Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device

Results From the AATAC Multicenter Randomized Trial

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Background—Whether catheter ablation (CA) is superior to amiodarone (AMIO) for the treatment of persistent atrial fibrillation (AF) in patients with heart failure is unknown.

Methods and Results—This was an open-label, randomized, parallel-group, multicenter study. Patients with persistent AF, dual-chamber implantable cardioverter defibrillator or cardiac resynchronization therapy defibrillator, New York Heart Association II to III, and left ventricular ejection fraction <40% within the past 6 months were randomly assigned (1:1 ratio) to undergo CA for AF (group 1, n=102) or receive AMIO (group 2, n=101). Recurrence of AF was the primary end point. All-cause mortality and unplanned hospitalization were the secondary end points. Patients were followed up for a minimum of 24 months. At the end of follow-up, 71 (70%; 95% confidence interval, 60%–78%) patients in group 1 were recurrence free after an average of 1.4±0.6 procedures in comparison with 34 (34%; 95% confidence interval, 25%–44%) in group 2 (log-rank $P<0.001$). The success rate of CA in the different centers after a single procedure ranged from 29% to 61%. After adjusting for covariates in the multivariable model, AMIO therapy was found to be significantly more likely to fail (hazard ratio, 2.5; 95% confidence interval, 1.5–4.3; $P<0.001$) than CA. Over the 2-year follow-up, the unplanned hospitalization rate was (32 [31%] in group 1 and 58 [57%] in group 2; $P<0.001$), showing 45% relative risk reduction (relative risk, 0.55; 95% confidence interval, 0.39–0.76). A significantly lower mortality was observed in CA (8 [8%] versus AMIO (18 [18%]; $P=0.037$).

Conclusions—This multicenter randomized study shows that CA of AF is superior to AMIO in achieving freedom from AF at long-term follow-up and reducing unplanned hospitalization and mortality in patients with heart failure and persistent AF.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00729911.

(*Circulation*. 2016;133:1637-1644. DOI: 10.1161/CIRCULATIONAHA.115.019406.)

Key Words: amiodarone ■ atrial fibrillation ■ catheter ablation ■ heart failure

Transcatheter ablation represents a valid treatment option in patients with drug-refractory symptomatic atrial fibrillation (AF).[1] The majority of catheter ablation trials have mainly enrolled patients with preserved left ventricular (LV) systolic function. In these patients, the ablative treatment has been shown to be effective in reducing morbidity,[2–4] improving the quality of life (QoL),[3–6] and improving functional capacity.[5–7]

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Received July 29, 2015; accepted February 25, 2016.

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Presented at the ACC (American College of Cardiology) Annual Meeting, March 14-16, 2015, San Diego, CA.

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However, a significant number of patients with AF also have LV systolic dysfunction. AF and heart failure (HF) frequently coexist and are often associated with several common predisposing risk factors such as hypertension, coronary artery disease, structural heart disease (nonischemic, valvular), diabetes mellitus, obesity, and obstructive sleep apnea .[8,9] Importantly, the prevalence of AF increases with HF severity, ranging from 5% in functional class I patients to ≈50% in class IV patients.

Also, the prevalence of HF in patients with AF has been estimated at 42%.[8] The combination of HF and AF leads to deleterious hemodynamic and symptomatic consequences. Rhythm control with antiarrhythmic drugs (AADs) has not shown satisfactory results in randomized trials both in patients with or without HF.[9–12]

The Comparison of Pulmonary Vein Isolation Versus AV Nodal Ablation With Biventricular Pacing for Patients With Atrial Fibrillation With Congestive Heart Failure (PABA CHF) trial showed that pulmonary vein isolation (PVI) was superior to atrioventricular node ablation with biventricular pacing[13] in patients with AF and HF, improving their cardiac function, exercise capacity, and QoL; however, Jones et al[14] showed that this benefit was achieved after more than a single procedure.

We sought to evaluate whether catheter ablation is superior to amiodarone (AMIO) for the treatment of persistent AF in patients with HF in a randomized controlled trial.

Methods

Study Design

Ablation vs Amiodarone for Treatment of Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted ICD/CRTD (AATAC) was a randomized study assessing whether catheter ablation is superior to AMIO for the treatment of AF. Patients ≥18 years of age with persistent AF, dual-chamber implantable cardioverter defibrillator or cardiac resynchronization therapy defibrillator, New York Heart Association functional class II to III, and LV ejection fraction (LVEF) ≤40% within the past 6 months were enrolled at multiple centers. Patients were excluded if AF was caused by a reversible etiology, and if they had valvular or coronary heart disease requiring surgical intervention, early postoperative AF (within 3 months of surgery), or a life expectancy ≤2 years. Other exclusions included prolonged QT interval, hypothyroidism, history of severe pulmonary disease, and liver failure. Patients receiving a regular dose of AMIO (≥200 mg/d) were also excluded. The follow-up period of the study was 24 months. A flow chart showing the study design is presented in Figure 1.

Sample Size and Power

With the use of a log-rank test, the study was designed to detect at least 20% increase in success rate (30%–50% null hazard rate, 0.6; hazard ratio, 0.575) at 24 months follow-up at a 2-sided type I error (α) of 0.05, and 80% power. With 30% oversampling for attrition, a total of 200 patients (100 per group) were required to provide the power.

Randomization Procedure

Eligible subjects were enrolled after signing informed consent approved by the institutional review boards of the respective institutions, and were randomly assigned (1:1 ratio) to undergo catheter ablation for AF (group 1) or to receive AMIO (group 2).

A computerized central randomization scheme was generated using block randomization, and sets of randomly selected blocks were provided to the investigating sites.

Primary End Point

Long-term procedural success was the primary end point for this study. Procedural success was defined as freedom from AF, atrial flutter, or atrial tachycardia of >30 seconds duration off AADs at follow-up.

In the ablation arm, a second ablation procedure could be performed during the blanking period (3 months). After the blanking period, any atrial arrhythmia was considered a recurrence.

Secondary end points included complications, all-cause mortality, AF- and HF-related unplanned hospitalizations during the postablation follow-up, change in LVEF, 6-minute walk distance (6MWD), and QoL measured by Minnesota Living with Heart Failure Questionnaire (MLHFQ). Unplanned hospitalization was defined as a hospital admission during the postindex procedure follow-up for arrhythmia-related causes or symptoms, signs, or complications of HF. Planned readmissions, such as hospitalization for repeat ablation procedures, were not counted as outcomes in this measure.

Ablation

In brief, dofetilide was discontinued 4 to 5 days before ablation, whereas patients on low-dose AMIO (up to 200 mg daily) were allowed to discontinue the drug after the blanking period.

In all patients, a double transseptal puncture was performed. Intravenous heparin was given with a target activated clotting time of 300 to 400 seconds. A circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA) was used to guide the ablation. Intracardiac echocardiography could be used to guide transseptal catheterization and for anatomic orientation. An open-irrigation tip catheter (Thermocool, Biosense Webster) was used for ablation.

The main goal of the ablation procedure was pulmonary vein antrum isolation. Pulmonary vein antrum isolation was extended down to the coronary sinus and to the left side of the interatrial septum, along with extensive ablations on the left atrial posterior wall with the aim to achieve isolation of the entire left atrial posterior wall, which was defined as complete electric silence on the left atrial posterior wall confirmed by the absence of near-field atrial activity on the circular mapping catheter that was placed on the left atrial posterior wall. In addition, the superior vena cava was empirically isolated when pulmonary vein (PV)–like potentials were found. Additional linear lesion ablation of complex fractionated electrograms and elimination of non-PV triggers were advised but performed according to the preference of the center or the operator. Antiarrhythmic medications could be restarted at the discretion of the treating physician during the blanking period. A redo procedure within the first 3 months follow-up (blanking period) was not considered recurrence.

AMIO Treatment

Treatment with AMIO was initiated in the ambulatory setting.

AMIO therapy was initiated with a loading dose of ≈10 g in the first 2 weeks after randomization. This loading dose was given in divided doses: 400 mg given orally twice a day for 2 weeks followed by 400 mg each day for the next 2 weeks. Once the loading phase was completed, the maintenance dose of AMIO was 200 mg a day. However, 27 patients (12 in the ablation group and 15 in the AMIO group) receiving low-dose AMIO (<200 mg/d) were also included in the study. Digoxin was discontinued if possible, or the dose was at least reduced by 50%.

Screening pulmonary function tests and chest radiography were performed at baseline, and pulmonary function tests were performed yearly thereafter. Liver and thyroid function tests were assessed at baseline and every 6 months thereafter.

Congestive Heart Failure Management

All patients were on the optimal tolerated medical therapy for congestive heart failure. Optimal therapy included angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in angiotensin-converting enzyme–intolerant patients along with β-blockers, diuretics, and digoxin when appropriate.

For those patients intolerant to angiotensin-converting enzyme / angiotensin receptor blockers, a combination of hydralazine and isosorbide dinitrate was recommended. New York Heart Association class

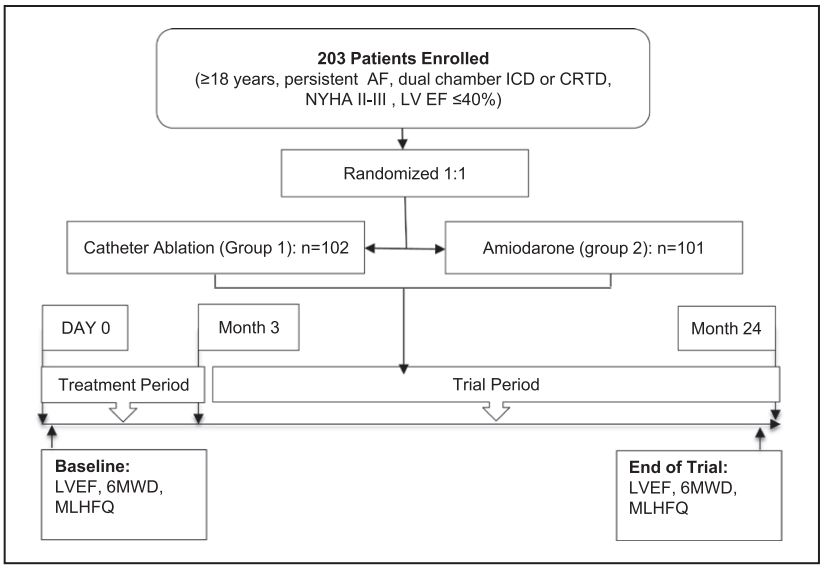

Figure 1. Flow chart of the study design showing enrollment, randomization, and evaluation time points for outcome measures. AF indicates atrial fibrillation; CRTD, cardiac resynchronization therapy defibrillator; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MLHFQ, Minnesota Living with Heart Failure questionnaire; 6MWD, 6-minute walk distance; and NYHA, New York Heart Association.

III patients were considered for treatment with spironolactone, whereas New York Heart Association class IV patients were excluded.

Left Ventricular Ejection Fraction

In all patients standard 2D and Doppler echocardiography was performed. LVEF was quantified by using a modified biplane Simpson rule in 2- and 4-chamber apical views. The LVEF measurements were performed by operators blinded to the randomization group and to the study end points.

Minnesota Living With Heart Failure Questionnaire

QoL was measured at baseline and 24 months of follow-up by using the MLHFQ survey. It is a 21-item, self-administered, validated questionnaire that measures the effects of HF and its treatment on an individual's QoL. The MLHFQ produces a total score ranging from 0 to 105. Lower scores indicate better QoL.[15,16]

6-Minute Walk Distance

Following the same schedule as the MLHFQ survey, 6MWD was obtained at baseline and 24 months, for objective evaluation of improvement in functional exercise capacity. It is a widely accepted test with good reliability in patients with congestive heart failure.[17] It measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes.[18]

Time Course

The time course for the trial was divided into a treatment period followed by the trial period.

The treatment period included the first 3 months postenrollment or postprocedure during which outcome data were not collected, repeat ablation could be performed and titration of AMIO dosages could be considered. The trial period started at the end of the treatment period and continued for 21 months (the total study duration was 24 months). For patients undergoing repeat ablation, cardioversion, or AMIO titration within the first 3 months, the treatment period started after the repeat procedure or AMIO dosage optimization. All outcome data were collected during this 21-month trial period.

Follow-Up

ECG, echocardiogram, clinical assessment with determination of New York Heart Association class, MLHFQ, and 6MWD were obtained at baseline and at 24 months follow-up. Clinic visit at 3 months postprocedure or post-AMIO initiation included echocardiogram, ECG, and assessment of adverse and serious adverse events.

Arrhythmia recurrence was evaluated by using remote monitoring capabilities on implanted devices, with device interrogation at 3, 6, 12, and 24 months follow-up. Adverse events were further collected at the end of the study.

Statistical Analysis

Demographic Baseline Characteristics

Descriptive analysis was performed summarizing the age, sex, comorbidities, procedural parameters, and other relevant baseline risk factors. The continuous variables were reported as mean±standard deviation. The categorical variables were reported as number of cases (n) and percentage. Normality of the analysis variables were tested using Shapiro-Wilk test. If the normality assumption was found to be violated, then appropriate nonparametric tests were used.

Efficacy Evaluation

The efficacy analysis was conducted for the intent-to-treat population. The intent-to-treat population consisted of all randomly assigned patients.

Primary End Point

Subjects who were recurrence-free at the end of follow-up were censored at the analysis time point, and AF-free time was defined as time from randomization to censor date. Survival curves were constructed by using the Kaplan–Meier method, and the primary null hypothesis was tested using the log-rank test; a 2-sided P value of <0.05 was considered statistically significant.

Secondary End Points

The mortality and unplanned hospitalization rates were summarized across study groups. Patients requiring at least 1 rehospitalization were counted for this end point; time to first such hospitalization was analyzed by using the survival analysis technique. Death from any cause within the follow-up period was considered for mortality analysis and was compared between the groups using the log-rank test. Change in LVEF, 6MWD, and MLHFQ were assessed by using analysis of covariance model (SAS GLM procedure) with grouping variable as factor and baseline value as covariate.

Multivariable Analysis

Multivariable Cox regression model was used for assessing independent predictors of AF-free survival and overall survival after adjusting for potential confounders.

Apart from covariates showing significant univariate association, potential confounders of known or expected clinical relevance, regardless of their statistical significance at univariate analysis were considered for entering into the multivariable model.

Confounders adjusted in the multivariable model included age, sex, diabetes mellitus, and hypertension. The proportional-hazard assumption was tested by Schoenfeld residual analysis. The hazard ratio and 95% confidence interval (CI) were computed and presented in the results.

All tests were 2-sided and a P value <0.05 was considered statistically significant. Analyses were performed by using SAS 9.2 (SAS Institute Inc, Cary, NC).

Results

Patient Characteristics

In total, 866 patients were screened, 331 were eligible for inclusion, and 203 consented and were included in the study and randomly assigned to receive catheter ablation (group 1, n=102, left atrial diameter 47±4.2 mm, LVEF 29±5%) or AMIO (group 2, n=101, left atrial diameter 48±4.9 mm, LVEF 30±8%). Baseline characteristics of the study population are presented in Table 1.

In the 102 patients undergoing catheter ablation, PVI was performed in 22 patients, and PVI plus posterior wall isolation was done in 80 patients. The total procedure time and radiofrequency time were 168±72 and 66±34 minutes, respectively.

Arrhythmia Recurrence

During the blanking period 52 (51%) in the AMIO group and 3 (3%) in the ablation group underwent cardioversion. After the blanking period, 25 (25%) and 15 (15%) patients had cardioversion in the AMIO and ablation group, respectively. All randomized patients were included in the survival analysis.

Table 1. Baseline Characteristics of Study Population

	Group 1 (Catheter Ablation, n=102)	Group 2 (Amiodarone, n=101)
Age, y	62±10	60±11
Male, n (%)	77 (75)	74 (73)
AF duration, mo	8.6±3.2	8.4±4.1
BMI, kg/m^2	30±8	29±4
Hypertension, n (%)	46 (45)	48 (48)
Diabetes mellitus, n (%)	22 (22)	24 (24)
Coronary artery disease, n (%)	63 (62)	66 (65)
LA diameter, mm	47±4.2	48±4.9
LVEF, %	29±5	30±8
6MWD, meters	348±111	350±130
MLHFQ Score	52±24	50±27
OSA, n (%)	46 (45)	48 (48)
ACEI or ARB, n (%)	94 (92)	89 (88)
Aldosterone antagonists, n (%)	46 (45)	51 (50)
β-Blockers, n (%)	78 (76)	81 (80)

Continuous variables are summarized as mean±standard deviation, and categorical variables are reported as number of cases (n) and percentage. ACEI indicates angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; LVEF, left ventricular ejection fraction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; 6MWD, 6-minute walk distance; and OSA, obstructive sleep apnea,

At the end of the study, 71 (70%; 95% CI, 60%–78%) patients in group 1 were recurrence free after average 1.4±0.6 procedures in comparison with 34 (34%; 95% CI, 25%–44%) in group 2 (log-rank P<0.001). Of the 67 patients having recurrence in group 2, treatment failed in 7 (10.4%) after withdrawal of AMIO because of adverse effects (4 had thyroid toxicity, 2 pulmonary toxicity, and 1 patient developed liver dysfunction).

Because repeat interventions were allowed during the blanking period, and followed up for 24 months after such intervention, these patients accrued a maximum 27 months of follow-up. We performed a sensitivity analysis at the 24-month cutoff. At this time point, 73 (72%; 95% CI, 62%–79%) in group 1 and 37 (37%; 95% CI, 28%–47%) in group 2 were arrhythmia free (log-rank P<0.001).

In group 1, higher success was reported in patients undergoing PVI and posterior wall isolation in comparison with PVI alone (63 [79%; 95% CI, 68%–86%] and 8 [36%; 95% CI, 17%–56%], respectively; P<0.001). Success rate of ablation in the different centers after a single procedure ranged from 29% to 61%. No patient was lost to follow-up during the study period. The Kaplan–Meier curve comparing recurrence across the study groups is presented in Figure 2.

Predictor of Arrhythmia Recurrence

We first investigated the association of AF recurrence in an unadjusted Cox model. In the univariate model, treatment with AMIO, LVEF, and diabetes mellitus showed significant association. The results of univariate analysis are presented in Table 2.

After adjusting for covariates in multivariable Cox model, the treatment of patients on AMIO therapy was found to be significantly more likely to fail (hazard ratio, 2.5; 95% CI, 1.5–4.3; P<0.001) in comparison with catheter ablation. Besides that, diabetes mellitus showed a statistically significant association with higher recurrence (hazard ratio, 1.1; 95% CI, 1.07–1.26; P=0.01).

Unplanned Hospitalization and Death

Over the 2-year follow-up, the unplanned hospitalization rate was substantially lower in group 1 (32 [31%; 95% CI, 20%–41%] and 58 [57%; 95% CI, 51%–69%] in group 2, log-rank P<0.001), showing 45% relative risk reduction (relative risk, 0.55; 95% CI, 0.39–0.76). The NNT to avoid 1 unplanned hospitalization was 3.8 patients. In addition, there were significantly fewer deaths (from all causes) in group 1 (8 [8%] group 1 and 18 [18%] group 2; log-rank P=0.037), with 56% relative risk reduction for mortality in patients receiving catheter ablation (relative risk, 0.44; 95% CI, –0.20 to 0.96; NNT 10 patients).

Change in LVEF, 6MWD, and MLHFQ

At baseline, the LVEF, 6MWD, and MLHFQ scores were not different between the catheter ablation and AMIO groups (Table 1).

With the exception of the 26 patients who died during the study period, end-of-study measurements were available for all 177 (94 in group 1 and 83 in group 2). In comparison with group 2, better improvement in terms of change in

LVEF (8.1±4 [median, 8.3%] versus 6.2±5.0 [median, 5.0%], *P*=0.02), 6MWD (22±41 [median, 19 m] versus 10±37 [median, 6 m], *P*=0.02), and reduction in MLFHQ score (11±19 [median, 10] versus 6±17 [median, 5.0]; *P*=0.04) was observed in the group 1 population. When stratifying the population by recurrence status, recurrence-free patients (n=91) experienced significantly better improvement in all parameters than those who experienced recurrence (n=86; Table 3).

Procedural Complications

In group 1, 2 (1.96%) patients had groin hematoma, and 1 patient (0.98%) had pericardial effusion that was conservatively managed with fresh-frozen plasma and protamine.

Discussion

Main Findings

This is the first multicenter randomized study showing that in patients with HF and persistent AF, catheter ablation is superior to AMIO in achieving freedom from AF at the long-term follow-up. Importantly, ablation improved QoL and exercise capacity and reduced unplanned hospitalization and overall mortality. These findings are clinically relevant, especially in light of the socioeconomic advantages that arise from the reduced rehospitalization and mortality in HF patients.

HF and AF are the most common cardiac conditions in Western countries and often coexist. Pharmacological rate versus rhythm control is a controversial topic in the literature for the treatment of AF especially in light of the main results of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) and Rate Control versus Electrical Cardioversion (RACE) trials.[11,12]

A subanalysis of the AFFIRM trial, however, clearly showing the association of sinus rhythm but not AADs with improved survival may reflect the fact that currently available AADs are neither highly efficacious nor completely safe. In addition, the results suggested that an effective and safe method to maintain sinus rhythm may improve survival. The rationale for a rhythm-control approach includes the possibility of fewer symptoms, improved exercise tolerance, lower risk of stroke, superior QoL, and better survival, if sinus rhythm can be maintained.[11,12]

In patients with HF and AF, the available AADs to maintain sinus rhythm recommended by the international guidelines are limited to AMIO and dofetilide. These drugs are associated with significant adverse side effects and drug interaction that often lead to drug discontinuation.[19–24] The long-term use of AMIO is associated with significant pulmonary, hepatic, and thyroid toxicity, in addition to severe bradycardia.[24] Dofetilide requires hospitalization for careful monitoring because of severe QT-interval prolongation and torsades de pointes in up to 3% of patients, and its use is limited in patients with renal dysfunction, which is a common finding in HF patients.[22]

AF ablation might represent the ideal therapy that restores sinus rhythm without the adverse effects of AADs. Successful AF ablation results in significant improvements of left ventricular function, exercise tolerance, symptoms, and QoL[4] irrespective of the level of preprocedural rate control, suggesting that factors other than rate control (eg, loss of atrial contraction, atrioventricular dyssynchrony) drive the deterioration of cardiac function.

AF ablation has shown superior outcome achieving freedom from AF in comparison with AADs in several randomized controlled trials that enrolled paroxysmal AF patients with a normal heart. The success rate in patients who have persistent and long-standing persistent AF is variable in the literature. The variation in procedural outcome depends on different factors such as age, sex, AF types, structural heart disease, ablation technique, and operator experience.[25–29]

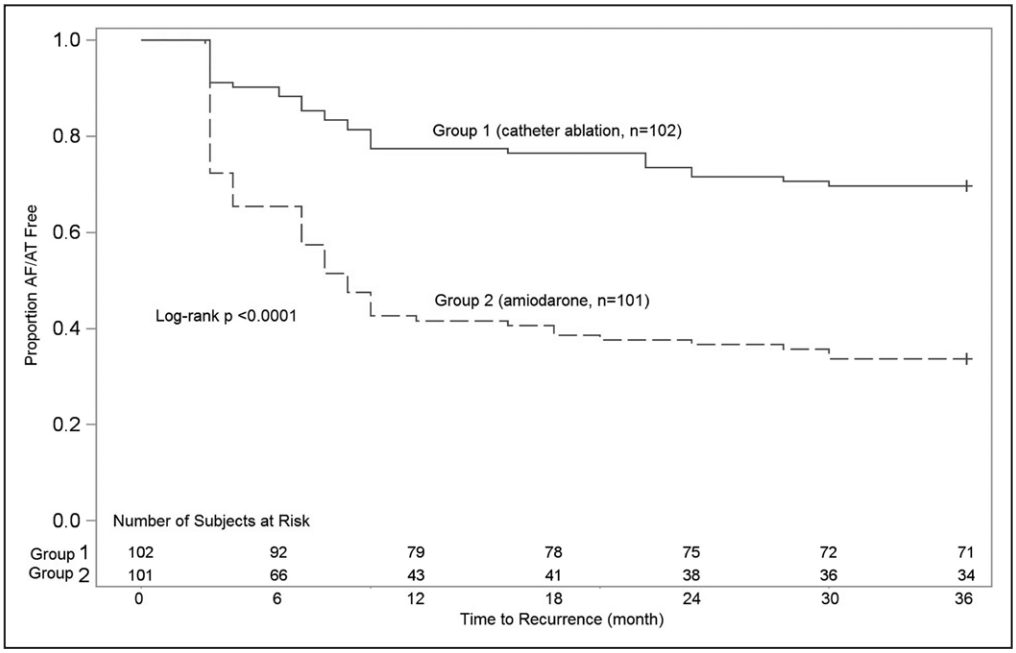

Figure 2. Kaplan–Meier curve comparing AF-free survival between patients undergoing catheter ablation (group 1) and those receiving amiodarone therapy (group 2). At end of the study, 71 (70%; 95% CI, 60%–78%) patients in group 1 were recurrence free in comparison with 34 (34%; 95% CI, 25%–44%) in group 2 (log-rank *P*<0.001). AF indicates atrial fibrillation; AT, atrial tachycardia; and CI, confidence interval.

Table 2. Variables Showing Univariate Association With AF Recurrence: Results From Cox Model

Variables	Hazard Ratio	95% Confidence Intervals	*P* Value
Amiodarone treatment	3.00	(1.96–4.61)	<0.0001
Sex	1.14	(0.92–1.41)	0.22
Age, y	0.99	(0.98–1.019)	0.94
BMI	0.99	(0.94–1.03)	0.59
LVEF, %	0.96	(0.93–0.99)	0.01
Hypertension	1.12	(0.93–1.36)	0.24
Left atrial size	1.02	(0.99–1.05)	0.18
Diabetes mellitus	2.22	(1.31–3.75)	0.003

AF indicates atrial fibrillation; BMI, body mass index; and LVEF, left ventricular ejection fraction.

Overall, a higher recurrence rate has been shown in HF patients,[3–6] and this might explain why AF ablation is not widely used as a rhythm control strategy in this subset of the patient population.

In agreement with these reports, we observed substantial improvement in 6MWD, LVEF, and MLHFQ scores in recurrence-free patients. The pathophysiology underlying HF and AF resulting in compromised stroke volume is the likely basis of altered exercise tolerance.[15–18,30] Thus, the significant improvement in 6MWD could reflect betterment in cardiac contractility and rhythm resulting in restoration of a more efficient cardiac contraction following successful ablation. Our results further corroborated the correlation between ablation success and improvement in QoL. This observation can be attributed to reinstatement of stable sinus rhythm, lesser burden of symptoms, and reduction in the use of health care resources and better well-being.[31–33] Results from a randomized trial conducted by MacDonald et al[7] comparing ablation versus rate-control medications in patients with persistent AF and LVEF <35% reported no significant differences between groups in terms of improvement in ejection fraction measured by magnetic resonance (MR), exercise tolerance, or QoL. However, it is difficult to compare our findings with their results for several reasons: (1) different study design: ablation versus rhythm control medication in our trial and ablation versus rate-control measures in their study: (2) small sample size (n=41); and (3) different ablation approach: majority (78%) of our patients received PVI and posterior wall isolation plus ablation of complex fractionated atrial electrograms and non-PV triggers as needed, which was the most likely reason behind the higher success rate than their patients who underwent PVI with a roof line and ablation of complex fractionated atrial electrograms. Recently published randomized trials have demonstrated suboptimal outcomes and no added advantage when linear lesions are performed in conjunction with PVI.[34,35] Other factors responsible for the higher success rate in our study population could be the operator experience and the improved mapping and ablation technology in recent years that resulted in better PV encirclement. The results from this early study also contrast with more recent findings from the Catheter Ablation Versus Medical Rate Control for Atrial Fibrillation in Patients With Heart Failure (ARC-HF) and Catheter Ablation Versus Medical Treatment of Atrial Fibrillation in Heart Failure (CAMTAF) trials, which both showed significant improvement in exercise capacity and QoL with AF ablation in comparison with pharmacological rate control.[14,36]

The CAMTAF trial also showed a significant improvement of LVEF after 6 months of follow-up with AF ablation in comparison with pharmacological rate control (+8.1 [95% CI, 3.0–13.1] versus –3 [95% CI, –7.7 to 0.5]; *P*<0.001).[36]

Similarly, the ARC-HF trial reported a trend toward a higher LVEF improvement with AF ablation (mean difference, +5.6% (95% CI, –0.1 to +11.3; *P*=0.055) after 12 months of follow-up.[14]

Our trial shows that, after an average of 1.4 procedures, a clinically relevant freedom from AF can be achieved in these patients. Of interest is the finding that, when sorting the results by ablation technique, a poor success was observed in patients who underwent PV ablation alone in comparison with patients undergoing a more extensive ablation approach.

The coexistence of AF and HF increases the risk of unplanned hospitalization and significantly impacts healthcare costs.[37] Therefore, the reduction of unplanned hospitalization and mortality are relevant potential benefits of the ablation strategy.

Study Limitation

We acknowledge certain limitations in our trial. (1) Although no formal comparison with a rate control strategy was performed in this study, we would like to emphasize that AMIO is also considered in the guidelines as a rate control drug. In addition, 76% of the ablation group and 80% of the AMIO group received β-blockers at the tolerated dosage. (2) The 2 other alternative AADs available for these patients, sotalol and dofetilide, were not tested in this trial, because dofetilide is not available in countries other than the United States and the patients were already on different β-blockers that they could tolerate. Moreover, AMIO is the most effective antiarrhythmic drug; therefore, these results could be extended to dofetilide

Table 3. Change in LVEF, 6MWD, and MLHFQ Score by Recurrence Status

	No Recurrence (n=91)		Recurrence (n=86)		*P* (Comparing Change Between Groups)
	Baseline	Change (Median)	Baseline	Change (Median)	
LVEF, %	28.8±10	9.6±7.4 (9.4)	30.2±9	4.2±6.2 (4.0)	<0.001
6MWD, meters	347±113	27±38 (24)	352±128	8±42 (2)	<0.001
MLHFQ	53±24	–14±18 (–12)	49±26	–2.9±15 (–2.2)	<0.001

Data are summarized as mean±standard deviation. LVEF indicates left ventricular ejection fraction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; and 6MWD, 6-minute walk distance.

and sotalol. (3) Finally, our patients were followed up for 24 months. Although a longer follow-up would be desirable, the follow-up duration in our study was longer than many other studies in the field of ablation. In addition, all patients had an implanted device, and success/failure was obtained by device interrogation.

Conclusion

This multicenter randomized study shows that catheter ablation of AF is superior to AMIO in achieving freedom from AF at long-term follow-up and reducing unplanned hospitalization and mortality in patients with HF and persistent AF. The potential socioeconomic repercussion of these results will require further investigation.

Disclosures

Dr Di Biase is a consultant for Biosense Webster, Stereotaxis and St Jude Medical. Dr Di Biase received speaker honoraria/travel from Medtronic, EPiEP, Janssen, Pfizer, Bristol Meyers, Boston Scientific, and Biotronik. Dr Natale received speaker honoraria from Boston Scientific, Biosense Webster, St. Jude Medical, Biotronik, and Medtronic. Dr Natale is a consultant for Biosense Webster, St Jude Medical, and Janssen. Dr Burkhardt is a consultant for Biosense Webster and Stereotaxis. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Heart failure and atrial fibrillation are common cardiac conditions that often coexist. This is the first randomized study to show that, in patients with heart failure and persistent atrial fibrillation, catheter ablation is superior to amiodarone (the most used drug in these patients) in achieving freedom from atrial fibrillation at long-term follow-up. Importantly, ablation reduced rehospitalization and overall mortality and improved quality of life and exercise capacity. This study suggests that clinicians should consider catheter ablation sooner in this patient population.

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