Success of Ablation for Atrial Fibrillation in Isolated Left Ventricular Diastolic Dysfunction
A Comparison to Systolic Dysfunction and Normal Ventricular Function

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Background—The efficacy of radiofrequency ablation for atrial fibrillation (AF) in patients with left ventricular (LV) systolic dysfunction and isolated diastolic dysfunction is uncertain.

Methods and Results—A prospective cohort of patients with normal and abnormal LV function underwent ablation for antiarrhythmic drug (AAD)-refractory AF. Three groups were compared: 111 patients with systolic dysfunction, defined as LV ejection fraction (LVEF) $\leq 40\%$; 157 patients with isolated diastolic dysfunction but preserved LVEF $>50\%$; and 100 patients with normal LV function. The primary end point was AAD-free AF elimination at 1 year after ablation. This end point was achieved in 62\% of patients with systolic dysfunction, 75\% of those with diastolic dysfunction, and 84\% of controls ($P=0.007$). AF control on or off AADs was achieved in 76\% of patients with systolic dysfunction, 85\% of those with diastolic dysfunction, and 89\% of controls ($P=0.08$).

In the systolic dysfunction group, 49\% experienced an increase in LVEF by $\geq 5\%$ after ablation, of which 64\% achieved normal LVEF. In the diastolic dysfunction group, 30\% of patients demonstrated at least 1 grade improvement in diastolic dysfunction. Multivariable analysis demonstrated an increased relative risk of arrhythmia recurrence of 1.8 (95\% CI, 1.1 to 3.1; $P=0.02$) in systolic dysfunction and 1.7 (1.0 to 2.7; $P=0.04$) in isolated diastolic dysfunction compared with normal function.

Conclusions—Although an ablative approach for AF in patients with systolic or diastolic dysfunction is associated with an increased long-term recurrence risk, there is potential for substantial quality-of-life improvement and LV functional benefit. (Circ Arrhythm Electrophysiol. 2011;4:724-732.)

Key Words: atrial fibrillation • cardiomyopathies • catheter ablation • heart failure diastolic • heart failure systolic

Atrial fibrillation (AF) and heart failure (HF) frequently coincide, often with deleterious hemodynamic and symptomatic consequences. In some patients, AF can result in symptomatic HF because of irregular and rapid ventricular response rates that lead to left ventricular (LV) systolic dysfunction.1-3 Conversely, patients with systolic HF have a 6-fold increased, long-term (>5 year) risk of developing AF.4 Even in patients with preserved LV systolic function, AF has been associated with LV diastolic dysfunction. One third of patients with HF related to isolated diastolic dysfunction present with AF. In these patients with stiffened LV, the onset of AF results in a loss of the left atrial (LA) contribution to the LV that can be further compounded by the shortened diastolic filling times owing to rapid ventricular rates. In $\approx 10\%$ of patients with abnormal LV diastolic function determined by echocardiography, new-onset AF develops during 4 years of follow-up.5 Although AF frequently is associated with congestive heart failure, few data are available on the comparative efficacy of catheter ablation of AF in patients with various forms of LV dysfunction. For patients with systolic dysfunction, the data on AF ablation are limited but favorable.6,7 In patients with isolated LV diastolic dysfunction, no data are available on the efficacy of ablation. Therefore, the objective of the present study was to determine the efficacy of catheter ablation for AF and the LV function and quality-of-life (QOL) benefits from the ablation outcome in patients with isolated LV diastolic dysfunction compared with systolic dysfunction.
Methods

Patient Population
From November 2000 to September 2007, 1384 symptomatic patients undergoing AF ablation at Mayo Clinic (Rochester, MN) were enrolled in a longitudinal study to prospectively follow their ablative outcomes, as approved by the Mayo Clinic Institutional Review Board. Each patient had highly symptomatic paroxysmal, persistent, or permanent AF.9 Based on prospectively acquired clinical data, patients with isolated LV diastolic dysfunction (as defined by echocardiographic criteria) were retrospectively identified by searching the database for LV ejection fraction (LVEF) ≥50% and abnormal diastolic function that could be quantified as grades 1 to 4. Of these patients, 157 had isolated LV diastolic dysfunction impairment with preserved LV systolic function (LV diastolic dysfunction group), and 111 had LV systolic dysfunction with LVEF of ≤40% (LV systolic dysfunction group). One hundred ablation recipients who had normal LV systolic (LVEF >50%) and diastolic function were randomly selected and served as the normal LV function group. No specific matching was performed. Patients were excluded from the study for a variety of reasons, including (1) an LVEF in a range that did not fit into any group (40% to 50%) and (2) the absence of diastolic dysfunction information at baseline in the presence of AF at the time of echocardiogram, indeterminate diastolic dysfunctional grades, very severe systolic dysfunction, or the lack of a baseline transthoracic echocardiogram.

Clinical Evaluation
Before ablative intervention, all patients underwent clinical evaluation, including (1) a detailed history of cardiovascular comorbidities, including HF, and a physical examination; (2) 12-lead electrocardiography; (3) 24-hour Holter monitoring; (4) chest radiography; (5) multislice CT scan; and (6) transesophageal and transthoracic 2D and Doppler echocardiography for complete assessment of LV function.

Baseline Assessment of LV Function
LV systolic function and volumes were quantified from LV end-diastolic and systolic dimensions. Diastolic function was assessed principally using transmitral flow profile from the apical 4-chamber view, including peak E velocity, peak A velocity, E/A ratio, and mitral valve deceleration time as well as tissue Doppler velocity of the mitral annulus (E' and A') to assess underlying myopathy. LV filling pressures were estimated by septal and lateral E/E'. Using laboratory standards, the interpreting echocardiographer graded diastolic function as normal (grade 0) or abnormal (grades 1 to 4, with a higher number indicating worse severity). A trained observer, blinded to ablative outcome, retrospectively reanalyzed all diastolic grading for consistency and accuracy. General grading criteria are detailed as follows, consistent with the American Society of Echocardiography guidelines10,11:

- Normal diastolic function: E/A, 0.75 to 1.5; septal E/E', <15; and normal LA volume, <32 mL/m²
- Grade 1 or mild diastolic dysfunction: E/A, <0.75; septal E/E', <15; and variable LA size
- Grade 2 or moderate diastolic dysfunction: Two of 3 criteria: (1) a pseudonormalized relaxation pattern with present E/A of 0.75 to 1.5; (2) septal E/E' of >12 to 15; and (3) LA volume index ≥32 mL/m²
- Grade 3 to 4 or severe diastolic dysfunction: E/A, >1.5; septal E/E', >15; and DT' <160 ms

Reversibility assessment (grade 3 versus 4) was based on E/A decrease with preload reduction during Valsalva maneuver and 2D echocardiography. Of note, diastolic function by these criteria was not analyzable in AF and, thus, could only be quantified in patients who were in sinus rhythm at the time of their transthoracic echocardiograms.

Catheterization and Radiofrequency Ablation

Catheter Placement
All patients underwent ablation under general anesthesia. Patients underwent standard catheterization with placement of 5-F or 6-F catheters into the right ventricle, right atrium, and His bundle region, and a 20-pole catheter was advanced into the coronary sinus. LA access was obtained using a double transseptal puncture technique with 2 8-F sheaths advanced into the LA. A 10-pole circular mapping catheter (Lasso; Biosense Webster; Diamond Bar, CA) was advanced through 1 transseptal sheath to engage each pulmonary vein (PV). An 8-F ablation catheter was advanced through the second sheath for radiofrequency (RF) energy delivery. Intravenous heparin was titrated to maintain the activated clotting time between 300 and 400 s after sheath placement at the end of the procedure. All surface and intracardiac electrogams were recorded on a 48-multichannel electrophysiology workstation (Prucka CardioLab EP System; GE Healthcare; Waukesha, WI). A 10-F intracardiac ultrasound catheter was positioned in the right atrium to guide transseptal catheterization, establish the venaovenal junction, guide catheter positioning, and monitor for pericardial effusion and other complications.

AF Ablation Approach
Lasso-Guided Circumferential PV Isolation
In patients undergoing PV isolation, circumferential ablation outside the PV ostium was guided exclusively by a circular mapping catheter positioned at the PV orifice under intracardiac echocardiographic guidance. RF energy was delivered in the atrial tissue near the venaovenal junction through a 5-mm-tip catheter. Up to 30 W of RF (500 kHz) power (temperature capped at 48°C to 50°C) was delivered for up to 20 to 30 s until the local PV potentials were eliminated. The PV ostia were circumferentially isolated to achieve entrance block as the acute end point.

Wide-Area Circumferential Ablation
The geometry of the native PV anatomy was rendered using a standard electroanatomic system (Carto XP EP Navigation System; Biosense Webster). An electroanatomic map of the LA also was created. The anatomic location of the esophagus as guided by esophageal temperature probes on biplane fluoroscopy was annotated on the posterior surface of the LA map. Substrate ablation was accomplished using a wide-area circumferential ablation ring placed 5 to 15 mm outside the venaovenal junction of the PVs, with up to 30 to 55 W (temperature capped at 50°C to 55°C) delivered through a nonirrigation 8-mm-tip ablation catheter or with up to 25 to 40 W (with a maximum temperature of 42°C) during saline flow at 15 to 30 mL/min delivered through a 3.5-mm-tip open-irrigation catheter. If complete entrance block was not accomplished at the end of wide-area circumferential ablation, additional “touch-up” ablation of residual activity at the PV orifice was guided by a circular mapping catheter. The entrance block with complete elimination of all PV potentials was considered an end point. In patients with persistent or permanent AF, linear lesions were then crafted along the LA roof and from the left inferior PV ring to the mitral valve annulus.

Non-PV foci were sought by burst pacing with intravenous infusion of isoproterenol 2 to 10 μg/min. Further ablation of arrhythmogenic foci, principally within the superior vena cava, vein of Marshall, and coronary sinus, was undertaken only if localized early recurrent AF was documented. After accomplishing AF ablation, all patients underwent cavotricuspid isthmus ablation for prevention of isthmus-dependent flutter.

Patient Follow-Up
All patients were hospitalized for at least 24 hours, and 12-lead electrocardiography, chest radiography, and transthoracic echocardiography were repeated. All patients were discharged on warfarin with low-molecular-weight heparin bridging until a target international normalized ratio of 2 to 3 was reached. Patients were instructed to return for follow-up 3 months after ablation. At 3 months, patients underwent a detailed physical examination, 12-lead electrocardiography, 24-hour Holter monitoring, CT of the chest, and
event monitoring as needed. In addition, a 1-year follow-up visit was standard. Annual assessment of rhythm status and symptoms as well as of antiarrhythmic drug (AAD) use status was performed with clinical follow-up and an annual questionnaire that included QOL assessment. Any atrial arrhythmia after a 2-month blanking period was considered a recurrence. Between visits, designated research and clinical support staff facilitated telephone or written correspondence as clinically warranted among patients, referring clinicians, and the Mayo Clinic electrophysiologist.

### QOL Assessment

QOL was evaluated by using the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36). The SF-36 assesses 8 aspects of health status: general and mental health, physical and social functioning, physical and emotional role, pain, and vitality. By using this score system, we intended to relate objective physiological measures, such as the frequency, duration, and intensity of AF episodes, and the degree of symptomatic HF to subjective QOL. These evaluations were performed before the procedure and at 3-month and 1-year follow-up.

### Statistical Analysis

Continuous variables are presented as medians with 25th and 75th percentiles. Comparison between groups was performed using the nonparametric Kruskal-Wallis tests. Categorical variables were assessed using Fisher exact test. When significant, all possible comparisons among groups were completed using individual Wilcoxon rank sum test and Fisher exact test, adjusting the individual P values for ≥3 comparisons using the Bonferroni method. Comparisons between the continuous parameters before and after the ablation were completed using the Wilcoxon signed rank test. Comparisons of QOL at follow-up with baseline were performed using paired t tests. AF-free survival after last ablation was estimated using the Kaplan-Meier method. A log-rank test was used to compare estimates between groups. Univariate and multivariable predictors were identified using Cox proportional hazards regression methods. Multivariable models were performed using a stepwise selection of significant univariate values from baseline characteristics. Systolic dysfunction and diastolic dysfunction were forced into the model. Relative risks are expressed as hazard ratios (HRs) with 95% CIs. Analyses were performed using SAS release 8.2 (SAS Institute Inc; Cary, NC) statistical software. A P<0.05 was considered significant.

### Results

#### Patient Characteristics

Overall, 368 patients were followed for a median (25th, 75th percentile) follow-up time of 1.1 years (0.4, 2.1 years). The baseline characteristics of the LV systolic dysfunction (n=111), isolated LV diastolic dysfunction (n=157), and normal LV function (n=100) groups were compared as shown in Table 1. Notable differences in clinical characteristics in the LV dysfunction groups compared with the normal LV function group included (1) older age in patients with diastolic dysfunction, (2) a higher proportion of patients with persistent or longstanding persistent AF in the systolic and diastolic dysfunction groups, and (3) a greater proportion of patients with hypertension in the diastolic dysfunction group.

In the systolic dysfunction group, the median (25th, 75th percentile) LVEF was 35 (30, 40) compared with 63 (60, 65) in controls (P<0.001). In the diastolic dysfunction group, the median diastolic functional grade was 2 (2, 2). Increased LA volume index was significant in both systolic and diastolic dysfunction groups compared with those with normal LV function (P<0.001).

From a procedural standpoint, substrate-based ablation through a wide-area circumferential ablation approach (often with linear ablation) was used more commonly in patients with LV systolic dysfunction (82%) or diastolic dysfunction (78%) than in those with normal LV function (61%, P=0.001). Repeat ablation rates were similar across the groups (20% systolic dysfunction, 12% diastolic dysfunction, 13% normal LV function, P=0.18).

#### AF Elimination and Control Using AADs

One-year ablative efficacy outcomes for patients after their final AF ablation are shown in Figure 1. Follow-up rates were similar in the 3 groups (75% normal LV, 75% diastolic dysfunction, 77% systolic dysfunction). AF elimination rates differed significantly among the groups (P=0.007), but differences in AF control rates only tended to significance (P=0.08). Compared with the 1-year AAD-free AF elimination rate of 84% in patients with normal LV function, the AF elimination rate was significantly lower in patients with systolic dysfunction (62%, P=0.002) and nonsignificantly lower in those with diastolic dysfunction (75%, P=0.15).

Figure 1 also demonstrates AF control outcomes on or off AADs at 1 year after final ablation. At 1 year, compared with the AF control rate of 89% in patients with normal LV function, the AF control rate was significantly lower in those with systolic dysfunction (76%, P=0.03) but not significantly different in patients with diastolic dysfunction (85%, P=0.35).

#### Long-Term Ablation Efficacy in Systolic and Diastolic Dysfunction

Estimates of long-term freedom from recurrence after last AF ablation are demonstrated in the Kaplan-Meier curve in Figure 2. Overall, there was a significant difference in the freedom from recurrence on or off AADs among the 3 groups (P=0.03). Significant differences between the systolic dysfunction and normal LV function groups (P=0.01) and the diastolic dysfunction and normal LV function groups (P=0.01) were identified. At 5 years, overall freedom from any recurrence on or off AADs was 65% in the control patients compared with 33% in the systolic dysfunction group and 40% in the diastolic dysfunction group.

In addition, the difference in overall freedom from recurrence off AADs among the 3 groups was nearly significant (P=0.09). Although no significant differences between the systolic dysfunction and normal LV groups (P=0.13) were observed, there was a significant difference between the control and diastolic dysfunction groups (P=0.03). The corresponding 5-year freedom from recurrence off any AAD was 46% in control patients compared with 26% of patients in the systolic dysfunction group and 29% in the diastolic dysfunction group.

#### Contribution of LV Systolic and Diastolic Dysfunction to Recurrence

Univariate analysis was performed to assess for contributors to recurrence among the clinical and echocardiographic characteristics listed in Table 2. The presence of LV systolic
dysfunction (LVEF ≤40%) or isolated LV diastolic dysfunction (as opposed to normal LV function) was a significant univariate predictor for recurrence after last ablation. Additional univariate contributors to recurrence included older age, coronary artery disease, and moderate or severe LA enlargement. Protective factors included male sex and paroxysmal AF.

In a multivariable model for recurrence using a stepwise selection process and incorporating systolic and diastolic dysfunction into the model, systolic dysfunction (HR, 1.8; 95% CI, 1.1 to 3.1; \( P = 0.02 \)) and diastolic dysfunction (HR, 1.7; 95% CI, 1.0 to 2.7; \( P = 0.04 \)) remained significant predictors of increased recurrence risk, whereas male sex (HR, 0.5; 95% CI, 0.3 to 0.8; \( P = 0.004 \)) and paroxysmal AF (HR, 0.6; 95% CI, 0.4 to 0.9; \( P = 0.03 \)) were associated with less recurrence risk (Table 2).

LV Functional Improvements After Ablation
The systolic dysfunction group had an increase in LVEF from a median of 35% to 56% (\( P < 0.001 \)). An increase in LVEF of ≥5% after ablation occurred in 49% of the systolic dysfunction group, and 64% of this group achieved near normalization of LVEF to ≥50% (\( P < 0.001 \) compared to other groups for both comparisons). The 1-year AF elimination rate off AADs was 71% in patients with LVEF near normalization compared with 26% in those without (\( P < 0.001 \)).

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Function (EF &gt;50%)</th>
<th>Systolic Dysfunction (EF ≤40%)</th>
<th>Diastolic Dysfunction (EF ≥50%)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>100</td>
<td>111</td>
<td>157</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>75 (75)</td>
<td>105 (95)*</td>
<td>107 (68)†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>52.8 (43.9, 59.7)</td>
<td>54.7 (49.3, 61.2)*</td>
<td>62.2 (54.4, 70.5)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Paroxysmal AF type</td>
<td>61 (61)</td>
<td>31 (28)*</td>
<td>78 (50)†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of AF, y</td>
<td>4.5 (1.9, 7.9)</td>
<td>5.4 (2.4, 9.5)</td>
<td>4.2 (1.7, 8.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>Preablation stroke/TIA</td>
<td>4 (4)</td>
<td>7 (6)</td>
<td>8 (5)</td>
<td>0.75</td>
</tr>
<tr>
<td>HTN</td>
<td>29 (29)</td>
<td>42 (38)</td>
<td>75 (48)‡</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (5)</td>
<td>7 (6)</td>
<td>15 (10)</td>
<td>0.35</td>
</tr>
<tr>
<td>CAD</td>
<td>15 (15)</td>
<td>14 (13)</td>
<td>27 (17)</td>
<td>0.39</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>14 (14)</td>
<td>21 (19)</td>
<td>32 (20)</td>
<td>0.42</td>
</tr>
<tr>
<td>Failed antiarrhythmic drugs</td>
<td>94 (94)</td>
<td>106 (95)</td>
<td>146 (93)</td>
<td>0.70</td>
</tr>
<tr>
<td>AAD</td>
<td>61 (61)</td>
<td>74 (67)</td>
<td>85 (54)</td>
<td>0.11</td>
</tr>
<tr>
<td>( \beta )-blocker</td>
<td>70 (70)</td>
<td>89 (80)</td>
<td>102 (65)†</td>
<td>0.02</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>20 (20)</td>
<td>25 (23)</td>
<td>31 (20)</td>
<td>0.85</td>
</tr>
<tr>
<td>Echocardiographic characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, %</td>
<td>63 (60, 65)</td>
<td>35 (30, 40)*</td>
<td>62 (60, 65)†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume index, cm(^3)/m(^2)</td>
<td>25 (22, 28)</td>
<td>38 (31, 45)*</td>
<td>40 (35, 50)‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A</td>
<td>1.4 (1.2, 1.8)</td>
<td>1.5 (1.0, 2.5)*</td>
<td>1.2 (0.9, 1.4)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/e’</td>
<td>8.6 (6.6, 9.1)</td>
<td>9.5 (6.7, 12.9)*</td>
<td>12.0 (8.6, 15.7)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic grade (0–4)</td>
<td>0 (0, 0)</td>
<td>2 (1, 2)</td>
<td>2 (2, 2)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WACA</td>
<td>61 (61)</td>
<td>91 (82)*</td>
<td>122 (78)‡</td>
<td>0.001</td>
</tr>
<tr>
<td>PVI</td>
<td>39 (39)</td>
<td>20 (18)*</td>
<td>35 (22)‡</td>
<td>0.001</td>
</tr>
<tr>
<td>Linear ablation (LA roof)</td>
<td>14 (14)</td>
<td>65 (59)*</td>
<td>48 (31)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear ablation (LA isthmus)</td>
<td>13 (13)</td>
<td>75 (68)*</td>
<td>56 (36)†‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-PV foci ablation</td>
<td>20 (22)</td>
<td>23 (25)</td>
<td>35 (26)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Data are presented as median (25th, 75th percentile) or n (%). Pairwise differences were adjusted for 3 comparisons using the Bonferroni correction. AAD indicates antiarrhythmic drug; AF, atrial fibrillation; CAD, coronary artery disease; HTN, hypertension; LA, left atrial; LVEF, left ventricular ejection fraction; PV, pulmonary vein; PVI, pulmonary vein isolation; TIA, transient ischemic attack; WACA, wide-area circumferential ablation.

\*\( P < 0.05 \) for normal compared with systolic group.
\( \dagger \)\( P < 0.05 \) for diastolic compared with systolic group.
\( \ddagger \)\( P < 0.05 \) for diastolic compared with normal group.
rate off AADs was 80% in patients with at least a 1-grade improvement in diastolic function, which did not differ significantly from those with unchanged diastolic function (74%, P=0.53).

**QOL Outcome**

QOL scores at baseline and at 1 year are shown for all 3 groups in Figure 3. At baseline, the mean physical component summary and mental component summary scores were uniformly low across the 3 groups. At 1 year, the mean physical component summary score was significantly higher in the normal function group (77.3±16.2) and the systolic dysfunction group (77.1±17.5) than in the diastolic dysfunction group (69.3±21.8, P=0.03), although all 3 groups experienced significant improvements from baseline by paired t test. At 1 year, mental component summary scores only improved significantly from baseline for patients with systolic dysfunction, and no significant differences in mental QOL change were seen across the 3 groups.

**Procedural Safety**

A comparison of ablation characteristics and procedural complications is shown in Table 3. The number of RF deliveries was higher in the systolic dysfunction group compared with the diastolic dysfunction and control groups (P<0.001). However, major procedure-related complications were similar among the 3 groups.

**Discussion**

It is uncertain whether AF management in various forms of LV function or dysfunction should be treated the same. To our knowledge, this is the first comprehensive study of the long-term outcomes of AF ablation in patients with both systolic LV dysfunction and isolated LV diastolic dysfunction. This investigation demonstrated a 1-year AF elimination (including atrial tachycardia) rate of 75% in patients with isolated LV diastolic dysfunction. This rate was higher than the 62% AF elimination rate observed in patients with LV systolic dysfunction but was comparable to the success rate observed in the patients with normal LV function. The 5-year freedom from AF recurrence rate was lower in the LV systolic and diastolic dysfunction groups compared with the normal LV function group, despite similar repeat ablation rates. From a reverse-remodeling standpoint, however, patients with LV systolic dysfunction appeared to have the most to gain, demonstrating robust improvements in LVEF to normal or near normal in 40% of the group compared with the diastolic dysfunction group in which more modest, patient-specific diastolic function improvements were seen in less than one third.

AF Ablation as a Management Strategy in Diastolic Dysfunction

There are no specific recommendations for the management of AF in diastolic dysfunction, although there is increasing recognition that patients with isolated diastolic dysfunction represent a unique clinical substrate with an increased risk for HF hospitalization and mortality.12-14 Frequently elderly or hypertensive, these patients have noncompliant, stiffened LVs that give rise to elevated LA pressure and LA enlargement, conditions predisposing to AF.15,16 The current information about the severity of diastolic dysfunction at the time of presentation for ablation is minimal.17 In the present population, most patients with diastolic abnormalities had moderate (or grade 2) diastolic dysfunction. Although there are data to show that even patients with only mild impairments in diastolic dysfunction present with a first episode of AF, it is not unexpected that symptomatology requiring ablation would be associated with greater diastolic dysfunction.6

The present report demonstrates that AF ablation in patients with diastolic dysfunction is relatively efficacious in the midterm, with 1-year AF-free rates of 80% and with AADs of 75% and 85%. However, with a 5-year atrial arrhythmia-free rate of 40% after their last ablation by Kaplan-Meier analysis, the long-term ablative efficacy in these patients may be compromised by their contributing cardiovascular comorbidities. Although the diastolic dysfunction and normal LV function groups experienced a greater incidence of procedures in the LV systolic dysfunction group, the respective 1-year AF-free rates without and with AADs were similar among the 3 groups.
groups were not matched in this study, it is notable that, as expected, the diastolic dysfunction group was older and had more hypertension than the normal LV function group. Both variables could account for the progression of LV diastolic dysfunction and the redevelopment of vulnerable atrial substrate that would predispose to AF recurrence, suggesting that effective management of hypertension and maintaining therapies directed toward LV diastolic dysfunction remain important adjuncts to the ablative strategy in achieving long-term sinus rhythm. The present findings are consistent with a recent study of 35 patients in whom the presence of any diastolic abnormality and LA scarring by voltage were predictive of greater recurrence rates.17

AF Ablation as a Management Strategy in Systolic Dysfunction

In patients with systolic dysfunction, there are specific pharmacological recommendations of the first-line rhythm management of AF. However, amiodarone—a frequent choice—only has an efficacy of 60% and the risk of toxic adverse effects.18–21 In the present study, a 1-year ablative success rate of 62% without AADs (and 76% with or without them) in patients with LV systolic dysfunction refractory to AADs was comparable to the reported AF elimination rates from 69% to 73% at 1 year in similar populations with low LVEF.7,8,22 One important difference in our ablation strategy compared with that of others was a lower repeat ablation rate of 20% versus 40% to 50% in other studies.7,8,22 In this group with systolic dysfunction and a low repeat ablation rate, one third remained free of any atrial arrhythmia recurrence at 5 years. These patients often have coexisting LV diastolic dysfunction, predisposing to LA enlargement, and thus a tendency to persistent AF. Additional LA linear ablations were performed more often in these patients, which may be beneficial for modifying the atrial substrate. An opposing opinion is that this preference may be proarrhythmic.23,24

Reversibility of Left-Sided Cardiomyopathy With Ablation

We were able to demonstrate the extent of reversibility of the myopathic process in patients with LV dysfunction. It has

Table 2. Long-Term Predictors of Recurrence

<table>
<thead>
<tr>
<th>Clinical Predictors</th>
<th>Univariate HR (95% CI)</th>
<th>( P )</th>
<th>Multivariable HR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.6 (0.4–0.9)</td>
<td>0.02</td>
<td>0.5 (0.3–0.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Age (per 10-y increment)</td>
<td>1.3 (1.1–1.5)</td>
<td>0.01</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Paroxysmal AF (vs persistent AF)</td>
<td>0.6 (0.4–0.9)</td>
<td>0.02</td>
<td>0.6 (0.4–0.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.4 (1.0–2.0)</td>
<td>0.08</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.9 (0.5–1.8)</td>
<td>0.76</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.6 (1.0–2.5)</td>
<td>0.04</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>1.1 (0.7–1.8)</td>
<td>0.63</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.0 (0.9–1.0)</td>
<td>0.23</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td><strong>Heart failure status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic dysfunction (vs normal function)</td>
<td>1.8 (1.1–3.0)</td>
<td>0.02</td>
<td>1.8 (1.1–3.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Diastolic dysfunction (vs normal function)</td>
<td>1.8 (1.1–3.0)</td>
<td>0.01</td>
<td>1.7 (1.0–2.7)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Echocardiographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate-severe LA enlargement</td>
<td>1.3 (1.1–1.6)</td>
<td>0.004</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LVEF (per 10% increment)</td>
<td>0.9 (0.8–1.0)</td>
<td>0.09</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>E/e ( \geq 15 )</td>
<td>1.5 (0.9–2.5)</td>
<td>0.09</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Repeat ablation at Mayo Clinic</td>
<td>0.8 (0.5–1.5)</td>
<td>0.52</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

All significant univariates (\( P \leq 0.05 \)) were included as potential predictors in the multivariable model. HR indicates hazard ratio. Other abbreviations as in Table 1.

*Variables were selected out using a stepwise selection process and were not included in the final model.

Figure 3. QOL improvement after atrial fibrillation ablation in left ventricular dysfunction. Mean physical (A) and mental (B) QOL scores, calculated as physical and mental component Short Form-36 scores, are shown at baseline and at 1 year (with bars showing SD at 1 year) for patients with normal left ventricular function, systolic left ventricular dysfunction (EF \( \leq 40\% \)), and diastolic dysfunction. An ANOVA compared 1-year QOL scores (\( P_{1y} \)) and QOL improvement at 1 year from baseline (\( P_{1y} \)) across the 3 groups. QOL indicates quality of life. Other abbreviation as in Figure 1.
been shown that in patients with lone AF, subtle abnormalities of systolic and diastolic function are present that improve after AF ablation.\textsuperscript{25,26}

In the present study, we found that a clinically meaningful increment of improvement in LVEF (by 5%) after ablation occurred in the majority of patients with systolic dysfunction. One third of patients with LV systolic dysfunction appeared to have tachycardia-induced cardiomyopathy, given the restoration of LVEF to normal or near normal after ablation. Ablative efficacy was higher in patients with normalization of LVEF compared with those without normalization of LVEF. Another third of patients who experienced modest LVEF improvement without complete normalization likely represents a group whose primary cardiomyopathy is aggravated by tachyarrhythmia.

In contrast to those in the systolic dysfunction group, the effect of AF ablation on patients with isolated diastolic dysfunction was more difficult to discern. Improvements of potential clinical significance, by at least 1 diastolic grade, were seen in 30%, whereas a decline by 1 grade was only seen in 8%. It is possible that diastolic grade parameters (with only grades 0 to 4) are not sufficiently sensitive to detect subtle changes in diastolic function and that the need for sinus rhythm to assess transmitral inflow confounded serial diastology assessments in this population. Nonetheless, given that our patients with normal LV function still demonstrated some underlying QOL impairments attributable to comorbid conditions that cannot be overcome by restoration of sinus rhythm.

Restoring Sinus Rhythm and QOL Improvement

Patients with AF have markedly impaired QOL.\textsuperscript{26,27} In contrast to the echocardiographic improvements after ablation, a marked QOL improvement was more consistent in all states of normal and abnormal LV function. In the present study, a significant improvement in physical composite scores was seen in patients with normal LV function, systolic dysfunction, and diastolic dysfunction. Interestingly, physical QOL in patients with diastolic dysfunction never fully improved to the level achieved in those with normal function and systolic dysfunction, who demonstrated the greatest physical health impairment at baseline. This suggests that despite broad-based improvements in QOL, there may be some underlying QOL impairments attributable to comorbid conditions that cannot be overcome by restoration of sinus rhythm.

Procedural Safety

One important final observation is that AF ablation is relatively safe in patients with LV diastolic and systolic abnormalities. The overall rate of procedural complications was similar in patients with normal LV function and those with systolic or diastolic dysfunction. This finding should reassure practitioners concerned about the periprocedural risks of AF ablation in patients with complex conditions.

Study Limitations

There are some limitations to interpreting these data. First, this study was not randomized; therefore, investigator bias could have affected the selection of patients for ablation. In addition, the decision to perform PV isolation and wide-area circumferential ablation typically reflected an operator’s approach rather than selection bias. However, the decision to perform linear ablation or additional focal ablation was tailored to a given patient by the combination of patient substrate (moderate to severe LA enlargement, the persistence of AF, a history of previous ablation) and intraprocedure observations (eg, early recurrence of AF or atrial flutter). This approach resulted in more linear ablations performed in the diastolic and systolic dysfunction groups compared with the normal LV function group. Although this reflects our standard of care, a differential ablative approach could confound comparisons between the LV dysfunction and normal LV groups, particularly in light of concerns that incomplete linear ablation can be proarrhythmic.

A second limitation of this study is that the efficacy data reflect elimination of all symptomatic AF and asymptomatic arrhythmia recorded by 24-hour Holter monitoring and event recorder tracings. Importantly, the same approach of 3-month

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n=100)</th>
<th>EF ≤40 (n=111)</th>
<th>Diastolic Dysfunction (n=157)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation delivery, no. of burns</td>
<td>36 (27, 53)</td>
<td>55 (39, 64)*</td>
<td>43 (30, 57)†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ablation time, min</td>
<td>76 (49, 125)</td>
<td>100 (46, 144)</td>
<td>94 (57, 133)</td>
<td>0.80</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>43 (26, 63)</td>
<td>50 (31, 66)</td>
<td>38 (27, 58)</td>
<td>0.09</td>
</tr>
<tr>
<td>Procedural complications</td>
<td>8 (8)</td>
<td>3 (3)</td>
<td>4 (3)</td>
<td>0.18</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>2 (2)</td>
<td>1 (&lt;1)</td>
<td>0 (0)</td>
<td>0.11</td>
</tr>
<tr>
<td>Tamponade</td>
<td>3 (3)</td>
<td>2 (2)</td>
<td>2 (1)</td>
<td>0.56</td>
</tr>
<tr>
<td>Pulmonary vein stenosis</td>
<td>3 (3)</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
<td>0.33</td>
</tr>
<tr>
<td>Diaphragmatic paralysis</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (&lt;1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Esophageal atrial fistula</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>. . .</td>
</tr>
</tbody>
</table>
and 1-year electrophysiology follow-ups was recommended for all patients, allowing for consistent comparison of 1-year results among groups without significant differences observed in follow-up rates. However, we cannot exclude the possibility of asymptomatic AF that was not recorded. Patients with LV systolic or diastolic dysfunction may be more symptomatic with AF recurrence, whereas those with normal LV function may have less detection of asymptomatic AF.

Conclusions
RF ablation of AF is a nonpharmacological option to achieve rhythm control in patients with underlying LV dysfunction. Although AF ablation is less efficacious in patients with LV systolic dysfunction than it is in patients with normal function, its efficacy is comparable to or better than current AAD options, with a low, finite procedural risk, the potential to restore LV systolic function, and improved QOL. In patients with isolated diastolic dysfunction, 1-year AF ablation outcomes are as favorable as those in patients with normal function, but with echocardiographic improvement in a minority and potential for long-term recurrence that is similar to patients with systolic dysfunction.

Disclosures
Dr Cha receives research funding from Medtronic and St Jude Medical. Dr Asirvatham receives honoraria from Boston Scientific, St Jude Medical, Biotronik, and Medtronic and serves as a consultant for Sanofi-Aventis. Dr Friedman receives research funding from Bard, St Jude Medical, Medtronic, Boston Scientific, and Pfizer; has intellectual property rights for Bard EP, Hewlett Packard, Medical Positioning, Aegis Medical, and NeoChord; and has served as a speaker/consultant for Medtronic, Boston Scientific, and St Jude Medical. Dr Packer has received the Mayo Clinical Investigator Award for the study of AF ablation outcomes. Dr Packer has provided consulting services in the past 12 months for Biosense Webster, Boston Scientific, CyberHeart, Medtronic, nContact, Sanofi-Aventis, St Jude Medical, and Toray Industries; he received no personal compensation for these consulting activities. Dr Packer receives research funding from the National Institutes of Health, Medtronic, CryoCath, Siemens AG, EP Limited, St Jude Medical, Minnesota Partnership for Biotechnology and Medical Genomics/University of Minnesota, Biosense Webster, and Boston Scientific. Mayo Clinic and Dr Packer have a financial interest in mapping technology. In accordance with the University and Small Business Patent Procedures (Bayh-Dole) Act, this technology has been licensed to St Jude Medical, and Mayo Clinic and Drs Packer and Richard Robb (not an author) have received annual royalties of >$10,000, the federal threshold for significant financial interest. All other authors have no conflicts of interest to disclose.

References

**CLINICAL PERSPECTIVE**

Although ablation of atrial fibrillation has been followed by an improvement in left ventricular (LV) ejection fraction in selected patients with LV systolic dysfunction, there are concerns that ablation procedures in patients with heart failure have the potential for greater risk, less efficacy, and limited impact on quality of life. For patients with isolated diastolic dysfunction, these issues are also unclear. This investigation compared outcomes after catheter ablation in patients with depressed LV ejection fraction, preserved LV ejection fraction with diastolic dysfunction, and normal systolic and diastolic function. At 1 year, the atrial fibrillation elimination rate of 75% in patients with isolated LV diastolic dysfunction was comparable to that in patients with normal LV function and was better than that in patients with LV systolic dysfunction (62%). All 3 groups experienced improvement in physical and mental quality of life. LV ejection fraction improved to near normal in 31% of the LV dysfunction group. In the diastolic dysfunction group, 30% of patients showed improvement in diastolic dysfunction. Over 5 years, there were more atrial fibrillation recurrences in the LV systolic and diastolic dysfunction groups than in the normal group. Therefore, repeat ablation or supplemental antiarrhythmic therapy may be required more often in the long-term management of atrial fibrillation in populations with LV dysfunction.
Success of Ablation for Atrial Fibrillation in Isolated Left Ventricular Diastolic Dysfunction: A Comparison to Systolic Dysfunction and Normal Ventricular Function


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