Prospective Randomized Study of Ablation and Pacing Versus Medical Therapy for Paroxysmal Atrial Fibrillation
Effects of Pacing Mode and Mode-Switch Algorithm

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Background—Atrioventricular (AV) node ablation and pacing has become accepted therapy for drug-refractory paroxysmal atrial fibrillation (PAF). However, few data demonstrate its superiority over continued medical therapy. The influence of pacing mode and mode-switch algorithm has not been investigated.

Methods and Results—Symptomatic patients who had tried ≥2 drugs for PAF were randomized to continue medical therapy (n = 19) or AV junction ablation and implantation of dual-chamber mode-switching (DDDR/MS) pacemakers (slow algorithm [n = 19] or fast algorithm [n = 18]). Follow-up over 18 weeks was at 6-week intervals and used quality-of-life questionnaires (Psychological General Well Being [PGWB], McMaster Health Index [MHI], cardiac symptom score), exercise testing, echocardiography, and Holter monitoring. Paced patients were randomized to DDDR/MS or VVIR and subsequently crossed over. Ablation and DDDR/MS pacing produced better scores than drug therapy for overall symptoms (−41%, P < 0.01), palpitations (−58%, P = 0.0001), and dyspnea (−37%, P < 0.05). Changes in score from baseline were better with ablation and DDDR/MS pacing for overall symptoms (−48% versus −4%, P < 0.005), palpitation (−62% versus −5%, P < 0.001), dyspnea (−44% versus −3%, P < 0.005), and PGWB (+12% versus +0.5%, P < 0.05). DDDR/MS was better than VVIR pacing for overall symptoms (−21%, P < 0.05), dyspnea (−30%, P < 0.005), and MHI (+5%, P < 0.03). There were no differences between algorithms. More patients developed persistent AF with ablation and pacing than with drugs at 6 weeks (12 of 37 versus 0 of 19, P < 0.01).

Conclusions—Ablation and DDDR/MS pacing produces more symptomatic benefit than medical therapy or ablation and VVIR pacing but may result in early development of persistent AF. (Circulation. 1999;99:1587-1592.)

Key Words: fibrillation • catheter ablation • atrioventricular node • pacing • antiarrhythmia agents

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1% to 2% of the population and up to 10% of the elderly.1 Symptoms are often severe and difficult to control with drugs, especially with paroxysmal AF (PAF), when patients are subjected to sudden hemodynamic upset associated with loss of atrial transport, poor ventricular rate control, and heart rate irregularity.2 This has led to interest in nonpharmacological techniques to treat such patients, the most accepted of which is atrioventricular (AV) node ablation and pacing. However, there are surprisingly few data to support its use for PAF. Of the studies to date, most have been uncontrolled, retrospective, or have not distinguished between chronic AF and PAF.3–9 The only prospective study comparing medical treatment for PAF with ablation and pacing suggested superiority for the latter but did not assess the optimum pacing mode10, because both VVIR4 and DDDR/MS3 pacing have been shown to be effective, an assessment of pacing mode is required. Similarly, no study has assessed whether the mode-switching algorithm used affects the efficacy of ablation and pacing. We have therefore conducted a prospective randomized study comparing the clinical effects of ablation and pacing or continued medical therapy for patients with PAF. We have also examined the influence of pacing mode and mode-switching algorithms on the efficacy of ablation and pacing.

Methods

Study Setting and Population
This study was set in a tertiary referral center for cardiac electrophysiology serving a population of ~5 million.

Inclusion Criteria
Inclusion criteria were as follows. (1) Electrocardiographically documented PAF diagnosed at least 6 months previously. AF was...
defined electrocardiographically as an absence of P waves, the presence of a fibrillating baseline, and an irregular ventricular rhythm. (2) Symptoms occurring at least monthly or intolerable drug side effects. (3) At least 2 different attempts at drug therapy (single drugs or drug combinations) to maintain sinus rhythm or control ventricular rate during AF.

Exclusion Criteria
Exclusion criteria were as follows. (1) Coronary/valve disease requiring intervention. (2) Ventricular tachycardia documented on ECG. (3) Previous major thromboembolic event. (4) Coexisting medical condition limiting longevity to <1 year.

Design of the Study
The study was approved by the local research ethics committee. The scheme of investigation is illustrated in the Figure. Patients gave informed consent and were assessed at baseline by methods described below. Patients were then randomized to receive further efforts at optimizing drug therapy or to undergo AV node ablation and implantation of a DDDR/MS pacemaker. The randomization ratio for ablation and pacing to medical therapy was 2:1 to allow subrandomization of the ablation patients to Medtronic Thera (slow mode-switch) or Vitatron Diamond (“fast” mode-switch) pulse generators. Patients were followed up at three 6-week intervals after their first intervention and reassessed as below. Paced patients had a run-in period of 6 weeks programmed to DDDR/MS. They were randomized in a single-blinded fashion to either DDDR/MS or VVIR pacing for the next 6 weeks and crossed over to the remaining pacing mode for the final period. All randomization was by sealed envelope administered by an independent party.

End Points
Primary end points for the study were quality-of-life scores with medical treatment or ablation and pacing in DDDR/MS or VVIR mode.

Secondary end points were (1) intrapatient changes in quality-of-life scores between each treatment and baseline and intergroup comparisons of these changes, (2) exercise capacity and left ventricular systolic function at baseline and with each treatment, and (3) occurrence of persistent AF and complications of treatment.

Outcome Measurements
Quality of life was measured with 3 complementary self-administered tools that have been well validated in patients with pacemakers and other cardiological conditions. The Psychological General Well Being Questionnaire (PGWB) measures patients’ perception of well-being. It asks 22 questions relating to anxiety, positive well-being, depressed mood, self control, vitality, and general health over the previous 4 weeks. This produces an overall score out of 110, a higher score representing a perception of greater well-being. The McMaster Health Index (MHI) questionnaire measures functional ability by asking questions relating to daily activities such as running, walking, housework, etc, and produces a score out of 20, a higher score representing greater ability. The third tool was a visual analogue-scale cardiac symptom score. This asks 11 questions, relating to chest pain, palpitation, dizziness, and breathlessness, with answers marked on a linear scale. Measurements from these scales produce an overall score (maximum, 110) that can be broken down into component scores for each symptom; in each case, a lower score represents fewer symptoms.

Patients underwent echocardiography to assess left ventricular systolic function (measured as fractional shortening) and exercise testing with the Chronicologic Assessment Exercise Protocol at each visit. Holter monitoring was undertaken at each visit to assess the incidence of development of persistent AF (defined as absence of sinus rhythm on Holter recordings).

Medical Therapy
Patients randomized to continue medical therapy were seen by the same physician (H.J.M.) as often as required to optimize drug therapy. Drugs chosen to treat these patients were determined by those previously failed and by coexisting medical conditions. In all patients, therapy was changed initially to a drug not previously tried. Drugs previously tried were used only if previous dosages had been suboptimal or at the request of the patient. All patients in both the medical therapy and ablation arms of the study received anticoagulation with warfarin to achieve an international normalized ratio of 2 to 3.

Ablation and Pacing
All antiarrhythmic therapy (including amiodarone) was withdrawn 2 to 3 days before ablation and pacing. AV node ablation was performed by a femoral venous approach. With a temporary pacing wire in the right ventricle, a Polaris (Cordis) catheter was advanced to the compact AV node. Temperature-controlled (70°C) radiofrequency energy was applied for 60 seconds. If this did not achieve complete heart block, further signals were sought and ablation was repeated. In 2 patients, ablation required a retrograde arterial approach at a second procedure. Patients had a DDDR/MS pacemaker implanted immediately after ablation with bipolar steroid-eluting leads. The devices chosen were the Diamond (Vitatron) and the Thera DR (Medtronic Inc). These devices were selected because they have different mode-switch algorithms. The Diamond algorithm mode-switches instantly in response to the first atrial beat that exceeds the prevailing atrial rate by >15 bpm. In contrast, the Thera DR algorithm monitors the mean atrial rate. Before mode-switching occurs, the mean atrial rate must exceed a preset limit (for this study, 175 bpm). During this time, tracking of AF protocol and after mode-switching, the ventricular rate gradually falls back to the sensor-driven rate. In total, the time taken from the onset of AF to return to the sensor rate is 10 to 15 seconds.

Pacemaker Programming
For the run-in period, patients were programmed to DDDR/MS to allow optimization of rate response and to allow patients to recover from the procedure. The lower rate limit for all patients was 70 bpm. The upper rate limit was determined by the patient’s age and other medical conditions. Atrial sensitivity was set at 0.5 ms (bipolar), atrial blanking at 150 ms, and AV delay at 150 ms (with rate adaptation). Mode-switching was programmed “On—Detect Rate 175 bpm” for the Thera and “Auto” for the Diamond. After the first postoperative assessment, patients were programmed in a single-blinded fashion to the randomized pacing mode. Patients were programmed to the remaining mode at the next visit. All other parameters were constant for both pacing modes.

Statistics
The sample size was calculated to provide 80% power to detect a 20% difference in quality-of-life scores between treatments at the 5% level of significance. This was derived from previous studies of ablation and pacing. The data were found to be normally distributed by the Anderson-Darling test. The scores for medical therapy and ablation and pacing were compared by use of 2-sample Student’s t tests on an intention-to-treat basis. Comparisons of each pacing mode with baseline were made by ANOVA. Comparison of the 2
pacing modes was made by the Hills and Armitage\textsuperscript{30} method for analysis of a 2×2 crossover trial; this examines for period and carryover effects as well as treatment effect. Comparisons between the fast- and slow-mode-switching devices were made by 2-sample Student’s \textit{t} tests. Proportions were analyzed with Fisher’s exact test for a 2×2 table.

\section*{Results}

\subsection*{Patient Recruitment and Progress in the Study}

Sixty-seven patients were invited to enter the study between April 1995 and September 1997. Sixteen patients undergoing AV node ablation for PAF were not invited to join the study. Of these, 7 had documented ventricular tachycardia; 2 already had pacemakers; in 2 patients, AF was thought to be permanent, but they were in sinus rhythm at the time of the procedure; and 1 patient had coronary artery bypass graft surgery a week before ablation. In the remaining 3, there was poor correlation between AF and symptoms.

Of those who were invited to join the study, 1 patient was unwilling to continue medical therapy and 6 did not wish to undergo ablation and pacing. Therefore, 60 patients gave consent for the study and were randomized (n=21 medical, 20 Thera, and 19 Diamond). Four patients were withdrawn from the study before commencing therapy: 2 medical (1 developed thyrotoxicosis on amiodarone and 1 suffered a thromboembolic event to the leg), 1 Thera (AF was found to be secondary to AV nodal reentry tachycardia and was cured by slow-pathway ablation), and 1 Diamond (patient withdrew consent). The data analyzed are therefore from 56 patients (medical, n=19; Thera, n=19; and Diamond, n=18). Of the medically treated patients, 4 crossed over to ablation and pacing before the end of 18 weeks, because all medical options had been tried; data from these patients were analyzed on an intention-to-treat basis. Of the patients undergoing ablation and pacing, 8 were unable to tolerate programming to VVIR and requested alternative programming. These patients could not provide valid quality-of-life data, because the questionnaires require patients to report for a period of 1 month. They were therefore omitted from the comparison of the pacing modes. All baseline characteristics (including arrhythmia history) were similar between the medical and ablation groups and are shown in Table 1.

AV node ablation was achieved without complications with a right-sided approach in all but 2 patients. A mean of 3.4±3.2 energy applications were required to achieve AV block in these patients. The remaining 2 patients had a second procedure when AV node ablation was achieved from the left side with a further 3 and 9 burns, respectively. Pacing was uncomplicated in all but 2 patients; 1 sustained a pneumothorax requiring an intercostal drain, and the other had an atrial lead displacement requiring repositioning. The drugs used during the study for the medically treated patients are shown in Table 2.

The data for quality of life, exercise tolerance, and left ventricular systolic function for medical therapy, ablation, and DDR/MS or PVIR pacing are shown in Table 3. The follow-up data shown for the medically treated patients are the mean values for the 3 follow-up visits. There were no significant differences between the medically treated and ablation patients at enrollment.

\begin{table}
\centering
\caption{Baseline Characteristics of Patients}
\begin{tabular}{lcc}
\hline
 & Medical (n=19) & Ablation (n=37) \\
\hline
Age, y & 60.3±9.8 & 65.2±7.5 \\
Male sex, % & 63.2 & 48.6 \\
Duration of history, y & 9.8±8.0 & 7.1±6.3 \\
No. of episodes per month & 3.6±3.8 & 3.4±4.1 \\
Usual duration of episodes, h & 6.4±6.1 & 6.2±6.5 \\
Presence of cardiac disease, % & \\
Ischemic heart disease & 15.8 & 21.6 \\
Valvular heart disease & 5.3 & 5.4 \\
Dilated cardiomyopathy & 5.3 & 2.7 \\
Other atrial arrhythmias & 5.3 & 2.7 \\
Drugs tried before randomization, % & \\
Amiodarone & 63.1 & 51.4 \\
Sotalol & 68.4 & 75.7 \\
Propafenone & 36.8 & 35.1 \\
Flecainide & 52.6 & 54.0 \\
Quinidine & 36.8 & 13.5 \\
Disopyramide & 21.1 & 21.6 \\
Other \beta-blocker & 42.1 & 29.7 \\
Digoxin & 42.1 & 67.6 \\
Verapamil & 36.8 & 35.1 \\
No. of drugs/combinations failed & 3.9±1.6 & 3.5±1.4 \\
\hline
\end{tabular}
\end{table}

\begin{table}
\centering
\caption{Drugs Used During the Study to Treat Patients Randomized to Medical Therapy (n=19)}
\begin{tabular}{ll}
\hline
Drug & No. of Patients \\
\hline
Amiodarone & 3 \\
Sotalol & 8 \\
Flecainide & 9 \\
Propafenone & 9 \\
Quinidine & 4 \\
Disopyramide & 11 \\
Digoxin & 4 \\
Others & 6 \\
Mean number tried per patient during study & 2.8 \\
\hline
\end{tabular}
\end{table}

\subsection*{Primary End Points}

Although the scores for the drug and ablation groups were similar at enrollment, the scores after ablation and DDR/MS pacing were significantly better for overall symptoms (−41%, \(P<0.01\)), palpitations (−58%, \(P<0.0001\)), and breathlessness (−37%, \(P<0.05\)).

Eight patients were unable to tolerate VVIR pacing and requested pacemaker reprogramming within 24 hours. In those who tolerated VVIR pacing, the scores for overall symptoms (−29%, \(P<0.05\)) and palpitation (−58%, \(P<0.0001\)) were better than medical therapy.
In the crossover analysis of the 2 pacing modes, there was no discernible carryover or period effect in any of the parameters measured. The scores for those patients who completed the crossover phase of the study are shown in Table 4. There were no differences in the scores of the patients receiving the Thera and Diamond pulse generators (see Table 5).

Secondary End Points
Ablation and DDDR/MS pacing resulted in an improvement in all quality-of-life parameters, except chest pain, compared with baseline (P<0.01 for overall symptoms, palpitations, dizziness, and PGWB and P<0.05 for breathlessness and MHI), but no significant changes were seen with drug therapy (see Table 3). Ablation and VVIR pacing produced an improvement in overall symptoms (P<0.01) that was solely due to an improvement in palpitations (P<0.0001).

In addition, the changes in score from baseline seen with ablation and DDDR/MS pacing were better than with medical therapy for overall symptoms (P<0.005), palpitations (P<0.001), dyspnea (P<0.005), and PGWB (P<0.05) (see Table 6). Ablation and VVIR pacing produced a greater change from baseline than medical therapy only for palpitation (P<0.005).

Exercise tolerance and left ventricular systolic function were not significantly affected by ablation and pacing or medical therapy.

Development of Persistent AF
Absence of sinus rhythm on Holter monitoring at 6 weeks was more common in those treated with ablation and pacing (12 of 37 versus 0 of 19, P<0.001). In these patients, sinus rhythm was not seen again, and pacemaker diagnostic data suggested that AF was permanent. No more ablation-treated patients developed persistent AF after the first 6 weeks. However, in the last 6-week period of the study, 2 medically treated patients had no sinus rhythm on Holter monitoring; thus, there was no significant difference in the prevalence of persistent AF at this stage.

Discussion
Our study shows that for patients with drug-refractory PAF, AV node ablation and DDDR/MS pacing produces greater improvements in quality of life than continuation of medical therapy. The benefits are most obvious in terms of cardiac symptoms, specifically palpitation and breathlessness, but ablation and pacing also improves psychological well-being more than drug therapy does. This supports the findings of Brignole et al,10 who compared ablation and DDDR/MS pacing with drug therapy for patients with PAF. They demonstrated superiority for ablation and pacing in terms of palpitation, breathlessness, fatigue, exercise intolerance, and socioeconomic and psychological well-being.

Our study showed no significant improvement (but importantly, no deterioration) in exercise tolerance or left ventricular systolic function after ablation and pacing. This is consistent with the study by Brignole et al10 but in contrast with other previous studies of ablation and pacing for AF.21,22 However, we suggest that a lack of improvement in these parameters should not be unexpected in our study population, because the majority had normal left ventricular function at entry.

Before this study, there has been no comparison of pacing modes for patients undergoing ablation and pacing for PAF.

### Table 3. Scores for Quality of Life, Cardiac Symptoms, Exercise Capacity, and LV Function Before and After Intervention

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Enrollment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drugs</td>
<td>Ablation</td>
</tr>
<tr>
<td></td>
<td>(n=19)</td>
<td>(n=37)</td>
</tr>
<tr>
<td>Overall symptoms</td>
<td>42.9±24.5</td>
<td>46.1±23.0</td>
</tr>
<tr>
<td>Palpitations</td>
<td>16.5±7.8</td>
<td>17.5±6.8</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10.0±8.2</td>
<td>11.2±6.7</td>
</tr>
<tr>
<td>Chest pain</td>
<td>8.2±9.9</td>
<td>10.1±9.0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7.1±5.9</td>
<td>7.4±6.4</td>
</tr>
<tr>
<td>PGWB</td>
<td>69.5±14.3</td>
<td>68.8±18.1</td>
</tr>
<tr>
<td>MHI</td>
<td>15.5±3.7</td>
<td>14.8±3.3</td>
</tr>
<tr>
<td>Exercise tolerance, s</td>
<td>678±342</td>
<td>581±264</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>30.7±8.6</td>
<td>30.3±7.5</td>
</tr>
</tbody>
</table>

Values are mean scores±SD. Significant differences: *P<0.05 vs enrollment; †P<0.05 vs drugs; ‡P<0.05 vs VVIR.

### Table 4. Scores for Patients (n=29) Who Completed the Crossover Phase Comparing DDDR/MS and VVIR Pacing

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DDDR/MS</th>
<th>VVIR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall symptoms</td>
<td>22.5±20.8</td>
<td>28.5±20.2</td>
<td>0.044*</td>
</tr>
<tr>
<td>Palpitations</td>
<td>6.2±6.3</td>
<td>6.3±6.5</td>
<td>0.95</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6.3±5.5</td>
<td>9.0±6.8</td>
<td>0.0023*</td>
</tr>
<tr>
<td>Chest pain</td>
<td>7.1±8.4</td>
<td>7.3±7.5</td>
<td>0.1621</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3.7±4.9</td>
<td>5.6±5.1</td>
<td>0.1064</td>
</tr>
<tr>
<td>PGWB</td>
<td>77.2±22.3</td>
<td>72.4±21.0</td>
<td>0.1284</td>
</tr>
<tr>
<td>MHI</td>
<td>16.3±3.1</td>
<td>15.6±3.2</td>
<td>0.0228*</td>
</tr>
<tr>
<td>Exercise tolerance, s</td>
<td>653±247</td>
<td>594±269</td>
<td>0.0627</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>28.9±9.5</td>
<td>30.2±12.0</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*Significant differences.
Studies of pacing for spontaneous heart block have shown greater symptomatic benefits with DDD pacing than with VVIR pacing. However, these studies assessed treatment for bradycardia, did not use mode-switching devices, and excluded patients with atrial arrhythmias. Their results therefore cannot be applied to a population specifically treated for tachyarrhythmias by ablation and pacing.

In our study, the improvements in quality of life seen with ablation and DDDR/MS pacing were greater than those with VVIR pacing. DDDR/MS pacing was superior in terms of overall cardiac symptoms, breathlessness, and functional ability, even though our comparison of pacing modes was biased in favor of VVIR pacing by the omission of the 8 patients unable to tolerate VVIR pacing. Indeed, we were able to demonstrate an improvement in symptoms (specifically palpitation) for ablation and VVIR pacing only when compared with enrollment. This is in contrast with the study by Kay et al; we suspect that this reflects the nature of the populations studied. That study population had failed all medical therapy, and ablation and pacing was considered a treatment of last resort. Our patients had only to have failed 2 drug therapies and may therefore have been considered for ablation and pacing much earlier.

We were unable to demonstrate any difference between the 2 different mode-switch algorithms, each producing similar improvements in quality of life; this implies either that the benefits are independent of the speed of mode-switch algorithm or that any differences between algorithms are too small to be detected by a study of this design. Previous comparisons of mode-switching algorithms have failed to demonstrate significant differences in quality of life, even when algorithms were compared in the same patients. We suggest, therefore, that differences in symptomatic improvements produced by pacemakers with different mode-switch algorithms are insignificant compared with the overall effect of ablation and DDDR/MS pacing for PAF.

Ablation and pacing resulted in a significantly greater incidence of early development of persistent AF. This finding is consistent with the findings of Brignole et al, who found that 24% versus 0% were in permanent AF after 6 months. It is possible that the use of cardioversion may have influenced the progression to permanent AF. Ablated patients were not cardioverted in our study because they were not symptomatic. Cardioversion was offered to the 2 medically treated patients who developed persistent AF, but this was not carried out during the study because the persistent AF was only discovered at the last follow-up visit. We were unable to determine whether pacing mode influenced the development of persistent AF in the ablated patients. However, when it did occur, it was during the run-in period when patients were pro-

### TABLE 5. Scores for Patients Before and After Ablation and DDDR/MS Pacing With Fast (Diamond) and Slow (Thera) Mode-Switching Devices

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diamond Before</th>
<th>Diamond After</th>
<th>Thera Before</th>
<th>Thera After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall symptoms</td>
<td>44.3±21.6</td>
<td>26.3±23.8</td>
<td>47.8±24.7</td>
<td>21.5±18.7</td>
</tr>
<tr>
<td>Palpitations</td>
<td>16.3±7.0</td>
<td>8.0±7.7</td>
<td>18.6±6.5</td>
<td>5.4±5.2</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>11.1±7.5</td>
<td>6.3±5.5</td>
<td>11.3±6.1</td>
<td>6.1±5.7</td>
</tr>
<tr>
<td>Chest pain</td>
<td>9.2±7.6</td>
<td>7.8±8.9</td>
<td>11.0±10.3</td>
<td>6.9±7.5</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7.7±6.5</td>
<td>5.3±5.8</td>
<td>7.0±6.4</td>
<td>3.4±4.8</td>
</tr>
<tr>
<td>PGWB</td>
<td>68.7±18.1</td>
<td>74.1±26.4</td>
<td>68.9±18.7</td>
<td>80.3±16.4</td>
</tr>
<tr>
<td>MHI</td>
<td>15±3.6</td>
<td>16.3±3.8</td>
<td>14.6±3.1</td>
<td>15.8±2.6</td>
</tr>
<tr>
<td>Exercise tolerance, s</td>
<td>615±300</td>
<td>697±245</td>
<td>553±240</td>
<td>604±235</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>28.2±7.4</td>
<td>28.9±8.1</td>
<td>33.1±7.1</td>
<td>30.0±11.5</td>
</tr>
</tbody>
</table>

Values are mean scores ± SD. There were no statistically significant differences between groups.

### TABLE 6. Changes in Scores From Baseline With Drugs, Ablation, and DDDR/MS or VVIR Pacing

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Drugs (n=19)</th>
<th>DDDR/MS (n=37)</th>
<th>VVIR (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall symptoms</td>
<td>-2.5±19.3 (−4)</td>
<td>-22.3±25.6 (−48)</td>
<td>-15.9±28.1 (−34)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>-1.0±9.7 (−5)</td>
<td>-10.8±9.5 (−62)</td>
<td>-10.4±9.9 (−59)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>-0.3±3.6 (−3)</td>
<td>-4.9±6.4 (−44)</td>
<td>-1.9±8.2 (−17)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>+0.3±8.4 (−3)</td>
<td>-2.8±8.6 (−28)</td>
<td>-2.1±9.7 (−21)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>-0.4±4.9 (−5)</td>
<td>-3.0±6.9 (−41)</td>
<td>-1.9±5.8 (−26)</td>
</tr>
<tr>
<td>PGWB</td>
<td>+0.4±10.4 (+0.5)</td>
<td>+8.6±17.7 (+12)</td>
<td>+2.9±21.2 (+4)</td>
</tr>
<tr>
<td>MHI</td>
<td>+0.2±2.0 (+1)</td>
<td>+1.2±2.2 (+8)</td>
<td>+0.6±2.7 (+4)</td>
</tr>
<tr>
<td>Exercise tolerance, s</td>
<td>-5.0±152 (-1)</td>
<td>+59±173 (+10)</td>
<td>+7±242 (+1)</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>-0.9±5.0</td>
<td>-1.6±9.6</td>
<td>+0.4±10.2</td>
</tr>
</tbody>
</table>

Values are mean changes in scores ± SD (mean change as % of mean baseline in parentheses).

*P* = <0.05 vs drugs.
grammed to DDDR/MS. It would seem, therefore, that DDDR/MS pacing with a lower rate limit of 70 bpm is not protective against the development of persistent AF. The factor most likely to be responsible for the excess of persistent AF in the ablation group is the cessation of antiarrhythmic therapy (although it may be that this is partly responsible for the improvement in quality of life).

Limitations of the Study
One unavoidable limitation of this and any study comparing an invasive procedure with medical therapy might be that the procedure carries a placebo effect. However, in a previous study from Brignole et al in which patients with chronic AF were randomized to either ablation and pacing or pacing alone, the latter failed to produce the improvement in quality of life seen with ablation and pacing. This suggests that the placebo effect of pacemaker implantation in patients with AF is small.

Another potential limitation of any study of this nature is the somewhat arbitrary nature of antiarrhythmic drug selection for medically treated patients. Our preference for sotalol and class Ia and Ic drugs reflects the fact that the majority of patients had previously tried and failed amiodarone, and we wished to avoid its potentially serious side effects in our younger patients. However, other investigators may have chosen to use different agents.

Finally, this study has assessed the effects of ablation and pacing only in the short term. Until long-term prospective results are available, it should probably still be used as a treatment of last resort.

Conclusions
AV node ablation and pacing produces greater improvements in quality of life than continuing medical therapy in patients with drug-refractory PAF, at least in the short term. DDDR/MS is the optimum pacing mode, but the benefits of this mode are not dependent on the mode-switching algorithm used.

However, because ~33% of patients with PAF undergoing ablation and pacing rapidly develop persistent AF, it should still be regarded as a last-resort therapy, particularly if maintenance of sinus rhythm is considered to be a major therapeutic aim.

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Prospective Randomized Study of Ablation and Pacing Versus Medical Therapy for Paroxysmal Atrial Fibrillation: Effects of Pacing Mode and Mode-Switch Algorithm
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