The electromechanical effects of pacing at different sites within the right atrium

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Aims To compare high right atrium (HRA) with right atrial appendage (RAA) pacing with respect to atrial electromechanical function.

Methods Eleven patients undergoing elective electrophysiological studies were studied in order directly to compare atrial conduction acutely associated with HRA and RAA pacing. Twenty-five patients with chronically implanted, active fixation leads in the HRA were compared with an age and sex matched group of 25 patients with chronically implanted, passive fixation leads in the RAA. For both studies recordings were taken in sinus rhythm then repeated when paced. Measured time intervals were intra- and interatrial activation times, P wave duration and time to onset of atrial systolic blood flow.

Results Right atrial pacing, when compared with sinus rhythm, significantly prolongs the interatrial activation time, the P wave duration and the time to onset of right and left atrial blood flow irrespective of site paced. Comparing the RAA group with the HRA group, there were no statistical differences for any of the measured parameters.

Conclusion High right atrial free wall or the right atrial appendage pacing, when compared with sinus rhythm, is significantly detrimental to atrial electromechanical function. There is, however, no demonstrable difference between the two sites.

(Key Words: High right atrial free wall pacing, right atrial appendage pacing, intra-atrial activation time, inter-atrial activation time, P wave duration, time to onset of atrial systolic bloodflow.)

Introduction

During normal sinus rhythm each heart beat is initiated by spontaneous depolarization of specialized cells within the sinoatrial (SA) node1,2. The activation wave-front then spreads through the atria with preferential conduction along geometrically discrete bands of atrial myocardium which connect the SA node to the atroventricular (AV) node3,4 and the left atrium5. Once depolarized the onset of mechanical wall motion within each atrium is effectively synchronous6; between the atria there is a physiological delay in contraction of approximately 20 ms7,8. Atrial systole completes diastole and, in normal subjects, can account for 40–50% of ventricular filling9,10.

When pacing the right atrium (RAP) the majorities of operators implant the lead (active or passive fixation) in the atrial appendage (RAA) which is anatomically consistent and electrically stable. RAA pacing however, when compared with sinus rhythm (SR), prolongs the duration of atrial activation11–13 and delays the onset of atrial systolic contraction7.

Indications for pacemaker therapies are expanding. They now include the prevention of atrial arrhythmias that are not related to bradycardia and the rate-independent improvement of cardiac function. For these indications especially the optimization of lead position is critical. As the RAA has been shown to be sub-optimal, investigation into other, alternative, sites is necessary. It is possible to achieve safe and effective atrial pacing from high on the right atrial lateral free wall (HRA)14 which more closely approximates to the sinoatrial node15–17. The main objective of this investigation was to evaluate whether pacing from the HRA, because it is closer to the physiological origin of atrial depolarization, would be less detrimental to atrial electromechanical function than pacing from the right atrial appendage.

The second objective was to identify whether pacing induced prolongation of atrial activation occurred within one atrium or both atria.

**Methods**

**Patients**

Eleven patients undergoing elective electrophysiological studies (EPS) were investigated in order directly to compare intra and inter atrial conduction acutely associated with HRA and RAA pacing. All patients gave informed consent and the study was approved by the local research ethics committee. Those taking anti-arrhythmic medication had undergone a period of pharmacological washout exceeding five half lives. No radiofrequency ablation had been performed prior to the study.

Twenty-five patients with active fixation leads chronically implanted in the HRA were studied. This group was compared with an age and sex matched group of 25 patients with passive fixation leads chronically implanted in the RAA. All patients gave informed consent and the local research ethics committee approved the study. Lead position was verified from written documentation at time of implantation; confirmation being gained from paced P wave morphology (Fig. 1)[18].

Measurements

After each diagnostic EPS, bipolar catheters were positioned in the RAA and the HRA. A quadripolar catheter was positioned across the tricuspid annulus to record the His bundle electrogram[19] and a decapolar catheter with a lumen was placed within the coronary sinus. Access for these catheters were via the right femoral vein, the left femoral vein and the right subclavian vein using fluoroscopy.

In each patient, there was simultaneous recording of the intracardiac electrograms from the HRA/RAA, His bundle, proximal coronary sinus (PCS), mid coronary sinus (MCS) and distal coronary sinus (DCS) at 200 mm/s paper speed using a Prucka Engineering CardioLab system. Recordings were taken initially when the patients were in sinus rhythm (Fig. 2). The recordings were then repeated when the patients were paced at the sinus rate +10 bpm (Fig. 3). All patients were paced from the HRA and RAA in a random order as dictated by an independent observer using a binary number generator. In each study recordings were taken when the patient had been in a steady rhythm state for at least 5 min; thus allowing haemodynamic stabilization[20]. Measurements were performed using callipers and online software; they were averaged over five consecutive beats. The measured time intervals were
HRA/RAA electrograms to the atrial spike of the PCS electrogram.

Atrial spike of the PCS electrogram to the atrial spike of the DCS electrogram.

Comparisons were made between SR and HRA/RAA pacing then between HRA pacing and RAA pacing with respect to the above timings.

Patients studied with chronically implanted physiological pacemakers initially underwent baseline echocardiography in sinus rhythm. Assessed were cardiac dimensions, the presence or absence of valvular disease, the presence or absence of ventricular hypertrophy\(^{[21]}\), the presence or absence of abnormal diastolic filling patterns\(^{[9]}\) and ejection fraction.

Atrial electromechanical function was determined indirectly by measuring the P wave duration and the time to the onset of echocardiographic atrial systolic blood flow. The P wave duration was measured from a 3 lead ECG (I, II, III) recorded at a speed of 50 mm/s (Fig. 4). The time to the onset of echocardiographic right and left atrial systolic blood flow (ttA) was measured from transtricuspid (TT) and transmitral (TM) pulsed wave Doppler flow patterns respectively (Fig. 5). These measurements and their correlation to cardiac electromechanical function have been previously described\(^{[7,12]}\).

For each study the ECG/Doppler echo was first recorded when the patients were in sinus rhythm. The recordings were then repeated when the atrium was paced at sinus rate +10 bpm. Recordings were taken after a steady rhythm state had been achieved for 5 or more minutes\(^{[20]}\). The atrioventricular (AV) delays were not standardized within or between groups; for individuals AV delays were adjusted, if necessary, to ensure the same mode of ventricular depolarization during sinus rhythm and atrially paced rhythm. All measurements were averaged over five consecutive beats.

**Data analysis**

Means and standard deviations were calculated.

For the EPS data related t-tests were used as the data were paired and the distribution was normal. For the ECG and echocardiography data related and unrelated t-tests were used to explore the differences between sinus rhythm and paced rhythm (from analysis of the differences) and between HRA and RAA pacing sites (from analysis of the raw data).

A \( P \) value \(<0.05\) was considered significant.

Categoricals were compared using a Chi-squared test.

**Results**

**Patients**

Eleven patients undergoing elective electrophysiological studies (EPS) were studied in order directly to compare intra and inter atrial conduction acutely associated with HRA and RAA pacing. There were 6 male and 5 female patients with ages ranging from 36–69 years (mean ± SD
EPS demonstrated that 2 patients had left sided accessory pathways, 3 had right-sided accessory pathways, 3 had intra-nodal pathways and 3 had no electrophysiological abnormalities. During normal sinus rhythm all patients had an interatrial conduction time less than 100 ms and an activation sequence that proceeded from the HRA to the His bundle then to proximal, mid and finally the distal coronary sinus.

Twenty-five patients with chronically implanted leads in the HRA were studied. The HRA group consisted of 18 males and 7 females aged 41–91 years (mean 64 ± 14); mean time since implant was 9 ± 20 months. This group was compared with an age and sex matched group of 25 patients with chronically implanted leads in the RAA. The RAA group consisted of 18 males and 7 females aged 34–91 years (mean 66 ± 17); mean time since implant was 17 ± 18 months. Comparing these two groups of patients there were no significant differences in demographics or baseline echocardiography (Table 1).

Electrophysiological measurements

Right atrial pacing, when compared with sinus rhythm, significantly prolonged right intra-atrial conduction without significantly altering left intra-atrial conduction. This was the case irrespective of the site paced (Table 2).

When comparing HRA pacing with RAA pacing there were no significant differences.

**P wave duration**

Right atrial pacing, compared with sinus rhythm, significantly increased P wave duration irrespective of site paced (Table 3). There was no statistically significant difference when comparing HRA pacing with RAA pacing.

**Time to onset of atrial systole**

Right atrial pacing, compared with sinus rhythm, was associated with a significant increase in time to onset of right and left atrial blood flow irrespective of site paced (Table 4). Comparing the RAA group with the HRA group, there was no statistical difference.

Discussion

Our studies have demonstrated that pacing from the HRA or RAA significantly increases the atrial activation time and delays the onset of atrial systolic blood flow.

Figure 4  Three lead ECG of sinus rhythm and right atrial pacing.
when compared with sinus rhythm. These results are consistent with those reported by previous investigators\cite{7,11,12} and indicate that right atrial pacing exerts a detrimental effect on atrial electromechanical function.

We demonstrated an average increase in the interatrial conduction time of 37 ms with right atrial pacing when compared with sinus rhythm. In the studies by Ausubel\cite{11} and Camous\cite{12} the average increases in interatrial conduction time associated with right atrial pacing were 27 ms and 50 ms respectively. The reasons for the variations probably relate to measurement methods and population demographics. Ausubel measured the interatrial conduction time from the onset of the electrocardiographic P wave (lead II) to the left atrial signal recorded from an intra-oesophageal pill electrode placed at the mid atrial level. During sinus rhythm the beginning of the surface the P wave and the intrinsic deflection of a right atrial electrode will be synchronous\cite{23}; during right atrial pacing there is an interval of 10–25 ms between the right atrial electrode pacing artefact and the beginning of the surface P wave\cite{24}. It is likely, therefore, that the differences in our results and those of Ausubel relate to their use of the surface P wave compared with our use of the right atrial electrode to indicate onset of right atrial activation. Camous\cite{12} measured the interatrial conduction time from the right atrial electrode to the left atrial signal recorded by an intra-oesophageal electrode which is comparable to our methods. The population in Camous’s study had a mean age of 78 years and was undergoing permanent pacemaker implantation for bradycardia; within their population they demonstrated a positive correlation between age and interatrial conduction time (during intrinsic and paced rhythm). In our study there were no known conduction defects and the mean age was 50 years; it is likely, therefore, that the differences between the studies are due to the differences in the study population demographics. When measuring P wave duration

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**Table 1 Comparing the demographics and baseline echocardiography of the chronically implanted pacemaker study groups**

<table>
<thead>
<tr>
<th></th>
<th>HRA</th>
<th>RAA</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of males</td>
<td>18</td>
<td>18</td>
<td>ns</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>66</td>
<td>64</td>
<td>ns</td>
</tr>
<tr>
<td>Mean left atrial diameter (mm)</td>
<td>36</td>
<td>37</td>
<td>ns</td>
</tr>
<tr>
<td>Mean ejection fraction (%)</td>
<td>63</td>
<td>58</td>
<td>ns</td>
</tr>
<tr>
<td>No. with ventricular hypertrophy</td>
<td>5</td>
<td>4</td>
<td>ns</td>
</tr>
<tr>
<td>No. with abnormal diastolic function</td>
<td>3</td>
<td>4</td>
<td>ns</td>
</tr>
</tbody>
</table>

Abbreviations: HRA=high right atrial free wall, RAA=right atrial appendage, ns=not significant.
Ausubel and ourselves both used the same methods and therefore the changes were similar. In our study right atrial pacing, when compared with sinus rhythm, increased the P wave duration by a mean of 23 ms compared with the mean increase of 26 ms demonstrated by Ausubel.

In the study by Wang, right atrial pacing, compared with sinus rhythm, delayed the onset of right and left atrial systolic blood flow by a mean of 7 ms and 19 ms respectively. In our study the mean increase in time to onset of right and left atrial systolic blood flow was 25 ms and 42 ms respectively. Although the measurement methods were similar our data were paired whereas Wang’s data were unpaired which may explain the differences.

Despite the differences between the absolute increases in interatrial conduction time, P wave duration and time to onset of atrial systolic bloodflow associated with right atrial pacing the findings in all studies were consistent and significant.

In contrast to these other studies we have additionally shown that pacing from the HRA or RAA increases the duration of right atrial activation without affecting the duration of left atrial activation, a previously unrecognized phenomenon. We hypothesize that the lack of difference in duration of left atrial activation is due to the normalization of conduction once the depolarization wave-front has traversed the interatrial septum. With the interatrial septum acting as an electrical insulator the site or mechanism of right atrial depolarization would not affect preferential conduction within the left atrium.

Considering these results it should be remembered that identifying the exact point of termination of right atrial activation/initiation of left atrial activation is difficult. In our study the PCS was considered to be the transition point but others may argue that using the atrial spike of the His bundle electrogram would be better.

The increase in the duration of the right atrial conduction time without the alteration of the duration of the left atrial conduction time associated with right atrial pacing. ns=not significant.

### Table 2 Comparing the intra-atrial conduction times during sinus rhythm and during high right atrial right atrial appendage pacing

<table>
<thead>
<tr>
<th></th>
<th>RA–PCS SR</th>
<th>RAP P value</th>
<th>PCS–DCS SR</th>
<th>RAP P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRA</td>
<td>44.55 ms</td>
<td>&lt;0.01</td>
<td>21.36 ms</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>(17:10)</td>
<td>(12:67)</td>
<td>(15:65)</td>
<td></td>
</tr>
<tr>
<td>RAA</td>
<td>46.36 ms</td>
<td>&lt;0.01</td>
<td>21.82 ms</td>
<td>ns</td>
</tr>
</tbody>
</table>

Abbreviations: HRA=high right atrial free wall, RAA=right atrial appendage, RA=right atrium, PCS=proximal coronary sinus, DCS=distal coronary sinus, SR=sinus rhythm, RAP=right atrial pacing.

### Table 3 Comparing the P wave duration during sinus rhythm and during high right atrial right atrial appendage pacing

<table>
<thead>
<tr>
<th></th>
<th>HRA SR</th>
<th>RAP P value</th>
<th>RAA SR</th>
<th>RAP P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P wave</td>
<td>98 ms</td>
<td>&lt;0.01</td>
<td>102 ms</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>(24)</td>
<td>(23)</td>
<td>(21)</td>
<td>(20)</td>
</tr>
</tbody>
</table>

Abbreviations: HRA=high right atrial free wall, RAA=right atrial appendage, SR=sinus rhythm, RAP=right atrial pacing.

### Table 4 Comparing the time to onset of right and left atrial blood flow during sinus rhythm and during high right atrial right atrial appendage pacing

<table>
<thead>
<tr>
<th></th>
<th>HRA SR</th>
<th>RAP P value</th>
<th>RAA SR</th>
<th>RAP P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT:ttA</td>
<td>65 ms</td>
<td>&lt;0.01</td>
<td>64 ms</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>(31)</td>
<td>(18)</td>
<td>(18)</td>
<td>(18)</td>
</tr>
<tr>
<td>TM:ttA</td>
<td>91 ms</td>
<td>&lt;0.01</td>
<td>82 ms</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>(32)</td>
<td>(19)</td>
<td>(16)</td>
<td>(19)</td>
</tr>
</tbody>
</table>

Abbreviations: HRA=high right atrial free wall, RAA=right atrial appendage, SR=sinus rhythm, RAP=right atrial pacing, TT=transtricuspid flow, TM=transmitral flow, tta=time to onset of atrial systolic blood flow, ns=not significant.
atrial pacing explains the observations of Wang who demonstrated that RAA pacing caused delayed and non-synchronous right atrial contraction without affecting left atrial contraction. This finding also aids in the understanding of why there is variable success in the prevention of atrial arrhythmias with right atrial pacing. Although the increased heart rate decreases atrial ectopic activity and refractoriness dispersion it increases the likelihood of anisotropic re-entry due to pacing induced conduction delays.

We are unaware of a direct comparison between the HRA and RAA having been published. We found no demonstrable differences between the two sites for any of the measured parameters. This lack of difference may relate to the inevitable heterogeneity of HRA lead positioning even when using standardized electrocardiographic criteria but we feel this is unlikely to be a major contributory factor. We postulate that the detrimental effects of pacing from the HRA and RAA and the lack of difference between the two sites are due to a failure preferentially to conduct along the intra-atrial bands from either site. When pacing from either site the axis of the activation wavefront is not parallel to the right intra-atrial bands and thus will slow conduction through the atra.

Alternatively it is possible that pacing per se is detrimental to atrial electromechanical function. There is an altered mechanism of initiating depolarization during a paced rhythm compared with a spontaneous rhythm, this alteration may interfere with cellular Ca\(^{2+}\) handling and thus affect conduction and contractility. The detrimental effects may be cellular rather than macroscopic, with the mode rather than the site of depolarization being the problem.

**Conclusion**

Pacing from the high right atrial free wall or the right atrial appendage, when compared with sinus rhythm, is significantly detrimental to atrial electromechanical function. There is no demonstrable difference between the two sites.

**References**