ATRIAL FIBRILLATION

RESEARCH ARTICLE

Atrioventricular Nodal Ablation and Pacemaker Therapy: Role in the Management of Atrial Fibrillation

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ABSTRACT. Background: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia worldwide and causes increased morbidity and mortality. The prevalence of AF is on the rise in the United States, with a projected 5.6–12 million Americans carrying this diagnosis by 2050. First-line treatment of AF remains medical therapy with rate control or rhythm control strategies. In patients who fail first-line medical therapy, atrioventricular nodal (AVN) ablation with permanent pacemaker insertion is an established treatment modality. Benefits: AVN ablation and ventricular pacing decreases symptoms, improves quality of life, and decreases hospitalization compared to medical therapy in patients with medically refractory AF. In patients with AF and heart failure undergoing cardiac resynchronization therapy, AVN ablation offers a probable survival benefit. AF has a high prevalence in elderly people, and AVN ablation can potentially decrease polypharmacy in this population while effectively controlling heart rate. Complications: AVN ablation is a safe procedure with high success rates. The risk of sudden cardiac death after ablation is mitigated by pacing at a higher rate temporarily. Long-term right ventricular apical pacing has been linked to worsening of heart failure, and there is a need to identify risk factors that contribute to worsening of heart failure in these patients. Future directions: The PACIFIC trial is currently underway and compares pharmacotherapy, AVN ablation with conventional pacing, and AV nodal ablation with cardiac resynchronization therapy (CRT). This review article describes the current evidence regarding AVN ablation and pacing as a therapeutic modality, with a highlight on ablation in patients undergoing CRT and ablation in elderly people.

KEYWORDS. atrial fibrillation, atrioventricular nodal ablation, cardiac resynchronization therapy, radiofrequency ablation, review.

Introduction and epidemiology

Atrial fibrillation (AF) is a common condition causing increased morbidity and mortality. In 2010, the prevalence of AF in the United States was estimated to be between 2.7 and 6.1 million. This is expected to rise to about 5.6–12 million in 2050. At 40 years of age, the lifetime risk of developing AF is 26% for men and 23% for women. AF is associated with increased incidence of death in men and women and is a risk factor for stroke, dementia, and heart failure.

AF and heart failure frequently coexist and beget each other. It is estimated that 40% of individuals with AF will develop heart failure and vice versa. In patients with New York Heart association (NYHA) class I heart failure, AF is present in < 5% patients. In patients with NYHA class IV heart failure, the proportion of patients with coexistent AF increases to 50%. In addition, new-onset
AF in patients with heart failure confers a mortality risk in both men and women. The hazard ratio for mortality is 1.6 in men and 2.7 in women. In patients who are refractory to medical management of AF, options include catheter or surgical ablation of AF and atrioventricular nodal (AVN) ablation and pacemaker insertion—also known as the “ablate and pace” strategy. In patients who are refractory to pharmacologic interventions, the “ablate and pace” strategy is increasingly used. It can be considered as an extreme form of rate control. The AV node is ablated using radiofrequency energy, following which a permanent pacemaker is required for maintenance of adequate ventricular rate. There is lifelong pacemaker dependency and need for anticoagulation following this procedure.

Although AVN ablation and pacemaker therapy is effective in rate control and alleviates symptoms, pacing-mediated dyssynchrony and heart failure have been observed in selected patient populations. The role of biventricular pacing (BVP) (cardiac resynchronization therapy CRT) and septal pacing following AVN ablation are currently under investigation. We will review the current indications for AVN ablation and pacing in AF based on currently available evidence.

AVN ablation and pacing in current clinical practice

According to the 2011 ACCF/AHA/HRS updates for management of AF, AVN ablation may be beneficial in patients with medically refractory AF. This approach should be considered in patients who cannot maintain sinus rhythm or cannot be adequately rate controlled by pharmacotherapy.5 The long-term safety of the procedure was underlined in a prospective cohort study of 350 patients by Ozcan et al.8 in 2001, which revealed that the survival of patients undergoing AVN ablation and pacing was similar to patients receiving drug therapy for AF. Previous myocardial infarction, congestive heart failure, and requirement for other cardiac drugs were predictors of death in multivariate analysis. In the absence of these risk factors, survival was similar to expected survival of the age and sex-matched general population. A recent meta-analysis by Chatterjee et al.9 compared AVN ablation with pharmacotherapy in patients with drug refractory AF. Of the five studies included in the efficacy analysis, four were randomized trials, comprising 314 subjects in total. The efficacy analysis demonstrated that AVN ablation improves symptoms and quality of life (QoL) significantly in patients with medically refractory disease when compared with pharmacotherapy alone. There was non-significant yet modest improvement in exercise tolerance and ejection fraction (EF) with AVN ablation. In patients with reduced systolic function at baseline, there was modest and significant improvement in EF in the AVN ablation group compared with pharmacotherapy alone (4% greater; 95% CI 3.11–4.89). There was minimum heterogeneity for this result (I²=0%). Exercise capacity was similar in both groups, irrespective of baseline systolic function. There were only 10 deaths in the studies included in the efficacy analysis, and conclusions regarding the effects of AVN ablation on mortality could not be drawn.

The effectiveness analysis included 11 observational or prospective single-armed studies and yielded a total of 810 patients. There was a mean increase in exercise duration of 1.19 min in patients undergoing AVN ablation (95% CI 0.52–1.86). There was a mean increase in EF by 4.80% (95% CI 2.01–7.58) in patients undergoing AVN ablation (I²=78%). Again, subgroup analysis revealed that patients with baseline systolic dysfunction had greater improvement in EF after AVN ablation (7.44%; 95% CI 5.4–9.5) with minimal heterogeneity for this result (I²=0%). There was no significant difference in systolic function between the two groups in the subgroup of patients with normal systolic function at baseline. Thus, the results of trials conducted so far demonstrate that AVN ablation is a safe procedure, resulting in improvements in symptoms and QoL irrespective of left ventricular (LV) function and modest improvements in systolic function and exercise capacity in patients with baseline LV dysfunction (Table 1).

Catheter ablation procedures involving pulmonary vein isolation (PVI) and wide area circumferential ablation are another option for treatment of drug refractory AF. These procedures provide good control of AF in the short term.10 A randomized trial by Khan et al.9 comparing AVN ablation and catheter ablation in patients with drug refractory AF demonstrated superiority of catheter ablation over AVN ablation. Patients in the catheter ablation group had greater improvements in EF, exercise tolerance and QoL at 6 months’ follow-up. These effects are probably due to reversal of tachycardia-induced cardiomyopathy in patients who are likely to have poor rate control. About half the patients in this trial had paroxysmal AF and the other half had persistent AF. Further evidence in support of catheter ablation for drug refractory AF was provided by an observational nested case-control study of 1000 patients who reported a survival benefit with PVI compared with AVN ablation or pharmacotherapy over a 7-year follow-up period. It is difficult to utilize the findings of this study in clinical practice, as the study was likely to be confounded due to non-randomized selection of therapy.

The enthusiasm for catheter ablation has been tempered by the results of recent studies that report a high rate of recurrence of AF, especially in patients with persistent and longstanding persistent AF.11 Other factors that have been linked with recurrence of AF after catheter ablation include greater age, permanent AF, hypertension, greater left atrial diameter, and underlying

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AF is a risk factor for dementia, as evidenced in a recent meta-analysis that studied risk of dementia in patients with AF (HR = 1.42; 95% CI 1.17–1.72, p < 0.001). Another benefit of AVN ablation is improvement in brain perfusion and cognitive performance, as evidenced in a small study by Efimova et al. Ninety-four percent of patients with medically refractory AF and poorly controlled ventricular conduction had cognitive deficits in this study. Verbal memories, visual memories, attention, psychomotor speed, and learning ability were improved in all 17 patients studied after AVN ablation and pacemaker insertion. This may have important implications while choosing treatment in an aging population.

### Right ventricular apical pacing in AV nodal ablation

Studies from before the turn of the century have raised concerns about chronic right ventricular apical (RVA) pacing. It was demonstrated that RVA pacing can cause or worsen mitral regurgitation and can worsen hemodynamic status in patients with pre-existing ventricular dilatation. A recent meta-analysis of four trials comparing RVA pacing to BVP did not demonstrate a decrease in mortality with BVP (risk ratio: 0.85, 95% CI, 0.40–1.82). In the subgroup of patients with baseline systolic dysfunction, BVP offered a non-significant reduction in cardiac mortality (risk ratio 0.59, 95% CI 1.45–3.99). There was no difference in exercise tolerance, but a subgroup analysis of patients with NYHA II/III symptoms showed increases in exercise tolerance with BVP in this population. EF was modestly improved in the BVP group, and there was moderate heterogeneity for this result (I² = 53%). QoL was significantly improved in patients receiving BVP in two studies, with one study reporting no difference in QoL between the two groups. One of the studies included in this analysis was the PAVE (Post AV Nodal Ablation Evaluation) study, which showed that with BVP, improvement in EF, functional parameters, and QoL were greater in patients with EF <45% at baseline or NYHA II/III symptoms (Table 2).

These findings are in contrast to results of an observational study that demonstrated modest significant improvement in the short term in patients with AVN ablation and RVA pacing. There was no difference in EF with long-term (>1 year) follow-up. High preablation heart rate was a univariate predictor of improved EF, and EF >40 was a predictor for decline in EF in the multivariate model. Half the patients without mitral regurgitation developed mild mitral regurgitation, which did not result in a decrease in LV function in these patients. There are differences in populations studied in observational studies and clinical trials. Observational studies commonly have greater numbers of patients who have exhausted all therapeutic options. This difference in study populations may account for some of the differences in the results of the observational study compared with the clinical trials.

There is much interest in determining which subsets of patients are predisposed to worsening of LV function after RVA pacing. The main determinants of worsening LV function after RVA pacing include baseline low EF, history of diabetes mellitus. These groups may be better suited to AVN ablation, which is a more permanent solution than PVI procedures.

### Table 1: Prospective double-armed trials comparing AV nodal ablation and pharmacotherapy in drug refractory atrial fibrillation

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Number studied</th>
<th>Type of study</th>
<th>Outcome</th>
<th>Results</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brigugnole et al</td>
<td>1997</td>
<td>43</td>
<td>Prospective randomized</td>
<td>Symptoms, QoL, NYHA class</td>
<td>Favors AVNA-improved symptoms, QoL, NYHA class.</td>
<td>55</td>
</tr>
<tr>
<td>Brigugnole et al</td>
<td>1998</td>
<td>66</td>
<td>Prospective randomized</td>
<td>LV function, exercise tolerance, symptoms, QoL, NYHA class</td>
<td>Favors AVNA-improved symptoms, QoL and NYHA class; no difference in EF and exercise tolerance.</td>
<td>56</td>
</tr>
<tr>
<td>Marshall et al</td>
<td>1999</td>
<td>56</td>
<td>Prospective randomized</td>
<td>Symptoms, QoL</td>
<td>Favors AVNA-improved symptoms and QoL</td>
<td>57</td>
</tr>
<tr>
<td>Ueng et al</td>
<td>2001</td>
<td>50</td>
<td>Prospective, non-randomized</td>
<td>LV function, exercise tolerance, symptoms, QoL, NYHA class</td>
<td>Favors AVNA-improved cardiac output, PCWP, LVEDP, exercise tolerance, symptoms, QoL and NYHA class.</td>
<td>58</td>
</tr>
<tr>
<td>Weerasooryla et al</td>
<td>2003</td>
<td>99</td>
<td>Prospective, randomized</td>
<td>LV function, exercise tolerance, symptoms, QoL, NYHA class</td>
<td>Favors AVNA-improved symptoms, QoL and NYHA class, no difference in LV function and exercise tolerance.</td>
<td>59</td>
</tr>
</tbody>
</table>

QoL: Quality of life; AVNA: Atrioventricular nodal ablation; NYHA: New York Heart Association; LV: Left ventricular; EF: Ejection fraction; PCWP: Pulmonary capillary wedge pressure; LVEDP: Left ventricular end diastolic pressure.
of heart failure, or myocardial infarction and QRS prolongation.\textsuperscript{20} Owing to a propensity to worsen regurgitating lesions with RVA pacing, patients with severe mitral or tricuspid regurgitation, RV dysfunction, and pulmonary hypertension are poor candidates for AVN ablation. Further studies are required to delineate predictors of poor response to RVA pacing and also to assess benefit of CRT instead of RVA pacing in these groups.

Ablating the AV node in patients undergoing CRT

CRT is an established treatment modality for patients in sinus rhythm with EF \(<35\%\), QRS>120 ms and NYHA class III or ambulatory NYHA class IV patients.\textsuperscript{21,22} The ACC/AHA/HRS and ESC guidelines both advise that AVN ablation may be required in patients with AF with pre-existing indications for CRT (Class 2A recommendation, level of evidence B). A survey of patients in Europe established that 23\% of patients receiving CRT also had AF.\textsuperscript{23} In 2004, a small prospective cohort study determined that response to CRT was poorer in patients with concomitant AF.\textsuperscript{24} The subgroup of AF patients who had previous AVN ablation had decreased severity of symptoms, improved QoL, improved exercise tolerance, and improved EF when compared with patients undergoing therapy with rate-controlling medications.

There have been several retrospective and small prospective studies that have addressed the role of AVN ablation in patients with AF undergoing CRT. Recently, Ganesan et al.\textsuperscript{25} performed a meta-analysis of six of the largest retrospective and prospective studies that had outcomes reported. Three studies that had reported mortality data supported decreased all-cause mortality in patients undergoing AVN ablation in addition to CRT (risk ratio 0.42; 95\% CI 0.26–0.68). There was also decreased cardiovascular mortality in the AVN ablation group (risk ratio 0.44; 95\% CI 0.24–0.81). There was low heterogeneity for this result.\textsuperscript{26–28} There was a trend towards improvement of EF that was not significant and had high heterogeneity. There was significant improvement in NYHA class (risk ratio \~0.52; 95\% CI \~0.87 to \~0.17; $I^2=59\%$) in the AVN ablation group, and QoL scores were significantly improved in one study and not improved in another.

A reason for improved survival and performance of patients who have undergone AV nodal ablation in this population is a greater percentage of BVP. BVP reduces mortality in patients with CRT when it gets close to 100\%. It is difficult to attain a high BVP percentage in AF patients who are medically controlled.\textsuperscript{29} A 12-lead Holter study of patients not responding to CRT shows high prevalence of fusion (ventricular-sensed response) and pseudo-fusion beats in patients with coexisting AF. Rate irregularities in AF patients result in this finding and can decrease %

### Table 2: Prospective randomized trials comparing right ventricular apical pacing to biventricular pacing

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Number studied</th>
<th>Baseline EF, mean ± SD</th>
<th>Outcome</th>
<th>Results</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doshi et al (PAVE study)</td>
<td>2005</td>
<td>184</td>
<td>BIV: 46 ± 16, RVA: 45 ± 16</td>
<td>EF, exercise tolerance, QoL</td>
<td>Favors BiV-Improved EF, exercise tolerance in BiV group, especially in patients with baseline EF &lt;45 or NYHA II/III symptoms. No difference in QoL</td>
<td>60</td>
</tr>
<tr>
<td>Brignole et al</td>
<td>2005</td>
<td>56</td>
<td>Combined: 41 ± 12</td>
<td>EF, exercise tolerance, symptoms, QoL, NYHA class</td>
<td>No difference between the groups. Modest benefit of BiV pacing in patients with preserved systolic function.</td>
<td>61</td>
</tr>
<tr>
<td>Orlov et al</td>
<td>2010</td>
<td>108</td>
<td>BIV: 56 ± 9, RVA: 57 ± 8</td>
<td>EF, echo parameters, exercise tolerance, symptoms, QoL, NYHA class</td>
<td>Increased left atrial volume, LVESV, LV mass, NYHA class in RVA group. EF decreased non-significantly in RVA and increased significantly in BiV group. No difference in symptoms, QoL or exercise tolerance between groups.</td>
<td>62</td>
</tr>
<tr>
<td>Brignole et al</td>
<td>2011</td>
<td>186</td>
<td>BIV: 38 ± 14, RV: 37 ± 14</td>
<td>Primary composite endpoint of death from HF, HF hospitalization, worsening HF</td>
<td>Favors BiV-primary endpoint in 11% of BiV group and 26% of RV group, SHR 0.37 (95% CI 0.06–0.72), p = 0.005. No difference in total mortality.</td>
<td>63</td>
</tr>
</tbody>
</table>

EF: Ejection fraction; SD: Standard deviation; BiV: Biventricular; RVA: Right ventricular apical; QoL: Quality of life; NYHA: New York Heart Association; LVESV: Left ventricular end systolic volume; SHR: sub-hazard ratio; PAVE: Left ventricular-based cardiac stimulation post AV nodal ablation evaluation.
However, in the meta-analysis, as well as the study by Dong et al., better survival is observed in AVN ablation patients even if the non-ablated patients have high percent BVP. However, it is difficult to accurately calculate % BVP in AF patients without AVN ablation because of the aforementioned high rate of fusion and pseudo-fusion beats (Figure 1). These fusion (ventricular sensed response) and pseudo-fusion beats would be calculated as BVP beats, but in reality the benefit of BVP-mediated synchrony is likely to be incomplete from these fusion and pseudo-fusion beats. Thus the true % BVP is less than the calculated % BVP in patients with AF who have not undergone AVN ablation. This could potentially explain the findings in the study by Dong et al.

Since there was no difference in defibrillator or pacing device utilization in patients with or without AV nodal ablation, one would expect the survival benefit to be due to a decrease in heart failure events. The non-significant rise in EF in patients with AVN ablation does not support this notion. Again, the survival benefit in the absence of improved EF could be explained by a lower percentage of true BVP beats in patients without AV nodal ablation. This effect may also be due to measurement of follow-up EF only in survivors in the non-AVN ablation group, who would be expected to have better LV function and EF, which might have led to their better prognosis.

There are no published trials that examine the role of PVI in AF patients undergoing CRT for treatment of heart failure.

Complications of AVN ablation

AVN ablation is a safe procedure with high success rates and low rates of post-procedural complications. As outlined by Chatterjee et al. in the safety review portion of their meta-analysis comprising 5,632 patients, the most common cause of morbidity was the need for a left-sided procedure after a failed right-sided approach (6.9%). Spontaneous recurrence of AVN conduction requiring redo procedures occurred in 2.9% cases. The incidence of death within 30 days of the procedure was 0.27%. Other reported complications included malignant arrhythmias, lead failure, stroke, hematoma, infection, pleural effusion, pericarditis, pseudoaneurysm, RV perforation, and pneumothorax (all under 1%). Rare complications like the Gerbode defect (left ventricle to right atrium shunt) can also occur after AVN ablation.

Patients who have undergone AVN ablation are predisposed to sudden cardiac death (SCD) after the procedure. This risk is highest in the days and few weeks following the procedure, in patients paced at ≤70 bpm, but some cases of late SCDs have also been reported. There are several mechanisms that contribute to the post-procedural proarrhythmic state. Notably, studies report post-procedural bradycardia-dependent prolongation of ventricular repolarization, leading to prolongation of the QT interval. This puts patients at risk for torsade de pointes and SCD. Other reported mechanisms include change in sequence of ventricular activation following RVA pacing, increased sympathetic activity due to sudden decrease in heart rate, increased heterogeneity of repolarization due to lower heart rate, and hypokalemia as a result of antiarrhythmic medication. QT interval prolongation decreases over time, and the degree of prolongation is reduced by temporary pacing at higher rates. The Journal of Innovations in Cardiac Rhythm Management, March 2013

Figure 1: Twelve-lead electrocardiogram showing biventricular paced beats in a patient with atrial fibrillation without AV nodal ablation. Thin arrow demonstrates biventricular (BV) pacing after ventricular sensed event. This ventricular sensed response is counted as a BV paced beat but unlikely to provide a complete BV-mediated synchrony effect. Broken arrow demonstrates complete BV pacing in the setting of AF. Thick arrow demonstrates a pseudo-fusion beat when pacing was initiated after a premature ventricular contraction (PVC). Both ventricular sensed response and pseudo-fusion beats are less effective than BV pacing.
follow-up is similar to those for patients treated with pharmacotherapy. In a recent report in abstract form, Wang et al. reported the incidence of SCD likely related to the procedure was less than 1% after implementing the practice of temporary faster pacing rate after AVN ablation. Another concern with AVN ablation is lifelong pacemaker dependency and risk of morbidity associated with pacemaker failure. This is a very rare complication and was not reported in both meta-analyses published in 2012.

Evolving role in elderly and new methods of pacing

AVN ablation obviates the need for further pharmacotherapy to control the ventricular rate. This may be of potential benefit in populations that are adversely affected by polypharmacy or drug–drug interactions. Such populations include elderly people and patients with hepatic or renal insufficiency. An average elderly patient has eight drug prescriptions, and more than 75% of elderly individuals have at least one drug prescription. Medications for AF superimposed on already prescribed medications for other comorbidities make this age group vulnerable to drug–drug interactions. Elderly populations commonly have comorbidities like hypertension and diabetes mellitus, impairments in hepatic and renal function, and often have longstanding disease, all of which make them poorer candidates for PVI procedures compared with AVN ablation. Also, catheter ablation frequently requires repeat procedures which may not be well tolerated in elderly populations. Elderly patients are also at higher risk for adverse effects from antiarrhythmic drugs such as bradycardia, orthostatic hypotension, urinary retention, and falls, which are due to drug–drug interactions and changes in pharmacokinetics with age. In addition, AF is a risk factor for development of dementia, a common problem in the elderly population. There is suggestion that there is a high incidence of cognitive deficits in patients with poor rate control and that adequate rate control can lead to improvement in cognitive symptoms. AVN ablation can provide reliable and long-lasting rate control, and it would be expected that cognitive symptoms in elderly patients with poor rate control will be improved by AVN ablation (Table 3).

RVA pacing has been identified as a factor associated with worsening of LV function. While activation spreads from apex to base of the ventricles in RVA pacing, there is considerable intra- and interventricular delay in the spread of activation. These delays promote interventricular dyssynchrony resulting in adverse modeling of the LV and decrease in the EF over time. Right ventricular outflow tract (RVOT) pacing close to the interventricular septum can potentially result in more physiologic activation of both ventricles, as this location is closer to the normal conducting system of the ventricles. Compared to septal pacing, RVA pacing has been shown to cause more regional wall motion abnormalities, prolonged QRS duration, and interventricular mechanical delay in the short term. The spread of activation is from apex to base of the ventricles in both RVA pacing and RVOT pacing. However, the speed at which the mechanical wavefront of activation spreads is faster in RVOT pacing, which may account for some of its benefits. Long-term follow-up in small studies has demonstrated significantly lower EF, LA dilatation and remodeling, higher LV end systolic and diastolic volumes, and lower survival in RVA-paced patients than septal pacing. Most of these studies are retrospective studies or prospective studies with a small sample of patients. Also, the population studied is a mix of sick sinus syndrome and complete heart block patients. Sick sinus syndrome patients do not have high percent ventricular pacing rates and can offset the negative effects of RVA pacing in AVN ablation in the statistical analysis. A well-designed large prospective trial will go a long way in answering which is the best pacing modality for patients with AV nodal ablation, RVA pacing, RVOT pacing, or BVP.

Special consideration in patients with ventricular dysfunction and possible need for resynchronization

Complex decision making is involved when dealing with a patient who has significant ventricular dysfunction that is least expected to be as a result of AF and rapid rates. Because of the ventricular dysfunction following AVN ablation, a resynchronization device should be strongly considered. On the other hand, one may anticipate significant recovery of ventricular function following AVN ablation, and thus would not need resynchronization ablation in the long run in the absence of anticipated heart failure symptoms. In our practice, we use the clinical history, examination, and analysis of echocardiographic findings to try and make these decisions. For

Table 3: Advantages of Ativoventricular nodal ablation in elderly people

<table>
<thead>
<tr>
<th>Advantages of AV nodal ablation in elderly patients</th>
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</thead>
<tbody>
<tr>
<td>Avoidance of polypharmacy in a population with several comorbidities and medications</td>
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<tr>
<td>Decreasing risk of drug-drug interactions</td>
</tr>
<tr>
<td>Greater incidence of hepatic and renal insufficiency increases risk for drug toxicity</td>
</tr>
<tr>
<td>Side effects of antiarrhythmics such as bradycardia, orthostatic hypotension, urinary retention and falls is greater</td>
</tr>
<tr>
<td>Permanent safe solution for controlling rate in AF. Orthostatic hypotension, urinary retention and falls is greater</td>
</tr>
<tr>
<td>Elderly patients commonly have long standing AF with atrial dilatation, hence they are poor candidates for PVI procedures</td>
</tr>
<tr>
<td>Possibility of improvement in cognitive symptoms</td>
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</tbody>
</table>

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example, if the patient has known ventricular dysfunction from coronary disease or other causes similar to the rapid AF, we favor placing a defibrillator with a LV lead (CRT, implantable cardioverter-defibrillator). On the other hand, if ventricular wall thickness is normal, diastolic function is relatively normal, and there is no other even partial explanation for ventricular dysfunction from other disease processes, we place a non-resynchronization standard pacemaker and observe the patient. We counsel the patient on the possibility that an upgrade to a resynchronization therapy device or possibly a defibrillator may be required.

**Conclusion and future directions**

In summary, the pros and cons of drug therapy in AF have been established for a long time. Additional long-term data are being gathered about PVI therapy. Outcomes of PVI procedures such as improvement of symptoms and QoL are encouraging in younger patients with paroxysmal AF. However, a high recurrence rate in patients with persistent AF, in patients with high risk, and the lack of data on the impact of stroke and survival would warrant caution in a wide application of PVI. There is logical consideration of an earlier use of AVN ablation in older patients with persistent and symptomatic AF.

Conventional RVA pacing is effective in alleviating symptoms, improving QoL, and reducing hospital admission and drug use. RVA pacing-induced ventricular dysfunction and heart failure is present in selected patients, although risk factors to identify these patients are currently absent. Septal pacing in the RVOT may have a lesser effect on production of ventricular dyssynchrony than RVA pacing. Randomized trials and observational studies differ significantly in patient selection, scope, and size of the study population and length of follow-up, which may account for the differences in their results.

There are no current randomized trials that adequately compare AVN ablation to catheter ablation in patients who have failed medical therapy. There exists a need for larger randomized trials with longer follow-up to adequately address this issue. The choice of procedure must be individualized for patients with refractory AF.

There is evidence supporting the use of AVN ablation in patients undergoing CRT with a recent meta-analysis reporting benefits in all-cause and cardiovascular mortality in AVN ablation patients treated with CRT compared to patients without AVN ablation. Further studies are needed to ascertain this prospectively.

The Pacing and AV Node Ablation Compared to Drug Therapy in Symptomatic Elderly Patients with Atrial Fibrillation Clinical Trial (PACIFIC trial) is currently under development; a pilot study has recently been completed, although results have not been reported. The PACIFIC pivotal trial will randomize elderly patients with drug refractory symptomatic AF to pharmacologic therapy, AVN ablation with conventional pacemaker implantation, or AVN ablation with CRT pacemaker implantation. The trial will be sufficiently large to assess the endpoints of survival, QoL, exercise capacity, stroke, and hospitalization. Because the number of elderly patients with symptomatic AF is expected to rapidly increase over the next several years, results from the PACIFIC trial will be of great help in guiding the management of these patients.

The indications for CRT continue to be refined. The results of the Resynchronization/defibrillation for Ambulatory Heart Failure Trial (RAFT) and Multicenter Automatic Defibrillator Implantation Trial – Cardiac Resynchronization Therapy (MADIT-CRT) trials endorsed lower mortality and hospitalizations in heart failure patients with NYHA class I/II, EF <35%, and QRS <120 undergoing CRT. Patients with AF had a lesser effect on the outcome in patients without AF in the MADIT-CRT trial. The outcomes for AF were not different in the RAFT trial. There is a need for studies evaluating the role of AVN ablation in patients undergoing CRT with better NYHA class at baseline.

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