Atrial Fibrillation

Research Article

Atrioventricular Node Ablation in Atrial Fibrillation Patients with Cardiac Resynchronization Therapy: Benefits Beyond Rate Control

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ABSTRACT. Aims: We sought to determine whether atrial fibrillation (AF) patients following cardiac resynchronization therapy (CRT) benefit from atrioventricular node (AVN) ablation by mechanisms other than rate control alone. Methods and results: In this single-center retrospective cohort study we analyzed the device database registry to identify heart failure patients with AF who underwent CRT. Among 137 patients with successful CRT, 42 (31%) had persistent AF. Patients with AF were divided into two groups on basis of AVN ablation. Patients underwent AVN ablation because of rapid ventricular rates in spite of maximizing medical therapy, and were expected to have a low percent biventricular pacing. Transthoracic echocardiography and the 6-min walk test were obtained at baseline and 3 months after CRT. At 3 months, resting and peak heart rates ±SD during the 6-min walk were similar for both groups, nine AVN ablation patients (71 ± 4 and 91 ± 9 bpm respectively) and 31 without AVN ablation (71 ± 9 and 92 ± 16 bpm respectively; p = 0.77). Biventricular pacing was greater with AVN ablation than no ablation (96 ± 7% and 87 ± 24%, respectively; p = 0.27). Heart rates during the 6-min walk did not correlate with the percent biventricular pacing. Left ventricular end-systolic volume after CRT improved by 15% in 56% of AVN ablation versus 27% without ablation (p = 0.12). Conclusions: AVN ablation patients had a non-statistically significant improvement in reverse remodeling compared with no ablation. Rate control does not fully account for CRT response. Regularization of the ventricular rate may contribute to increased biventricular pacing and optimize the benefits of CRT in AF patients with heart failure.

KEYWORDS. atrial fibrillation, cardiac resynchronization therapy, catheter ablation, atrioventricular node.

Introduction

Although approximately one-third of advanced heart failure patients exhibit atrial fibrillation (AF), the impact of cardiac resynchronization therapy (CRT) in this group remains unclear.1–3 The efficacy of CRT in patients with AF and the need for atrioventricular node (AVN) ablation is not yet beyond controversy. In heart failure, the presence of AF is a poor prognostic factor for CRT.4
Studies have demonstrated that CRT results in improvement in quality of life, heart failure symptoms, exercise capacity, mortality, and hospitalization rates. AF and heart failure are commonly found together, with each potentially exacerbating the other and causing a substantial increase in morbidity and mortality. Heart failure leads to structural and electrical atrial remodeling that can induce AF; alternatively, AF can lead to hemodynamic deterioration that causes tachycardia-induced cardiomyopathy. Previous studies have demonstrated similar benefits of biventricular pacing in patients with advanced heart failure and AF compared with those in sinus rhythm, if the AF patients undergo an AVN ablation. Both heart rate control and ventricular rhythm regularization (elimination of the irregular ventricular rhythm in AF) are potential mechanisms for symptomatic improvement.

In our study, we looked into potential mechanisms for improvement in left ventricular (LV) function after AVN ablation in patients with AF who underwent CRT. We sought to determine whether rate control alone accounts for the benefits from AVN ablation.

**Methods**

Our study group comprised patients with New York Heart Association class III/IV heart failure with concurrent long-standing persistent or permanent AF who underwent clinically indicated CRT defibrillator implantation at our institution during the period from September 2005 to September 2007. Leads were implanted in a standard manner with the right ventricular (RV) lead near the RV apex, and the lateral wall was targeted for the LV lead. The CRT device pacing modes were DDDR with lower base rate ranged between 50–70 beats/min and upper sensor rates were in the range between 120–130 beats/min. Patients were retrospectively analyzed in 2 groups on the basis of whether they underwent AVN ablation prior to or within 1 week after CRT defibrillator implantation. Prior to undergoing CRT, patients were treated with rate control medications, including metoprolol, atenolol, bisoprolol, carvedilol as well as digoxin as indicated. Patients underwent AV node ablation at the discretion of their cardiologist. Patients with inadequate rate control, or who were anticipated to have a low percent biventricular pacing underwent AV node ablation.

Data were prospectively collected at the time of the CRT defibrillator implant and at 3-month follow-up with a comprehensive echocardiogram, 6-min walk test, peak oxygen consumption exercise treadmill test, and Minnesota Living with Heart Failure Questionnaire. Patients in the study group received a CRT defibrillator between September 2005 and September 2007 at the Mayo Clinic, Rochester, MN.

This study was approved by the Mayo Clinic Institutional Review Board. The study participants were prospectively enrolled in anticipation of CRT for advanced heart failure and subsequently were followed for at least 3 months after CRT. Of 184 patients prospectively enrolled in the institutional CRT Registry, 137 patients met standard criteria for CRT of QRS duration >120 ms and ejection fraction <35%, and underwent successful implantation of a CRT defibrillator. Of those 137 patients, 42 had persistent or permanent AF. Two were excluded from analysis because AVN ablation was performed more than 1 week after CRT, resulting in a total of 40 patients included in our analysis.

After CRT, the 40 patients with AF were classified into two groups for comparison analysis. The first group included nine patients who underwent an AVN ablation, and the second group of 31 patients had AF but no AVN ablation. The primary endpoint of the study was CRT response, which was defined as a >15% reduction at 3 months in LV end-systolic volume by the biplane Simpson method of echocardiography. The secondary endpoints for 3-month CRT responders were a peak oxygen consumption increase >10%, a 6-min walk distance increase >75 m, and quality-of-life score improvement >10%.

**Figure 1:** Patient Flowchart. Of 184 patients selected for cardiac resynchronization therapy (CRT), 137 had CRT; 42 of the 187 had atrial fibrillation, and were eligible for the study, but two patients were excluded because of the delay between CRT and atrioventricular node ablation, resulting in a final study enrollment of 40 patients.
**Transthoracic echocardiography**

The Simpson biplane method was used to calculate LV end-systolic and diastolic volumes and ejection fraction. Variability in echocardiography measures was minimized by all baseline and 3-month echocardiograms being read by a single researcher (B.D.P.) blinded to the clinical results.

**Biventricular pacing and heart rate**

The study participants underwent CRT defibrillator device interrogation 3 months after implant. The mean percentage of biventricular pacing over this period was determined at that time. Patients also underwent a 6-min walk test 3 months after implant, which allowed for assessment of heart rate at rest and with exercise.

**Statistical methods**

Values were reported as mean ± SD. Student’s t-test was used to compare baseline characteristics. Fisher’s exact test was used for bivariate analysis of dichotomous outcomes. The dispersion measurements of continuous variables were graphically represented through the Pearson correlation coefficient. Statistical analysis was performed using JMP version 9.0.1 (SAS Inc., Cary, NC).

**Results**

**Patient baseline demographics**

The first group of nine patients had an AVN ablation, whereas the second group of 31 patients had AF but no AVN ablation after CRT defibrillator implant. Ischemic cardiomyopathy was present in 55% of the ablation group and in 65% of the non-ablation group (p = 0.85). The use of β-blockers was similar between groups: 89% in the ablation group and 87% in the non-ablation group. The use of angiotensin-converting enzyme inhibitors was higher in the non-ablation group than in the ablation group (100% versus 31%, respectively; p < 0.001). Digoxin use was significantly higher in the non-AVN ablation group than the AVN ablation group: 85% compared with 65% (p = 0.65). In both groups, the majority of patients (80%) had the RV lead placed in the apical position, and in all of them the LV lead was placed in the coronary sinus. Additional baseline characteristics are listed in Table 1. The echocardiography parameters and functional characteristics were similar between the two groups, except that the mean LV end-systolic volume was 99 mL in the ablation group and 159 mL in the non-ablation group (p = 0.01) (Table 2). Most patients in each group had New York Heart Association class III function. The heart rate before ablation was similar in both groups during rest (71 ± 15 bpm) and following a 6-min walk (83 ± 17 bpm) (Figure 2).

**Clinical outcome After CRT**

Patients who underwent AVN ablation were more likely to have a >15% reduction in left ventricular end-systolic volume at 3-month follow-up, although the difference did not reach statistical significance (55% in the AVN ablation group versus 25% in the non-ablation group; p = 0.12). There was no significant difference in change in peak oxygen consumption or quality-of-life score (Figure 3). Both groups had a similar mean resting and peak heart rate during the 6-min walk test (71 ± 4 and 91 ± 9 bpm for AVN ablation compared with 71 ± 9 and 92 ± 16 bpm for the non-ablation group) (Figure 2).

However, the mean percentage of biventricular pacing was higher in the AVN ablation group than in the non-ablation group (96% ± 7% versus 87% ± 24%, respectively; p = 0.27) (Figures 3 and 4). Figure 5 demonstrates a narrower distribution of the range of biventricular pacing in the AVN ablation group, with the highest concentration in the 95–100% range. In contrast, in the non-ablation group, the dispersion is more widely spread from 60% to 98%, although there was no statistically significant correlation between the percentage of biventricular pacing and the change in LV end-systolic volume in this study (Figure 6). Although the heart rate in both groups was similar both at rest and during the 6-min walk, the percentage of biventricular pacing was different at 3-month follow-up after CRT defibrillator implant. Resting and peak heart rates during the 6-min walk test did not correlate with the percentage of biventricular pacing.

The study also showed a trend toward improved LV reverse remodeling, defined as greater than 15% reduction in LV end-systolic volume, following AVN ablation.

**Table 1: Baseline characteristics of nine patients with and 31 patients without atrioventricular node ablation for atrial fibrillation**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With AVN ablation (n = 9)</th>
<th>Without AVN ablation (n = 31)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (years)</td>
<td>72 ± 10</td>
<td>73 ± 10</td>
<td>0.89</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>5 (55%)</td>
<td>20 (65%)</td>
<td>0.85</td>
</tr>
<tr>
<td>ACE-inhibitor or ARB</td>
<td>6 (67%)</td>
<td>31 (100%)</td>
<td>0.001</td>
</tr>
<tr>
<td>β-blocker</td>
<td>8 (89%)</td>
<td>27 (87%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Mean NYHA class</td>
<td>2.7</td>
<td>3.0</td>
<td>0.08</td>
</tr>
</tbody>
</table>

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; AVN: atrioventricular node; NYHA: New York Heart Association.

*Values are number (percentage) unless indicated otherwise.*
in CRT (56% AVN ablation patients had reverse remodeling versus 27% without ablation; \(p = 0.12\)), although there were no differences in quality of life, peak oxygen consumption or 6-min walk test (Figure 3).

**Discussion**

The main findings of this study are 1) AF patients who underwent CRT and had AVN ablation had greater improvement in LV reverse remodeling, although the difference was not statistically significant because of the limited sample size; 2) patients with or without AVN ablation had similar resting and peak heart rates 3 months after CRT; and 3) AVN ablation produced a higher percentage of biventricular pacing than that for patients without AVN ablation, although the difference did not reach statistical significance.

AVN ablation can optimize CRT in AF patients with advanced heart failure. The finding of greater LV reverse remodeling with AVN ablation is similar to that reported in previous studies.\(^9,14,15\) However, in current clinical practice, AVN ablation is not routinely performed on all CRT patients who have persistent or permanent AF.\(^2\) At the present time it has a level 2A indication given jointly by American College of Cardiology and American Heart Association Guidelines. Some patients may not undergo AVN ablation because they achieve adequate rate control with medical therapy. AVN ablation may be beneficial in AF and CRT due to optimal ventricular rhythm regularization by reducing RR interval variability, increasing the percentage of biventricular pacing, and improving intraventricular conduction delay.\(^10\) Our findings provide added insights on the potential mechanisms for benefit from AVN ablation in AF patients who undergo CRT. The mean ventricular rates at rest and with the 6-min walk test were not significantly different between the two groups at the beginning of the study, nor at 3-month follow-up, which implies a different mechanism for benefit from AVN ablation.

![Figure 2: Heart rate at rest and with exercise at baseline. Average heart rates were similar in both groups at baseline. (a) At rest (mean heart rate, 71 ± 15 bpm) and, (b) with exercise (mean heart rate, 83 ± 17 bpm) at baseline prior to cardiac resynchronization therapy and atrioventricular node ablation.](image)

![Figure 3: Follow-up assessment. At 3-month follow-up, patients who had atrioventricular node (AVN) ablation had significantly improved left ventricular end-systolic volume compared with that in patients who did not undergo AVN ablation. 6MWT: 6-min walk test; QOL: quality of life; VO₂: peak oxygen consumption.](image)

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**Table 2:** Baseline function of nine patients with and 31 patients without atrioventricular node ablation for atrial fibrillation

<table>
<thead>
<tr>
<th>Variable</th>
<th>With AVN ablation (n=9)</th>
<th>Without AVN ablation (n=31)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction</td>
<td>29 ± 7%</td>
<td>25 ± 7%</td>
<td>0.11</td>
</tr>
<tr>
<td>LV end-systolic volume</td>
<td>99 ± 69 mL</td>
<td>159 ± 9 mL</td>
<td>0.01</td>
</tr>
<tr>
<td>6-min walk distance</td>
<td>307 ± 137 m</td>
<td>298 ± 137 m</td>
<td>0.85</td>
</tr>
<tr>
<td>Peak VO₂</td>
<td>15.0 ± 5.4 ml/kg/min</td>
<td>12.4 ± 5.4 ml/kg/min</td>
<td>0.11</td>
</tr>
<tr>
<td>MLHFQ</td>
<td>56.8 ± 21</td>
<td>55.3 ± 21</td>
<td>0.86</td>
</tr>
</tbody>
</table>

AVN: atrioventricular node; LV: left ventricular; MLHFQ: Minnesota Living with Heart Failure Quality of Life questionnaire; VO₂: peak oxygen consumption.
Ablation other than rate control alone. The regularizing of ventricular rate and activity with a subsequent percentage increase in biventricular pacing is a plausible explanation for the added benefit of AVN ablation.\(^{16}\) Patients in the AVN ablation group had a higher percentage of biventricular pacing, despite having resting and peak heart rates similar to those patients without AVN ablation.\(^{17}\) We also noted improvement in LV end-systolic volume and reverse remodeling in the AVN ablation group compared with the non-ablation group despite no difference in heart rates during rest and exercise. As such, the percentage of biventricular pacing did correlate with positive changes observed in AVN ablation in respect to LV end-systolic volume and ventricular remodeling, but as noted earlier did not reach statistical significance. This finding suggests that ventricular rate regularization with AVN ablation improves biventricular pacing, which has been shown to be associated with improved outcome after CRT.\(^{16}\) Similar observations have been made by Ueng et al\(^{18}\) in AF patients with normal LV function where AVN ablation and pacing conferred both acute and long-term benefits beyond rate control by eliminating rhythm irregularity. Rhythm irregularity may decrease LV systolic and diastolic function, in spite of a normal heart rate. In addition, biventricular pacing greater than 92% in patients with heart failure has been shown to be associated with improved outcomes compared with patients with less than 92% biventricular pacing.\(^{14}\) In our study, the AVN ablation group had a mean percentage biventricular pacing above this value, whereas those AF patients who did not undergo AVN ablation had a mean of less than 92% biventricular pacing. Koplan et al\(^{19}\) showed similar benefits with AVN ablation in AF patients undergoing CRT. AF reduces the actual percentage of biventricular pacing and is more likely to have fusion of biventricular pacing with partial intrinsic conducted beats. AVN ablation improves this phenomenon by creating iatrogenic heart block, which allows for a higher percentage of true biventricular pacing. This consistency in pacing also results in ventricular rhythm regularization in spite of underlying AF.

Our study did not identify any difference in resting and peak walking heart rates between the two groups. Overall, the heart rates of patients both at rest and with exercise were relatively well controlled in both groups (around 70 and 90 bpm, respectively). Melenovsky et al\(^{20}\) found that irregularity of the RR interval worsens cardiac function in heart failure patients who have AF. These findings raise the possibility that AF patients may benefit from undergoing AVN ablation even if their ventricular rates appear moderately well controlled with medication. Similar results were observed in a recent meta-analysis by Stavrakis et al\(^{21}\) showing statistically significant improvement of hospitalization and non-significant reduction in

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Figure 4: Percentage of biventricular pacing. At 3-month follow-up, biventricular pacing was significantly higher in the nine patients who underwent atrioventricular node (AVN) ablation than that in the 31 patients who did not undergo AVN ablation.

Figure 5: Heart rate at rest and with exercise 3 months after cardiac resynchronization therapy. At 3-month follow-up, the heart rate at rest and with exercise were similar for the group of nine patients who underwent atrioventricular node (AVN) ablation and the group of 31 who did not undergo AVN ablation.

Figure 6: Correlation of biventricular pacing and left ventricular end-systolic volume in all patients in both groups after cardiac resynchronization therapy.
overall mortality in spite of no difference in the 6-min walk test and the Minnesota living with heart failure score in a selected AF population who underwent AVN ablation following CRT compared with RV pacing only. The study also provided similar findings to those seen by Ciaramitaro et al in AF with heart failure but preserved LV function: ventricular rhythm regularization achieved after AVN ablation reduces biventricular rate variability following CRT. In our study populations, the paced rate in both groups was similar at rest and exercise, but the rate stabilization achieved by ablation provided a favorable outcome in advanced heart failure with AF after CRT. Although there were no differences in quality of life, peak oxygen consumption, or 6-min walk test, which are similar to the results of prior studies like Tse et al in 2004.

**Limitations**

This study has a relatively small number of patients who underwent AVN ablation. However, these patients underwent prospective follow-up including baseline and 6-min walk tests which allowed for detailed analysis of the potential mechanisms for response to CRT. AVN ablation was performed at the physician’s discretion without randomization due to the limited number of patients who had atrial fibrillation in the original cohort group. Nevertheless, the end result of our study is similar to other randomized trials showing a trend regarding the benefits of CRT therapy in AF. Our focus was on the mechanism of these benefits. Device algorithms that promote biventricular pacing at the time of sensed ventricular events result in fused biventricular pacing. These potentially less effective biventricular paced beats may be less frequent in patients with AVN ablation. This may in part account for greater reverse remodeling in the AVN ablation group. Detailed data on true biventricular pacing percent and triggered biventricular pacing were not available for analysis.

**Conclusions**

Patients with AF who underwent AVN ablation had a higher percentage of biventricular pacing, despite having resting and peak heart rates similar to those in patients without AVN ablation before and after CRT. This finding was likely secondary to improved ventricular rhythm regularization. This mechanism may explain the added benefit of AVN ablation in AF patients who undergo CRT. Future randomized studies are needed to determine whether routine AVN ablation might be beneficial in all AF patients undergoing CRT.

**References**

18. Ueng KC, Tsai TP, Tsai CF, et al. Acute and long-term effects of atrioventricular junction ablation and VVIR


