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Comparison of Long-Term Risk Adverse Outcomes In Patients with Atrial Fibrillation Having Ablation vs Antiarrhythmic Medications:

Freeman, Outcomes After Atrial Fibrillation Ablation

James V. Freeman, MD, MPH, MS[a], **Grace H. Tabada, MPH**[b], **Kristi Reynolds, PhD**[c], **Sue Hee Sung, MPH**[b], **Daniel E. Singer, MD**[d], **Paul J. Wang, MD, MS**[e], **Taylor I. Liu, MD, PhD**[f], **Nigel Gupta, MD**[g], **Mark A. Hlatky, MD**[e,h], **Alan S. Go, MD**[b,h,i]

[a]Department of Medicine, Yale University School of Medicine, New Haven, CT

[b]Division of Research, Kaiser Permanente Northern California, Oakland, CA

[c]Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA

[d]Division of General Internal Medicine, Massachusetts General Hospital, and Harvard Medical School, Boston, MA

[e]Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA

[f]Division of Cardiology, Kaiser Permanente Santa Clara Medical Center, Santa Clara, CA

[g]Division of Cardiac Electrophysiology, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA

[h]Department of Medicine, Health Research and Policy, Stanford University School of Medicine, Stanford, CA

[i]Departments of Epidemiology, Biostatistics, and Medicine, University of California, San Francisco, San Francisco, CA

Abstract

The impact of atrial fibrillation (AF) catheter ablation vs. chronic antiarrhythmic therapy alone on clinical outcomes such as death and stroke remains unclear. We compared adverse outcomes for AF ablation versus chronic antiarrhythmic therapy in 1070 adults with AF treated between 2010 and 2014 in the Kaiser Permanente Northern California and Southern California healthcare delivery systems. Patients undergoing AF catheter ablation were matched to patients treated with only antiarrhythmic medications, based on age, gender, history of heart failure, history of coronary heart disease, history of hypertension, history of diabetes, and high-dimensional propensity score. We compared crude and adjusted rates of death, ischemic stroke or transient ischemic attack,

Corresponding Author: James V Freeman, MD, MPH, MS, Yale School of Medicine, Section of Cardiovascular Medicine, P.O. Box 208017, New Haven, CT 06520, Tel: 203-785-4126, james.freeman@yale.edu.

intracranial hemorrhage, and hospitalization. The matched cohort of 535 patients treated with AF ablation and 535 treated with antiarrhythmic therapy had a median follow-up of 2.0 (interquartile range 1.1–3.5) years. There was no significant difference in adjusted rates of death (adjusted hazard ratio [HR] 0.24, 95% confidence interval [CI]: 0.03–1.95), intracranial hemorrhage (adjusted HR 0.17, CI:0.02–1.71), ischemic stroke or transient ischemic attack (adjusted HR 0.53, CI: 0.18–1.60) and heart failure hospitalization (adjusted HR 0.85, CI: 0.34–2.12), although there was a trend towards improvement in these outcomes with ablation. However, there was a significantly increased risk of all-cause hospitalization following ablation (adjusted HR 1.60, CI: 1.25–2.05). In a contemporary, multicenter, propensity-matched observational cohort, AF ablation was not significantly associated with death, intracranial hemorrhage, ischemic stroke or transient ischemic attack, or heart failure hospitalization, but was associated with a higher rate of all cause-hospitalization.

Keywords

atrial fibrillation; catheter ablation; mortality; hospitalization

Introduction

Atrial fibrillation (AF) affects more than five million people in the United States (1). Catheter ablation is increasingly performed for AF rhythm control in patients with significant rhythm-related symptoms, and randomized trials have consistently shown that ablation decreases AF burden and symptoms compared with medical treatment (2–4). The Catheter Ablation vs Antiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) trial showed no significant difference between AF ablation (n=1,108) and drug therapy with rate or rhythm control (n=1,096) for a primary composite endpoint of death, disabling stroke, serious bleeding or cardiac arrest at 5 years (5). Secondary analyses of death and serious stroke also did not show significant differences, but there was very substantial crossover in the study and an on-treatment analysis showed significant differences favoring AF ablation for the primary endpoint of all-cause mortality and death or cardiovascular mortality. Two recent randomized trials have shown a lower risk of all-cause mortality and hospitalization in patients with atrial fibrillation and systolic heart failure treated with catheter ablation compared with medical therapy (6, 7), although it is not clear if these findings can be extrapolated to a lower-risk, general AF population. Some observational studies suggest AF ablation may reduce the risk of stroke (8, 9) and death (10, 11) compared with pharmacological management, but others have not (12, 13). Most of these observational studies, however, did not have adequate data or use the most contemporary methods to control for residual confounding.

We evaluated the contemporary rates of death, ischemic stroke/transient ischemic attack (TIA), intracranial hemorrhage, and hospitalization in community-based adults undergoing AF ablation compared with matched adults with AF who were chronically treated with antiarrhythmic medications.

Methods

The source population for this study was members from Kaiser Permanente Northern California and Southern California—two large, integrated health care delivery systems that care for >8.9 million persons who are highly representative of the local and statewide population (Figure 1) (14). Each system has implemented a Virtual Data Warehouse derived from comprehensive electronic health record systems (15), which served as the primary data source for subject identification and characterization, as well as having comprehensive electrophysiology procedure databases. The Virtual Data Warehouse is a distributed, standardized data resource comprised of electronic datasets at each site that are populated with linked demographic, administrative, ambulatory pharmacy, outpatient laboratory test results, and health care utilization (ambulatory visits, hospitalizations and claims with diagnoses and procedures) data for their membership (15).

Institutional review boards of Kaiser Permanente Northern California, Kaiser Permanente Southern California and Yale University approved the study. A waiver of informed consent was obtained due to the nature of the study.

Using information from comprehensive health plan electronic health records, we identified adults age ≥18 years diagnosed with AF from January 1, 2010 through June 30, 2014 based on meeting any of the following criteria: ≥1 hospitalization with a primary discharge diagnosis of AF (International Classification of Diseases, Ninth Edition [ICD-9] codes 427.31); ≥1 emergency department diagnosis of AF; or ≥2 outpatient encounters for diagnosed AF. The subset of these patients who underwent their first ablation for AF was identified by manual review of the electrophysiology laboratory procedure logs for the specified time period. The index date was assigned based on the date of the procedure for the ablation group, which was also the index date for the matched patients from the chronic antiarrhythmic therapy group. We excluded patients with unknown gender, <12 months of continuous membership or drug benefit before index date, or no membership after index date (16).

Our goal was to identify a matched cohort of adults with AF receiving chronic antiarrhythmic therapy for comparing outcomes. A high-dimensional propensity score (hd-PS) was calculated for each person using a logistic regression model for receiving AF ablation that included demographic and multiple patient characteristics. As opposed to standard propensity scoring, which includes a limited group of pre-selected variables, an hd-PS is generated by an algorithm that scans through all available data in electronic health records from the three dimensions of medication prescriptions, diagnoses and procedures across care settings. The algorithm selects the most frequent 200 items from each of these three dimensions within a five-year look-back period, then selects up to 300 of the best matched parameters for use in the hd-PS (17). This methodology has been shown to approximate point estimates of risk from randomized trials substantially better than standard propensity scoring or regression methodologies (17). Using this approach, we developed an hd-PS model to accurately predict receipt of AF ablation (c=0.83). Each AF ablation patient was then matched (without replacement) to one patient chronically treated with antiarrhythmic medications for AF, based on age, gender, history of heart failure, history of

coronary heart disease, history of hypertension, history of diabetes, and high-dimensional propensity score (within ≤0.001), on the calendar date of the matched AF ablation patient.

Patients were followed through December 31, 2014 for the outcomes of death from any cause, ischemic stroke or TIA, intracranial hemorrhage, all-cause hospitalization and heart failure-related hospitalization. Patients were censored at the time of health plan disenrollment or the end of follow-up. Death from any cause was identified from health plan databases (inpatient deaths, proxy report of deaths, cancer registry), California state death certificate files, and Social Security Administration Death Master File (15, 16, 18, 19). Hospitalization and adverse events, including stroke, TIA, and intracranial hemorrhage, were identified using validated algorithms based on comprehensive electronic medical records and billing claims databases (20). Ischemic stroke and intracranial hemorrhage were based on a primary discharge diagnosis, while TIA was based on either a principal discharge diagnosis or emergency department diagnosis (see Supplementary Materials Table 1 for ICD-9 codes). Hospitalization for heart failure was defined as a hospitalization with a primary discharge diagnosis of heart failure (20).

Data on patient age, gender, and self-reported race/ethnicity were obtained from health plan electronic records. We ascertained relevant medical history documented up to five years before and including cohort entry date using previously validated approaches based on ICD-9 diagnosis and procedure codes, Current Procedure Terminology (CPT) procedure codes, laboratory records and pharmacy records (16, 20–25). This included cardiovascular diseases (prior coronary heart disease, peripheral artery disease, valvular heart disease), prior ventricular arrhythmias (ventricular tachycardia or fibrillation), prior implantable cardiac device (pacemaker, implantable cardioverter-defibrillator, cardiac resynchronization device), other cardiovascular risk factors (hypertension, dyslipidemia, and diabetes mellitus), and other coexisting medical illnesses (hospitalized bleeding, hyperthyroidism, hypothyroidism, chronic lung disease, chronic liver disease, dementia, depression). We ascertained body mass index and blood pressure up to 365 days prior to and including the cohort entry date from outpatient visit information in electronic medical records. We also characterized baseline kidney function using outpatient serum creatinine concentration values and estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2) using the CKD-EPI equation (26). We ascertained other selected laboratory test results from health plan databases up to one year prior to and including cohort entry, including low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, and urine dipstick proteinuria.

We also characterized baseline exposure to cardiovascular medications within 120 days before cohort entry based on estimated day supply information per dispensed prescription and refill patterns found in health plan outpatient pharmacy databases using previously validated methods (16, 27). For this analysis, we included the following medications: antiarrhythmic medications, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aldosterone receptor antagonists, α-adrenergic receptor antagonists, diuretics, beta-blockers, calcium channel blockers, nitrates, hydralazine, statins, other lipid lowering agents, anti-platelet agents, and diabetic medications (20).

All analyses were conducted using SAS, version 9.4 (Cary, N.C.). We compared baseline characteristics between matched patients treated with AF ablation or antiarrhythmic medications without ablation during follow-up using analysis of variance, or relevant non-parametric test, for continuous variables, and the X^2 test for categorical variables.

We next calculated rates (per 100 person-years) with associated 95% confidence limits (CI) for death, ischemic stroke or TIA, intracranial hemorrhage, all-cause hospitalization and heart failure hospitalization for those who received AF ablation during follow-up compared with those treated with antiarrhythmic medications without ablation. We generated cumulative hazard curves for the outcomes of death and ischemic stroke or TIA, censoring patients at the time of death or loss to follow-up. We next conducted extended Cox regression models with time-varying covariates to examine the independent association between AF ablation compared with antiarrhythmic therapy in the hd-PS-matched cohort and the risk of adverse outcomes. Finally, we conducted sensitivity analyses in a separately matched cohort in which we excluded patients treated with amiodarone from the chronic antiarrhythmic therapy without ablation subgroup.

Results

We identified 182,666 adults with diagnosed AF between January 2010 and June 2014 (Figure 1), of whom 811 underwent AF ablation and 156,963 received only chronic antiarrhythmic therapy during follow-up. The age, gender, and hd-PS-matched cohort included 1,035 adults, of whom 535 were treated with AF ablation, and 535 were treated with only chronic antiarrhythmic therapy.

Matched patients were generally similar in terms of clinical characteristics at study entry (Table 1). However, those treated with chronic antiarrhythmic medications were more likely to have a history of documented mitral or aortic valvular disease, ventricular arrhythmias, implantable cardioverter defibrillator, hospitalized bleeding, cancer, and organ transplant, but less likely to have a history of ischemic stroke or TIA, or depression. Those treated with antiarrhythmic medications were more likely to be treated with angiotensin converting enzyme inhibitors/angiotensin receptor blockers, diuretics, beta-blockers, aldosterone receptor antagonists, and statins, but less likely to be treated with anticoagulants.

Median follow up time was 2.0 years (interquartile range 1.1–3.4 years). There were 41 deaths (11 in the AF ablation patients, 30 in antiarrhythmic therapy patients) during follow-up, with a significantly lower crude rate of death in those treated with AF ablation compared with those treated with chronic antiarrhythmic medical therapy (0.85 vs. 2.52 per 100 person-years, respectively, P=0.002, Table 2, Figure 2). In multivariable analysis, AF ablation was not significantly associated with all-cause mortality (adjusted hazard ratio [HR] 0.24, 95%CI:0.03–1.95, Figure 3).

During follow-up, 21 patients had an ischemic stroke or TIA (8 ablation patients, 13 antiarrhythmic therapy patients), and there was no significant difference between those treated with AF ablation compared to those treated with antiarrhythmic therapy (0.63 vs. 1.10 per 100 person-years, respectively, P=0.21, Table 2, Figure 2). In multivariable

analysis, AF ablation was not significantly associated with the risk of ischemic stroke or TIA (adjusted HR 0.53, 95%CI: 0.18–1.60, Figure 3).

There were 8 intracranial hemorrhages (2 in the AF ablation patients, 6 in antiarrhythmic therapy patients) during follow-up, and there was no significant difference between those treated with AF ablation compared to those treated with antiarrhythmic therapy (0.15 vs. 0.51 per 100 person-years, respectively, P=0.13, Table 2). In multivariable analysis, AF ablation was not significantly associated a lower risk of intracranial hemorrhage (adjusted HR 0.17, 95% CI:0.02–1.71, Figure 3).

During follow-up, there were 369 hospitalizations for any cause in the matched cohort (211 ablation patients, 158 antiarrhythmic therapy patients), with a significantly higher crude rate of hospitalization in those treated with AF ablation compared to those treated with chronic antiarrhythmic therapy (24.7 vs. 17.3 per 100 person-years, respectively, P=0.01, Table 2, Figure 2). In multivariable analysis, AF ablation was associated with significantly higher rate of subsequent hospitalization (adjusted HR 1.60, 95%CI: 1.25–2.05, Figure 3). AF ablation was associated with no difference in the crude rate of hospitalization for heart failure (0.86 vs. 1.11 per 100 person-years, respectively, P=0.54, Table 2, Figure 2), and no significant difference in the adjusted rate risk of hospitalization for HF (adjusted HR 0.85, 95%CI: 0.34–2.12, Figure 3). When we evaluated the absolute counts of all-cause and heart failure hospitalization, the rate of both outcomes decreased after AF ablation and the initiation of chronic antiarrhythmic therapy, but the decrease was greater for those treated with medications alone (Supplementary Materials Tables 1 and 2). Finally, results were similar in a sensitivity analysis in a separate matched cohort in which patients receiving chronic amiodarone therapy in the antiarrhythmic therapy group were excluded (Supplementary Table 3).

Discussion

In this contemporary, multicenter, observational cohort of adults undergoing AF ablation, we found no statistically significant differences in the adjusted rates of death, ischemic stroke or TIA, intracranial hemorrhage or hospitalization for heart failure, although all of the point estimates were favorable towards ablation. However, we observed a significantly increased adjusted rate of all-cause hospitalization during follow-up in ablation patients compared with those treated with only chronic antiarrhythmic therapy.

Our findings were consistent with the results of the recently published CABANA trial which showed no significant difference between AF ablation (n=1,108) and drug therapy with rate or rhythm control (n=1,096) for a composite endpoint of death, disabling stroke, serious bleeding or cardiac arrest at 5 years (8% vs 9.2%; hazard ratio [HR] 0.86, 95% confidence interval [CI] 0.65–1.15) (5). Secondary analyses also did not show statistically significant differences for death (5.2% vs 6.1%, p=0.38) and serious stroke (0.3% vs 0.6%, p=0.19). However, crossover occurred frequently in the study (ablation to drug 9.2% and drug to ablation 27.5%), and a secondary on-treatment analysis showed significant differences favoring AF ablation for the primary composite endpoint (7.0 vs 10.9%, p=0.006), all-cause

mortality (4.4 vs 7.5%, p=0.005) and death or cardiovascular hospitalization (41.2% vs 74.9%, p=0.002) (5).

The point estimates for the risk of death, ischemic stroke or transient ischemic attack, and intracranial hemorrhage all favored AF ablation in our study, but our study population was relatively small and the confidence intervals for our risk estimates were broad. It is possible that with greater power, we may have been able to detect a statistically significant difference in these outcomes. Data from existing observational studies about the association of AF ablation with stroke and death risk have been mixed. While some studies have shown a favorable association of ablation with the risks of stroke (8, 9) and death (10), there remains considerable concern about patient selection bias and residual confounding in these studies. Other studies have shown a non-significant trend towards lower risk or no difference between treatment with ablation and medical management (12, 13), but these studies were also relatively small and may have been underpowered to detect statistically significant differences in these outcomes.

We consistently found higher rates of all-cause hospitalizations in patients treated with AF ablation. This result was unexpected given prior studies showing lower symptom burden and improved quality of life with ablation (2–4). AF ablation use was relatively uncommon in our cohort, and patients treated with ablation may have been more symptomatic and likely to use health care resources before and after ablation, introducing residual confounding that could not be accounted for with our adjustment methods. However, we showed comparable rates of hospitalization for ablation and medically managed patients prior to the procedure suggesting that this was not the case. The 1–3 month “blanking” period often employed in AF ablation studies has contributed to understudy of this critical period after the procedure, and we have previously shown considerable rates of readmission and emergency department evaluation after ablation (28). Our data suggests substantial differences in resource utilization during this period and suggests that peri-procedural interventions including use of short term anti-arrhythmic drugs or diuretics after AF ablation may improve short-term morbidity and resource utilization (29). Additional investigation into the timing and specific causes of hospitalization, may help to identify potentially modifiable contributing factors that may be targets for other interventions.

Our study has several limitations. Our efforts to create a well-matched observational cohort of patients resulted in a small study cohort and we had low event rates which limited our statistical power to detect differences in outcomes. The study was conducted within two large healthcare delivery systems in California, so the results may not be fully generalizable to all populations and practice settings. However, the patients within Kaiser Permanente Northern California and Southern California have been shown to be broadly generalizable to the California statewide and national population (30). The study was observational in design and used combined clinical and administrative data for the identification of comorbidities and outcomes, which may have led to some misclassification. However, the algorithms used within the Kaiser Permanente system for the identification of comorbid conditions and outcomes have been well validated in prior studies (16, 20–25). Finally, as an observational study of outcomes associated with different care strategies, we cannot eliminate the possibility of residual confounding. The patients in our study who underwent ablation were

matched to patients treated with only anti-arrhythmic medications based on age, gender and a high-dimensional propensity score which included 200 prescription and medical history variables derived from electronic medical records (17). This methodology has been shown to approximate point estimates of risk from randomized clinical trials substantially better than standard propensity scoring or regression methodologies. Despite this matching methodology, there were persistent differences in selected characteristics between the final cohorts, with the ablation group being generally lower risk for cardiovascular disease and risk factors than the medical therapy group, and the Cox regression methods are meant to adjust for this residual confounding.

In conclusion, in a contemporary, observational cohort, we found AF ablation was not associated with a significant difference in adjusted rates of death, intracranial hemorrhage, ischemic stroke or TIA and heart failure hospitalization compared with antiarrhythmic medical therapy, although there was a trend towards improvement in these outcomes with ablation. AF ablation was associated with a higher adjusted rate of subsequent all-cause hospitalization.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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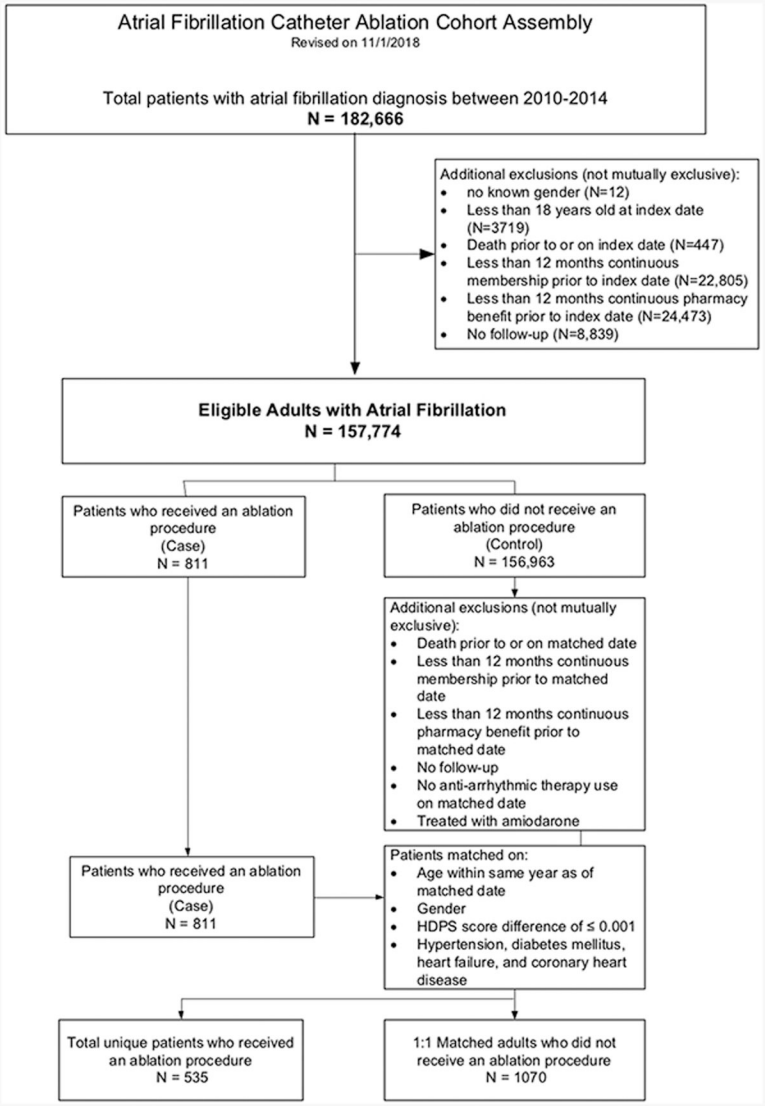
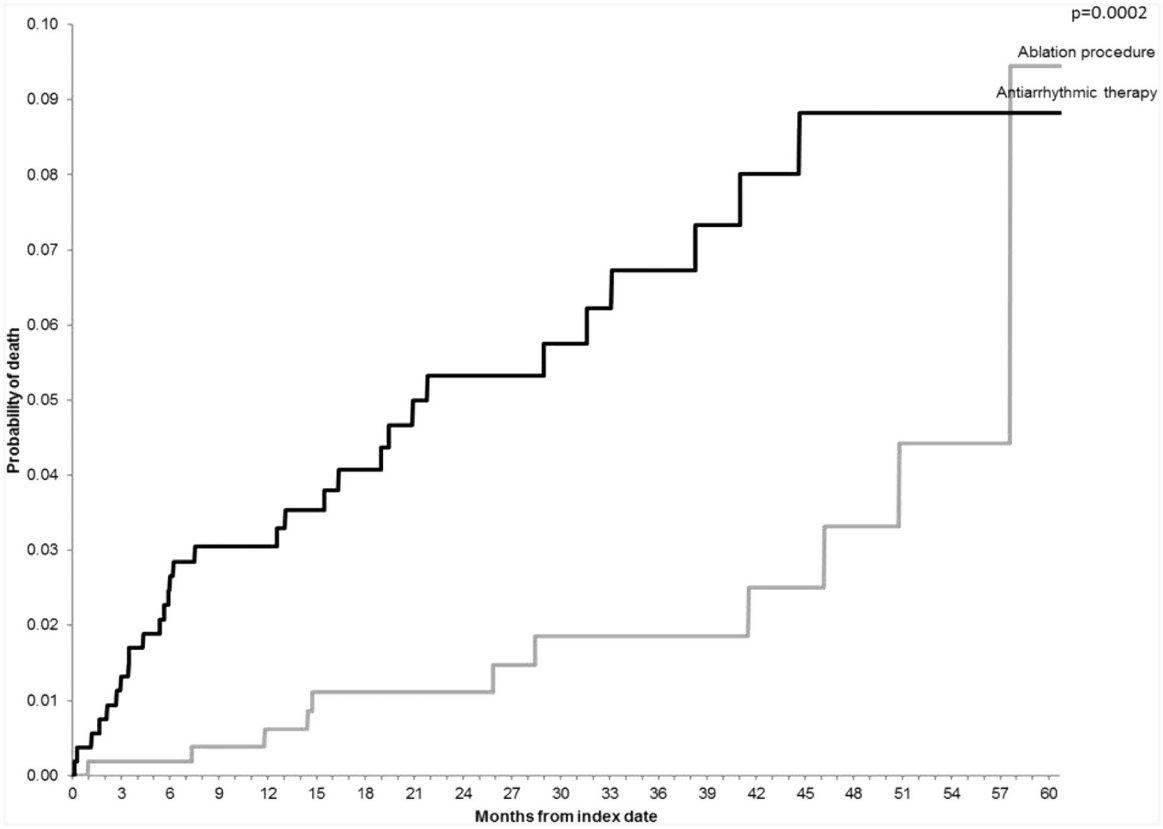
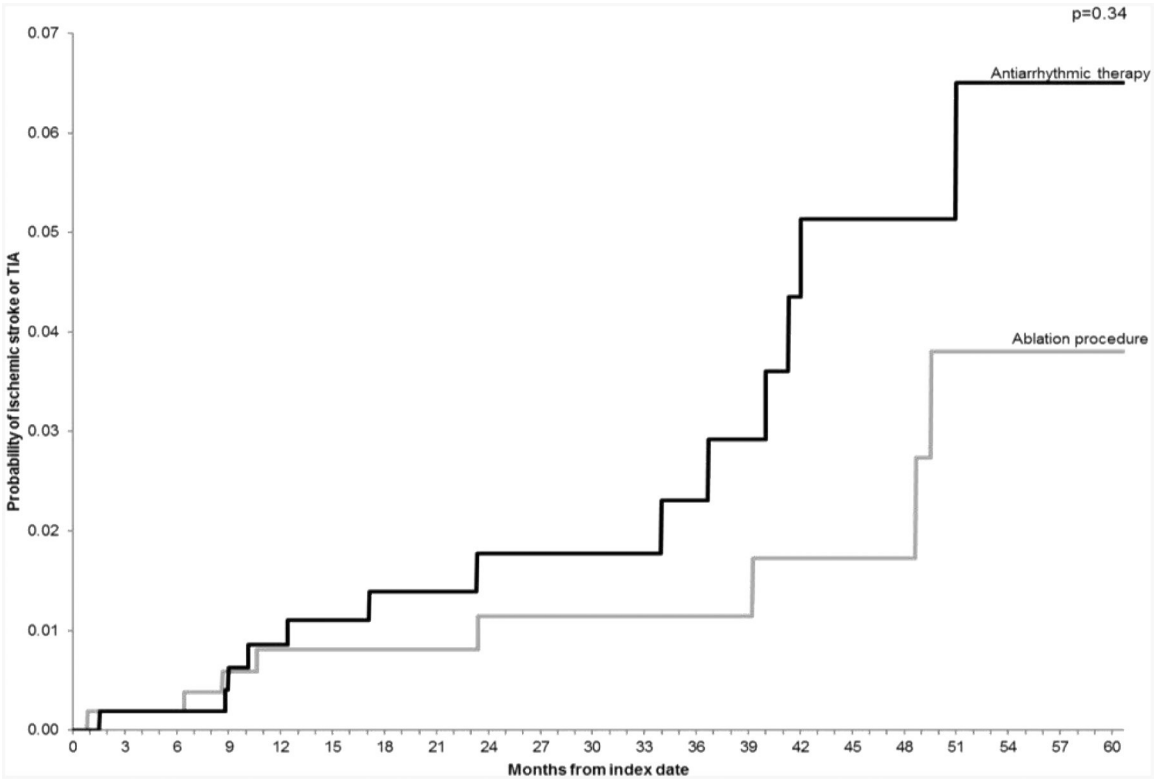


Figure 1.

Age, gender, and high-dimensional propensity score-matched cohort assembly of patients with atrial fibrillation treated with catheter ablation or antiarrhythmic medications between January 1, 2010 and June 31, 2004.





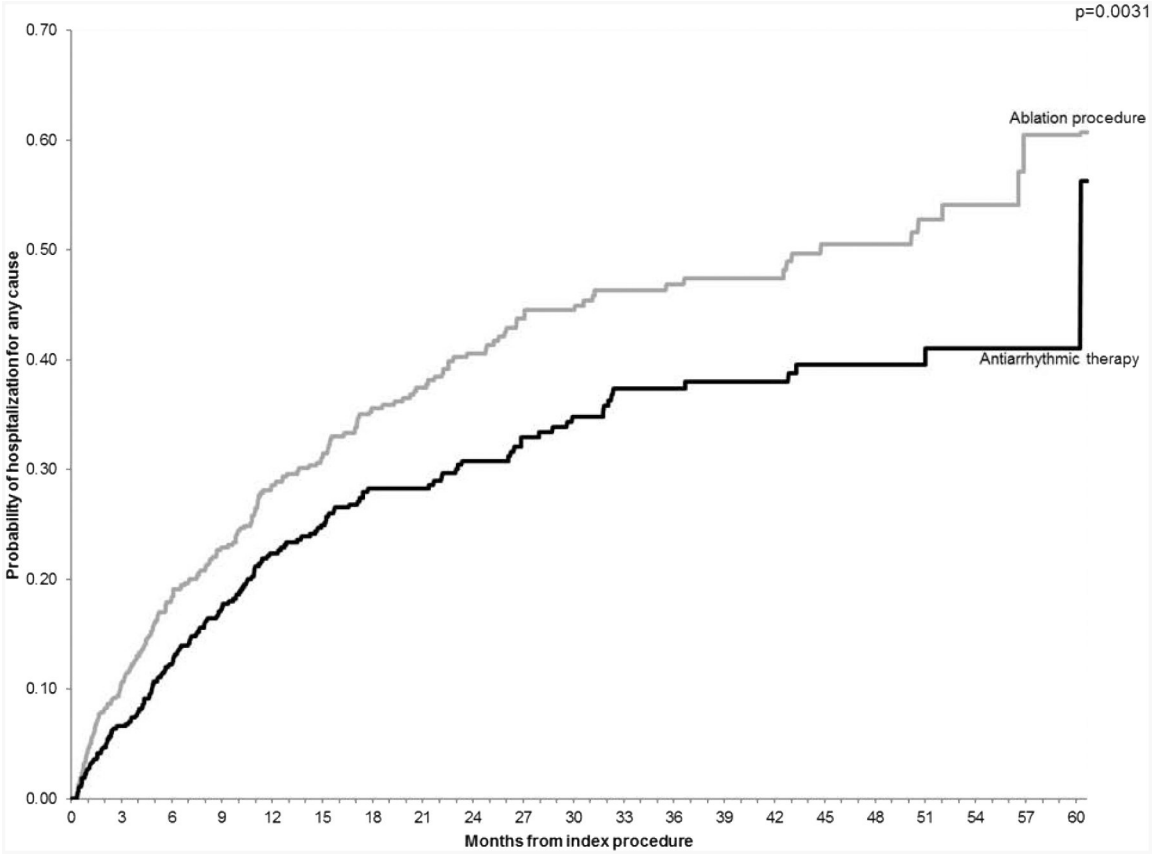


Figure 2.

Cumulative incidences of (A) death from any cause, (B) ischemic stroke or transient ischemic attack, and (C) hospitalization from any cause in age, gender and high-dimensional propensity score matched adults with atrial fibrillation treated with catheter ablation or antiarrhythmic medications between 2010–2014.

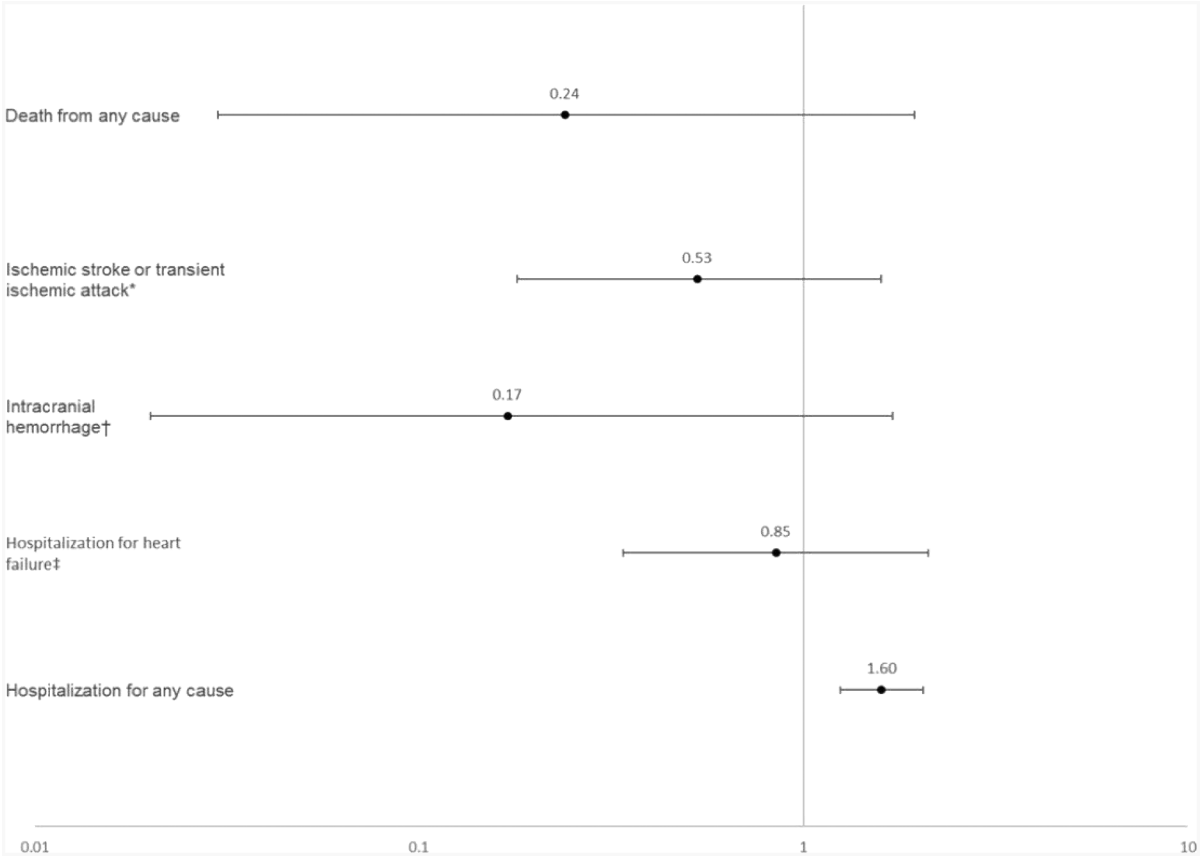


Figure 3.

Multivariable association of atrial fibrillation catheter ablation versus chronic antiarrhythmic therapy with clinical outcomes among 1,070 adults with atrial fibrillation matched on age, gender, and high-dimensional propensity score.

Death model adjusted for dyslipidemia, chronic lung disease, systemic cancer, organ transplant, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, anti-arrhythmic medications, diuretics (loop and thiazide), and warfarin

* Stroke/transient ischemic attack model adjusted for mitral and/or aortic valvular disease, chronic lung disease, systolic blood pressure, and anti-arrhythmic medications

† Intracranial hemorrhage model adjusted for mitral and/or aortic valvular disease, diagnosed depression, and systemic cancer

‡ Heart failure hospitalization model adjusted for mitral and/or aortic valvular disease, chronic lung disease, diagnosed depression, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, anti-arrhythmic medications, and warfarin

§ Hospitalization for any cause adjusted for ischemic stroke or transient ischemic attack, intracranial hemorrhage, peripheral artery disease, mitral and/or aortic valvular disease, dyslipidemia, chronic lung disease, diagnosed depression, systemic cancer, organ transplant, systolic blood pressure, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, anti-arrhythmic medications, diuretics (loop and thiazide), beta-blockers, calcium

channel blockers, statins, warfarin, non-warfarin oral anticoagulants, antiplatelet agents, and diabetes therapy

Table 1.

Baseline characteristics of adults with atrial fibrillation between January 2010 and June 2014, stratified by treatment of catheter ablation versus antiarrhythmic therapy only.

Characteristic	Overall (N=1070)	AF ablation (N = 535)	Anti-arrhythmic medication (N = 535)	p-value
Age, median (IQR), (years)	64.2 (59.5–68.2)	64.1 (59.3–68.1)	64.2 (59.5–68.2)	0.67
Age group, (years)				1.00
18–49	42 (3.9%)	21 (3.9%)	21 (3.9%)	
50–59	256 (23.9%)	128 (23.9%)	128 (23.9%)	
60–69	578 (54.0%)	289 (54.0%)	289 (54.0%)	
70–79	192 (17.9%)	96 (17.9%)	96 (17.9%)	
≥ 80	2 (0.2%)	1 (0.2%%)	1 (0.2%)	
Women	352 (32.9%)	176 (32.9%)	176 (32.9%)	1.00
Race				0.17
White	954 (89.2%)	485 (90.7%)	469 (87.7%)	
Black	15 (1.4%)	7 (1.3%)	8 (1.5%)	
Asian / Pacific Islander	63 (5.9%)	23 (4.3%)	40 (7.5%)	
Other	38 (3.6%)	20 (3.7%)	18(3.4%)	
Known Hispanic ethnicity	52 (4.9%)	26 (4.9%)	26 (4.9%)	1.00
Current or former smoker	538 (50.3%)	259 (48.4%)	279(52.1%)	0.22
Medical history *(5 years prior to or on index date)*				
Heart failure	74 (6.9%)	37 (6.9%)	37 (6.9%)	1.00
Prior coronary heart disease	44(4.1%)	22(4.1%)	22(4.1%)	1.00
Ischemic stroke or transient ischemic attack	57 (5.3%)	36 (6.7%)	21 (3.9%)	**0.04**
Intracranial hemorrhage	6 (0.6%)	2 (0.4%)	4 (0.7%)	0.41
Peripheral arterial disease	18(1.7%)	7(1.3%)	11 (2.1%)	0.34
Mitral and/or aortic valvular disease	154(14.4%)	61 (11.4%)	93(17.4%)	**<0.01**
Ventricular tachycardia or fibrillation	55(5.1%)	19(3.6%)	36 (6.7%)	**0.02**
Implantable cardioverter defibrillator	33(3.1%)	4 (0.7%)	29 (5.4%)	<0.001
Pacemaker	57 (5.3%)	34 (6.4%)	23 (4.3%)	0.13
Cardiac resynchronization therapy	13(1.2%)	4 (0.7%)	9(1.7%)	0.16
Hypertension	618(57.8%)	309 (57.8%)	309 (57.8%)	1.00
Dyslipidemia	734 (68.6%)	356 (66.5%)	378 (70.7%)	0.15
Diabetes mellitus	92 (8.6%)	46 (8.6%)	46 (8.6%)	1.00
Hospitalized bleeding	22(2.1%)	5 (0.9%)	17(3.2%)	**<0.01**
Hyperthyroidism	56 (5.2%)	33 (6.2%)	23 (4.3%)	0.17
Hypothyroidism	188(17.6%)	100(18.7%)	88(16.4%)	0.34
Chronic lung disease	308 (28.8%)	149 (27.9%)	159(29.7%)	0.50
Chronic liver disease	55(5.1%)	27 (5.0%)	28 (5.2%)	0.89
Diagnosed dementia	20 (1.9%)	12 (2.2%)	8(1.5%)	0.37

Characteristic	Overall (N=1070)	AF ablation (N = 535)	Anti-arrhythmic medication (N = 535)	p-value
Diagnosed depression	185(17.3%)	109(20.4%)	76(14.2%)	**<0.01**
Systemic cancer	80 (7.5%)	28 (5.2%)	52 (9.7%)	**<0.01**
Organ transplant	12(1.1%)	2 (0.4%)	10(1.9%)	**0.02**
Body Mass Index, categories (kg/m^2)				**<0.01**
<18.5	8 (0.7%)	1 (0.2%)	7(1.3%)	
18.5–25	233 (21.8%)	124 (23.2%)	109 (20.4%)	
25–30	401 (37.5%)	218 (40.7%)	183 (34.2%)	
30–40	359 (33.6%)	164 (30.7%)	195 (36.4%)	
>=40	48 (4.5%)	23 (4.3%)	25 (4.7%)	
Missing	21 (2.0%)	5 (0.9%)	16 (3.0%)	
Systolic blood pressure, median (IQR), (mmHg)	120.5 (110.0–132.0)	120.0 (111.0–130.0)	122.0 (110.0–133.0)	0.10
Diastolic blood pressure, median (IQR) (mmHg)	71.0 (64.0–78.0)	70.0 (64.0–77.0)	71.0 (64.0–78.0)	0.07
Estimated glomerular filtration rates, median (IQR), (ml/min/1.73 m2)	76.9 (65.7–88.4)	76.8 (65.9–88.0)	77.1 (65.3–89.2)	0.89
HDL cholesterol, median (IQR), (mg/dL)	47.0 (40.0–58.0)	48.0 (41.0–58.0)	47.0 (39.0–58.0)	0.25
LDL cholesterol, median (IQR), (mg/dL)	97.0 (79.0–120.0)	98.0 (79.0–120.0)	96.0 (79.0–120.0)	0.49
Medications (*120 days prior to index date)*				
Alpha-adrenergic receptor antagonists	78 (7.3%)	34 (6.4%)	44 (8.2%)	0.24
Angiotensin converting enzyme inhibitors (ACEi) / angiotensin receptor blockers (ARB)	383 (35.8%)	163 (30.5%)	220 (41.1%)	**<0.001**
Anti-arrhythmic medications	1015 (94.9%)	480 (89.7%)	535 (100.0%)	**<0.001**
Diuretics (loop and thiazide%)	291 (27.2%)	115 (21.5%)	176 (32.9%)	**<0.001**
Beta-blockers	807 (75.4%)	385 (72.0%)	422 (78.9%)	**<0.01**
Aldosterone receptor antagonists	25 (2.3%)	2 (0.4%)	23 (4.3%)	**<0.001**
Calcium channel blockers	325 (30.4%)	175 (32.7%)	150 (28.0%)	0.10
Nitrates	53 (5.0%)	24 (4.5%)	29 (5.4%)	0.48
Hydralazine	20 (1.9%)	10 (1.9%)	10 (1.9%)	1.00
Statins	522 (48.8%)	238 (44.5%)	284 (53.1%)	**<0.01**
Other lipid lowering agents	47 (4.4%)	23 (4.3%)	24 (4.5%)	0.88
Warfarin	696 (65.0%)	431 (80.6%)	265 (49.5%)	**<0.001**
Other anticoagulant	58 (5.4%)	46 (8.6%)	12 (2.2%)	**<0.001**
Antiplatelet agents	46 (4.3%)	18 (3.4%)	28 (5.2%)	0.13
Diabetes therapy	69 (6.4%)	30 (5.6%)	39 (7.3%)	0.26

Table 2.

Crude rates by outcomes among patients with atrial fibrillation treated with catheter ablation or antiarrhythmic therapy.

Outcomes	AF Ablation Therapy (N = 535)			Antiarrhythmic Therapy (N = 535)			p-value comparison for crude rates
	Number of outcomes	Person-years	Rate per 100 person-years (95% CI)	Number of outcomes	Person-years	Rate per 100 person-years (95% CI)	
Death	11 (2.1)	1293.1	0.85 (0.47–1.54)	30 (5.6)	1190.6	2.52(1.76–3.60)	**0.002**
Ischemic stroke or TIA	8 (1.5)	1278.9	0.63(0.31–1.25)	13 (2.4)	1178.3	1.10(0.64–1.90)	**0.21**
Intracranial hemorrhage	2 (0.4)	1292.3	0.15(0.04–0.62)	6 (1.1)	1183.1	0.51 (0.23–1.13)	**0.13**
Hospitalization for heart failure	11 (2.1)	1280.8	0.86 (0.48–1.55)	13 (2.4)	1176.0	1.11 (0.64–1.90)	**0.54**
Hospitalization for any cause	211 (39.4)	853.3	24.7(21.61–28.30)	158 (29.5)	912.2	17.3(14.82–20.24)	**0.0007**