Clinical Outcomes Following Catheter or Surgical Ablation of Atrial Fibrillation

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ABSTRACT

Background: The efficacy related to ablation treatment for AF has been well studied; however, the comparative safety of AF ablation procedures in large general populations is limited.

Objectives: The purpose of this study was to compare clinical outcomes of U.S. adult patients who underwent an ablation procedure for AF.

Methods: Using data from the MORE^2 Registry, we conducted a retrospective cohort study of U.S. adult patients who underwent an ablation procedure for AF from 2007 to 2014. We used weighted Cox proportional hazards models to estimate adjusted hazard of CTPP, hematoma or hemorrhage, and rehospitalization through two years of follow-up.

Results: Our analysis included 10,134 patients who underwent an ablation procedure for AF, 68% of whom received a CA. Baseline characteristics were comparable for the two cohorts after propensity score adjustment. Relative to SA, patients who underwent CA had lower 90-day adjusted risks for rehospitalization (HR=0.54; 95% CI: 0.43-0.68) and higher adjusted risks for hematoma or hemorrhage at two years (HR=1.51; 95% CI: 1.07-2.12). There was no significant difference between the two cohorts in the adjusted risks for CTPP at two years (HR=0.61; 95% CI: 0.37-1.02).

Conclusion: AF patients that underwent CA had a lower risk of 90-day rehospitalization compared to those that underwent SA, but had a higher risk of having a hematoma or hemorrhage at two years. Further large-scale randomized clinical trials are warranted to confirm study findings.

KEY WORDS

Ablation, arrhythmia, clinical outcomes, complication rates

ABBREVIATIONS

1. AF = Atrial Fibrillation
2. CA = Catheter Ablation
3. SA = Surgical Ablation
4. MORE^2 Registry = Medical Outcomes Research for Effectiveness and Economics Registry
5. CTPP = Cardiac Tamponade or Pericardiocentesis Procedure
6. CCI = Charlson Comorbidity Index Score
7. SD = Standard Deviation
8. HR = Hazard Ratio
9. CI = Confidence Interval
10. TIA = Transient Ischemic Attack

INTRODUCTION

Ablation procedures for atrial fibrillation (AF) have evolved as a common alternative therapy for patients with drug-refractory symptomatic paroxysmal or persistent AF, especially in younger, healthier adults.[1-4] While the safety and efficacy of ablation procedures are expected to result in an overall low major complication rate, concerns have been raised that ablation procedures for AF may be associated with an increased risk of cardiac perforation with possible cardiac tamponade. Although a relatively rare event, cardiac tamponade is associated with a high risk of morbidity and mortality.[5] Despite several recent studies including meta-analyses and large population studies,[1-2, 6-22] there remains uncertainty about the trade-offs between the safety and the effectiveness of AF ablation procedures.

The efficacy related to ablation treatment for AF has been well researched. Results have varied across studies and is dependent on the methods applied including study design, sample size, type of ablation procedure, and duration of the study.[1-2, 6-22] The reported efficacy for catheter ablation (CA) ranged from 16% to 88%, whereas surgical ablation (SA) success rates have been reported to be between 75% and 92%.[1, 5-6, 9, 18, 12-14, 20-22] However, the comparative safety of CA and SA is not well understood. Published studies have focused primarily on the in-hospital complication rates of patients receiving CA. Therefore, the risks of these procedures may be underestimated, based on adverse events that occur after discharge.[1-2, 8, 17, 19] Also, studies that have examined the relative safety of SA compared to CA typically used smaller sample sizes.[11, 16, 21, 23-27] Nevertheless, those studies usually reported significantly higher adverse event rates for SA compared to CA.[16, 21, 23-27]

Using data from the Medical Outcomes Research for Effectiveness and Economics Registry (MORE^2 Registry®), we conducted a retrospective cohort study to evaluate rates of

cardiac tamponade or pericardiocentesis procedure (CTPP), hematoma or hemorrhage, and readmission to the hospital in U.S. adults with AF who underwent an ablation procedure.

METHODS

Data Source

This study used the MORE^2 Registry for 2007-2014 to identify patients 18 years or older enrolled in commercial, Medicare Advantage, or managed Medicaid programs and that had received an ablation procedure for AF. The MORE^2 Registry is a data warehouse that is statistically de-identified in accordance with 45 CFR 164.541 (b)(1)[28] and contains longitudinal patient-level data for more than 131 million unique individuals nationwide.

The Cohort

Patients, aged 18 years or older, undergoing an ablation procedure for AF were identified by the presence of a claim for a CA or SA during June 30, 2007 to December 31, 2014. For this analysis, patients who were coded as having multiple ablation procedures during the reporting period, their index date was selected as the most recent service date from an outpatient visit or the discharge date from an inpatient stay. Patients eligible for this study must have had a diagnosis of AF within 30 days, inclusive, prior to the ablation procedure and continuously enrolled as well as having medical and pharmacy benefits six months before the ablation procedure. We used exclusion criteria based on the analysis of previous retrospective studies.[1-2, 8, 17, 19] Patients were excluded if they (1) had a secondary diagnosis claim for Wolf-Parkinson-White Syndrome, nonparoxysmal atrioventricular nodal tachycardia, paroxysmal supraventricular tachycardia, paroxysmal ventricular tachycardia, atrial flutter, atrioventricular nodal reentrant tachycardia, ventricular premature beats or complexes, and/or anomalous atrioventricular excitation present on the index event for ablation procedure; (2) had a claim for

both types of ablation procedures present on the index event; and (3) had a claim for atrioventricular node ablation, implantation pacemaker, and/or implantable cardioverter-defibrillator (Table A2).

Covariates

Using information from the index event for ablation procedure, we identified the following covariates: age, gender, region, payer, number of previous ablations, year of index ablation procedure, history of hospitalizations, Charlson Comorbidity Index Score (CCI), history of risk factors for thromboembolism (i.e., hypertension, diabetes, congestive cardiac failure, thromboembolic event, and/or stroke/TIA), history of coronary artery disease, history of hyperlipidemia, history of cardiomyopathy, history of valvular heart disease, history of chronic pulmonary disease, history of renal disease, and history of anticoagulation medications (i.e., warfarin, aspirin, rivaroxaban, clopidogrel, dabigatran, danapariod, enoxaparin, fondaparinux, and dalteparin) (Table A2).

Outcome Measures

We estimated rates of all-cause 30, 60, and 90-day rehospitalizations as well as rates for CTPP and hematoma or hemorrhage within 30, 60, and 90 days on or after the index event for AF ablation. CTPP and hematoma or hemorrhage were based on the presence of specific codes (Table A2).

Long-term clinical outcomes of interest were CTPP and hematoma or hemorrhage. Eligible patients were followed-up to two years from the index event for AF ablation to assess risk of CTPP and hematoma or hemorrhage. Patients were censored at the date of disenrollment or at the end of the reporting period (December 31, 2014).

Statistical Analysis

Categorical variables are presented as frequencies and percentages; continuous variables are presented as mean ± SD. Differences in baseline patient characteristics between the two cohorts were examined using chi-square test for categorical and binary variables and a t-test or Mann-Whitney U test for continuous variables. For the CA cohort, rates of 30-day CTPP and hematoma or hemorrhage were compared to published in-hospital 30-day rates.[1, 8, 17, 19] In addition, rates of 30-day rehospitalization were compared to the California State Inpatient Database.[19]

We used GREEDY 5→1 digit propensity scoring to control for any differences between the populations of patients undergoing an ablation procedure. GREEDY 5→1digit match is a process that paired patients who underwent CA to patients that received SA on five-digits of the propensity score. For patients that did not match, they were then paired on four-digits of the propensity score. This continued down to a one-digit match of the propensity score for those individuals that remained unmatched.[29] The propensity score, accounting for differences in the covariates, was calculated using logistic regression with cohort membership as the dependent variable.

We estimated adjusted hazard of CTPP, hematoma or hemorrhage, and all-cause rehospitalizations using Cox proportional hazards models, weighting by the propensity score. We expressed differences in hazard between the two cohorts as a hazard ratio (HR) with 95% confidence intervals (95% CIs) and p-value <0.05. The hazard distributions were compared using the log-rank test and Kaplan-Meier curves of adverse outcomes were plotted to show survival comparisons between the two cohorts.[30]

All analyses and the generation of output were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Study Population

From June 30, 2007 to December 31, 2014, 10,134 patients received at least one ablation procedure and met the eligibility criteria. Of those, 6,929 (68.4%) received a CA and 3,205 (31.6%) received a SA (Figure 1).

Patient Characteristics

Prior to propensity score adjustment, there was a statistically significant difference in baseline characteristics between the two ablation cohorts. However, after propensity score adjustment, there was no significant difference in any of the baseline characteristics. Therefore, the GREEDY 5→1 digit propensity score approach was able to achieve balance for baseline characteristics that were potential confounders between procedure and outcome measures.

After matching, 3,846 patients who received an ablation procedure for AF were, on average, in their late-60s ±11.1 with the largest number of patients between the ages of 65-79 (1,897, 49.3%) and 50-64 (1,267, 32.9%) respectively. The regional composition of the study sample was diverse, with most of the population living in the Midwest (1,267, 32.9%). There were 1,501 (39.0%) women and 2,345 (61.0%) men in this study. The average CCI was 2.9 ±2.3 with the largest number of patients having a history of hyperlipidemia (2,699, 70.2%), coronary artery disease (2,562, 66.6%), and valvular heart disease (1,825, 47.5%) (Table 1).

Rehospitalization

During the 90 days of observation, 10.5% of patients in the CA cohort had a rehospitalization with and an average time to rehospitalization of 27.9±25.6 days. In the SA cohort, 28.3% of patients had a rehospitalization at an average of 22.8±21.2 days (Table 2).

The unadjusted risks of rehospitalization were significantly lower (p<0.001) in the CA than in the SA cohorts: 6.5% vs. 21.3% at 30 days; 8.9% vs. 25.8% at 60 days; and 10.5% vs. 28.3% at 90 days (Table 2).

Figure 2 shows unadjusted estimates of the cumulative hazard of rehospitalizations through 90 days of follow-up (Log-rank p <0.001) by which the odds associated with CA was 21.9% lower (Table 2, HR=0.28; 95% CI: 0.25-0.33). The adjusted model indicated there remained a significant difference in the risk of 60, and 90-day rehospitalization between the two cohorts. The 30-day risk became non-significant. The odds of having a rehospitalization were lower for patients who underwent CA relative to SA: (37.5% chance) (Table 2, HR=0.60; 95% CI: 0.46-0.77) within 60 days; and (35.1% chance) (Table 2, HR=0.54; 95% CI: 0.43-0.68) within 90 days.

CTPP

During the two years of observation, 1.3% of patients in the CA cohort had a CTPP with an average time to CTPP of 12.9±49.8 days. In the SA cohort, 2.4% of patients had a CTPP at an average of 14.4±38.3 days (Table 2).

The unadjusted risks of CTPP were significantly lower (p<0.001) in the CA than in the SA cohorts: 1.2% vs. 2.2% at 30 days; 1.2% vs. 2.3% at 60; 1.2% vs. 2.4% at 90 days; and 1.3% vs. 2.4% at 365 and 730 days (Table 2).

Figure 3 shows unadjusted estimates of the cumulative hazard of CTPP through 730 days of follow-up (Log-rank p <0.001) by which the odds associated with CA was 34.2% lower (Table 2, HR=0.52; 95% CI: 0.38-0.71). The adjusted model indicated there was no significant difference in the risks of CTPP between the two cohorts (Table 2).

Hematoma or Hemorrhage

During the two years of observation, 3.1% of patients in the CA cohort had a hematoma or hemorrhage with an average time to hematoma or hemorrhage of 37.1±99.1 days. In the SA cohort, 3.0% of patients had a hematoma or hemorrhage at an average of 57.2±129.9 days (Table 2).

There were no significant differences in unadjusted risks of hematoma or hemorrhage in the CA than in the SA cohorts: 2.6% vs. 2.2% at 30 days; 2.7% vs. 2.5% at 60 days; 2.8% vs. 2.5% at 90 days; 3.0% vs. 2.8% at 365 days; and 3.1% vs. 3.0% at 730 days (Table 2).

The unadjusted estimates of the cumulative hazard of hematoma or hemorrhage through 730 days of follow-up (Log-rank p=0.694) showed that the odds associated with CA were non-significantly higher than SA (52.8% chance) (Table 2 HR=1.12; 95% CI: 0.86-1.45). The adjusted model indicated there became a significant difference in the risk of 30, 90, 365, and 730-day hematoma or hemorrhage between the two cohorts. The 60-day risk remained non-significant. The odds of having a hematoma or hemorrhage were higher for patients that underwent CA than in SA: (59.8% chance) (Table 2, HR=1.49; 95% CI: 1.00-2.21) within 30 days; (60.2% chance) (Table 2, HR=1.51; 95% CI: 1.04-2.21) within 90; (59.5% chance) (Table 2, HR=1.47; 95% CI: 1.03-2.09) within 365 days; and (60.2% chance) (Table 2, HR=1.51; 95% CI: 1.07-2.12) within 730 days.

DISCUSSION

We assessed the impact of ablation procedures for AF on the outcomes of rehospitalizations, CTPP, and hematoma or hemorrhage. We compared these outcomes for the population of patients undergoing CA with the population of patients undergoing SA. We wanted to address the important question of whether the population of ablation patients with AF have improved outcomes following SA compared to CA since the wide-spread use of SA is increasing

relative to CA. We used a propensity score adjusted retrospective cohort design to minimize confounding and selection bias from observed pretreatment differences across the two cohorts. Based on the experience of 3,846 enrollees, we found that the relative risk of 90-day rehospitalization rate decreased by 36.0% in the CA cohort compared to the SA cohort. The relative risk of 730-day hematoma or hemorrhage rate increased by 32.6% in the CA cohort compared with the SA cohort. There were no significant differences in the relative risk of CTPP rates between the two groups. To our knowledge, this is the first large, multi-center, retrospective study to investigate the comparative safety of CA vs. SA for AF and their clinical adverse events that can occur after discharge.

CA is found to be a good strategy for focal isolation of paroxysmal AF, but is a time-consuming procedure and carries the risk of multiple complications like cardiac tamponade which could be fatal, atrioesophageal fistula and local thrombus formation at the site of ablation.[31] Those potential complications of CA may account for our results showing increased hematoma or hemorrhage rates and other morbidities such as pulmonary vein stenosis, the esophagus vagal and phrenic nerves, stroke or TIA, and air embolism when compared to SA. To that effect and for patients with persistent or longstanding persistent AF, the SA technique has been greatly improved over time requiring less surgery.[31] The SA minimally invasive ablation procedure became the most effective non-pharmacological treatment of AF.[31] Cardiac perforation is a recognized complication of CA procedures, most commonly encountered during ablation of AF. Tokuda M et al. (2012) did a retrospective analysis on consecutive patients undergoing CA for ventricular arrhythmias at a tertiary referral center. “Of 1,152 consecutive CA procedures in 892 patients over 12 years, 11 procedures (1.0%) were complicated by

ventricular perforation. Emergent pericardial drainage and surgical repair were required in 10 (91%) and 6 (55%) cases, respectively." [32]

Several studies have reported complication rates following CA for AF, but most of the studies have primarily focused on in-hospital rates or were conducted at specialized centers. 30-day CTPP rates following CA for AF have ranged from 1.3% to 3.1%.[1, 8, 17, 19] A California State Inpatient Database that examined 4,156 patients who received a CA for AF between 2005 and 2008 reported a CTPP rate of 2.5% at 30 days.[19] The Worldwide Survey on Ablation of AF reported a CTPP rate of 1.3% on 16,309 patients with AF between 2003 and 2006.[1] A Medicare Fee-for-Service study that observed 15,423 patients aged 65 years or older who received a CA for AF between 2007 and 2009 reported a CTPP rate of 1.7% at 30 days.[17] Further, the Medicare Provider Analysis and Review reported a CTPP rate of 3.1% on 6,065 admissions from 168 hospitals between 2001 and 2006.[8] We found a 1.0% CTPP rate at 30 days. Therefore, the complication rate for CTPP observed in the present study appears to be lower than those previously reported. However, the present study used a propensity score method to control for any differences between the populations of patients undergoing an ablation procedure.

Two studies have examined in-hospital 30-day hematoma or hemorrhage rates following CA for AF. The Medicare Provider Analysis and Review reported a hematoma or hemorrhage rate of 4.8% and a California State Inpatient Database reported a hematoma or hemorrhage rate of 2.2% at 30 days.[8, 19] A Nationwide Inpatient Sample that examined 93,801 CA for AF between 2000 and 2010 reported an overall frequency of postoperative hemorrhage of 3.4% with an annual rate significantly increasing from 1.8% in 2000 to 4.9% in 2010.[2] We found a 3.2% hematoma or hemorrhage rate at 30 days. Our findings were therefore consistent with previously published data that observed 30-day hematoma or hemorrhage rates.

To date, rehospitalization rates following an AF ablation as well as the comparative effectiveness studies of CA and SA are limited. Only one study assessed 30-day rehospitalization rate following CA for AF and found the rate to be 9.4%.[19] We found a 10.1% rehospitalization rate at 30 days, which appears to be slightly higher than what the California State Inpatient Database reported. However, the present study had a more regionally diverse sample that could be more representative of the general AF population.

Five studies have compared the rates of cardiac tamponade associated with CA and SA for the treatment of AF. A meta-analysis of those five studies by Kearney et al. (2014) found no difference between SA and CA in terms of CTPP (2.0% vs. 3.0%; OR=1.16; 95% CI: 0.25-5.41; p=0.85).[11] Similarly, we found no significant differences in the risks of CTPP rates between AF patients that underwent CA and SA (1.0% vs. 1.7%; HR=0.60; 95% CI: 0.35-1.05; p=0.075). The present study had a larger sample that could be more representative of the general AF population. It also did not have the limitation of heterogeneity reported in the study by Kearney et al (2014).

Study Limitations

The MORE^2 Registry contains patient-level information similar to administrative claims data, which lack clinical detail such as disease severity that is available in trials and registries. There is also the potential for miscoding of the diagnoses and procedures we used to define ablation for AF or complications. There are no specific procedure codes indicating an ablation for AF. We combined nonspecific codes for CA and SA with diagnosis codes for AF to identify the procedures of interest. However, our approach is comparable to previously published coding algorithms.[2, 8, 17, 19, 26] In addition, this study was unable to obtain detailed dosage information of anticoagulants used ,as well as, to distinguish between the types of AF (i.e., paroxysmal or

persistent). Outcomes after ablation procedures are influenced by the type of AF, which may have led to an underestimate of complication rates.

CONCLUSIONS

The results provide new evidence on the comparative safety of ablation procedures for AF. It suggest that the risks of having a rehospitalization are lower for AF patients that underwent a CA procedure compared to those that underwent a SA procedure, but the risks of having a hematoma or hemorrhage are higher. Despite the potential limitations, the current study had a large sample size and an absence of reporting bias that could be introduced by results from specialized cardiac centers.

PERSPECTIVES

Clinical Competencies

Clinicians and patients should take into account the higher event rates when selecting the most appropriate ablation technique to treat AF. These results could serve as the basis for an outcome-based quality measure designed to evaluate relative performance and provide benchmarks to support both consumer choice and quality improvement efforts.

Translational Outlook Implications

Further large-scale randomized clinical trials are warranted to confirm study findings.

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REFERENCES

1. Cappato R, Calkins H, Chen SA, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010; 3: 32-38.
2. Deshmukh A, Patel NJ, Pant S, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: Analysis of 93,801 procedures. *Circulation* 2013; 128(19): 2104-2112.
3. Jons C, Hansen PS, Johannessen A, et al. The medical antiarrhythmic treatment or radiofrequency ablation in paroxysmal atrial fibrillation (MANTRA-PAF) trial: Clinical rationale, study design, and implementation. *Europace* 2009; 11: 917-923.
4. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): A report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. *J Am Coll Cardiol* 2011; 57: 223-242.
5. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for personnel, policy, procedures and follow-up. *Heart Rhythm* 2007; 4(6): 816-861.
6. Boersma LVA, Castella M, Boven WV, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): A 2-center randomized clinical trial. *Circulation* 2012; 125: 23-30.
7. Bohnen M, Stevenson WG, Tedrow UB, et al. Incidence and predictors of major complications from contemporary catheter ablation to treat cardiac arrhythmias. *Heart Rhythm* 2011; 8: 1661-1666.

8. Ellis ER, Culler ST, Simon AW, Reynolds MR. Trends in utilization and complications of catheter ablation for atrial fibrillation in Medicare beneficiaries. *Heart Rhythm* 2009; 6(9): 1267-1273.
9. Ganesan AN, Shipp NJ, Brooks AG, et al. Long-term outcomes of catheter ablation of atrial fibrillation: A systematic review and meta-analysis. *J Am Heart Assoc* 2013; 2: 1-14.
10. Jones DG, Haldar SK, Hussain W, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. *J Am Coll Cardiol* 2013; 61: 1894-1903.
11. Kearney K, Stephenson R, Phan K, et al. A systematic review of surgical ablation versus catheter ablation for atrial fibrillation. *Ann Cardiothorac Surg* 2014; 3(1): 15-29.
12. Leong-Sit P, Roux JF, Zado E, et al. Antiarrhythmics after ablation of atrial fibrillation: Six-month follow-up study. *Circ Arrhythm Electrophysiol* 2011; 4: 11-14.
13. Lim T, Day JD, Weiss JP, et al. More aggressive left atrial ablation in elderly patients does not increase procedural complications and favorably impact outcomes. *J of Innov in CRM* 2011; 2: 206-211.
14. Maroto LC, Carnero M, Siva JA, et al. Early recurrence is a predictor of late failure in surgical ablation of atrial fibrillation. *Interact Cardiovasc Thorac Surg* 2011; 12: 681-686.
15. Nadem-Anee K, Amnueypol M, Lee F, et al. Benefits and risks of catheter ablation in elderly patients with atrial fibrillation. *Heart Rhythm* 2015; 12: 44-51.
16. O'Neill MD, Wright M, Knecht S, et al. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. *Eur Heart J* 2009; 30: 1105-1112.
17. Piccini JP, Sinner MF, Greiner MA, et al. Outcomes of Medicare beneficiaries undergoing catheter ablation for atrial fibrillation. *Circulation* 2012; 126(18): 2200-2207.

18. Santini M, Loiaconi V, Tocco MP, et al. Feasibility and efficacy of minimally invasive stand-alone surgical ablation of atrial fibrillation: A single-center experience. *J Interv Card Electrophysiol* 2012; 34: 79-87.
19. Shah RU, Freeman JV, Shilane D, et al. Procedural complications, rehospitalizations, and repeat procedures after catheter ablation for atrial fibrillation. *J Am Coll Cardiol* 2012; 59(2): 143-149.
20. Tilz RR, Rillig A, Thum AM, et al. Catheter ablation of long-standing persistent atrial fibrillation: 5-year outcomes of the Hamburg sequential ablation strategy. *J Am Coll Cardiol* 2012; 60: 1921-1929.
21. Wang J, Li Y, Shi J, et al. Minimally invasive surgical versus catheter ablation for the long-lasting persistent atrial fibrillation. *PLoS One* 2011; 6 (7): e22122-e22122.
22. Weera-Sooriya R, Khairy P, Litalien J, et al. Catheter ablation for atrial fibrillation: Are results maintained at 5 years of follow-up? *J Am Coll Cardiol* 2011; 57: 160-166.
23. Stulak JM, Dearani JA, Sundt TM 3rd, et al. Ablation of atrial fibrillation: Comparison of catheter-based techniques and the Cox-Maze III operation. *Ann Thorac Surg* 2011; 91:1882-8.
24. Mahapatra S, LaPar DJ, Kamath S, et al. Initial experience of sequential surgical epicardial-catheter endocardial ablation for persistent and long-standing persistent atrial fibrillation with long-term follow-up. *Ann Thorac Surg* 2011; 91: 1890-8.
25. Gu J, Liu X, Jiang WF, et al. Comparison of catheter ablation and surgical ablation in patients with long-standing persistent atrial fibrillation and rheumatic heart disease: A four-year follow-up study. *Int J Cardiol* 2013; 168: 5372-7.

26. Krakor R, Chares M, Schneider J, et al. Mid-term results of endoscopic mitral valve repair in combination with endocardial or epicardial ablation. *Eur J Cardiothorac Surg* 2011; 40: e125-9.
27. Guidance regarding methods for de-identification of protected health information in accordance with the health insurance portability and accountability act (HIPAA) privacy rule. Washington, DC: U.S. Department of Health & Human Services n.d. (Accessed September 25, 2014, at http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/De-identification/guidance.html).
28. Parsons LS. Reducing bias in a propensity score matched-pair sample using Greedy matching techniques. Cary, NC: SAS Institute Inc. 2001. (Access on September 25, 2014, at http://www2.sas.com/proceedings/sugi26/p214-26.pdf).
29. Bland JM, Altman DG. The logrank test. *BMJ* 2004; 328(7447): 1073.
30. Ladapo JA, David G, Gunnarsson CL, et al. Healthcare utilization and expenditures in patients with atrial fibrillation treated with catheter ablation. *J Cardiovasc Electrophysiol* 2012; 23: 1-8.
31. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Heart Rhythm* 2012; 9(4): 632-717.
32. Tokuda M1, Kojodjojo P, Epstein LM, et al. Outcomes of cardiac perforation complicating catheter ablation of ventricular arrhythmias. *Arch Cardiovasc Dis* 2012; 105(8-9): 446-53.

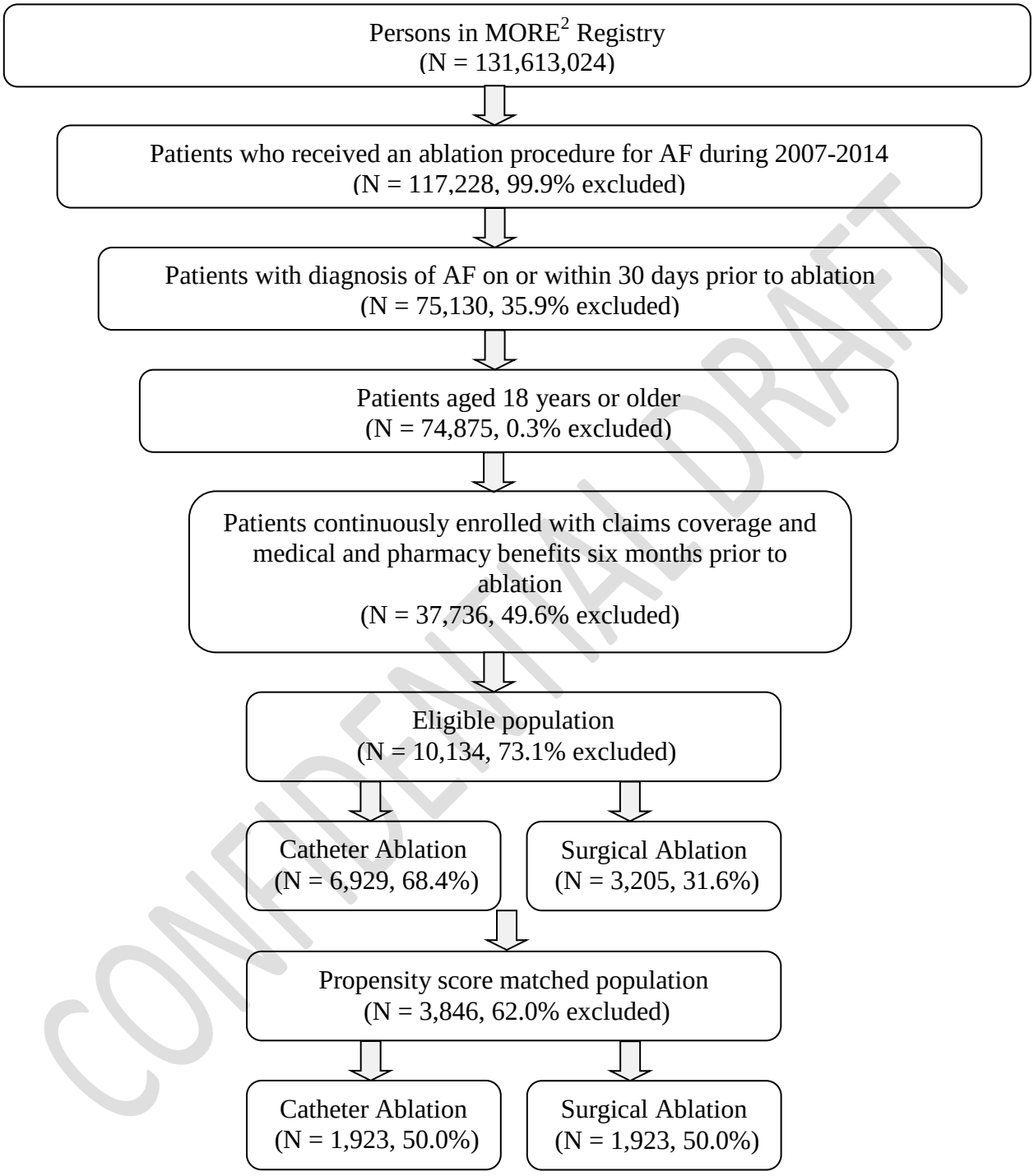

Figure 1. Study Flow Chart

Flow chart outlining the study sample selection process.

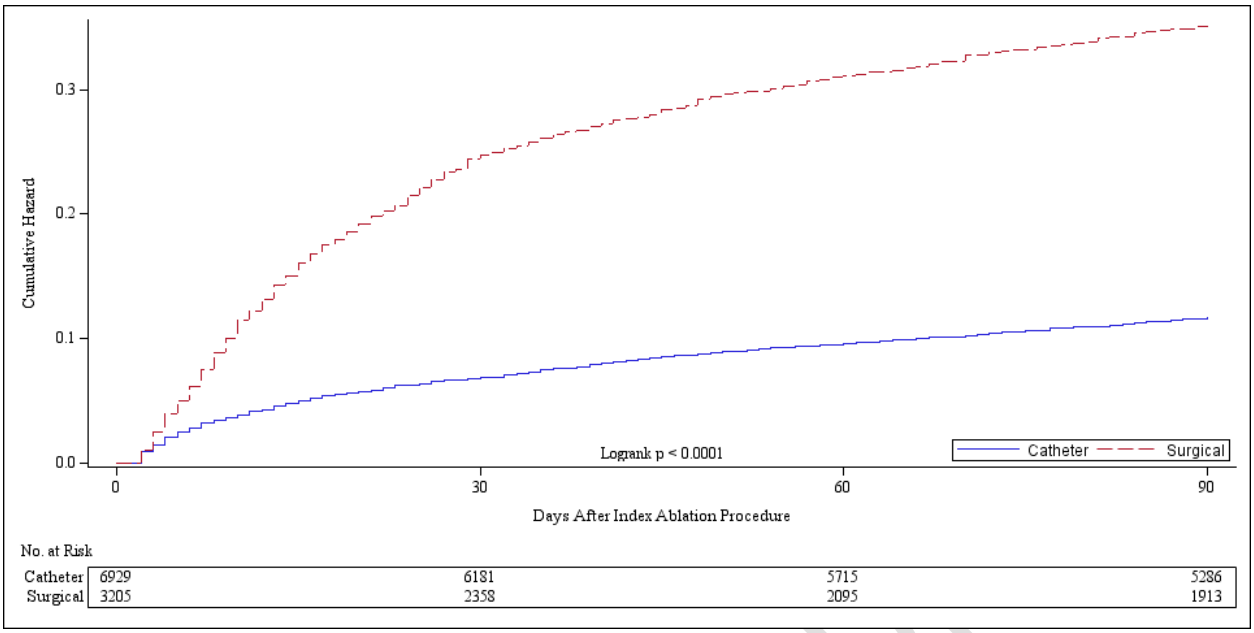

Figure 2. Unadjusted Cumulative Hazard of Rehospitalizations for Patients Undergoing Ablation Procedure for Atrial Fibrillation

30-Day: HR= 0.45; 95% CI: 0.36-0.55; p>0.001, the odds associated with CA cohort was 31.0% lower than the SA cohort. 60-Day: HR= 0.30; 95% CI: 0.26-0.36; p>0.001, the odds associated with CA cohort was 23.1% lower than the SA cohort. 90-Day: HR= 0.28; 95% CI: 0.25-0.33; p>0.001, the odds associated with CA cohort was 21.9% lower than the SA cohort.

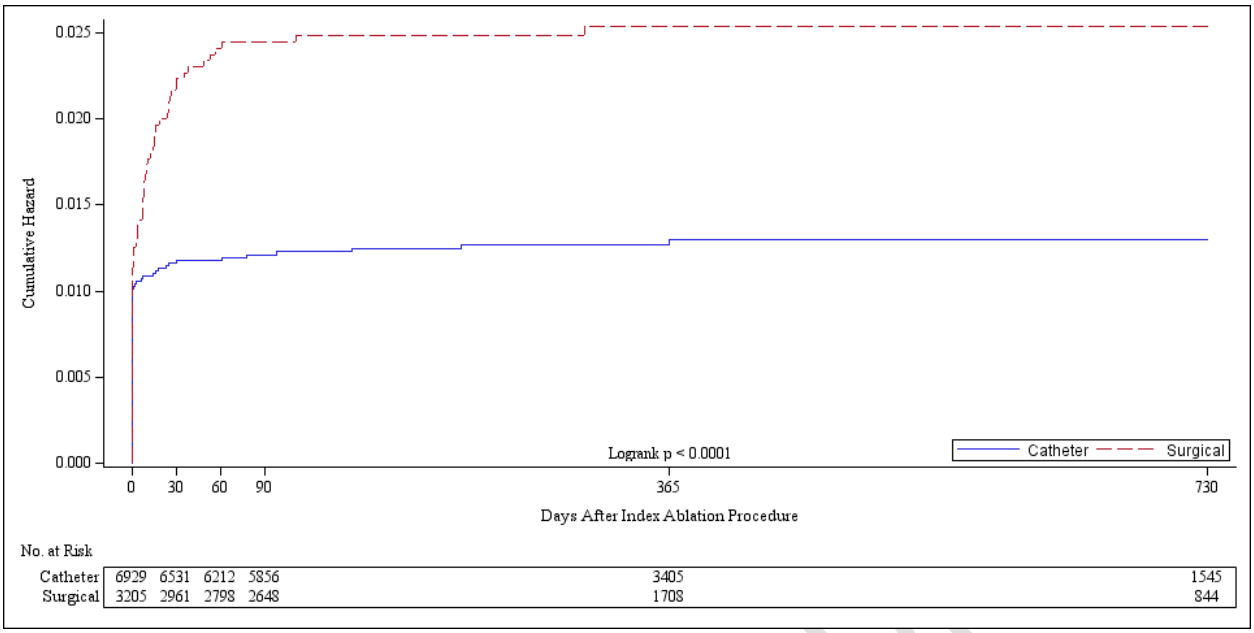

Figure 3. Unadjusted Cumulative Hazard of Cardiac Tamponade or Pericardiocentesis Procedure for Patients Undergoing Ablation Procedure for Atrial Fibrillation

30-Day: HR= 0.71; 95% CI: 0.49-1.02; p=0.067, there was no significant difference in the risks of CTPP between the two cohorts at 30 days. 60-Day: HR= 0.72; 95% CI: 0.50-1.03; p=0.072, there was no significant difference in the risks of CTPP between the two cohorts at 60 days. 90-Day: HR= 0.63; 95% CI: 0.44-0.89; p=0.009, the odds associated with CA cohort was 38.7% lower than the SA cohort. 365-day: HR= 0.52; 95% CI: 0.38-0.71; p>0.001, the odds associated with CA cohort was 34.2% lower than the SA cohort. 730-Day: HR= 0.52; 95% CI: 0.38-0.71; p>0.001, the odds associated with CA cohort was 34.2% lower than the SA cohort.

Table 1. Baseline patient characteristics of the study population after propensity-score matching

	Total		Surgical Ablation Cohort		Catheter Ablation Cohort	
	N	%	N	%	N	%
Total	3,846	100.0	1,923	50.0	1,923	50.0
Age						
Mean (SD)	67 (11.1)		67 (11.1)		67 (11.1)	
18-49	220	5.7	108	5.6	112	5.8
50-64	1,267	32.9	640	33.3	627	32.6
65-79	1,897	49.3	946	49.2	951	49.5
80+	462	12.0	229	11.9	233	12.1
Gender						
Male	2,345	61.0	1,167	60.7	1,178	61.3
Female	1,501	39.0	756	39.3	745	38.7
Region						
Northeast	668	17.4	347	18.0	321	16.7
Midwest	1,267	32.9	628	32.7	639	33.2
South	1,050	27.3	517	26.9	533	27.7
West	811	21.1	407	21.2	404	21.0
Other	50	1.3	24	1.2	26	1.4
Payer						
Commercial	1,539	40.0	776	40.4	763	39.7
Medicare	1,881	48.9	935	48.6	946	49.2
Medicaid	208	5.4	98	5.1	110	5.7
Unknown	218	5.7	114	5.9	104	5.4
Number of previous ablations						
0	3,042	79.1	1,499	78.0	1,543	80.2
1	663	17.2	352	18.3	311	16.2
≥ 2	141	3.7	72	3.7	69	3.6
Year of ablation procedure						
2007	234	6.1	109	5.7	125	6.5
2008	708	18.4	343	17.8	365	19.0
2009	686	17.8	357	18.6	329	17.1
2010	573	14.9	279	14.5	294	15.3
2011	506	13.2	262	13.6	244	12.7
2012	498	12.9	249	12.9	249	12.9
2013	414	10.8	208	10.8	206	10.7

	Total		Surgical Ablation Cohort		Catheter Ablation Cohort	
	N	%	N	%	N	%
2014	227	5.9	116	6.0	111	5.8
Number of previous hospitalizations						
0	2,410	62.7	1,196	62.2	1,214	63.1
1	949	24.7	476	24.8	473	24.6
2	309	8.0	164	8.5	145	7.5
≥ 3	178	4.6	87	4.5	91	4.7
Risk factors for thromboembolism	3,504	91.1	1,742	90.6	1,762	91.6
Hypertension*	3,230	84.0	1,556	80.9	1,674	87.1
Diabetes*	1,295	33.7	608	31.6	687	35.7
Congestive cardiac failure*	1,666	43.3	933	48.5	733	38.1
Thromboembolic event*	72	1.9	54	2.8	18	0.9
Stroke/TIA	225	5.9	121	6.3	104	5.4
CCI						
Mean (SD)	2.9 (2.3)		3.0 (2.4)		2.8 (2.2)	
0	393	10.2	201	10.5	192	10.0
1	800	20.8	391	20.3	409	21.3
2	838	21.8	424	22.0	414	21.5
≥ 3	1,815	47.2	907	47.2	908	47.2
Comorbidities						
Coronary artery disease	2,562	66.6	1,267	65.9	1,295	67.3
Hyperlipidemia	2,699	70.2	1,348	70.1	1,351	70.3
Cardiomyopathy	805	20.9	387	20.1	418	21.7
Valvular heart disease	1,825	47.5	929	48.3	896	46.6
Chronic pulmonary disease	732	19.0	361	18.8	371	19.3
Renal disease	71	1.8	35	1.8	36	1.9
Anticoagulation	2,897	75.3	1,442	75.0	1,455	75.7
Warfarin	2,336	60.7	1,167	60.7	1,169	60.8
Aspirin*	98	2.5	62	3.2	36	1.9
Rivaroxaban*	141	3.7	53	2.8	88	4.6
Clopidogrel	426	11.1	211	11.0	215	11.2
Dabigatran*	249	6.5	77	4.0	172	8.9
Danaparoid	0	0.0	0	0.0	0	0.0
Enoxaparin*	827	21.5	322	16.7	505	26.3
Fondaparinux	16	0.4	11	0.6	5	0.3
Dalteparin	31	0.8	17	0.9	14	0.7

**Significant at p<0.05*

Table 2. Crude Risks and Hazard Ratios of Cardiac Tamponade/Pericardiocentesis Procedure, Rehospitalization, and Hematoma/Hemorrhage for Catheter Ablation vs. Surgical Ablation

Outcome Measures	No. (%)			Hazard Ratios (95% Confidence Interval) of Catheter Ablation vs. Surgical Ablation			
	Catheter Ablation (6,929)	Surgical Ablation (3,205)	P-Value	Crude	P-Value	Adjusted*	P-Value
CTPP, Days							
30	81 (1.2)	70 (2.2)	<0.001	0.71 (0.49-1.02)	0.067	0.60 (0.35-1.05)	0.075
60	81 (1.2)	75 (2.3)	<0.001	0.72 (0.50-1.03)	0.072	0.75 (0.40-1.41)	0.378
90	83 (1.2)	76 (2.4)	<0.001	0.63 (0.44-0.89)	0.009	0.70 (0.38-1.29)	0.248
365	87 (1.3)	78 (2.4)	<0.001	0.52 (0.38-0.71)	<0.001	0.61 (0.37-1.02)	0.059
730	87 (1.3)	78 (2.4)	<0.001	0.52 (0.38-0.71)	<0.001	0.61 (0.37-1.02)	0.059
Rehospitalization, Days							
30	452 (6.5)	684 (21.3)	<0.001	0.45 (0.36-0.55)	<0.001	0.88 (0.64-1.22)	0.451
60	617 (8.9)	826 (25.8)	<0.001	0.30 (0.26-0.36)	<0.001	0.60 (0.46-0.77)	<0.001
90	730 (10.5)	906 (28.3)	<0.001	0.28 (0.25-0.33)	<0.001	0.54 (0.43-0.68)	<0.001
Hematoma/ Hemorrhage, Days							
30	181 (2.6)	71 (2.2)	0.233	1.27 (0.91-1.77)	0.154	1.49 (1.00-2.21)	0.048
60	186 (2.7)	79 (2.5)	0.520	1.35 (0.99-1.85)	0.062	1.42 (0.97-2.09)	0.069
90	192 (2.8)	79 (2.5)	0.375	1.17 (0.87-1.57)	0.289	1.51 (1.04-2.21)	0.031
365	207 (3.0)	91 (2.8)	0.682	1.12 (0.86-1.47)	0.393	1.47 (1.03-2.09)	0.032
730	214 (3.1)	95 (3.0)	0.735	1.12 (0.86-1.45)	0.417	1.51 (1.07-2.12)	0.019

Abbreviations: CTPP, Cardiac Tamponade/Pericardiocentesis Procedure

**Model adjusted for propensity scores*

APPENDIX

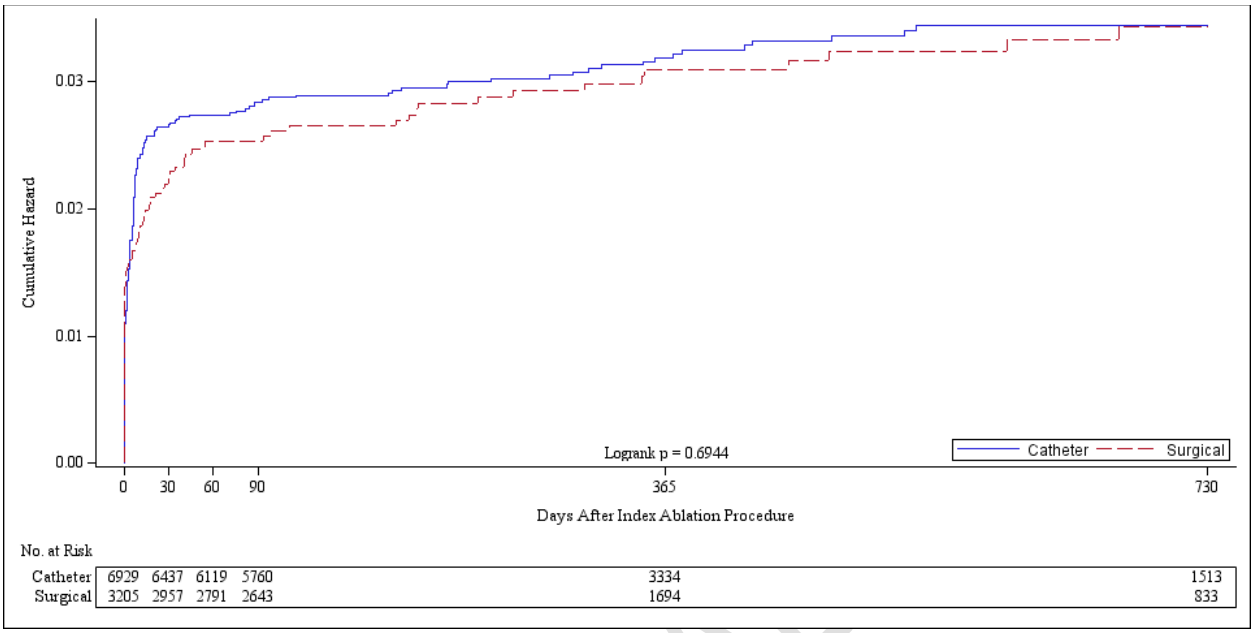

Figure A1. Unadjusted Cumulative Hazard of Cardiac Hematoma or Hemorrhage Patients Undergoing Ablation Procedure for Atrial Fibrillation

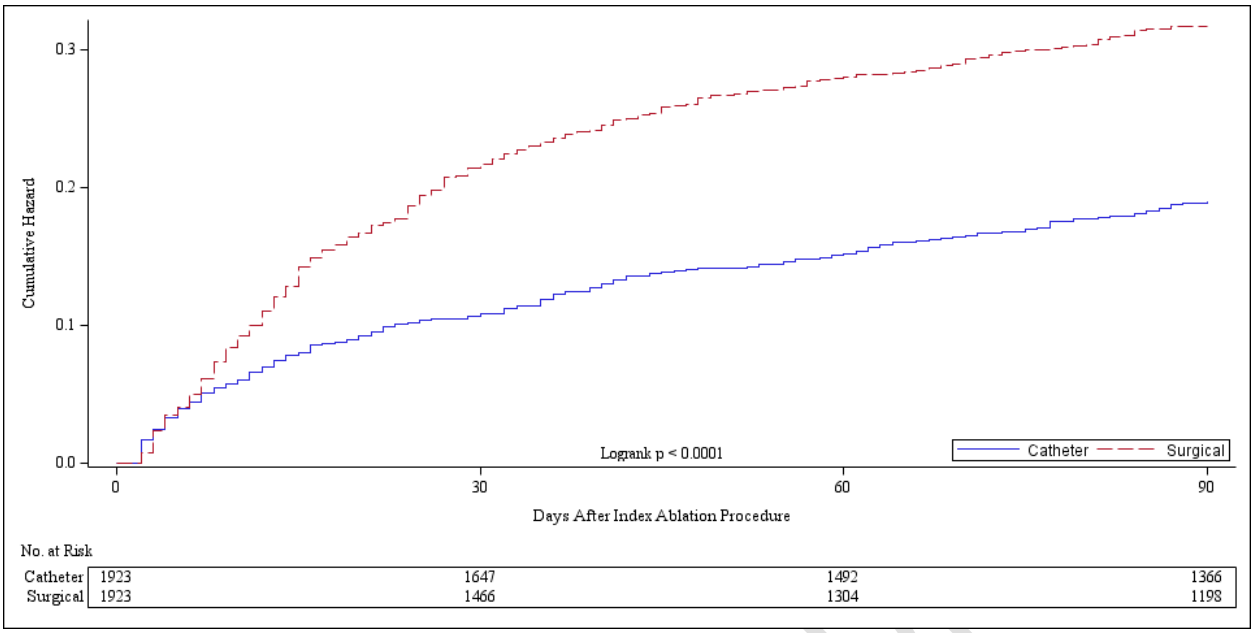

Figure A2. Adjusted Cumulative Hazard of Rehospitalizations for Patients Undergoing Ablation Procedure for Atrial Fibrillation

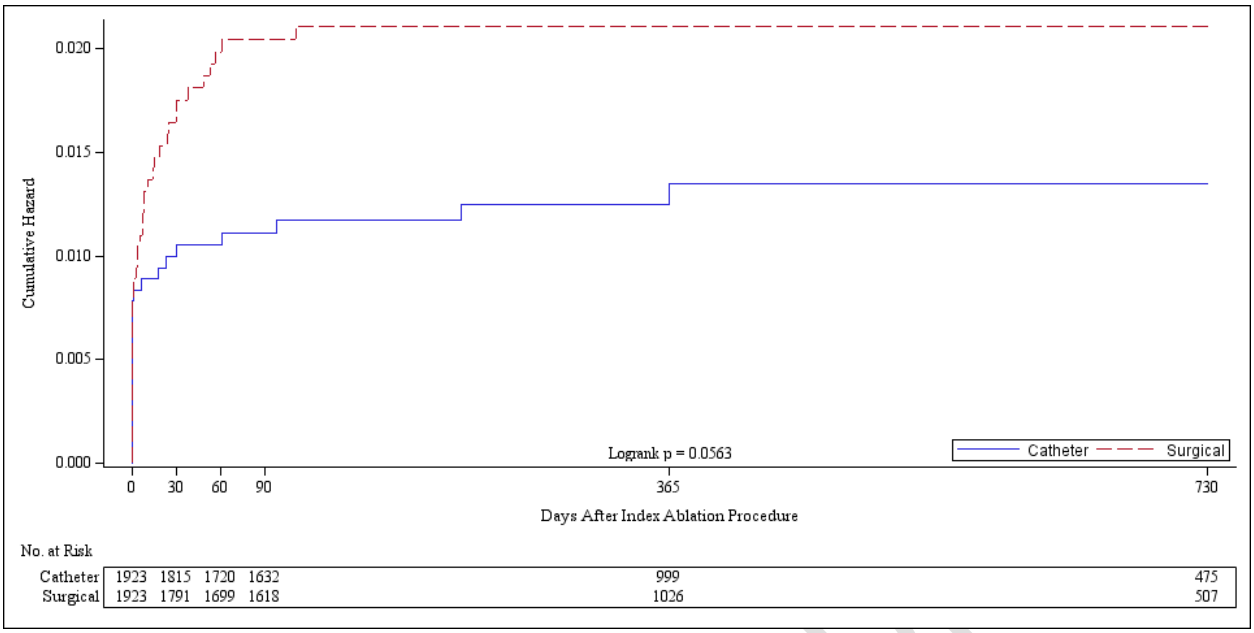

Figure A3. Adjusted Cumulative Hazard of Cardiac Tamponade or Pericardiocentesis Procedure for Patients Undergoing Ablation Procedure for Atrial Fibrillation

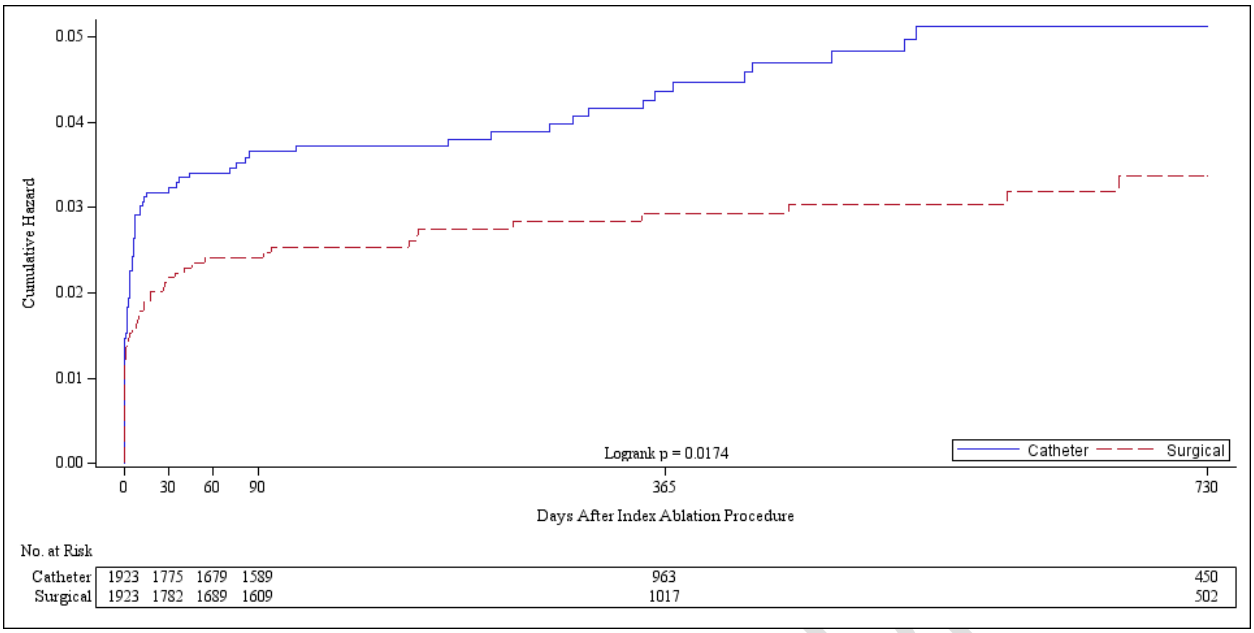

Figure A4. Adjusted Cumulative Hazard of Cardiac Hematoma or Hemorrhage Patients Undergoing Ablation Procedure for Atrial Fibrillation

Table A1. Adjusted Rates of Cardiac Tamponade/Pericardiocentesis Procedure, Hematoma/Hemorrhage, and Rehospitalization for Catheter Ablation Compared to Published Rates

Data Source	Outcomes		
	30-Day CTPP	30-Day Hematoma/ Hemorrhage	30-Day Rehospitalization
MORE[2] Registry	1.0%	3.2%	10.1%
California State Inpatient Database[19]	2.5%	2.2%	9.4%
Worldwide Survey[1]	1.3%	-	-
Medicare Fee-for-Service[17]	1.7%	-	-
Medicare Provider Analysis and Review[8]	3.1%	4.8%	-

Abbreviations: CTPP, Cardiac Tamponade/Pericardiocentesis Procedure

Table A2. International Classification of Disease, Version 9 (ICD-9), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) Codes used for Atrial Fibrillation Ablation Case and Co-Morbidity Identification

Condition/Procedure	Codes
Ablation	
Catheter	ICD-9-CM code 37.34, HCPCS code C1886, or CPT code 93650, 93651, 93653, 93655, 93656, or 93657
Surgical	ICD-9-CM code 37.33 or CPT code 33250, 33251, 33254, 33255, 33256, 33257, 33258, 33259, or 33265
Atrial Fibrillation	ICD-9-CM code 427.31
Wolf-Parkinson-White Syndrome	ICD-9-CM code 426.7
Nonparoxysmal Atrioventricular Nodal Tachycardia	ICD-9-CM code 426.89
Paroxysmal Supraventricular Tachycardia	ICD-9-CM code 427.0
Paroxysmal Ventricular Tachycardia	ICD-9-CM code 427.1 or 427.2
Atrial Flutter	ICD-9-CM code 427.32
Atrioventricular Nodal Reentrant Tachycardia	ICD-9-CM code 427.89
Ventricular Premature Beats or Complexes	ICD-9-CM code 427.60
Anomalous Atrioventricular Excitation	ICD-9-CM code 426.70
Atrioventricular Node Ablation	ICD-9-CM code V45.89
Implantation Pacemaker	ICD-9-CM code V45.01 or V45.02
Implantable Cardioverter-Defibrillator	ICD-9-CM code 996.0, 996.04, V53.31, or V53.32
Risk Factors for Thromboembolism	
Hypertension	ICD-9-CM code 401.XX
Diabetes	ICD-9-CM code 250.XX, 357.2X, 362.0X, 366.41, or 648.0X
Congestive Cardiac Failure	ICD-9-CM code 428.0, 428.40, or 428.90
Thromboembolic Event	ICD-9-CM code 434.10, 434.11, or 444.9
Stroke/TIA	ICD-9-CM code V12.54
Coronary Artery Disease	ICD-9-CM code 414.00, 414.01, or 746.85
Hyperlipidemia	ICD-9-CM code 272.0, 272.2, or 272.4
Cardiomyopathy	ICD-9-CM code 425.11, 425.18, 425.4, 425.5, 674.51, or 674.54
Valvular Heart Disease	ICD-9-CM code 397.0, 396.0, 396.1, 396.2, 396.3, 424.1, 424.2, or 424.3
Chronic Pulmonary Disease	ICD-9-CM code 491, 491.2, 492, 496, or 506.4
Renal Disease	ICD-9-CM code 585.5, 585.6, V42.0, or V45.1
Cardiac Tamponade/Pericardiocentesis Procedure	ICD-9-CM code 37.0 or CPT code 33010 and/or 33011
Hematoma/Hemorrhage	ICD-9-CM code 998.12