ORIGINAL RESEARCH

Catheter Ablation of Atrial Fibrillation in U.S. Community Practice—Results From Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)

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Background—The characteristics of patients undergoing atrial fibrillation (AF) ablation and subsequent outcomes in community practice are not well described.

Methods and Results—Using the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF), we investigated the prevalence and impact of catheter ablation of AF. Among 9935 patients enrolled, 5.3% had previous AF ablation. Patients with AF ablation were significantly younger, more frequently male, and had less anemia, chronic obstructive pulmonary disease, and previous myocardial infarction ($P<0.05$ for all analyses) than those without previous catheter ablation of AF. Ablated patients were more likely to have a family history of AF, obstructive sleep apnea, paroxysmal AF, and moderate-to-severe symptoms ($P<0.0001$ for all analyses). Patients with previous ablation were more often in sinus rhythm on entry into the registry (52% vs. 32%; $P<0.0001$). Despite previous ablation, 46% in the ablation group were still on antiarrhythmic therapy. Oral anticoagulation was prescribed in 75% of those with previous ablation versus 76% in those without previous ablation ($P=0.5$). The adjusted risk of death (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.52 to 1.18; $P=0.2$) and cardiovascular (CV) hospitalization (HR, 1.06; 95% CI, 0.90 to 1.26; $P=0.5$) were similar in both groups. Patients with incident AF ablation had higher risk of subsequent CV hospitalization than matched patients without incident ablation (HR, 1.67; 95% CI, 1.24 to 2.26; $P=0.0008$).

Conclusions—In U.S. clinical practice, a minority of patients with AF are managed with catheter ablation. Subsequent to ablation, there were no significant differences in oral anticoagulation use or outcomes, including stroke/non–central nervous system embolism/transient ischemic attack or death.

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Since its original description by Haïssaguerre et al., catheter ablation of atrial fibrillation (AF) by electrically isolating the pulmonary veins has evolved over the past 15 years and is now a commonly performed procedure in many major centers throughout the world.[1,2] Small, randomized, clinical trials have demonstrated that catheter ablation results in increased freedom from AF, when compared with medical therapy.[3] In general, the patients included in these trials have been relatively young (mid to late fifties) with drug-refractory paroxysmal AF and minimal comorbidity.[3,4] Hence, there may be considerable bias in the absolute event rates reported. Consistent with this evidence base, the only class I indication for ablation of AF in the 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society Guideline for the Management of Patients With Atrial Fibrillation is symptomatic paroxysmal AF in patients who are refractory or intolerant to at least 1 class I or III antiarrhythmic medication.[2]

Although differences in characteristics between patients with rhythm- or rate-controlling strategies have been described, with the patients on rhythm control being younger

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An accompanying Data S1 is available at http://jaha.ahajournals.org/content/4/5/e001901/suppl/DC1

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and with less comorbidity,[5,6] the characteristics of the subset of patients undergoing AF ablation in community practice, as opposed to randomized trial populations, is not well described. Some registry data indicate that patients referred for AF ablation in community practice may be substantially older than those in the randomized, clinical trials,[1,7] but further details on patient and/or arrhythmia characteristics are lacking. The objective of the present study was to describe the utilization of catheter ablation in a contemporary U.S. clinical practice and describe the characteristics and subsequent outcomes in these patients.

Methods

The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) study is a contemporary registry of outpatients in the United States with AF managed by a variety of providers, including internists, cardiologists, and electrophysiologists. Its design has been described in detail elsewhere.[8] In brief, a nationally representative sample of sites was invited to participate and an adaptive design was used to ensure provider and geographical heterogeneity, although enrollment was not formally stratified. Consecutive patients with AF, meeting all the inclusion criteria (at least 18 years of age, electrocardiographic [ECG] evidence of AF, providing informed consent) and none of the exclusion criteria (life expectancy of less than 6 months or AF secondary to reversible conditions) were enrolled. For the purpose of this analysis, patients with a history of surgical or hybrid maze or missing data for previous AF catheter ablation were excluded.

Data collection included demographics, past medical history, type of AF and previous interventions, ongoing antithrombotic therapy (with monitoring), vital signs, laboratory studies, ECG findings, and echocardiographic findings. Previous and incident electrophysiology interventions are also captured, including both catheter-based and surgical ablations for AF and atrial flutter. In ORBIT-AF, follow-up data collection occurs at 6-month intervals for a minimum of 2 years. For the current study, all available follow-up for the outcomes was used for analyses.

Statistical Analyses

The entire baseline ORBIT-AF population included 10 132 patients enrolled between June 29, 2010 and August 9, 2011 from 176 sites. The current analysis excluded 197 patients: 194 resulting from surgical or hybrid maze and 3 from missing data for AF catheter ablation at baseline. This yielded a final study population of 9935 patients from 176 sites.

Data are presented as frequencies and percentages for categorical variables and medians (interquartile range) for continuous variables. Groups are compared using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

To identify factors associated with the binary outcome "previous catheter ablation," a multivariable hierarchical logistic regression model was used, with site included as a random effect to account for site variability in ablation. Variable selection was conducted by backward selection with a significance level of 0.05. The list of candidate variables is provided in Data S1. Additionally, Cox frailty models (which account for clustered patients within a site) were used to examine the association of previous catheter ablation at baseline and time from enrollment to outcomes in follow-up (all-cause death, cardiovascular [CV] hospitalization or death, CV death, CV hospitalization, the composite of death, stroke, transient ischemic attack [TIA] or new-onset congestive heart failure [CHF], and major bleeding) among 9451 patients (484 patients were excluded because of no follow-up data). Each outcome model was adjusted for all independent predictors previously identified from a prespecified list of candidate variables using backward selection and a significance level of 0.05. Last, to examine the association between previous catheter ablation at baseline and repeat hospitalizations (all cause, CV, bleeding and non-CV, and nonbleeding), negative binomial regression models were used. Variables from the all-cause hospitalization adjustment model were used for adjustment.

In the preceding regression models, continuous variables were evaluated for nonlinearity with the outcome and nonlinear relationships were addressed by using linear splines. Missing data were multiply imputed and final estimates and SEs reflect the combined analysis over 5 imputed data sets. Variable selection was conducted on the first imputed data set. Rates of missingness were less than 2% for all candidate variables in the models, with the following exceptions: level of education (4%); serum creatinine (8%); hematocrit (11%); estimated glomerular filtration rate (8%); left ventricular ejection fraction (LVEF; 11%); and left atrial diameter (16%). Results were presented as odds/hazard/rate ratios (OR/HR/RR) with corresponding 95% confidence intervals (CIs) and *P* values.

To examine the association between incident catheter ablation and subsequent outcomes, we employed propensity score matching to construct a matched cohort between patients with catheter ablation after enrollment in the registry (incident catheter ablation) and overall (non-catheter-ablated) patients having a similar disease course. A propensity score for having catheter ablation during follow-up versus no catheter ablation was created by logistic regression. Risk factors included in this model are reported in Data S1. Missing data of the risk factors were imputed to the mode. Catheter-ablated patients were matched to non-catheter-ablated patients using a 2 to 1 match matching exactly on duration of AF, AF type, and ever on rhythm control treatment strategy and matching on the linear predictor (X*beta) from the propensity score model using a caliper for matching of 0.20*std(X*beta) using a greedy algorithm. Ultimately, 266 catheter-ablated patients were matched to 515 non-catheter-ablated patients. The outcome models were fit using the stratified Cox regression model with each case/control group forming a strata. Results were presented as HRs with corresponding 95% CIs and *P* values.

All statistical analyses of the aggregate, deidentified data were performed by the Duke Clinical Research Institute using SAS software (version 9.3; SAS Institute Inc., Cary, NC). All *P* values were 2 sided. The ORBIT-AF Registry is approved by the Duke Institutional Review Board, and all participating sites obtained institutional review board approval pursuant to local requirements. All subjects provided written, informed consent.

Results

Baseline Characteristics

Overall, 527 patients (5.3%) had a previous catheter ablation of AF at baseline. Median time between catheter ablation and inclusion in the study was 18 (5 to 51) months. Table 1 shows the complete set of baseline characteristics in the overall study population and by previous catheter ablation of AF. Compared to nonablated patients, patients with a previous catheter ablation were younger (67 [59 to 74] vs. 75 [67 to 82] years; $P<0.0001$), more often male, of white race, had a higher level of education, and were more often privately insured. They had a lower prevalence of hypertension, hyperlipidemia, anemia, diabetes, chronic obstructive pulmonary disease, and dementia. Moreover, patients with previous catheter ablation of AF were less likely to have suffered from a stroke or previous myocardial infarction. The notable exception was obstructive sleep apnea, which was more common in patients with previous catheter ablation of AF (26% vs. 18%; $P<0.0001$).

AF Characteristics at Baseline

Baseline AF characteristics are summarized in Table 2. Patients with previous catheter ablation more often had a family history of AF, had longer history of AF, and were more likely to have paroxysmal AF (63% vs. 50%; $P<0.0001$). Patients with previous ablation more frequently exhibited sinus rhythm on their baseline ECG (52% vs. 32%; $P<0.0001$). They were more likely to have undergone cardioversion, and the vast majority had been treated with antiarrhythmic drugs (82% vs. 43%; $P<0.0001$). They were also more symptomatic (31% vs. 16% with severe or disabling symptoms; $P<0.0001$) and were more often on a rhythm-controlling strategy at baseline (57% vs. 30%; $P<0.0001$). Their $CHADS_2$ score was lower compared to patients without previous catheter ablation of AF (mean±SD; 1.8±1.3 vs. 2.3±1.3; $P<0.0001$). Patients with previous AF ablation were more often treated by an electrophysiologist at baseline than those without previous ablation (42% vs. 15%; $P<0.0001$).

Antithrombotic Therapy by $CHADS_2$ Score and Previous AF Ablation

Antithrombotic therapy according to $CHADS_2$ score and previous AF ablation is summarized in Table 3. Three quarters of the patients in ORBIT-AF were on oral anticoagulation therapy at baseline, regardless of whether or not they had a history of catheter ablation of AF (75% vs. 76%; $P=0.5$). Dabigatran use was higher among patients with previous catheter ablation of AF (9.5% vs. 4.7%; $P<0.0001$), whereas warfarin was more common in nonablated patients (66% vs. 72%; $P=0.0036$). However, ablated patients were more likely to have been treated with warfarin in the past. In addition, use of aspirin was more common in patients with previous AF ablation. Both previously ablated and nonablated patients were highly likely to be on some form of antithrombotic therapy (95% vs. 95%; $P=0.8$).

Patients with a lower $CHADS_2$ score were less likely to be on oral anticoagulation therapy than those with higher scores, regardless of previous AF ablation. This was particularly evident for warfarin treatment (patients with previous catheter ablation: 66% [$CHADS_2$=0, $CHADS_2$=1, $CHADS_2\geq2$: 47%, 55%, 77%], $P<0.0037$; patients without previous catheter ablation: 72% [$CHADS_2$=0, $CHADS_2$=1, $CHADS_2\geq2$: 46%, 64%, 76%], $P<0.0001$), whereas the findings for dabigatran were less clear. Over half of the patients with a $CHADS_2$ score of 0 were on oral anticoagulation therapy in both groups. Of the patients with previous catheter ablation, 69 (13%) were within the 2-month period immediately postablation, when anticoagulation is recommended irrespective of $CHADS_2$-score.[2] As expected, the rate of oral anticoagulation treatment (warfarin or dabigatran) was high overall (87%), as well as across the different $CHADS_2$ score strata ($CHADS_2$=0, $CHADS_2$=1, $CHADS_2\geq2$: 79%, 83%, 94%, $P=0.2842$) in this group.

Factors Associated With Previous AF Catheter Ablation

Factors independently associated with previous catheter ablation of AF are summarized in Figure. In addition to being treated by an electrophysiologist (adjusted OR, 3.00; 95% CI, 2.31 to 3.90; $P<0.0001$), the factor with the strongest association with a higher likelihood of previous AF ablation was AF duration more than 12 months (adjusted

Table 1. Baseline Characteristics by Previous AF Ablation

	Overall (N=9935)	No Previous AF Ablation (N=9408)	Previous AF Ablation (N=527)	*P* Value
Age, y	75 (67 to 82)	75 (67 to 82)	67 (59 to 74)	<0.0001
Female	42	43	38	<0.0001
Race				
White	89	89	94	0.0008
Black or African-American	5.1	5.2	3.0	
Hispanic	4.3	4.4	1.5	
Other	1.4	1.4	1.0	
Level of education				
Some school	14	15	6.1	<0.0001
High school graduate	51	51	50	
College graduate	23	22	26	
Postgraduate	8.1	7.8	14	
Geographical region				
Midwest	25	25	30	0.0002
Northeast	26	26	27	
South	35	35	35	
West	14	15	8.2	
Private insurance	26	24	45	<0.0001
Medical history				
Smoking	48	48	48	0.8
Hypertension	83	84	74	<0.0001
Hyperlipidemia	72	72	67	0.0060
Anemia	18	18	13	0.0029
Diabetes	29	30	25	0.0265
Chronic obstructive pulmonary disease	16	16	13	0.0410
Obstructive sleep apnea	18	18	26	<0.0001
Previous myocardial infarction	16	16	11	0.0026
Heart failure	32	33	28	0.054
Implanted device	27	27	30	0.20
Moderate/severe mitral stenosis	1.3	1.3	0.6	0.14
Previous cerebrovascular events	16	16	13	0.0376
Stroke (all-cause)	8.7	8.9	5.5	0.0069
Nonhemorrhagic	7.9	8.0	5.1	0.0165
Hemorrhagic	0.7	0.8	0.2	0.13
Other intracranial bleeding	0.9	0.9	1.0	0.9
Gastrointestinal bleeding	9.0	9.2	6.1	0.0150
Cognitive impairment or dementia	3.1	3.2	0.6	0.0006
Frailty	5.8	5.9	2.9	0.0031
BMI, kg/m^2	29 (25 to 34)	29 (25 to 34)	31 (27 to 35)	<0.0001
Heart rate, bpm	70 (63 to 80)	70 (63 to 80)	71 (63 to 80)	0.9418
Systolic blood pressure, mm Hg	126 (116 to 138)	126 (116 to 138)	124 (115 to 134)	0.0121
Diastolic blood pressure, mm Hg	72 (66 to 80)	72 (66 to 80)	73 (68 to 80)	0.0213

Continued

Table 1. Continued

	Overall (N=9935)	No Previous AF Ablation (N=9408)	Previous AF Ablation (N=527)	*P* Value
Calculated creatinine clearance, mL/min per 1.73 m^2	69 (50 to 97)	69 (49 to 95)	92 (65 to 122)	<0.0001
Left ventricular ejection fraction >50%	70	70	76	0.0230
Left atrial diameter, cm	4.4 (3.9 to 5.0)	4.4 (3.9 to 5.0)	4.4 (3.9 to 4.9)	0.3

Continuous variables are presented as median and interquartile range. AF indicates atrial fibrillation; BMI, body mass index; bpm, beats per minute.

OR, 2.85; 95% CI, 2.05 to 3.96; $P<0.0001$). In contrast, the factors with the strongest association with a lower likelihood of previous AF ablation were increasing age (adjusted OR, 0.65; 95% CI, 0.58 to 0.72 per 5-year increase beyond 70 years; $P<0.0001$), severely reduced LVEF (adjusted OR, 0.41; 95% CI, 0.23 to 0.74; $P=0.0033$) and being of nonwhite race (Figure).

Previous AF Ablation and Associations With Outcome

Patients with a previous AF ablation had more repeat CV hospitalizations per 100 patient-years than without ablation in the unadjusted analysis (30.19 vs. 24.01; unadjusted RR, 1.26; 95% CI, 1.05 to 1.50; $P=0.0126$), but this difference was not statistically significant in the adjusted model (adjusted RR, 1.11; 95% CI, 0.93 to 1.33; $P=0.2289$). Table 4 summarizes repeat hospitalizations during follow-up. During follow-up, risks of all-cause mortality (unadjusted HR, 0.50; 95% CI, 0.33 to 0.75; $P=0.0008$), CV death (unadjusted HR, 0.46; 95% CI, 0.24 to 0.89; $P=0.0222$) as well as the composite endpoint of death, stroke/TIA, and CHF (unadjusted HR, 0.54; 95% CI, 0.39 to 0.74; $P=0.0001$) were significantly lower in patients with a previous AF ablation, compared to patients without. However, no statistically significant differences were noted in any outcome in the adjusted models. Table 5 summarizes the associations between outcome variables and previous AF ablation.

Incident AF Ablation and Associations With Outcome

During follow-up, 266 patients underwent a catheter ablation of AF. These patients were compared to 515 matched controls. Compared to controls, patients with an incident AF ablation had a lower rate of all-cause (1.60 vs. 2.00 events per 100 patient-years) and CV death (0.32 vs. 1.11 events per 100 patient-years), but these differences did not reach statistical significance (adjusted HR, 0.75; 95% CI, 0.27 to 2.08; $P=0.57$; and HR, 0.32; 95% CI, 0.05 to 2.01; $P=0.22$). Patients with incident ablation were more frequently hospitalized because of CV causes (36.14 vs. 21.62 events per 100 patient-years; adjusted HR, 1.67; 95% CI, 1.24 to 2.26; $P=0.0008$) than matched patients without incident ablation, whereas the other outcomes included were similar (Table 6).

Discussion

The major finding in our analysis is that catheter ablation is a relatively infrequent rhythm control intervention. Only a small minority (5%) of AF patients in this nation-wide community practice cohort were previously treated with catheter ablation. This is in line with the rather strict criteria for referring patients to catheter ablation according to current guidelines.[2] The proportion is very similar to the rates reported in the Euro Heart Survey, where the rate of ablation is 5% in paroxysmal AF and 4% in patients with persistent AF.[9] However, several studies illustrate that there are regional, as well as temporal, differences in utilization rates of AF ablation.[1,10,11] The rapidly growing number of patients being considered for AF ablation is well illustrated by the fact that, during follow-up in ORBIT-AF, the number of patients who had undergone a catheter ablation of AF increased by approximately 50%.

According to current guidelines, the main criteria for considering a patient with AF for ablation are symptoms, drug resistance, and type of AF (ie, primarily paroxysmal and persistent).[2] It is therefore reassuring to find that patients with a previous catheter ablation in ORBIT-AF were more symptomatic, had higher burden of previous antiarrhythmic drug therapy, and also more seldom had permanent or newly diagnosed AF. In addition, patients with previous ablation were younger and had less comorbidity. This indicates that current practice patterns are in line with professional society guidelines. Although patients with previous ablation were younger than their nonablated counterparts, their mean age was still substantially higher than the mean age of ablated patients in the randomized, clinical trials,[3,4] similar to previously reported registry data.[7] Randomized, clinical trial data for AF ablation in the elderly are lacking,[12] and, consequently, the current guidelines state that more research is needed to establish the role of catheter ablation of AF in the elderly.[2] Data on the comorbidity of patients undergoing

Table 2. AF History by Previous AF Ablation

	Overall (N=9935)	No Previous AF Ablation (N=9408)	Previous AF Ablation (N=527)	*P* Value
AF type				
First detected/new onset	4.8	5.1	0.4	<0.0001
Paroxysmal	50	50	63	
Persistent	17	16	22	
Long-standing persistent	28	29	14	
Family history of AF	15	14	24	<0.0001
Duration of AF diagnosis, months	47 (18 to 93)	45 (17 to 91)	69 (34 to 117)	<0.0001
Sinus rhythm on most recent ECG	33	32	52	<0.0001
EHRA symptom level				
No symptoms	38	39	26	<0.0001
Mild	45	45	43	
Severe	15	14	26	
Disabling	1.8	1.6	4.6	
$CHADS_2$ risk groups				
0	6.4	5.8	17	<0.0001
1	22	21	28	
≥2	72	73	55	
Previous treatment				
Oral anticoagulation therapy	82	81	92	<0.0001
Antiarrhythmic drug	45	43	82	<0.0001
Previous cardioversions	29	28	55	<0.0001
Current treatment				
Oral anticoagulation therapy	76	76	75	0.5
Antiarrhythmic drug	29	28	46	<0.0001
Rhythm strategy	31	30	57	<0.0001
Treatment provider specialty				
Cardiology	80	81	73	<0.0001
Electrophysiology	17	15	42	<0.0001
Internal medicine/primary care	67	68	59	<0.0001
Neurology	2.1	2.1	2.9	0.23
Site investigator specialty				
Cardiology	65	66	58	<0.0001
Electrophysiology	15	14	24	
Internal medicine/primary care	20	20	18	

Continuous variables are presented as median and interquartile range. AF indicates atrial fibrillation; EHRA, European Heart Rhythm Association.

catheter ablation of AF in community practice are sparse, but the findings in the present study fit well with previously described community-based populations of rhythm-controlled AF patients.[5,6] Patients undergoing AF ablation have fewer CV and non-CV comorbidities.

A more provocative finding is the lower proportion of minorities among patients with a previous catheter ablation of AF. This reflects similar findings involving other cardiac procedures as well as AF ablation[10,13,14]; however, the reasons for this disparity in the management of patients with AF are not clear. Another disparity was also observed with respect to patient educational status. In this cohort, a higher level of education was associated with a higher rate of catheter ablation of AF. Educational level has been shown to

Table 3. Antithrombotic Therapy by $CHADS_2$ Score and Previous AF Ablation

	No Previous AF Catheter Ablation					Previous AF Catheter Ablation					*P* Value (No Previous Ablation vs. Previous Ablation)
	Overall (n=9408)	$CHADS_2$=0 (n=556)	$CHADS_2$=1 (n=2062)	$CHADS_2$≥2 (n=6790)	*P* Value	Overall (n=527)	$CHADS_2$=0 (n=88)	$CHADS_2$=1 (n=150)	$CHADS_2$ ≥2 (n=289)	*P* Value	
Currently on antithrombotic therapy (other than warfarin)	50	54	50	50	0.18	59	61	61	57	0.7	0.0001
Asprin	43	48	43	43	0.07	50	54	52	47	0.4	0.0047
Clopidogrel	7.2	3.9	44	8.3	<0.0001	6.3	2.3	6.0	7.6	0.19	0.4
Prasugrel	0.1	0.2	0.3	0.1	0.3	0.2	0	0.7	0	0.3	0.8
Ticagrelor	0	0	0	0	–	0	0	0	0	–	–
Aggrenox	0.2	0.2	0.2	0.2	0.9	0	0	0	0	–	0.4
Other antithrombotic	0.6	0.0	0.5	0.6	0.16	0	0	0	0	–	0.087
Oral anticoagulation therapy											
Treated with warfarin in the past	81	61	75	84	<0.0001	92	90	92	93	0.6	<0.0001
Warfarin	72	46	64	76	<0.0001	66	47	55	77	<0.0001	0.0037
Dabigatran	4.7	5.8	6.6	4.1	<0.0001	9.5	9.2	8.7	10	0.9	<0.0001
Warfarin or dabigatran	76	51	71	80	<0.0001	75	56	64	86	<0.0001	0.5
Contraindications to anticoagulation therapy	13					11					0.26
Any antithrombotic therapy, including warfarin	95	87	94	96	<0.0001	95	93	95	96	0.6	0.8

AF indicates atrial fibrillation.

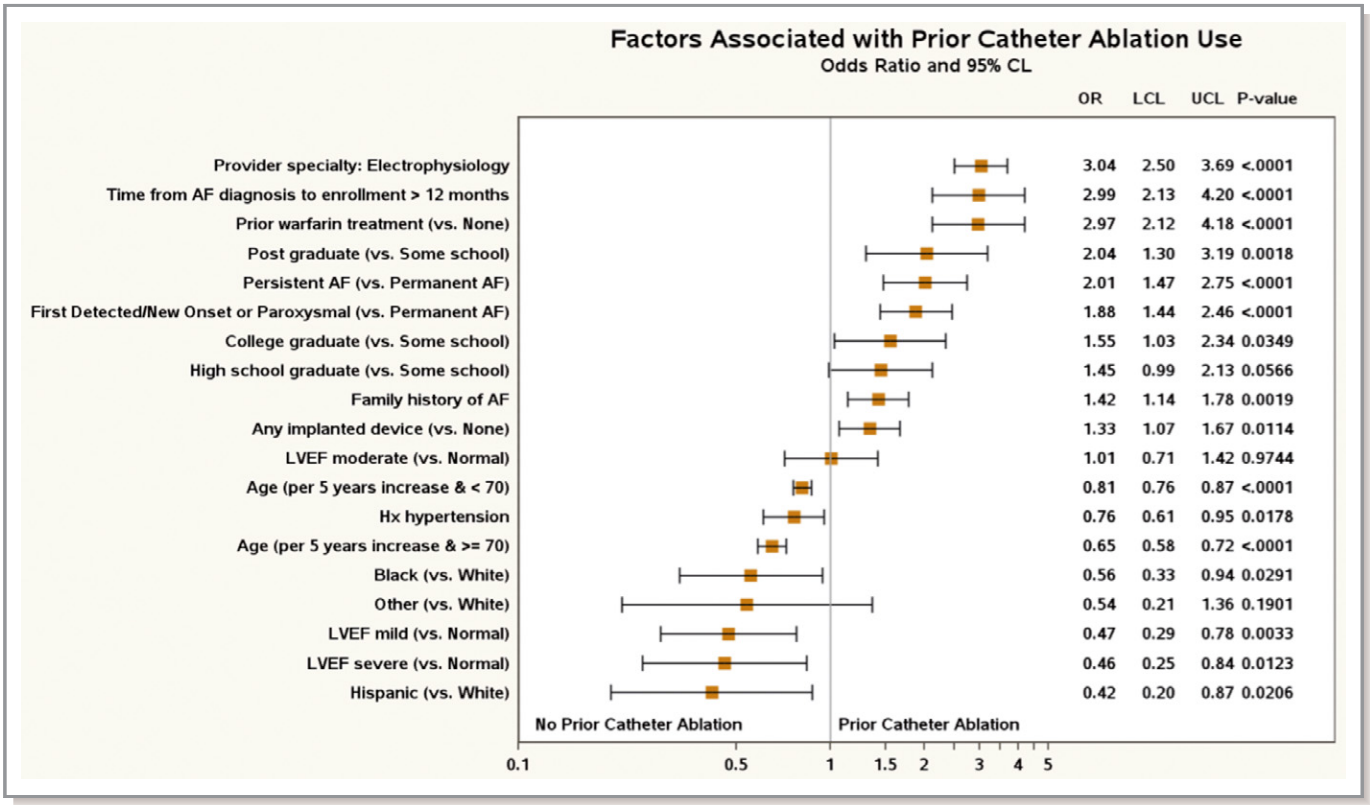

Figure. Forest plot of factors associated with a history of catheter ablation at baseline. AF indicates atrial fibrillation; CL, confidence level; Hx, history; LCL, lower confidence level; LVEF, left ventricular ejection fraction; OR, odds ratio; UCL, upper confidence level.

Table 4. Repeat Hospitalizations in Full Follow-up (N=9488)

Outcome	Previous AF Ablation	No Previous AF Ablation	Unadjusted RR (95% CI)	*P* Value	Adjusted RR (95% CI)	*P* Value
	No. of Events (Events/100 Patient-Years)	No. of Events (Events/100 Patient-Years)				
All-cause	446 (51.72)	7551 (52.76)	0.98 (0.85, 1.13)	0.7802	1.04 (0.91, 1.19)	0.5810
CV	260 (30.19)	3458 (24.01)	1.26 (1.05, 1.50)	0.0126	1.11 (0.93, 1.33)	0.2289
Bleeding	28 3.22)	592 (4.03)	0.80 (0.52, 1.23)	0.3110	1.10 (0.71, 1.72)	0.6722

AF indicates atrial fibrillation; CI, confidence interval; CV, cardiovascular; RR, relative risk.

be associated with symptom severity in AF and also with “health literacy” in general (ie, the ability to seek, understand, and use health information).[15,16] Further studies are needed to define the causes of these disparities and ultimately guide their correction.

Although the evidence base for catheter ablation is well established, there are few national reports from routine clinical practice. However, almost one third of the patients still had severe or disabling symptoms, despite ablation, and almost half of them had ongoing antiarrhythmic treatment. The continued symptom burden in patients with drug-refractory AF postablation illustrates the well-described shortcomings of AF ablation and the need for further improvement.[17] Fortunately, many procedural innovations are being investigated to improve the efficacy and safety of AF ablation, including contact-force sensing, alternative energy sources for ablation, and targeting of additional mechanisms of AF, including rotor ablation.[18–20]

Although preliminary registry data in relatively small cohorts without longer-term follow-up fail to identify significant stroke risk after discontinuation of oral anticoagulation therapy in patients after a successful ablation of AF,[21,22] current guidelines caution against weighing rhythm status and previous catheter ablation of AF when assessing stroke risk.[2] Therefore, it is reassuring that only minor differences in oral anticoagulation use between patients with and without a

Table 5. Association of Previous Catheter Ablation and Outcomes in Follow-up (N=9451)

Outcome	Previous AF Ablation	No Previous AF Ablation				
	No. of Events (Events/100 Patient-Years)	No. of Events (Events/100 Patient-Years)	Unadjusted HR (95% CI)	*P* Value	Adjusted HR (95% CI)	*P* Value
All-cause death	24 (2.73)	833 (5.55)	0.50 (0.33, 0.75)	0.0008	0.78 (0.52, 1.18)	0.2459
CV death	9 (1.03)	331 (2.22)	0.46 (0.24, 0.89)	0.0222	0.70 (0.36, 1.38)	0.3050
First CV hospitalization	163 (23.03)	2270 (17.76)	1.17 (0.99, 1.38)	0.0628	1.06 (0.90, 1.26)	0.4795
All-cause death/stroke/TIA or CHF	39 (4.51)	1229 (8.42)	0.54 (0.39, 0.74)	0.0001	0.78 (0.56, 1.09)	0.1417
Major bleeding	29 (3.39)	575 (3.95)	0.81 (0.55, 1.18)	0.2767	1.08 (0.74, 1.59)	0.6901

A complete list of the variables in the adjusted models can be found in Data S1. AF indicates atrial fibrillation; CHF, congestive heart failure; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; TIA, transient ischemic attack.

Table 6. Association of Incident Catheter Ablation and Outcomes in Follow-up (N=781)

Outcome	Incident Catheter Ablation (N=266)	No Incident Catheter Ablation (N=515)		
	No. of Events (Events/100 Patient-Years)	No. of Events (Events/100 Patient-Years)	Adjusted HR (95% CI)	*P* Value
All-cause death	5 (1.60)	18 (2.00)	0.75 (0.27, 2.08)	0.5774
CV death	1 (0.32)	10 (1.11)	0.32 (0.05, 2.01)	0.2246
First CV hospitalization	85 (36.14)	158 (21.62)	1.67 (1.24, 2.26)	0.0008
All-cause death/stroke/TIA or CHF	14 (4.59)	41 (4.65)	1.02 (0.53, 1.95)	0.9616
Major bleeding	7 (2.27)	21 (2.39)	1.07 (0.43, 2.68)	0.8843

A complete list of the variables in the adjusted models can be found in Data S1. CHF indicates congestive heart failure; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; TIA, transient ischemic attack.

previous catheter ablation of AF were observed. The rate of patients treated with any oral anticoagulation was similar in both groups, as was the rate of contraindication to oral anticoagulation. In summary, the findings in the current analysis indicate that physicians do not underestimate stroke risk nor do they withhold therapy in moderate- to high-risk patients after catheter ablation of AF.

Although the presence of sinus rhythm has been shown to be associated with a more favorable prognosis in AF,[23] and data from nonrandomized studies indicate that patients who have undergone pulmonary vein isolation experience improved outcomes,[24–26] reduction of stroke or mortality has not been demonstrated in a prospective, randomized, clinical trial. Several unadjusted differences in outcome between patients with a history of AF ablation and nonablated patients were noted in the present analysis (eg, a lower death rate and higher rates of hospitalization). However, after adjusting for relevant covariates, none of these associations remained. Similarly, the differences in outcome noted in patients with and without incident catheter ablation were entirely driven by differences in hospitalization rates, whereas rates of major adverse outcomes were similar. Importantly, a higher risk of hospitalization in patients on a rhythm-control strategy, when compared to patients on rate control, has been reported previously.[27] This is likely to reflect the fact that patients referred for AF ablation are more symptomatic and, although thoroughly matched, residual, unmeasured confounding factors may remain and, at least in part, explain this finding. It is important to highlight that there was limited statistical power to detect meaningful, clinically relevant differences in the major CV outcomes (eg, stroke, CV death, and all-cause mortality) owing to the low number of events. Despite the absence of statistical significance, several of the event rates were numerically lower in the ablation arm. Thus, it is possible that a beneficial association with catheter ablation may have been demonstrable in a larger population. Intuitively, the impact of AF ablation (if any) is likely to be different if the ablation is successful or not.[26] In that respect, the present analysis is hampered by the fact that there was no prespecified way of determining whether or not an ablation was considered successful (neither subjectively nor objectively). It is plausible that a successful AF ablation does have an impact on outcome, but the extent of that influence may be too small to detect when attenuated by the unsuccessful ablations.

The definite answer to whether or not catheter ablation of AF decreases death or stroke will require a prospective, randomized trial, as with the ongoing Catheter Ablation versus

Anti-arrhythmic Drug Therapy for Atrial Fibrillation trial (CABANA) (http://clinicaltrials.gov).

Limitations

These data are derived from a voluntary, observational study and thus are susceptible to the limitations inherent in such methods. These include both selection and reporting biases. Based on available data, there is no way to separate successful or unsuccessful ablations. Per protocol, ECGs were recorded every 6 months, and, consequently, more-detailed data on AF burden are not available. The data in this study are dependent on the quality of medical record documentation and abstraction. The utilization catheter ablation of AF was not randomized; therefore, despite multivariable adjustment, it is possible that residual, unmeasured confounding remains. Although the trends observed in ORBIT-AF are similar to those in other observational data, we cannot exclude that participation in ORBIT-AF may have highlighted symptoms that made rhythm control more likely. Finally, it is also possible that our analyses were limited by the sample size and reduced power to demonstrate a difference in outcomes.

Conclusion

In U.S. clinical practice, a minority of patients is managed with ablation. However, a significant portion of ablation patients had moderate or severe symptoms and required antiarrhythmic therapy, even after ablation. Factors associated with catheter ablation were primarily factors highlighted in current guidelines; however, nonwhite patients and those with less education were less likely to be treated with catheter ablation. There were no clinically relevant differences in oral anticoagulation post-AF ablation or differences in outcomes in patients with or without previous AF catheter ablation, but patients with incident AF ablation are hospitalized more often during the remainder of the follow-up.

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