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Long-Term Quality of Life After Ablation of Atrial Fibrillation

The Impact of Recurrence, Symptom Relief, and Placebo Effect

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Objectives We sought to determine the relationship between atrial fibrillation (AF) ablation efficacy, quality of life (QoL), and AF-specific symptoms at 2 years.

Background Although the primary goal of AF ablation is QoL improvement, this effect has yet to be demonstrated in the long term.

Methods A total of 502 symptomatic AF ablation recipients were prospectively followed for recurrence, QoL, and AF symptoms.

Results In 323 patients with 2 years of follow-up, 72% achieved AF elimination off antiarrhythmic drugs (AADs), 15% achieved AF control with AADs, and 13% had recurrent AF. The physical component summary scores of the Medical Outcomes Study Short Form 36 increased from 58.8 ± 20.1 to 76.2 ± 19.2 ($p < 0.001$) and the mental component summary scores of the Short Form 36 increased from 65.3 ± 18.6 to 79.8 ± 15.8 ($p < 0.001$). Post-ablation QoL improvements were noted across ablation outcomes, including recurrent AF (change in physical component summary: 12.1 ± 19.7 and change in mental component summary: 9.7 ± 17.9), with no significant differences in QoL improvement across 3 ablative efficacy outcomes. However, in 103 patients who completed additional assessment with Mayo AF Symptom Inventories (on a scale of 0 to 48), those with AF elimination off AADs had a change in AF symptom frequency score of −9.5 ± 6.3, which was significantly higher than those with AF controlled with AADs (−5.6 ± 3.8, $p = 0.03$) or those with recurrent AF (−3.4 ± 8.4, $p = 0.02$). Independent predictors of limited QoL improvement included higher baseline QoL, obesity, and warfarin use at follow-up.

Conclusions AF ablation produces sustained QoL improvement at 2 years in patients with and without recurrence. AF-specific symptom assessment more accurately reflects ablative efficacy. (J Am Coll Cardiol 2010;55:2308–16)

Atrial fibrillation (AF) affects >6.7 million people in the U.S. and Europe (1,2). People with AF have impaired quality of life (QoL) compared with the general population (3,4). Thus, the impetus to eliminate AF has been great. Maintenance of sinus rhythm with antiarrhythmic drugs (AADs), however, has not been shown to have consistent superior benefits in QoL, major physical end points, stroke, or survival over rate-control strategies (4–6).

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Primary curative AF ablation, with the potential for greater efficacy and freedom from the adverse side effects of AADs, is a viable option for select symptomatic patients (7,8). Post-ablation QoL improvement and/or a superior QoL benefit from ablation over pharmacologic rhythm control have been demonstrated in studies with limited sample sizes and follow-up durations ≤1 year (9–14). Nevertheless, establishing that QoL benefit lasts beyond 1 year and is attributable to ablation-specific effects would justify the broader application of this expensive procedure with uncommon, but significant risks.

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The purpose of this prospective observational study was to establish the impact of AF ablation on QoL in symptomatic patients and to identify the relative contributions of patient-related factors, rhythm status, AAD use, and relief of AF-specific symptom burden.

Methods

Patient population. We included 502 consecutive patients with symptomatic AF who underwent AF ablation at Mayo Clinic, a large tertiary care referral center. The decision to proceed with ablation was made by an electrophysiologist, usually after a symptomatic patient had failed to respond to a trial of at least 1 AAD or had side effects and rarely as a first-line AF therapy, per current consensus recommendations (7). Symptomatic patients undergoing AF ablation were prospectively followed for QoL and rhythm outcomes from December 2001 until July 2006. Data were collected prospectively until March 2008. This study was approved by the Mayo Institutional Review Board, and all patients provided informed consent.

Ablation protocol. Patients discontinued amiodarone for 2 months before ablation and other AADs for 5 half-lives. Patients underwent a previously described AF ablation protocol (15). Patients underwent either a lasso-guided, circumferential pulmonary vein (PV) isolation (n = 117, 22%) or an electroanatomically mapping–guided, wide area circumferential ablation (n = 385, 78%) with additional linear lesions along the left atrial roof and the left inferior isthmus. During PV isolation, ablation was guided by the lasso mapping catheter positioned near the orifice of the PVs, with localization by intracardiac echocardiography. During wide area circumferential ablation, electroanatomic maps of the PVs and left atrium were rendered using navigational mapping tools. With either approach, entrance block to the PVs, an acute end point of the ablation, was confirmed by a lasso catheter. Additional ablation targets included residual PV potentials and non-PV foci in the setting of recurrent spontaneous or induced AF during isoproterenol infusion (5 to 15 μg/min). Patients also uniformly underwent cavotricuspid isthmus ablation.

Outcomes assessment. Post-procedure, patients remained hospitalized and were monitored for 24 to 48 h. Clinical follow-up was recommended at 3 months and annually. Before and after ablation at 3 months and 1, 2, and 3 years, patients received a questionnaire that included QoL assessment, symptom information, and self-reports of arrhythmia recurrences (and interventions) that occurred outside of follow-up visits. All reported outcomes were timed in relation to the patient's last ablation at Mayo Clinic.

Health-related QoL was assessed with the Medical Outcomes Study Short Form-36 (SF-36). The SF-36 contains 8 individual scales, scored from 0 (worst health) to 100 (best health). Raw scores were presented as T scores in comparison with a healthy normal population with a mean score set at 50 with an SD of 10. In addition to a total score, physical component summary (PCS) and mental component summary (MCS) scores were assessed on a raw scale of 0 to 100 (14).

Abbreviations and Acronyms

AAD = antiarrhythmic drug
AF = atrial fibrillation
MAFSI = Mayo AF-Specific Symptom Inventory
MCS = mental component summary
PCS = physical component summary
PV = pulmonary vein
QoL = quality of life
SF-36 = Medical Outcomes Study Short Form-36

After August 2004, the Mayo AF-Specific Symptom Inventory (MAFSI) was introduced to clinically follow AF-specific symptoms (16). Although it has some common elements with the Symptom Checklist (survey developed by R.S. Bubien and G.N. Kay, and revised by L.S. Jenkins, 1993), the MAFSI inventory monitors additional symptoms (Packer DL, Kay GN, Bubien RS, personal communication, 2009) (17,18). Using a checklist of 12 symptoms, patients score the frequency of symptoms over 6 months as 0 (never), 1 (rarely), 2 (sometimes), 3 (often), and 4 (always). Total scores range from 0 to 48.

Recurrence was counted as any atrial arrhythmia that occurred after the post-procedural blanking period of 2 months, including atrial flutter and atrial tachycardia. Blanking recurrences were noted but not counted because of their unclear long-term significance. Asymptomatic recurrences were detected at routine clinical follow-up, which included a physical examination and electrocardiogram as well as Holter monitoring that was obtained typically at 3 and 12 months and then at the discretion of the patient's cardiologist. Symptomatic recurrences were identified at clinical follow-up and by a 3-month and then annual questionnaires and were confirmed electrocardiographically. Repeat ablations were generally delayed until 6 months after the initial ablation procedure.

Between follow-ups, patients were instructed to call in information regarding recurrences, cardioversions, and complications. Research staff or the patient's electrophysiologist contacted the patient to facilitate Holter or event monitoring to document arrhythmia when the diagnosis was uncertain. Quarterly chart review was also performed. AAD, warfarin, or aspirin use, cardioversions, and additional AF interventions were noted.

Ablative efficacy was categorized as AF elimination off AADs, AF control on AADs, and recurrent AF. AF elimination was achieved in patients who were arrhythmia free and off AADs for at least 6 months before evaluation. This group encompassed those patients in whom complete freedom from post-blanking recurrence was achieved for the duration of follow-up off AADs (96%) as well as those who had early recurrences that self-resolved without the need for long-term AAD therapy (4%). AF control on AADs was achieved in patients who maintained sinus rhythm for at least 6 months before assessment, but who had recurrence at some point and required AADs. Patients without AF control despite AAD use or repeat ablations were considered to have recurrent AF.

Statistical methods. Continuous data were expressed as mean ± SD. Using the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables, patient characteristics were compared in patients who did and did not complete QoL follow up at 2 years and in patients who did and did not complete a baseline MAFSI assessment. Changes in SF-36 or MAFSI scores from baseline to various time points were assessed using paired *t* tests. A 1-way analysis of variance was used to compare changes in SF-36 and MAFSI scores in patients based on a 3-tiered rhythm status outcome. The Bonferroni method was performed to adjust for multiple comparisons. Correlations were ascertained using Pearson correlation coefficients. Univariate linear regression relationships between: 1) baseline demographic characteristics; 2) baseline echocardiographic characteristics; 3) pharmacological therapies at 2 years; and 4) baseline PCS and MCS scores and QoL improvement at 2 years were described. If the p value was <0.15 in a univariate model, then an additional *t* test or analysis of variance was performed. Two linear multivariate regression models with stepwise selection of univariates with $p \leq 0.05$ were constructed to assess independent predictors of QoL improvement. The first model included all significant univariates except baseline PCS and MCS scores, but these were incorporated into the second model. For all statistical tests, a 2-tailed p value ≤ 0.05 was considered significant. Analyses were performed using SAS version 8.2 (SAS Inc., Cary, North Carolina).

Results

Clinical characteristics. Clinical characteristics of 502 symptomatic patients who underwent ablation are shown in Table 1. Previous AF ablations had been performed in 12% of the cohort at Mayo Clinic and in 12% elsewhere. The median duration of follow-up was 3.1 years (interquartile range 2.1 to 4.2 years). At 24 months, QoL and ablative efficacy data were available for 323 of 502 patients (64%). The clinical and echocardiographic characteristics of the patients who did and did not complete a QoL inventory at 24 months are compared in Table 1. The only significant difference between these groups was that patients with longer follow-up, as expected, less frequently underwent wide area circumferential ablation, which was incorporated into our practice approximately 3 years after the study began.

Health-related QoL. Baseline total SF-36 scores before the first ablation (63.9 ± 19.2) and last ablation (64.1 ± 18.7) were similar. Compared with baseline scores before the last ablation, total mean SF-36 scores increased significantly to 80.8 ± 15.6 at 3 months after the last ablation ($p < 0.001$). This improvement was sustained at 12 months (80.6 ± 15.7, $p < 0.001$) and 24 months (80.5 ± 16.5, $p < 0.001$). The early and sustained QoL improvement was

Table 1 Clinical Characteristics of Patients With and Without 2-Year Follow-Up

	Overall Cohort (n = 502)	<2 Years of Follow-Up (n = 179)	≥2 Years of Follow-Up (n = 323)	p Value
Demographic and echocardiographic features				
Age (yrs)	55.9 ± 10.3	54.9 ± 10.5	56.4 ± 10.2	0.09
Male	410 (82)	144 (80)	266 (82)	0.60
Paroxysmal AF	256 (51)	97 (54)	149 (46)	0.08
Persistent AF	175 (35)	64 (36)	109 (34)	0.64
Long-standing AF	65 (13)	26 (15)	39 (12)	0.43
AF duration (yrs)	6.6 ± 5.9	6.7 ± 5.7	6.6 ± 6.0	0.89
WACA ablation (vs. PVI)	385 (78)	153 (85)	232 (72)	<0.001
LV ejection fraction (%)	58.0 ± 9.7	57.7 ± 8.9	58.1 ± 10.1	0.12
LA size ≥45 mm	175 (35)	68 (38)	107 (33)	0.27
Underlying disease				
Heart failure	11 (2)	6 (3)	5 (2)	0.19
Coronary artery disease	56 (11)	20 (11)	36 (11)	0.99
Diabetes	33 (7)	16 (9)	17 (5)	0.11
Dilated cardiomyopathy	46 (9)	18 (10)	28 (9)	0.61
Hypertension	195 (39)	62 (35)	133 (41)	0.15
Valvular heart disease	59 (12)	22 (12)	37 (11)	0.79
Sleep apnea	67 (13)	24 (13)	43 (13)	0.96
Pre-ablation medications				
Any AAD therapy failed	459 (91)	158 (88)	301 (93)	0.06
Any rate control therapy failed	406 (81)	146 (82)	260 (81)	0.77
Beta-blockers	242 (68)	120 (68)	219 (68)	0.96
Calcium-channel blockers	186 (37)	71 (40)	115 (36)	0.30

Values are mean ± SD or n (%).

AAD = antiarrhythmic drug; AF= atrial fibrillation; echo = echocardiographic; LA = left atrial; LV = left ventricular; PVI = pulmonary vein isolation; WACA = wide area circumferential ablation.

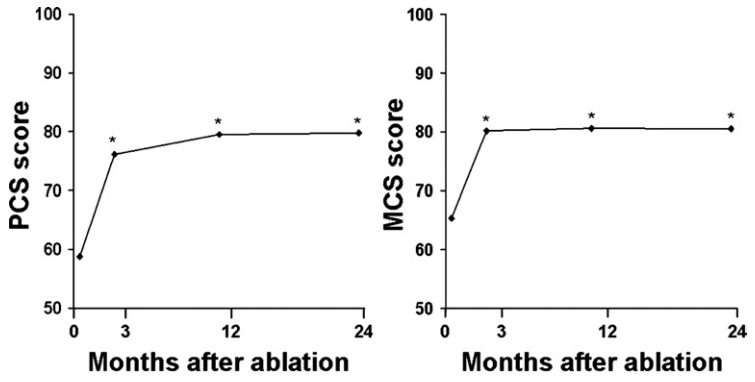

Figure 1 **Physical and Mental Health Over 24 Months After Ablation**

Quality of life measured by the Medical Outcomes Study Short Form 36 physical component summary (PCS) and mental component summary (MCS) scores is shown at baseline and 3, 12, and 24 months after ablation. *p ≤ 0.001 compared with baseline with Bonferroni adjustment.

similar for both physical and mental health, as Figure 1 illustrates. From baseline to 24 months, the mean PCS score of 58.8 ± 20.1 increased to 76.2 ± 19.2 ($p < 0.001$) and the mean MCS score increased from 65.3 ± 18.6 to 79.8 ± 15.8 ($p < 0.001$) All 8 scales of the SF-36 with the exception of body pain contributed significantly to overall QoL improvement, as shown in Figure 2. For reference, each scale was calibrated to population-based norms where an adjusted score of 50 ± 10 represents the mean ± SD scores of the entire U.S. population in any of the 8 categories. The areas of improvement ranked in order from greatest to least were physical role, vitality, social function, physical function, general health, emotional role, mental health, and body pain, resulting in a return to the norm for all domains.

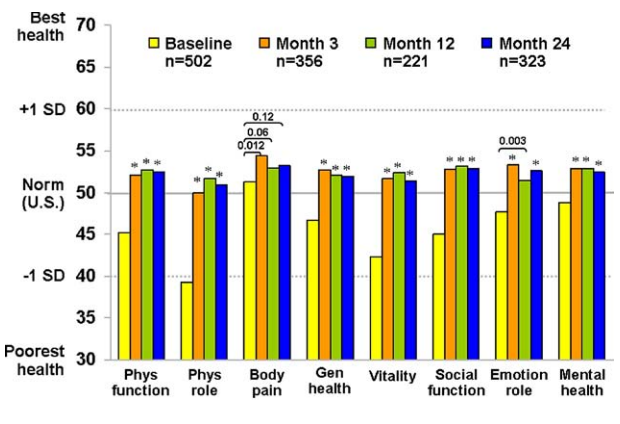

Figure 2 **Norm-Based Improvements on SF-36 Scales Over 24 Months**

Eight subscales of the Medical Outcomes Study Short Form 36 (SF-36) normalized to a healthy normal population (50 ± 10) are shown at baseline and 24 months after ablation. *p ≤ 0.001 compared with baseline with Bonferroni adjustment. Gen = general; Phys = physical.

Influence of ablative efficacy. Of the 323 patients, 224 (69%) were completely free of post-blanking recurrence and 99 (31%) had at least 1 post-blanking recurrence at 2 years. In the recurrence-free group, improvements in QoL scores (ΔPCS: −16.6 ± 17.4, ΔMCS: −13.1 ± 16.6) were higher than in those who had a recurrence (ΔPCS: −13.7 ± 18.9, ΔMCS: −11.8 ± 19.8), but these differences were not significant ($p = 0.131$ and $p = 0.681$, respectively).

At 2 years, 66 patients (20%) remained on either amiodarone (4%) or another AAD (16%) and 150 patients (46%) remained on beta-blockers (36%) or calcium-channel blockers (14%) for a variety of indications. Among 323 patients, 233 (72%) achieved AF elimination off AADs, 48 (15%) achieved AF control on AADs, and 42 had recurrent AF (13%) at 24 months. Among the 42 patients with recurrent AF, 5 patients underwent atrioventricular nodal ablation with pacemaker placement or the surgical Maze procedure (12%), 18 required AADs (43%), and 27 (64%) remained concurrently on some form of rate-control agent. As Figure 3 illustrates, post-ablation improvements in QoL were substantial across all ablation outcomes, including those with recurrent AF (ΔPCS: 12.1 ± 19.7 and ΔMCS: 9.7 ± 17.9). No significant differences in QoL improvement were noted among ablation efficacy outcomes.

Influence of repeat ablation. Fifty-nine patients in the cohort had multiple AF ablations and completed QoL assessments for both the first and repeat ablations. Although baseline QoL scores in this subgroup improved from 64.7 ± 21.8 before the first ablation to 72.5 ± 18.7 ($p = 0.04$) after 3 months, scores then decreased to 64.3 ± 17.1 before repeat ablation ($p = 0.77$), when the mean time to repeat ablation was 2.0 ± 1.6 years. At 2 years after repeat ablation, the QoL score improved to 77.3 ± 16.3 ($p = 0.03$ compared with baseline). This was comparable to improvements seen in the cohort overall.

Influence of long-term anticoagulation. From the standpoint of anticoagulation, 320 (64%) patients in the initial

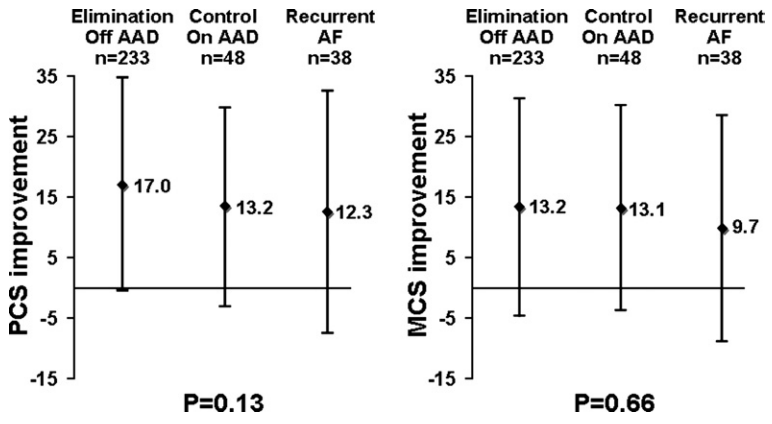

Figure 3 Quality of Life Based on Post-Ablation Rhythm Status

Improvements in PCS and MCS scores are compared in patients with atrial fibrillation (AF) elimination, AF control on antiarrhythmic drugs (AAD), and patients without AF control, or recurrent AF. Abbreviations as in Figure 1.

cohort reported warfarin use before ablation, and all patients were discharged on warfarin (with heparin bridging until therapeutic) for at least 3 months. Among the 306 patients with efficacy data, warfarin was continued in 96 patients (31%) and discontinued in 210 patients (69%) after a time to discontinuation of 1.1 ± 0.8 years. Patients maintained on warfarin had higher median CHADS2 (Congestive Heart Failure, Hypertension, Age ≥75 years, Diabetes, Secondary Prevention of Stroke or Transient Ischemia Attack [×2]) scores (1, interquartile range 0 to 1) than their counterparts off warfarin (0, interquartile range 0 to 1, $p = 0.003$) and were more likely to have persistent AF, severe left atrial enlargement, sleep apnea, or a history of stroke. Seven of the 8 patients who had stroke or transient ischemic attacks experienced them within the first 3 months, necessitating long-term anticoagulation, whereas 1 patient had a stroke 3 years after discontinuation of anticoagulation. The median CHADS2 score of this group was 1 (range 0 to 2), including 1 patient who had a mechanical mitral valve prosthesis. At 2 years, those who remained on warfarin had less SF-36 improvement than those who did not (−9.9 ± 16.5 vs. −16.3 ± 16.8, $p = 0.008$).

AF symptom frequency score to assess the impact of ablation. Of the original 502 patients, 226 who enrolled from August 2004 to June 2006 (45% of the cohort) completed baseline MAFSI surveys. Compared with the subgroup who did not complete baseline MAFSI surveys, the subgroup who did had a less paroxysmal AF (46% vs. 55%, $p = 0.04$), more left atrial enlargement >45 mm (40% vs. 30%, $p = 0.02$), and more hypertension (44% vs. 35%, $p = 0.04$). Both baseline and 24-month MAFSI surveys were completed in 106 patients (21%), of whom 103 had documented rhythm status at 24-month (20%) follow-up.

Mean AF symptom frequency scores before the first ablation (14.3 ± 6.5) and the last ablation (14.1 ± 6.4) were similar. Symptom frequency scores decreased from 14.1 ± 6.4 to 4.8 ± 5.3 ($p < 0.001$). Statistically significant improvements were observed in all individual symptom categories except ankle swelling and unexplained falls. Marked individual symptom improvements (by at least 1 of 4 grades) were observed with palpitations (2.4 ± 1.0 to 1.0 ± 0.9, $p < 0.001$), tiredness (2.2 ± 1.0 to 1.0 ± 1.1, $p < 0.001$), and inability to exercise (1.5 ± 1.2 to 0.5 ± 0.9, $p < 0.001$) (Fig. 4)

AF symptom frequency scores correlated strongly with total SF-36 scores in the 226 patients who completed baseline symptom surveys ($r = -0.64$, $p < 0.001$) and in the 204 patients who completed 24-month symptom sur-

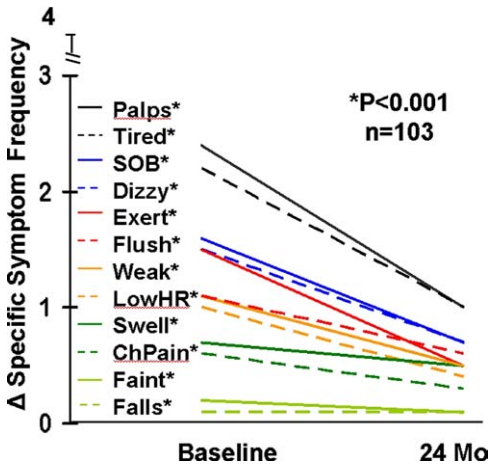

Figure 4 Change in Atrial Fibrillation-Specific Symptoms (0 to 4 Scale) Over 24 Months

The Mayo Atrial Fibrillation-Specific Symptom Inventory is a checklist of 12 symptoms: palpitations (Palps), tiredness or fatigue, shortness of breath (SOB), dizziness (Dizzy), exertional intolerance (Exert), flushing (Flush), weakness (Weak), a sense of low heart rate (HR), swelling (Swell), chest pain (ChPain), fainting or near fainting (Faint), and falls.

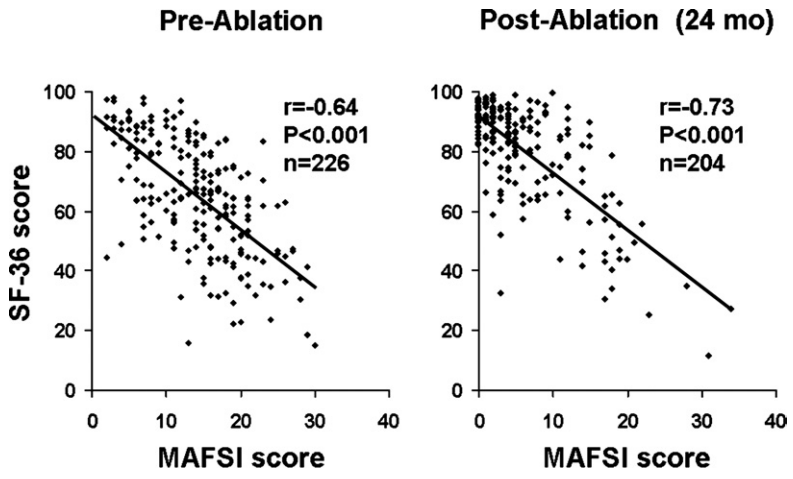

Figure 5 **Correlation of Frequency of AF Specific Symptoms With QoL**

The correlation Medical Outcomes Study Short Form 36 (SF-36) scores and Mayo AF-Specific Symptom Inventory (MAFSI) scores is shown at pre-ablation **(left)** and after ablation **(right)**. Higher quality of life (QoL) scores and lower symptom scores correspond to clinical improvement.

veys ($r = -0.73$, $p < 0.001$) (Fig. 5). In 103 patients for whom complete symptom, QoL, and recurrence status follow-up at 24 months and baseline was available, improvements in AF symptoms and QoL correlated moderately ($r = -0.55$, $p < 0.001$).

Unlike changes in QoL, changes in AF symptoms differed significantly among ablation efficacy outcomes (Fig. 6). In 103 patients, 75 with AF elimination off AADs had a change in the AF symptom frequency score of -9.5 ± 6.3, which was nearly significantly higher than the change in AF symptom frequency score in the 18 patients with AF control on AADs (-5.6 ± 3.8, $p = 0.06$) and significantly higher in the 10 patients with recurrent AF (-3.4 ± 8.4, $p = 0.04$).

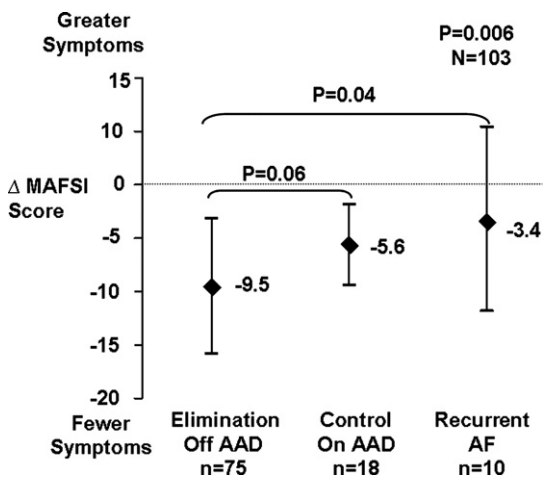

Figure 6 **Change in AF Symptom Score Based on Post-Ablation Rhythm Status**

One-way analysis of variance comparison of symptom improvements with mean ± SD are shown. Abbreviations as in Figures 3 and 5.

Predictors of QoL benefit. Three univariate predictors ($p \leq 0.05$) of an improvement in total QoL score at 24 months after ablation were identified: obesity defined as body mass index ≥30 kg/m^2 ($p = 0.04$), warfarin at follow-up ($p = 0.003$), and baseline SF-36 score ($p < 0.0001$). In the subgroup of patients who completed baseline MAFSI surveys, high baseline symptom scores were also identified as a predictor of QoL outcomes. Table 2 demonstrates the differences in QoL improvement for select patient characteristics including all significant factors.

In a multivariate analysis (which did not include baseline symptom score), warfarin use at follow-up predicts a 10-point decrease in SF-36 score improvement (SE = 2.0, $p < 0.0001$). Obesity (body mass index <30 kg/m^2) predicts a 6.8-point decrease in SF-36 score improvement (SE = 1.8, $p = 0.0002$). Higher baseline SF-36 scores also predict less robust QoL improvement. Each 10-point increase in baseline SF-36 is associated with a 3-point decrease in QoL improvement (SE = 0.7, $p < 0.0001$), with differences in baseline MCS and PCS scores having equivalent effects on QoL improvement.

Impact of complications. Major procedural complications and long-term follow-up events with potential for QoL impact were experienced by 43 patients (10 with cardiac tamponade requiring pericardiocentesis, 4 with in-hospital transient ischemic attack or stroke, 4 with transient ischemic attack or stroke sometime during follow-up, 1 with intracerebral hemorrhage, 24 with computed tomography evidence of pulmonary vein stenosis of whom 4 required intervention for symptoms, and none with gastroesophageal injury or fistula). QoL data were available for 30 of 43 patients with complications. In a univariate analysis, the

Table 2 Univariate Relationships of QoL Improvement

Characteristic	QoL Change	p Value
AF		
Paroxysmal	−13.4 ± 15.0	0.31
Nonparoxysmal	−15.5 ± 18.8	
LA size, mm		
>45	−14.0 ± 16.1	0.90
≤45	−14.6 ± 17.4	
Post-procedural complication	−17.2 ± 17.4	0.16
No post-procedural complication	−14.0 ± 16.8	
Hypertension	−12.6 ± 16.6	0.06
No hypertension	−15.7 ± 17.1	
Obese	−11.9 ± 18.5	0.05
Nonobese	−16.4 ± 16.2	
AF elimination off AAD	−14.9 ± 16.8	
AF controlled on AAD	−13.9 ± 16.4	0.62
Recurrent AF	−11.8 ± 17.7	
On warfarin at 2 yrs	−9.9 ± 16.5	0.008
Off warfarin at 2 yrs	−16.3 ± 16.8	
On beta-blocker at 2 yrs	−13.2 ± 17.6	0.33
Off beta-blocker at 2 yrs	−14.8 ± 16.4	
On calcium-channel blocker at 2 yrs	−10.8 ± 13.8	0.16
Off calcium-channel blocker at 2 yrs	−12.2 ± 17.2	
Repeat AF ablations	−10.5 ± 16.3	0.83
Single AF ablation	−12.2 ± 17.0	
Baseline SF-36, %		
0–25	−26.8 ± 20.2	<0.001
26–50	−17.9 ± 16.3	
51–75	−10.7 ± 12.2	
76–100	−3.0 ± 6.5	
Baseline MAFSI, %		
0–25	−8.1 ± 16.0	0.01
26–50	−16.5 ± 15.1	
51–75	−14.6 ± 15.2	
76–100	−22.0 ± 16.8	

MAFSI = Mayo AF-Specific Symptom Inventory; SF-36 = Medical Outcomes Study Short Form 36; other abbreviations as in Table 1.

presence of post-procedural complications including stroke did not have a long-term impact on QoL improvement. In addition, the decreased QoL improvement in obese patients and those on warfarin at follow-up was not significantly associated with an increased rate of any complication or stroke.

Discussion

In this prospective study of AF ablation recipients, a marked and sustained improvement in QoL at 2 years occurred in most patients. Although QoL seemed to improve with repeat ablations, QoL improvement was not closely linked to overall ablative efficacy. Despite a trend toward greater physical QoL improvement in patients with AF elimination, substantial QoL improvement was also seen in patients with AF control on AADs and those with recurrent AF. Determinants of limited QoL improvement included obesity, ongoing warfarin use, and a good baseline QoL. In contrast to the nonspecific relationship between QoL improvement by SF-36 scores and AF ablation efficacy, changes in AF-specific symptoms by MAFSI scores more consistently reflected ablative efficacy.

Long-term QoL benefit. The clinical relevance of these findings is substantial. According to the consensus report on AF ablation from the Heart Rhythm Society, "the primary justification for an AF ablation procedure. . .is the presence of symptomatic AF, with a goal of improving a patient's quality of life" (7). In most of our cohort, there was not only improvement, but also normalization of QoL seen as early as 3 months. The finding of a durable 2-year QoL benefit extends previous findings of a 1-year or less benefit (7,9–14). Therefore, the longevity of the QoL improvement after ablation potentially strengthens the argument for ablation in patients with symptomatic AF.

However, the lack of a strong relationship between the degree of QoL improvement and ablation efficacy raises questions about the specificity of the QoL effect of ablation and its mode of assessment. In this cohort, we found little difference in QoL improvement between the 69% of patients who were entirely free of recurrence at 2 years off AADs and the remaining 31% who experienced recurrences. Recognizing that freedom from sustained symptomatic recurrences due to rhythm control could be as favorably perceived by patients as absolute freedom from any recurrence, we also assessed QoL based on rhythm control off and on AAD. Although patients with AF elimination had a substantial QoL improvement, so too did those with AF control on AADs and those with limited recurrent AF.

QoL improvement in recurrent AF. The QoL improvement observed in patients with recurrent AF may be attributable to a variety of causes. In some cases, QoL improvement may have been due to other efficacious AF interventions including atrioventricular node ablation or the surgical Maze procedure. Alternatively, those with recurrent AF may represent a less symptomatic group post-ablation than those who sought those interventions or repeat ablation. Such transition to less severe or asymptomatic disease states could be due to direct ablation effects, secondary destruction of autonomic inputs to the atrium, or improved pharmacologic efficacy (19). Nonetheless, only minor improvements in AF-specific symptom burden were observed in patients with recurrent AF despite substantive QoL improvements. Therefore, regression to the mean, placebo effect, and the limitations of SF-36 as a metric of ablation efficacy need to be considered.

The principle of regression to the mean is that patients may be less symptomatic on average than they report at presentation, thus predisposing to an overestimation of symptom or QoL improvement. This effect seems unlikely because patients frequently wait for months from the time of ablation referral to the actual time of procedure and baseline questionnaire completion. Placebo effect is another potential explanation for the lack of correlation between treatment effect and QoL outcomes in this study. The actual contribution of placebo effect is hard to define given the

ethical problems with sham invasive procedures (7). Although the consistent nature of QoL improvement at 3, 12, and 24 months does not favor a placebo effect, there are examples of placebo effect lasting beyond 1 year (20,21). Alternatively, our findings suggest that the SF-36 does not entirely describe the QoL burden that a sporadic disease process such as AF imposes on a person's well-being.

Contributors to symptom improvement. Other factors obscured the relationship between rhythm status and QoL, including obesity and ongoing warfarin therapy. Procedural complications (including stroke) were not significantly higher in either subgroup, nor were overall complications of sufficient frequency or magnitude to diminish the QoL improvement in these entire subgroups. In obese patients, limited QoL improvement may reflect diminished underlying functional capacity. In some patients requiring warfarin, the inconvenience of international normalized ratio monitoring or nuisance bleeding may explain limitations in QoL improvement.

Warfarin and QoL. The impact of warfarin on QoL raises questions regarding the unaccepted ablation indication for discontinuation of anticoagulation. Although one randomized study of anticoagulation in patients with AF demonstrated no detrimental impact of warfarin use on QoL, our study suggests that in post-ablation patients, the QoL benefit of ablation is decreased in patients on long-term anticoagulation therapy (22). This may relate to patient perceptions of less stroke risk after AF elimination and, therefore, less benefit of anticoagulation or that sicker patients with less potential for QoL improvement were anticoagulated in the long term. Although limited data suggest that the judicious discontinuation of long-term anticoagulation therapy after AF ablation, applied on an individualized basis, does not increase stroke risk, additional study is required (23). Nonetheless, anticoagulation during and early after the procedure remains critically important, given that transient ischemic attacks or strokes in this study occurred predominantly within 3 months of the procedure.

AF-specific symptom scoring. Elimination of AF-specific symptoms may be a better end point for ablative therapy than generic QoL. We found that the use of AF-specific symptom assessment with MAFSI, a simple survey, provided clinically relevant, disease-specific information that more directly reflected rhythm status and clinical improvement at 2 years. Specifically, palpitations, tiredness, shortness of breath, dizziness, and perceived limitations in exertional capacity should be assessed because these are the most problematic at baseline and improve the most after ablation.

Study limitations. The main limitation is that the data are derived from a prospective cohort rather than from a randomized, controlled cohort comparing AF ablation therapy to best pharmacological therapy. In addition, it is important to note that the ablation practices described here do not incorporate the targeting of complex fractionated electrograms, which may augment ablative efficacy. Another limitation of this study is that the mode of detecting recurrence was largely clinically driven. The use of either implantable atrial monitoring or frequent screening with auto-detection full disclosure monitors may better identify the frequency of asymptomatic recurrences and their impact on QoL.

Conclusions

This study compares ablation efficacy status, QoL, and AF-symptom score assessments. We found the QoL improvement after ablation was not entirely dependent on ablative efficacy. Other factors, including symptom relief, baseline QoL status, baseline characteristics, and the potential for warfarin discontinuation must be considered. Atrial fibrillation symptom assessments provide more disease-specific information than QoL tools in baseline assessment and clinical follow-up of patients undergoing AF ablation.

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REFERENCES

1. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285:2370–5.
2. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). J Am Coll Cardiol 2006;48:e149–246.
3. Dorian P, Jung W, Newman D, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. J Am Coll Cardiol 2000;36:1303–9.
4. Hagens VE, Ranchor AV, Van Sonderen E, et al. Effect of rate or rhythm control on quality of life in persistent atrial fibrillation. Results from the Rate Control Versus Electrical Cardioversion (RACE) Study. J Am Coll Cardiol 2004;43:241–7.
5. The AFFIRM Investigators. Quality of life in atrial fibrillation: the Atrial Follow-up Investigation of Rhythm Management (AFFIRM) study. Am Heart J 2005;149:112–20.
6. Hohnloser SH, Kuck KH, Lilienthal J. Rhythm or rate control in atrial fibrillation—pharmacological intervention in atrial fibrillation (PIAF); a randomized trial. Lancet 2000;356:1789–94.
7. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures, and follow-up. Europace 2007;9:335–79.
8. Cappato R, Calkins H, Chen S-A, et al. Worldwide survey on methods, efficacy, and safety of catheter ablation for atrial fibrillation. Circulation 2005;111:1100–5.
9. Chen MS, Marrouche NF, Khaykin Y, et al. Pulmonary vein ablation for the treatment of atrial fibrillation in patient with impaired systolic function. J Am Coll Cardiol 2004;43:1004–9.
10. Purerfellner H, Martinek M, Aichinger J, et al. Quality of life restored to normal in patients with atrial fibrillation after pulmonary vein ostial isolation. Am Heart J 2004;148:318–25.

11. Goldberg A, Menen M, Mickelson S, et al. Atrial fibrillation ablation leads to long-term improvement of quality of life and reduced utilization of healthcare resources. J Interv Cardiac Electrophysiol 2003;8:59–64.
12. Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs. antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA 2005;293:2634–40.
13. Pappone C, Rosanio S, Augello G, et al. Mortality, morbidity and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: outcomes form a controlled nonrandomized long-term study. J Am Coll Cardiol 2003;42:185–97.
14. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. Circulation 2008;118:2498–505.
15. Bunch TJ, Munger TM, Friedman PA, et al. Substrate and procedural predictors of outcomes after catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. J Cardiovasc Electrophysiol 2009;19:1009–14.
16. Ware JE Jr. SF-36 Health Survey. Manual and Interpretation Guide. Boston, MA: The Health Institute; 1993.
17. Bubien RS, Knotts-Dolson SM, Plumb VJ, Kay GN. Effect of radiofrequency catheter ablation on health-related quality of life and activities of daily living in patients with recurrent arrhythmias. Circulation 1996;94:1585–91.
18. Wokhlu A, Hodge DO, Monahan K, et al. Unique AF-specific symptom score assesses long-term symptom relief after ablation (abstr). Circulation 2008;118:S589.
19. Lin J, Scherlag BJ, Niu G, et al. Autonomic elements within the ligament of Marshall and inferior left ganglionated plexus mediate functions of the atrial neural network. J Cardiovasc Electrophysiol 2009;20:318–24.
20. Turner JA, Ersek M, Herron L, et al. Patient outcomes after lumbar spinal fusions. JAMA 1992;268:907–11.
21. Cobb LA, Thomas GI, Dillard DH, Merendino KA, Bruce RA. An evaluation of internal-mammary-artery-ligation by a double-blind technique. N Engl J Med 1959;260:1115–8.
22. Lancaster TR, Singer DE, Sheehan MA, et al. The impact of long-term warfarin therapy on quality of life. Arch Intern Med 1991;151:1944–9.
23. Oral H, Chugh A, Ozaydin M, et al. Risk of thromboembolic events after percutaneous left atrial radiofrequency ablation of atrial fibrillation. Circulation 2006;114:759–65.

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