Evolution of ventricular function during permanent pacing from either right ventricular apex or outflow tract following AV-junctional ablation for atrial fibrillation

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Aims To compare acute and chronic ventricular function between patients, without cardiac failure, paced at either right ventricular apex or outflow tract.

Methods Twenty patients, 10 paced apically and 10 in the outflow tract, underwent two radionuclide ventriculograms. Eight parameters of systolic or diastolic function were compared at each assessment, as were changes within each group over time.

Results No differences were identified in systolic function between pacing sites 6 weeks after pacing or 23 weeks later. Peak filling rate was lower (P=0.04) at the second assessment with outflow tract pacing. No other diastolic differences were identified. Between assessments, time to peak filling rate prolonged (P=0.04) with apical pacing, while left ventricular area reduced (P=0.04) and peak filling rate decreased (P=0.04) with outflow tract pacing. Septal motion was better preserved with outflow tract pacing. No other parameter changed over time. ECG measures were similar at 14-7 months.

Conclusions No major differences were identified in systolic function between pacing sites. Some systolic parameters were better preserved with outflow tract pacing and diastolic function deteriorated subtly over time in both groups. Right ventricular pacing adversely affects left ventricular function.

Introduction

There has been a growing appreciation, in recent years particularly, of the important effects of abnormal electrical activation on ventricular function[1,2]. Abnormalities, previously considered trivial, such as first degree AV-block, left bundle branch block and intraventricular conduction delays are now known to add to the mechanical dysfunction of the primary underlying myopathy[3,4]. New additional indications for permanent pacing are evolving specifically to improve the abnormal spread of electrical activation, which contributes to ventricular dysfunction in patients with advanced heart failure and wide native QRS complexes[5–7].

Complete AV-junctional ablation is an established approach to the management of patients with paroxysmal or permanent atrial fibrillation, when drug therapies have failed either to prevent frequent paroxysms or to control the ventricular response rate to the arrhythmia[8–10]. Ventricular pacing is an essential part of this treatment, but one consequence is that the sequence of ventricular activation is changed from that occurring over the normal His-Purkinje network to that originating from the site of the ventricular lead. QRS morphology and duration usually also change from the short duration, normal axis pattern of the native ECG to a prolonged duration, abnormal axis pattern of the paced QRS complex. In appropriately selected patients, AV-junctional ablation and pacing improve the symptomatic status of patients with drug refractory...
atrial fibrillation by controlling ventricular rate and regularizing RR intervals. In some this can be shown to reverse a tachycardia-induced cardiomyopathy\(^{11,12}\). These beneficial effects, however, may be negated in some patients by the less efficient pattern of electrical activation resulting from paced ventricular rhythm, which may itself cause measurable deterioration in systolic and/or diastolic function. In patients with preserved ventricular function prior to AV-junctional ablation the site of chronic right ventricular pacing might influence how ventricular function subsequently evolves\(^{13}\). The aim of this study, therefore, was to compare acute and chronic radionuclide parameters of ventricular function between patients, who had no evidence of prior cardiac decompensation, paced at either right ventricular apex or outflow tract sites after complete AV-junctional ablation for drug refractory paroxysmal or permanent atrial fibrillation.

**Methods**

Patients, scheduled for complete AV-junctional ablation and pacing to control symptoms of atrial fibrillation, were sequentially allotted to have their ventricular lead positioned either at the right ventricular apex or at the septal right ventricular outflow tract (Fig. 1). In those paced in the outflow tract, the aim was to place the lead septally at or above the cranial limit of the tricuspid valve annulus. No attempt was made to capture the specialized conduction system or to find the site resulting in the shortest paced QRS duration. Apically sited leads were all passive fixation and septal ones all active fixation in type. Complete conduction block at the AV-junction was achieved in all by standard radiofrequency catheter ablation and, subsequently, all underwent Tc99m radionuclide ventriculography twice. Patients were scheduled to have their first set of images within one month of AV-junctional ablation and the second set 3–6 months later. In an attempt to standardize comparisons of ventricular function and negate the effects of variable atrial rhythms within and between patients, ventriculograms were performed with the pacemakers programmed temporarily to demand ventricular mode at 80 beats per minute.

**Radionuclide ventriculograms**

Ventricular function was assessed at the two time points by standard planar Tc99m radionuclide ventriculography. Images were acquired in the left anterior oblique and left lateral projections using a gamma camera and associated computer. Comparisons between and within groups of initial and later results were made for the following parameters of ventricular function: (1) left ventricular area (cm\(^2\)); (2) right ventricular area (cm\(^2\)); (3) global left ventricular ejection fraction (%); (4) left ventricular segmental wall motion score; (5) inhomogeneity of left ventricular systolic contraction (phase analysis); (6) left ventricular diastolic function: mean and peak left ventricular dV/dT diastolic function and time to left ventricular peak filling rate (ms).

**Ventricular areas**

Two-dimensional radionuclide chamber area, expressed in cm\(^2\), provides an uncomplicated index of left ventricular volume. Ventricular area is considerably easier and more reliably calculated than ventricular volume, which has to rely on assumptions of chamber shape. Right and left ventricular areas were calculated separately from the left anterior oblique image, using the amplitude image from phase/amplitude analyses more accurately to define cavity margins.

**Left ventricular ejection fractions**

Global left ventricular ejection fraction (LVEF\%) was measured from the left anterior oblique image automatically and expressed as a percentage\(^{14,15}\). In ventricles showing a uniform contraction pattern, the normal range for this hospital is any value in excess of 45% (range 45–70%)\(^{16}\).

**Segmental wall motion scores**

Systolic wall motion was scored independently by two experienced observers originally in both left anterior oblique and left lateral projections on a scale of increasing dysfunction from 0 to 5\(^{17,18}\). The final score for any segment was reached by consensus between observers, who were blinded both to the site of right ventricular pacing and time interval from AV-junctional ablation. However, left ventricular segments were obscured sometimes by overlap from a relatively enlarged right ventricle in the lateral projection. This image was discarded ultimately, therefore, from further analysis.

Because inter-ventricular septal motion might be influenced disproportionately by the site of right ventricular pacing, this was analysed separately and compared within and between the groups. The presence of either septal akinesia or paradoxical movement during systole was determined from the left anterior oblique images. The presence of either was deemed abnormal. Patients were excluded from this particular comparison, however, if septal motion was already abnormal on a pre-ablation echocardiogram\(^{19}\).

**Inhomogeneity of left ventricular contraction**

The inhomogeneity of left ventricular contraction was assessed by phase analysis of the ECG-gated image. This was expressed as the standard deviation of the phase distribution histogram from the left anterior oblique image of the left ventricle in isolation using a window of 0–240 degrees\(^{20,22}\). In a population with normal left ventricular function assessed at this hospital, the mean standard deviation of the phase distribution histogram was 8\(^\circ\)\(^{23}\).
Figure 1 Intended ventricular lead positions for right ventricular outflow tract or apical pacing and the corresponding paced 12-lead ECG morphology. RAA=right atrial appendage; RVA=right ventricular apex; RVOT=right ventricular outflow tract.
Left ventricular diastolic function
Diastolic function was measured from the left ventricular function curve and expressed as peak and mean change in wall motion velocity over time (dV/dT) during diastole and by time to peak left ventricular filling rate\[18,20,24\]. Since all images were acquired in a standardized VVI pacing mode at 80 beats/min, measurements were not considered to be influenced by atrial rhythm, whether sinus or fibrillation.

Electrical comparisons
QRS duration and rate corrected QT-intervals were compared between groups at baseline prior to AV-junctional ablation from the last ECG showing AV-nodal conduction. Following ablation, only single lead ECGs were available routinely from times of pacing follow-up and the lead recorded was not standardized. To allow comparison of ECG parameters between outflow tract and apical right ventricular pacing, therefore, a 12-lead ECG was recorded at 50 mm/s on one occasion, when the patient attended for routine pacing follow-up. QRS duration and QT interval were measured from three complexes in each of the 12 leads, by an operator blinded to the site of ventricular pacing, using a digitizing board and computer\[25,26\]. From these measurements mean paced QRS duration, maximum QT-interval and QT-interval heterogeneity or dispersion were measured. Change in QRS duration and QT-interval from before to after ablation were then compared.

Whether patients who received dual-chamber pacing systems initially retained sinus rhythm or progressed to permanent atrial fibrillation during follow-up was determined at the time of pacing clinic review\[27\]. Any patient in atrial fibrillation on two consecutive reviews six months apart, was deemed to be permanently in atrial fibrillation.

Statistical analysis
Unless otherwise stated, all values are quoted as mean and standard deviations. Early and later measures of each parameter within each group were compared using paired t-tests. Comparisons between results from patients paced at different sites were made using unpaired t-tests or chi-squared tests corrected for small number comparisons, where appropriate. For either test, differences were defined as significant at the 5% and highly significant at the 1% probability levels respectively.

Results
Twenty patients — 10 paced in the right ventricular outflow tract and 10 apically — enrolled into the study and who underwent AV-junctional ablation and radionuclide ventriculography on two occasions, form the study population. Four other patients, also enrolled initially, were excluded from analysis because either they withdrew consent before completing the protocol (n=2) or because one of their radionuclide ventriculograms was uninterpretable for technical reasons (n=2). The mean age of patients studied was 64 ± 7 years and 11 (55%) were female. Patient characteristics, including aetiology and duration of atrial fibrillation, echocardiographic results prior to AV-junctional ablation when available, medications continued during the study and mode of pacing are summarized in Table 1. No patient had evidence of cardiac failure prior to ablation but three, two subsequently paced in the outflow tract and one apically, had echocardiographic evidence of reduced left ventricular systolic function without symptoms of cardiac failure.

Initial comparison of ventricular function: outflow tract vs apical pacing (Table 2)
Initial radionuclide assessments were undertaken a mean of 6 weeks (range 0·14–38) after AV-junctional ablation. No significant differences were identified in age, duration of pacing, right ventricular area or any radionuclide parameter of left ventricular systolic function between those paced in the outflow tract or apically. Mean time to peak filling rate was longer in those paced in the outflow tract (P=0·054), but neither this nor the differences in other diastolic parameters between the groups was significant at this initial assessment.

Late comparison of ventricular function: outflow tract vs apical pacing (Table 3)
Radionuclide parameters of ventricular function were reassessed a mean of 23 weeks (range 12–50) following the initial evaluation. No significant differences were identified between the groups in parameters of systolic left ventricular function or left or right ventricular areas. Peak filling rate was significantly lower in those paced in the outflow tract of the right ventricle compared with those paced apically (238 ± 67 vs 301 ± 63 dV/dT; P=0·04). Other measures of diastolic function — mean filling rate and time to peak filling rate — were similar between the groups.

Evolution of ventricular function during apical pacing: initial to late comparison (Table 4)
Parameters of left ventricular function were compared between the first and second sets of radionuclide ventriculograms for patients paced at the right ventricular apex to determine how ventricular size and function evolved over time. No significant changes in systolic
function were detected over time. Time to peak left ventricular filling rate prolonged significantly from the first to the second assessment (0.13 ± 0.05 vs 0.16 ± 0.03 s; \( P = 0.04 \)) compatible with a deterioration in diastolic function. This was not corroborated by any detectable deterioration in the other parameters of diastolic function between the two sets of results.

Evolution of ventricular function during outflow tract pacing: initial to late comparison (Table 5)

Parameters of left ventricular function were compared between the first and second sets of radionuclide
ventriculograms for patients paced in the right ventricular outflow tract. Left ventricular area reduced significantly (151 ± 25 vs 143 ± 25 cm²; \( P = 0.04 \)) from the first to the second assessment while peak filling rate reduced significantly (278 ± 64 vs 238 ± 67 dV/dT; \( P = 0.04 \)). These results are compatible with improvement in systolic function but deterioration in diastolic function over time. However, no changes in other parameters of systolic or diastolic function were detected between the two sets of results.

**Effect of site of right ventricular pacing on inter-ventricular septal motion**

Four patients paced apically (40%) and three paced in the right ventricular outflow tract (30%) had radionuclide evidence of septal akinesis or paradoxical systolic septal motion on one or both radionuclide ventriculograms. Three of these, however, had echocardiographic evidence of abnormal septal motion even prior to ablation or pacing. After excluding these patients from this analysis only, two apically paced (20%) and one paced in the outflow tract (10%) had abnormal septal motion in their first radionuclide assessment (\( P = 0.53 \)). At the second assessment, three apically paced (30%) but no patient paced in the outflow tract (\( P = 0.06 \)) had abnormal septal motion. This nonsignificant trend, may indicate that outflow tract pacing preserves septal motion better than apical pacing.

**Subgroup comparison of most cranial outflow tract vs apical paced sites**

Although the intention, in those paced in the right ventricular outflow tract, was to place the lead on the septum at or above cranial limit of the tricuspid valve annulus, in practice chest X-rays subsequently showed some lower lead sites. Lead placement was influenced ultimately by the need to have stable fixation and satisfactory acute pacing parameters. In an attempt to allow for the effect of sub-optimal outflow tract pacing sites on the results, a subgroup analysis was performed. Parameters from five of the initial ten subjects with the most cranial and septal outflow tract lead positions were compared with the ten subjects in the group paced apically. Consistent with the findings of the main study, no differences emerged between the groups in parameters of systolic left ventricular function or left or right ventricular areas at either initial or later assessments. Peak filling rate was lower (301 ± 63 vs 229 ± 32 dV/dT; \( P = 0.03 \)) in those paced in the outflow tract at the second assessment. There were trends for left ventricular area to be smaller in those paced in the outflow tract at the second assessment only (149 ± 25 vs 124 ± 25 cm²; \( P = 0.07 \)) and for ‘time-to-peak-filling’ rate to be longer in those paced in the outflow tract at both initial (0·13 ± 0·05 vs 0·2 ± 0·1 s; \( P = 0.08 \)) and later (0·16 ± 0·03 vs 0·19 ± 0·03; \( P = 0.07 \)) assessments compared with those paced apically. Between assessments, left ventricular area reduced significantly (136 ± 14 vs 124 ± 17 cm²; \( P = 0.01 \)) in those paced in the outflow tract suggesting improved systolic function but diastolic parameters did not change significantly.

**Comparison of chronic ECG parameters between apical and outflow tract pacing**

Table 6 summarizes results of ECG comparisons between the groups, including pre- and post-ablation QRS duration and QT-interval measurements. QRS duration was longer (194 ± 33 vs 181 ± 30 ms; \( P = 0.01 \)) in those paced in the outflow tract while the QT interval was shorter (376 ± 27 vs 393 ± 22 ms; \( P = 0.03 \)) in those paced apically.
duration was almost identical between the groups (n=20) prior to AV-junctional ablation. Right bundle branch block occurred during ablation in 7 (35%) patients — 3 in the apical and 4 in the outflow tract paced groups. Although not part of the initial study protocol, 12-lead ECGs were obtained on one occasion during late follow-up in 14 (70%) patients — 7 apically and 7 septally paced — at a mean of 14·7 months (range 4–23) after the initiation of continuous ventricular pacing. As expected, mean QRS duration increased significantly in both apically (+63 ± 17 ms; P=0·03) and outflow tract (+56 ± 45 ms; P=0·0003) groups from natively conducted to ventricular paced rhythm. Surprisingly, however, no significant differences were identified between apical and outflow tract paced groups in mean QRS duration, maximum QT-interval or QT-interval dispersion. Even when only those paced in the highest outflow tract positions (n=5) were compared with those paced apically (n=10), no differences emerged in mean QRS duration (145 ± 16 vs 160 ± 14 ms; P=0·13), QT-max (505 ± 76 vs 491 ± 19 ms; P=0·64) or change in QRS duration with onset of pacing (35 ± 40 vs 63 ± 17 ms; P=0·17).

Of the 20 patients studied, 13 (65%) — 7 apically and 6 in the outflow tract paced groups — had paroxysmal atrial fibrillation at the time of AV-junctional ablation and were paced in DDD mode. During follow-up ranging 16–36 months in those continuing with paroxysmal atrial fibrillation, three (43%) apically paced and two (33%) paced in the outflow tract progressed to permanent atrial fibrillation as defined (P=0·72) at intervals of between one and 18 months.

### Table 4  Evolution of left ventricular function over course of study: apically paced group

<table>
<thead>
<tr>
<th>Interval from ablation (weeks)</th>
<th>Early</th>
<th>Late</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 ± 6</td>
<td>21 ± 7</td>
<td>—</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>51 ± 9</td>
<td>49 ± 10</td>
<td>0·35</td>
</tr>
<tr>
<td>Wall motion score (LAO image)</td>
<td>1·7 ± 2·3</td>
<td>1·0 ± 1·2</td>
<td>0·33</td>
</tr>
<tr>
<td>Inhomogeneity of contraction</td>
<td>16·6 ± 3·1</td>
<td>16·4 ± 4·4</td>
<td>0·51</td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>141 ± 31</td>
<td>152 ± 30</td>
<td>0·10</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean filling rate (dV/dT)</td>
<td>138 ± 39</td>
<td>127 ± 34</td>
<td>0·51</td>
</tr>
<tr>
<td>Peak filling rate (dV/dT)</td>
<td>325 ± 95</td>
<td>301 ± 63</td>
<td>0·35</td>
</tr>
<tr>
<td>Time to peak filling rate (s)</td>
<td>0·13 ± 0·06</td>
<td>0·16 ± 0·03</td>
<td>0·04*</td>
</tr>
<tr>
<td>Right ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>137 ± 27</td>
<td>144 ± 17</td>
<td>0·50</td>
</tr>
</tbody>
</table>

*Statistically significant difference.

dV/dT rate of change of volume over time; LAO=left anterior oblique; P=probability value.

### Table 5  Evolution of ventricular function over course of study: outflow tract pacing site

<table>
<thead>
<tr>
<th>Interval from ablation (weeks)</th>
<th>Early</th>
<th>Late</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7 ± 11</td>
<td>25 ± 13</td>
<td>—</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>49 ± 6</td>
<td>45 ± 9</td>
<td>0·18</td>
</tr>
<tr>
<td>Wall motion score (LAO image)</td>
<td>1·0 ± 1·3</td>
<td>1·3 ± 1·5</td>
<td>0·59</td>
</tr>
<tr>
<td>Inhomogeneity of contraction</td>
<td>15·1 ± 3·6</td>
<td>15·6 ± 5·7</td>
<td>0·61</td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>151 ± 25</td>
<td>143 ± 25</td>
<td>0·04*</td>
</tr>
<tr>
<td><strong>Diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean filling rate (dV/dT)</td>
<td>122 ± 29</td>
<td>114 ± 21</td>
<td>0·41</td>
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<tr>
<td>Peak filling rate (dV/dT)</td>
<td>278 ± 64</td>
<td>238 ± 67</td>
<td>0·04*</td>
</tr>
<tr>
<td>Time to peak filling rate (s)</td>
<td>0·19 ± 0·08</td>
<td>0·24 ± 0·02</td>
<td>0·52</td>
</tr>
<tr>
<td>Right ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>140 ± 22</td>
<td>142 ± 23</td>
<td>0·82</td>
</tr>
</tbody>
</table>

*Statistically significant difference.

dV/dT rate of change of volume over time; LAO=left anterior oblique; P=probability value.
Table 6 Chronic ECG parameters* following right ventricular apical- versus outflow-tract pacing

<table>
<thead>
<tr>
<th></th>
<th>RVA (n=7)</th>
<th>RVOT (n=7)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Pre-AV junction ablation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean QRS duration (ms)</td>
<td>96 ± 13</td>
<td>97 ± 25</td>
<td>0·97</td>
</tr>
<tr>
<td>Mean QTmax-interval (ms)</td>
<td>413 ± 28</td>
<td>426 ± 23</td>
<td>0·36</td>
</tr>
<tr>
<td>Post-AV junction ablation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean QRS duration (ms)</td>
<td>160 ± 14</td>
<td>160 ± 21</td>
<td>0·94</td>
</tr>
<tr>
<td>Max QT-interval (ms)</td>
<td>491 ± 19</td>
<td>507 ± 58</td>
<td>0·48</td>
</tr>
<tr>
<td>QT-interval dispersion*</td>
<td>36 (26–52)</td>
<td>38 (32–43)</td>
<td>0·63</td>
</tr>
<tr>
<td>Change in QRS duration (ms)</td>
<td>+63 ± 17</td>
<td>+56 ± 45</td>
<td>0·73</td>
</tr>
</tbody>
</table>

Max/min/mean = maximum, minimum or mean measurement from a 12 ECG lead recording for each patient.
All values quoted are group means.
*No rate corrections since all ECGs recorded in VVI mode at 80 bpm.
QTc=rate corrected QT-interval (pre-ablation ECGs had variable ventricular rates).
Change in QRS duration= difference in mean 12-lead QRS duration between the last AV-conducted and subsequently post-ablation ventricular-paced ECGs.

Discussion

The main conclusion from this study is that, in patients with preserved left ventricular function at baseline, no major differences were identified in acute or chronic radionuclide parameters of ejection fraction, wall motion score or in-homogeneity of contraction between patients paced apically or in the right ventricular outflow tract following AV-junctional ablation. The results do not justify changing the standard site of ventricular pacing from the right ventricular apex to the right ventricular outflow tract. However, some differences were observed in systolic and diastolic parameters of ventricular function between the pacing sites over time, which contribute to understanding the complex effects of pacing on mechanical function.

Left ventricular area, a surrogate for left ventricular volume in this study, reduced significantly between the first to the second assessments in those paced in the outflow tract (151 ± 25 cm² vs 143 ± 25 cm²; P=0·04) [1,28]. In addition, fewer patients paced in the outflow tract had detectable abnormalities of septal motion at both initial and later assessments [19]. Whereas the number of patients with septal akinesis or paradoxical motion increased between the first and second sets of images in those paced apically, it reduced over the same period in those paced in the outflow tract. Both these findings suggest that right ventricular outflow tract pacing may be better than apical pacing in preserving systolic function over time.

Diastolic function changed more than systolic function over time but the changes were similar for those paced in the outflow tract or at the right ventricular apex. Within both groups, diastolic function deteriorated between the initial and later assessments, as indicated by a longer time to peak filling (0·13 ± 0·06 vs 0·16 ± 0·03 s; P=0·04) in those apically paced and by a reduction in peak filling rate (278 ± 64 vs 238 ± 67 dV/dT; P=0·04) in those paced in the outflow tract. Although the deterioration in diastolic function might have been anticipated following ventricular pacing, on the basis of these results right ventricular outflow tract pacing does not seem to prevent the deterioration in diastolic function associated with apical pacing [13].

Perhaps surprisingly, no differences were identified in electrical parameters between the two pacing sites as assessed by QRS duration, maximum QT-interval or QT-interval dispersion. Nor was there a difference in the rate of progression from paroxysmal to permanent atrial fibrillation between the two groups over the course of the study. However, the study was not powered to answer this question definitively.

This study in the context of previous publications

This study differs in a number of important respects from previous publications but the results are comparable [29,32]. Victor et al. evaluated 16 patients implanted chronically with leads both at the right ventricular apex and outflow tract after AV-junctional ablation in a randomized, double-blind, cross over pacing site study design of patients without heart failure [33]. Consistent with the results presented here, no significant differences were detected between the two pacing sites in left ventricular ejection fraction, New York Heart Association functional class, exercise time or maximal oxygen uptake three months after randomization. In another study the acute haemodynamic effects of right ventricular apical, outflow tract, left ventricular single site and bi-ventricular pacing were compared in patients with severe heart failure [35]. Mean blood pressure, pulmonary artery wedge pressure and cardiac index were similar to baseline during pacing at either right ventricular site. Single site left ventricular pacing or combined
left and right ventricular pacing improved haemodynamics compared with no pacing in patients with advanced heart failure. Left ventricular pacing or bi-ventricular pacing were better than single site pacing at either right ventricular apex or outflow tract.

The finding that diastolic function deteriorates with chronic right ventricular apical pacing has been reported previously\(^\text{[19]}\). The deterioration has been explained by histopathological alterations resulting from the abnormal pattern of ventricular activation, regional blood flow and wall stress compared with normal activation. While diastolic function has been neglected in some comparative studies of right ventricular pacing site, others have shown subtle improvements in systolic and diastolic function with outflow tract pacing over apical pacing in patients with impaired function at baseline\(^\text{[34]}\).

In this study, diastolic function also deteriorated in those paced in the right ventricular outflow tract. This difference from some other reports may point to a real difference in the effects of pacing in patients with preserved as compared with severely impaired left ventricular function at baseline. It is entirely plausible that diastolic function deteriorates with both right ventricular pacing sites in those with near normal function at baseline, yet improves with outflow tract pacing in those with severely impaired function. All studies are agreed, however, that whatever parameters are measured right ventricular apical pacing is least desirable because of its adverse effects on systolic and diastolic left ventricular function.

**Limitations of the study**

The study evaluated only 20 patients and was underpowered therefore to identify subtle changes, which might still be clinically important. Patients were not randomized to site of pacing but were allotted sequentially to ensure a balance in the numbers in each group. However, the fact that echocardiographic indices of ventricular function and left atrial size prior to AV-junctional ablation did not differ significantly between the two groups, suggests that bias did not occur inadvertently as a result of the non-randomized study design. Radionuclide ventriculograms were not performed prior to AV-junctional ablation in this study because of the known inaccuracies in comparing parameters of ventricular function between atrial fibrillation with uncontrolled, irregular ventricular response rates prior to ablation and paced rhythm at a slower rate afterwards.

If the site of outflow tract pacing is critical to obtaining the benefits of this site for ventricular function, then the fact that some subjects were paced at lower sites than others, could explain the predominantly negative findings of the study. However, it is unlikely that this influenced the results significantly, since the findings did not change when only the subgroup with the highest lead positions in the outflow tract were compared with those paced apically. The fact that QRS duration was not shorter in those paced in the outflow tract is surprising and unexplained. It could be that because these subjects had normal ventricular function and no QRS prolongation at baseline, paced ventricular activation spreads equally rapidly from either site, in comparison with that in subjects with cardiac dilatation and abnormal inter-ventricular conduction. Alternatively, the occurrence of right bundle branch block at time of AV-junctional ablation in some patients might explain why QRS duration from the two sites were similar.

In contrast to the methodology used in other studies, ventricular function was assessed in VVI-mode at 80/ min, specifically to avoid the influence of differing atrial rhythms in the same patient at the two assessments or between patients in the two groups\(^\text{[35]}\). Whether assessments of ventricular function at maximum paced heart rate-for-age would have been more discriminating between the two sites cannot be answered. Nor did patients in this study cross over between pacing sites to allow the effects of both sites to be compared in the same patient. This was considered an invalid comparison in patients paced after AV-junctional ablation, in whom the withdrawal of antiarrhythmic drugs and the reversal of tachycardia related cardiomyopathy might also influence assessments making interpretation of a cross over design impossible.

Finally the conduct of drug therapy used in the course of the study was left to the discretion of the physician managing the patient. Significantly more patients paced in the outflow tract were taking angiotensin-converting enzyme inhibitors, mainly for hypertension, at the time of AV-junctional ablation than in those paced apically. It is not possible to exclude the possibility that the benefits of outflow tract pacing observed were due, not solely to the site of pacing, but also to differences in the ways in which ventricular function evolved after ablation through the actions of these agents.

**Conclusions**

This comparative study of the chronic effects of right ventricular pacing after AV-junctional ablation on ventricular function in patients without history of cardiac failure, suggests that systolic function is better preserved by outflow-tract compared with traditional apical site pacing. Diastolic function deteriorated over time in both groups. The results are consistent with and provide new insights into published reports on optimum pacing site selection both in patients with preserved and impaired ventricular function. A consensus is emerging that, in younger patients particularly, more consideration should be given to the site adopted for ventricular pacing to avoid the potential for deleterious haemodynamic legacies. While all studies agree that the traditional right ventricular apical site provides the worst haemodynamic outcome, it remains to be determined whether the change recommended should be to the right ventricular outflow tract, to a right ventricular site...
specifically to capture the His-bundle, to a single left-ventricular lateral wall site or to multi-site ventricular pacing incorporating several right ventricular or right and left ventricular sites.

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References