R His and TA His.
***P < 0.05 for the comparison between R His and pCS.

Table 2  Group 2. Discontinuous retrograde conduction (ventriculo-atrial jumps)

<table>
<thead>
<tr>
<th></th>
<th>Pre-ablation</th>
<th>Post-ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>St-A</td>
<td>St-A_{max D}</td>
</tr>
<tr>
<td>R His</td>
<td>129 ± 7</td>
<td>269 ± 27</td>
</tr>
<tr>
<td>TA His</td>
<td>128 ± 8°</td>
<td>238 ± 41**</td>
</tr>
<tr>
<td>pCS</td>
<td>155 ± 12***</td>
<td>270 ± 45*****</td>
</tr>
</tbody>
</table>

St-A intervals at constant pacing and at ventriculo-atrial conduction jump (St-A jump) during ventricular pacing. S₁–S₂ is the pacing interval at which maximum ventriculo-atrial conduction decrement was obtained. Abbreviations are as in Table 1.

*P > 0.05 for the comparison between R His and TA His.
**P < 0.05 for the comparison between R His and TA His.
***P < 0.05 for the comparison between R His and pCS.

Table 3  Group 3. Non-decremental retrograde conduction

<table>
<thead>
<tr>
<th></th>
<th>Pre-ablation</th>
<th>Post-ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>St-A</td>
<td>St-A_{max D}</td>
</tr>
<tr>
<td>R His</td>
<td>127 ± 12</td>
<td>136 ± 9</td>
</tr>
<tr>
<td>TA His</td>
<td>116 ± 15°</td>
<td>129 ± 7°</td>
</tr>
<tr>
<td>pCS</td>
<td>136 ± 26**</td>
<td>146 ± 26**</td>
</tr>
</tbody>
</table>

St-A intervals at constant pacing and at ventriculo-atrial conduction decrement (St-A_{max D}) during ventricular pacing. S₁–S₂ is the pacing interval at which maximum ventriculo-atrial conduction decrement was obtained. Abbreviations are as in Table 1.

*P > 0.05 for the comparison between R His and TA His.
**P > 0.05 for the comparison between R His and pCS.

Reproducibility of activation patterns

The sequence of atrial activation was reproducible during ventricular pacing, with no change in the retrograde atrial activation sequence when analysed at separate time intervals and by two different observers. Using the 95% limits of agreement that provided from the Bland and Altman method, we observed that 88% of the values were within the interval of agreement. High concordance was also found between the two observers (kappa statistic = 0.84, P < 0.01).

Discussion

Our results indicate that in patients with typical AVNRT, retrograde VA activation patterns compatible with both fast and slow pathway retrograde conduction can be observed during ventricular pacing, depending on the retrograde-effective refractory periods of the two pathways. The fact that initiation of tachycardia by ventricular pacing was possible in only two of our patients who demonstrated retrograde conduction decrement or dual pathways suggests that the retrograde refractory period of the slow pathway is usually shorter than that of the fast pathway. In 12–30% of patients with AVNRT, tachycardia can be initiated by ventricular extra-stimuli. This mode of tachycardia initiation requires that the slow pathway has a retrograde refractory
period longer than that of the fast pathway. Consequently, the ventricular extra-stimulus blocks in the slow pathway and is conducted over the fast one, thus preventing the demonstration of any retrograde jump or significant decrement.

When a retrograde conduction jump or maximum decrement occurs, there is a shift of retrograde activation with significantly shorter Stim-A intervals on the left septum, thus indicating that fibres from the slow pathway are primarily responsible for retrograde conduction. In this respect, our findings are compatible with the observation that the leftward inferior extension is shorter in length than the rightward inferior extension and support our earlier reports that the inferior nodal extensions may play a role in slow pathway conduction. Damage to this area through radiofrequency ablation resulted in abolition of these differences. Catheter ablation in the right inferoparaseptal area has been shown to affect the right inferior atrial extension. In a previous case report, histopathological examination of the septum following slow pathway ablation showed a white endocardial patch at the site of ablation in the apex of Koch’s triangle, a remnant of the inferior extension beyond the scar, and also distinct endocardial thickening on the left ventricular septal surface. Thus, ablation targeting the slow pathway from the right side of the septum may well affect the left nodal extension as well. These observations provide a rationale for the well-documented observation that a successful ablation procedure may not result in complete slow pathway elimination.

Our data provide further evidence in support of the initial hypothesis of Becker and co-workers supporting the role of the inferior AV nodal extensions as the anatomic substrate of the slow pathway in human.

**Study limitations**

First, our patient numbers are small to allow detailed comparisons between the three groups. Perhaps unavoidably, the nature of this study made recruitment extremely difficult. Secondly, our findings depend on conventional catheter mapping techniques, and we cannot exclude subtle catheter movements affecting our results. Nevertheless, retrograde activation patterns were shown to be consistent and reproducible. Thirdly, while performing right ventricular pacing, it may be difficult to obtain recordings of the retrograde His bundle potential. In the literature, retrograde conduction properties of the fast and slow pathways have been derived indirectly by analysing the conduction curves (V1–V2/A1–A2). Thus, in cases of discontinuous retrograde curves, the longest V1–V2 interval in which conduction fails in the fast pathway is assumed to be the retrograde-effective refractory period of the fast pathway, and the shortest attainable A1–A2 interval on the fast pathway conduction curves is assumed to be its functional refractory period. Similarly, analysis of curves left of the discontinuity, which represent slow pathway conduction, provides the refractory periods of the slow pathway. This method assumes that no other causes of discontinuities in VA conduction, such as intraventricular conduction delays, exist. Of course, retrograde refractoriness of the His-Purkinje system may also be an important factor with respect to VA conduction patterns. Anatomic slow pathway ablation, however, does not affect conduction in the His bundle.

In summary, our study has shown that in patients with typical AVNRT, VA activation patterns compatible with both fast and slow pathway retrograde conduction can be obtained. Retrograde conduction through the slow
pathway results in the earliest retrograde atrial activation on the left side of the septum, and catheter ablation in the right inferoparaseptal area results in abolition of this pattern. These findings are compatible with the concept of slow pathway conduction by means of the inferior AV nodal extensions.

Acknowledgements

We are grateful to D. Panagiotakos, PhD, and G. Kurlaba, BSc, for their help with statistical analysis.

References