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CLINICAL RESEARCH

In-hospital complications associated with pulmonary vein isolation with adjunctive lesions: the NCDR AFib Ablation Registry

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Aims No prior study has been adequately powered to evaluate real-world safety outcomes in those receiving adjunctive ablation lesions beyond pulmonary vein isolation (PVI). We sought to evaluate characteristics and in-hospital complications among patients undergoing PVI with and without adjunctive lesions.

Methods and results Patients in the National Cardiovascular Data Registry AFib Ablation Registry undergoing first-time atrial fibrillation (AF) ablation between 2016 and 2020 were identified and stratified into paroxysmal (PAF) and persistent AF, and separated into PVI only, PVI + cavotricuspid isthmus (CTI) ablation, and PVI + adjunctive (superior vena cava isolation, coronary sinus, vein of Marshall, atypical atrial flutter lines, other). Adjusted odds of adverse events were calculated using multivariable logistic regression. A total of 50 937 patients [PAF: 30 551 (60%), persistent AF: 20 386 (40%)] were included. Among those with PAF, there were no differences in the adjusted odds of complications between PVI + CTI or PVI + adjunctive when compared with PVI only. Among persistent AF, PVI + adjunctive was associated with a higher risk of any complication [3.0 vs. 4.5%, odds ratio (OR) 1.30, 95% confidence interval (CI) 1.07–1.58] and major complication (0.8 vs. 1.4%, OR 1.56, 95% CI 1.10–2.21), while no differences were observed in PVI + CTI compared with PVI only. Overall, there was high heterogeneity in adjunctive lesion type, and those receiving adjunctive lesions had a higher comorbidity burden.

Conclusion Additional CTI ablation was common without an increased risk of complications. Adjunctive lesions other than CTI are commonly performed in those with more comorbidities and were associated with an increased risk of complications in persistent AF, although the current analysis is limited by high heterogeneity in adjunctive lesion set type.

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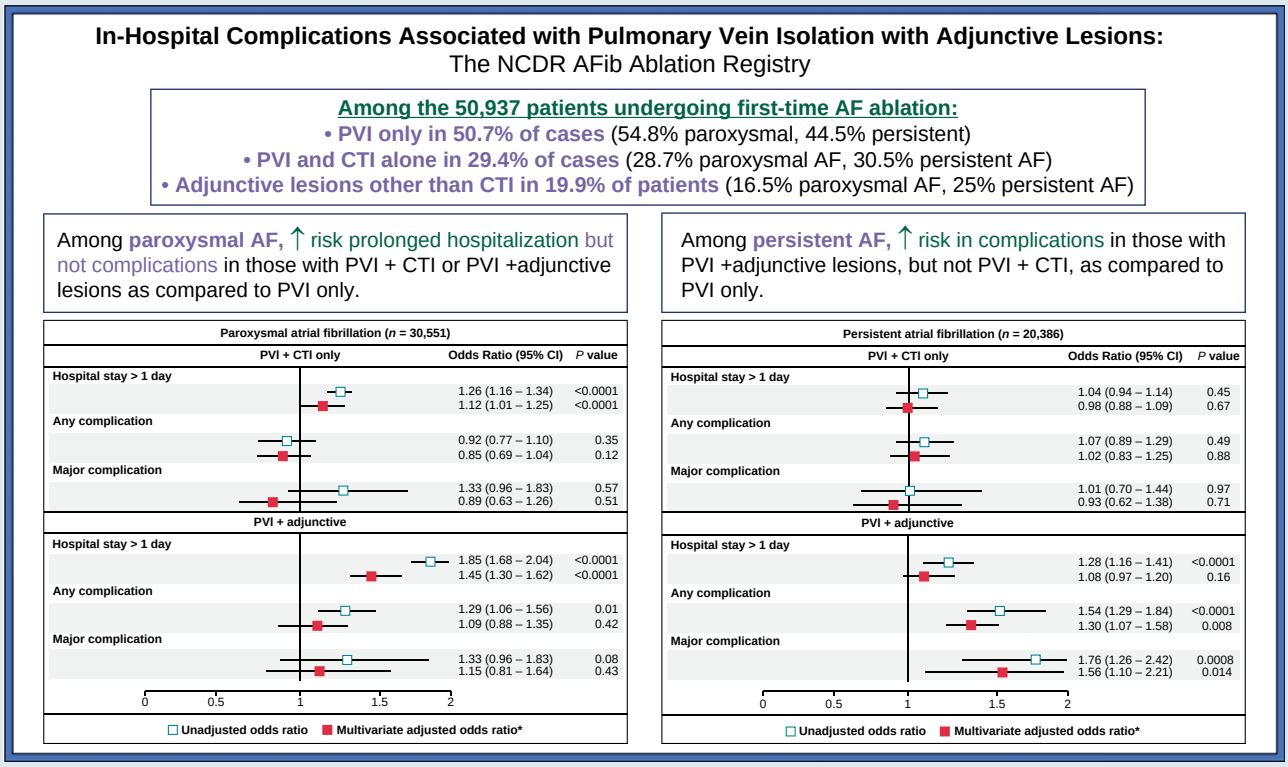
Graphical Abstract



Keywords Atrial fibrillation • Ablation • Pulmonary vein isolation • Adjunctive lesions • Paroxysmal • Persistent • Outcomes • Registry • Complications

What's new?

- In 50 937 patients undergoing atrial fibrillation (AF) ablation, adjunctive lesions beyond pulmonary vein isolation (PVI) were performed in nearly half of the cohort with high heterogeneity.
- Among those with paroxysmal AF, there was an increased risk of prolonged hospitalization, but no difference in the risk of complications in those with adjunctive lesions when compared with PVI only.
- Those with persistent AF who undergo PVI plus adjunctive lesions were at a higher risk of procedural complications than those with PVI alone, but no difference in risk was observed with PVI plus cavotricuspid isthmus ablation alone.

Introduction

Percutaneous catheter ablation for atrial fibrillation (AF) leads to a significant improvement in the quality of life, reduction in hospitalizations, decreased AF burden, and may increase the chances of survival in those with systolic heart failure.[1–3] Pulmonary vein isolation (PVI) has remained the cornerstone of AF ablation based on landmark data demonstrating triggers originating from the PVs, although atrial arrhythmia recurrence rates approach 40% in paroxysmal AF (PAF) and nearly half in those with persistent AF.[4,5] Several trials have evaluated various adjunctive lesions beyond PVI with the goal to improve AF-free survival with mixed results, including left atrial linear ablation, complex fractionated electrogram ablation, vein of Marshall ethanol ablation, left atrial appendage isolation, and posterior wall isolation.[6–9] Although limited trial data have failed to lead to a Class I indication for a non-PVI ablation strategy per the professional society guidelines, adjunctive lesions are still commonly performed in the real world with unclear procedural risk due to underpowered studies.[5,10]

Using data from the National Cardiovascular Data Registry (NCDR) AFib Ablation Registry, the present study evaluated the differences among patients stratified into PAF and persistent AF undergoing PVI only, PVI plus cavotricuspid isthmus (CTI) ablation, and PVI plus adjunctive lesions in terms of patient characteristics and in-hospital complications.

Methods

Data source

The patients included in this study were enrolled the NCDR AFib Ablation Registry. Briefly, the American College of Cardiology launched the NCDR AFib Ablation Registry to assess the prevalence, demographics, management, and outcomes of patients undergoing percutaneous catheter ablation procedures to manage AF in the USA. Details have been described in the original publication of the NCDR AFib Ablation Registry.[11] Briefly, the voluntary registry began collection of approximately 230 data elements from index hospitalization beginning in January 2016. A link to the full data collection forms for the index hospitalization is publicly available.[12] Data are collected by sites at discharge. The NCDR Data Quality Reporting process has been designed to ensure that submissions are complete, valid, and accurate. It involves an annual audit of ~5% of sites that are randomly selected during which submitted data are compared with source documentation and billing data as well as evaluation of sites that are outliers with regards to adverse event rates.[13] Waiver of written informed consent and authorization for NCDR studies were granted by Chesapeake Research Review Incorporated. The research in this study

was conducted according to the Helsinki Declaration guidelines on human research.

Study population

Between 1 January 2016, and 31 December 2020, a total of 162 hospitals submitted data on 67 970 patients undergoing AF ablation. We identified a final cohort of 50 937 patients after exclusion of patients with prior surgical or percutaneous catheter ablation ($n = 15\,101$), left atrial appendage thrombus ($n = 227$), atrioventricular node ablation with pacemaker implantation ($n = 429$), those labelled as permanent AF ($n = 101$), and those with missing values on AF type or adjunctive lesions ($n = 1175$).

The cohort was first stratified into PAF and persistent AF and then grouped into PVI only, PVI plus CTI ablation alone, and PVI plus adjunctive lesions with or without CTI ablation. Adjunctive lesions included superior vena cava (SVC) isolation, coronary sinus ablation, ligament/vein of Marshall ablation, atypical atrial flutter (AFL) lines, and other.

Outcomes

First, in-hospital events were compared among PVI only, PVI plus CTI, and PVI plus adjunctive lesions. Periprocedural information, death, hospital stay >1 day, any complication, and major complication were collected. Major complications included death, stroke, transient ischaemic attack, cardiac arrest, cardiac surgery, vascular injury requiring intervention, access site bleeding requiring transfusion, and pericardial effusion requiring intervention.

Statistical analysis

Baseline demographic and clinic factors are presented as numbers and percentages for categorical variables. Categorical variables were compared using the χ^2 test, and continuous variables were compared using the Wilcoxon rank sum test or the *t*-test as appropriate. Missing dichotomous variables (yes/no) were treated as no, and missing continuous variables were imputed with the overall median value. For missing categorical variables, the most common category of each variable was imputed.

Descriptive, unadjusted outcomes were summarized by the numbers and percentages of events. Then, unadjusted and adjusted multivariable logistic regressions were used to obtain odds ratios (ORs) with 95% confidence intervals (CIs) for PVI plus CTI and PVI plus adjunctive lesions vs. PVI only (reference) for in-hospital outcomes (hospital stay >1 day, any complication, and major adverse event). All tests were two-sided and $P \leq 0.05$ was considered statistically significant. Variables in the multivariable model were chosen based on both clinical risk-adjusted variable selection and backward elimination. Patient characteristics that differed between ablation strategies in the univariate analysis were entered into a logistic regression model with backward selection using a $P \leq 0.05$ for removal during the selection process. The final covariates in the multivariable model included age, race/ethnicity, insurance status, body mass index, chronic lung disease, obstructive sleep apnoea, cardiomyopathy, CHA2DS2-VASc score, HAS-BLED score, preprocedural creatinine, prior typical AFL, warfarin use, hospital region, and teaching hospital. Potential confounding variables were well represented and collected as part of the NCDR AFib Ablation Registry. All analyses were performed with the SAS statistical package, version 9.4 (SAS Institute Inc.).

Results

Between 1 January 2016 and 31 December 2020, a total of 50 937 patients undergoing first-time AF ablation were enrolled in the NCDR AFib Ablation Registry.

Baseline characteristics for those with paroxysmal atrial fibrillation

Of the 30 551 patients with PAF, the ablation strategies included PVI only ($n = 16\,374$, 54.8%), PVI plus CTI only ($n = 8775$, 28.7%), and PVI plus adjunctive lesions with or without CTI lesion ($n = 5041$, 16.5%). Baseline characteristics of the PAF cohort are shown in *Table 1*. Those with PVI plus adjunctive lesions were older, more likely to be female, more likely to have coronary artery disease, congestive heart failure, hypertension, and diabetes than those undergoing PVI only and PVI plus CTI. Those with PVI plus adjunctive lesions also had a slightly higher prevalence of AFL than PVI only and PVI plus CTI (55.0 vs. 13.7 vs. 40.9%, $P < 0.0001$). Also, PVI plus adjunctive lesions had a higher prevalence of prior attempts at AF termination, specifically with direct current cardioversion. Those with PVI plus adjunctive lesions were more likely to have moderately (16.0%) and severely enlarged left atrial size (10.2%) on echocardiogram. Slightly less than half of the patients were prescribed a direct oral anti-coagulant and warfarin was prescribed in over 5% of patients prior to the procedure. Those with PVI plus adjunctive lesions were less likely to be prescribed a preprocedural anti-arrhythmic drug than those undergoing PVI only and PVI and CTI (31.9 vs. 41.1 vs. 40.5%, respectively).

Baseline characteristics for those with persistent atrial fibrillation

Of the 20 386 patients with persistent AF, the ablation strategies included PVI only ($n = 9076$, 44.5%), PVI plus CTI only ($n = 6222$, 30.5%), and PVI plus adjunctive lesions ($n = 5088$, 25.0%). Baseline characteristics of the persistent AF cohort are shown in *Table 2*. Those with PVI plus adjunctive lesions in the persistent AF cohort were also older and had a higher prevalence of coronary artery disease, congestive heart failure, and hypertension. Those with PVI plus CTI reported a higher prevalence of prior history of AFL when compared with PVI only and PVI plus adjunctive lesions (45.8 vs. 13.4 vs. 30.6%, $P < 0.0001$). Prior attempts at AF termination occurred in ~80% of each group with slightly higher prevalence in the PVI only group. Approximately 18% of patients had a severely enlarged left atrium with no differences across the groups. Also, approximately a half of the patients were prescribed a direct oral anti-coagulation while warfarin was prescribed in ~6% prior to the procedure. Those with PVI plus adjunctive lesions were less likely to be prescribed a preprocedural anti-arrhythmic drug than PVI only and PVI and CTI (30.5 vs. 41.2 vs. 40.1%, respectively).

Procedural information

In the PAF cohort, general anaesthesia was used in over 94%. A double transseptal technique was used more in the PVI plus adjunctive cohort than PVI only and PVI plus CTI (44.9 vs. 30.6 vs. 38.8%). Pulmonary vein isolation was confirmed with bidirectional block in nearly 70%, and a circumferential vein catheter was used in nearly 90% of cases. Direct current cardioversion during the procedure was more common in the PVI plus adjunctive lesion cohort, occurring in 27.3% compared with 15.2% in PVI only and 17.6% in PVI plus CTI.

In the persistent AF cohort, general anaesthesia was used in over 94%. A double transseptal technique was used more in the PVI plus adjunctive cohort than PVI only and PVI plus CTI (44.9 vs. 30.6 vs. 38.8%). Pulmonary vein isolation was confirmed with bidirectional block in nearly 70%, and a circumferential vein catheter was used in nearly 90% of cases. Direct current cardioversion was more common in the PVI plus adjunctive lesion cohort, occurring in 27.3% compared with 15.2% in PVI only and 17.6% in PVI plus CTI.

Adjunctive lesion strategies

The lesion strategies used in those with PVI plus adjunctive lesions in both PAF and persistent AF cohorts are shown in *Table 3*. When compared with those with persistent AF, those with PAF were more likely to receive SVC isolation (5.7 vs. 2.8%, $P < 0.0001$), atypical AFL lines (12.5 vs. 8.1%, $P < 0.0001$), and less likely to receive multiple adjunctive lesions.

Table 1 Baseline characteristics of the paroxysmal atrial fibrillation cohort

	PVI only (*N* = 16 735)	PVI + CTI (*N* = 8775)	PVI + adjunctive (*N* = 5041)	*P*-value
Age	63.9 (11.0)	64.8 (10.3)	65.7 (10.9)	<0.0001
Sex, male	9894 (59.1%)	5710 (65.1%)	2935 (58.2%)	<0.0001
Race				
White	15 698 (93.8%)	8183 (93.3%)	4643 (92.1%)	0.0001
Black	578 (3.5%)	349 (4.0%)	234 (4.6%)	0.0003
Asian	236 (1.4%)	107 (1.2%)	80 (1.6%)	0.1876
Hispanic	666 (4.0%)	271 (3.1%)	126 (2.5%)	<0.0001
Other	317 (1.9%)	169 (1.9%)	129 (2.6%)	0.0103
Insurance payer				
Private	13 288 (79.4%)	6922 (78.9%)	3775 (74.9%)	<0.0001
Medicare	8020 (47.9%)	4337 (49.4%)	2779 (55.1%)	<0.0001
Medicaid	737 (4.4%)	395 (4.5%)	255 (5.1%)	0.14
State-specific plan	271 (1.6%)	152 (1.7%)	116 (2.3%)	0.005
Other	633 (3.8%)	451 (5.1%)	245 (4.9%)	<0.0001
Patient history and risk factors				
Chronic lung disease	1358 (8.1%)	771 (8.8%)	528 (10.5%)	<0.0001
Coronary artery disease	3380 (20.2%)	1781 (20.3%)	1192 (23.7%)	<0.0001
Obstructive sleep apnoea	4808 (28.7%)	2601 (29.6%)	1389 (27.6%)	0.03
Treatment	3561 (74.9%)	1916 (74.8%)	1001 (73.0%)	0.33
Cardiomyopathy	2020 (12.1%)	1236 (14.1%)	805 (16.0%)	<0.0001
Non-ischaemic	1094 (6.5%)	717 (8.2%)	409 (8.1%)	<0.0001
Ischaemic	467 (2.8%)	294 (3.4%)	210 (4.2%)	<0.0001
Restrictive	11 (0.1%)	3 (0.0%)	3 (0.1%)	0.59
Hypertrophic	196 (1.2%)	99 (1.1%)	87 (1.7%)	0.004
Other	317 (1.9%)	169 (1.9%)	129 (2.6%)	0.01
CHA_2DS_2-VASc score	2.4 (1.6)	2.5 (1.6)	2.7 (1.7)	<0.0001
Congestive heart failure	2132 (12.7%)	1255 (14.3%)	872 (17.3%)	<0.0001
NYHA Class I	751 (4.5%)	351 (4.0%)	245 (4.9%)	0.05
NYHA Class II	899 (5.4%)	539 (6.1%)	376 (7.5%)	<0.0001
NYHA Class III	254 (1.5%)	182 (2.1%)	157 (3.1%)	<0.0001
NYHA Class IV	31 (0.2%)	24 (0.3%)	14 (0.3%)	0.26
Left ventricular dysfunction	864 (5.2%)	517 (5.9%)	362 (7.2%)	<0.0001
Hypertension	10 915 (65.2%)	5822 (66.4%)	3440 (68.3%)	0.0003
Diabetes	2835 (17.0%)	1709 (19.5%)	1004 (19.9%)	<0.0001
Stroke	857 (5.1%)	461 (5.3%)	276 (5.5%)	0.60
Transient ischaemic attack	663 (4.0%)	358 (4.1%)	213 (4.2%)	0.69
Thromboembolic event	696 (4.2%)	422 (4.8%)	237 (4.7%)	0.0
Vascular disease	2594 (15.5%)	1366 (15.6%)	922 (18.3%)	<0.0001
Prior myocardial infarction	1353 (8.1%)	687 (7.8%)	456 (9.0%)	0.04
Peripheral arterial disease	491 (2.9%)	277 (3.2%)	181 (3.6%)	0.06
Known aortic plaque	193 (1.2%)	110 (1.3%)	172 (3.4%)	<0.0001
HAS-BLED score	1.0 (0.9)	1.1 (0.9)	1.2 (0.9)	<0.0001
Uncontrolled hypertension	1378 (8.2%)	771 (8.8%)	494 (9.8%)	0.002
Abnormal renal function	427 (2.6%)	266 (3.0%)	203 (4.0%)	<0.0001
Abnormal liver function	111 (0.7%)	80 (0.9%)	49 (1.0%)	0.03
Prior stroke	670 (4.0%)	357 (4.1%)	222 (4.4%)	0.45
Prior bleeding	606 (3.6%)	295 (3.4%)	185 (3.7%)	0.51

Continued

Table 1 *Continued*

	PVI only (*N* = 16 735)	PVI + CTI (*N* = 8775)	PVI + adjunctive (*N* = 5041)	*P*-value
Labile INR	122 (0.7%)	69 (0.8%)	59 (1.2%)	0.009
Alcohol use	855 (5.1%)	502 (5.7%)	268 (5.3%)	0.12
Anti-platelet medication use	1636 (9.8%)	1016 (11.6%)	727 (14.4%)	<0.0001
Non-steroidal inflammatory drug use	3416 (20.4%)	1794 (20.5%)	986 (19.6%)	0.37
Physical examination and labs				
Body mass index, kg/m^2	30.8 (22.0)	30.8 (8.4)	30.6 (7.3)	0.79
Systolic blood pressure, mmHg	133.4 (23.3)	133.0 (23.5)	133.9 (23.0)	0.07
Diastolic blood pressure, mmHg	74.6 (13.8)	75.0 (14.1)	75.5 (13.3)	0.0002
Heart rate, beats/min	68.4 (17.4)	71.3 (20.2)	73.1 (20.2)	<0.0001
Creatinine	1.0 (0.6)	1.1 (0.6)	1.1 (0.7)	<0.0001
Bilirubin	0.7 (0.9)	0.7 (0.5)	0.7 (1.1)	0.28
Arrhythmia history				
Symptomatic	16 392 (98.0%)	8569 (97.7%)	4932 (97.8%)	0.30
Attempts at AFib termination	8459 (50.6%)	4467 (50.9%)	2640 (52.4%)	0.08
Pharmacologic cardioversion	5542 (65.5%)	2824 (63.2%)	1653 (62.6%)	0.004
DC cardioversion	4543 (53.7%)	2604 (58.3%)	1544 (58.5%)	<0.0001
Prior AFL	2293 (13.7%)	4819 (55.0%)	2057 (40.9%)	<0.0001
Typical	1894 (82.6%)	4440 (92.1%)	1599 (77.7%)	<0.0001
Pharmacologic cardioversion	408 (2.4%)	851 (9.7%)	405 (8.0%)	<0.0001
Direct current cardioversion	468 (2.8%)	836 (9.5%)	486 (9.6%)	<0.0001
Catheter ablation	1312 (7.8%)	421 (4.8%)	666 (13.2%)	<0.0001
Pre-procedure imaging				
Transoesophageal echocardiogram performed	7417 (44.4%)	4246 (48.5%)	2193 (43.6%)	<0.0001
Left atrial size				
Normal	1719 (50.1%)	883 (46.4%)	551 (46.2%)	0.26
Mildly enlarged	979 (28.5%)	611 (32.1%)	329 (27.6%)	0.002
Moderately enlarged	499 (14.5%)	263 (13.8%)	191 (16.0%)	0.011
Severely enlarged	234 (6.8%)	148 (7.8%)	122 (10.2%)	<0.0001
Computed tomography performed prior	8084 (90.6%)	3989 (91.0%)	2228 (90.8%)	0.78
Magnetic resonance imaging performed prior	8909 (53.2%)	4371 (49.8%)	2445 (48.5%)	<0.0001
Pre-procedure medications				
Anti-thrombotic therapy				
Warfarin	995 (5.9%)	563 (6.4%)	378 (7.5%)	0.0004
Direct oral anti-coagulant	7789 (46.5%)	4086 (46.6%)	2325 (46.1%)	0.86
Aspirin	3653 (21.8%)	2055 (23.4%)	1221 (24.2%)	0.0003
Clopidogrel	491 (2.9%)	271 (3.1%)	209 (4.1%)	<0.0001
Prasugrel	33 (0.2%)	20 (0.2%)	12 (0.2%)	0.80
Ticagrelor	49 (0.3%)	28 (0.3%)	14 (0.3%)	0.90
Rate-control therapy				
Beta-blocker	8381 (50.1%)	4417 (50.3%)	2460 (48.8%)	0.19
Digoxin	367 (2.2%)	249 (2.8%)	157 (3.1%)	0.0001
Anti-arrhythmic therapy	3732 (41.1%)	2517 (40.5%)	1623 (31.9%)	<0.0001
Amiodarone	1790 (25.9%)	1123 (31.9%)	501 (32.6%)	<0.0001
Dofetilide	683 (9.9%)	202 (5.7%)	98 (6.4%)	<0.0001
Dronedarone	622 (9.0%)	266 (7.6%)	152 (9.9%)	0.004
Flecainide	1889 (27.4%)	1093 (31.1%)	402 (26.2%)	<0.0001
Propafenone	538 (7.8%)	283 (8.0%)	116 (7.6%)	0.003

Continued

Table 1 *Continued*

	PVI only (*N* = 16 735)	PVI + CTI (*N* = 8775)	PVI + adjunctive (*N* = 5041)	*P*-value
Sotalol	1426 (20.7%)	566 (16.1%)	284 (18.5%)	<0.0001
Procedure information				
General anaesthesia	16 081 (96.1%)	8615 (98.2%)	4759 (94.4%)	<0.0001
Double transseptal	5126 (30.6%)	3406 (38.8%)	2265 (44.9%)	<0.0001
All veins present able to be isolated by PVI	15 833 (94.6%)	8426 (96.0%)	4792 (95.1%)	<0.0001
Assessed with circumferential vein catheter	14 337 (90.8%)	7693 (91.5%)	4165 (87.1%)	<0.0001
Isolation confirmation				
Entrance block	2408 (14.4%)	967 (11.0%)	612 (12.1%)	<0.0001
Exit block	1264 (7.6%)	504 (5.7%)	198 (3.9%)	<0.0001
Bidirectional block	11 036 (65.9%)	6322 (72.0%)	3487 (69.2%)	<0.0001
Atrial arrhythmia present during procedure	1515 (9.1%)	4395 (50.3%)	2769 (55.2%)	<0.0001
Cardioversion performed during procedure	2540 (15.2%)	1543 (17.6%)	1371 (27.3%)	<0.0001
Radiation dose				
Hospital characteristics				
Hospital region				
Northeast	2130 (12.7%)	753 (8.6%)	369 (7.3%)	<0.0001
West	2839 (17.0%)	1634 (18.6%)	1034 (20.5%)	<0.0001
Midwest	4978 (29.7%)	2097 (23.9%)	1106 (21.9%)	<0.0001
South	6788 (40.6%)	4291 (48.9%)	2532 (50.2%)	<0.0001
Location				
Rural	840 (5.0%)	599 (6.8%)	372 (7.4%)	<0.0001
Suburban	5059 (30.2%)	2294 (26.1%)	1521 (30.2%)	<0.0001
Urban	10 836 (64.8%)	5882 (67.0%)	3148 (62.4%)	<0.0001
Hospital type				
Government	505 (3.0%)	456 (5.2%)	26 (0.5%)	<0.0001
Private	13 510 (80.7%)	7068 (80.5%)	4169 (82.7%)	0.003
University	2720 (16.3%)	1251 (14.3%)	846 (16.8%)	<0.0001
Teaching	9853 (58.9%)	4342 (49.5%)	2629 (52.2%)	<0.0001
Patient beds	561.0 (266.5)	548.5 (269.9)	523.0 (243.4)	<0.0001
Annual volume	1856.7 (978.8)	1823.3 (923.5)	1834.8 (1020.6)	0.03

CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation; AFL, atrial flutter; INR, international normalized ratio; NYHA, New York Heart Association.

Outcomes

The unadjusted rates of in-hospital adverse events in the PAF cohort are presented in *Table 4*. In-hospital death was rare across the groups. Hospital stay >1 day was more frequent in PVI plus adjunctive lesions than PVI only and PVI plus CTI (14.1 vs. 8.2 vs. 10.1%, $P < 0.0001$). The rates of any complication were higher in the PVI plus adjunctive lesion cohort with 2.9%, when compared with 2.3% in PVI only and 2.1% in PVI plus CTI cohorts ($P = 0.008$). Major complications occurred in 0.8% of PVI only, 0.7% of PVI plus CTI, and 1.1% of PVI plus adjunctive lesions with no statistically significant difference across the groups.

In the PAF cohort, when compared with PVI only, those with PVI plus CTI had a higher odds of hospital stay >1 day in both unadjusted and multivariable adjusted analyses (adjusted OR 1.12; 95% CI 1.01–1.25; $P < 0.0001$), as shown in *Figure 1*. There were no differences in the risk of any complication or major complication. When compared with PVI only, those receiving PVI plus adjunctive lesion were at a significantly higher risk of hospital stay >1 day in both unadjusted and adjusted analyses (adjusted OR 1.45; 95% CI 1.30–1.62; $P < 0.0001$). No differences were observed in any or major complications after adjustment in PVI plus adjunctive compared with PVI only patients.

The unadjusted rates of in-hospital adverse events in the persistent AF cohort are presented in *Table 5*. In-hospital death was rare across the groups. Hospital stay >1 day occurred in 16.2% of patients in the PVI plus adjunctive lesions, compared with 13.1% in PVI only and 13.5% in PVI plus CTI ($P < 0.0001$). Any complication was more frequent in the PVI plus adjunctive lesion cohort with 4.5%, when compared with 3.0% in PVI only and 3.2% in PVI plus CTI ($P = 0.008$). The rates of major complications were more common in PVI plus adjunctive lesions (1.4%) when compared with PVI only (0.8%) and PVI plus CTI (1.4 vs. 0.8 vs. 1.1%, $P = 0.0008$). Specific complications, including stroke/transient ischaemic attack, acute renal failure, and heart failure, were statistically higher in PVI plus adjunctive when compared with the other groups.

Table 2 Baseline characteristics of the persistent atrial fibrillation cohort

	PVI only (*N* = 9076)	PVI + CTI (*N* = 6222)	PVI + adjunctive (*N* = 5088)	*P*-value
Age	65.7 (9.9) 19.0–100.0	66.3 (9.6) 21.0–98.0	67.3 (9.5) 20.0–90.0	<0.0001
Sex, male	6399 (70.5%)	4481 (72.0%)	3467 (68.1%)	<0.0001
Race				
White	8652 (95.3%)	5848 (94.0%)	4773 (93.8%)	<0.0001
Black	243 (2.7%)	225 (3.6%)	156 (3.1%)	0.004
Asian	88 (1.0%)	63 (1.0%)	55 (1.1%)	0.82
Hispanic	286 (3.2%)	185 (3.0%)	119 (2.3%)	0.02
Other	497 (5.5%)	339 (5.4%)	245 (4.8%)	0.20
Insurance payer				
Private	7148 (78.8%)	4814 (77.4%)	3812 (74.9%)	<0.0001
Medicare	4808 (53.0%)	3414 (54.9%)	2988 (58.7%)	<0.0001
Medicaid	409 (4.5%)	309 (5.0%)	232 (4.6%)	0.38
State-specific plan	128 (1.4%)	88 (1.4%)	110 (2.2%)	0.001
Other	340 (3.7%)	329 (5.3%)	296 (5.8%)	<0.0001
Patient history and risk factors				
Chronic lung disease	957 (10.5%)	692 (11.1%)	571 (11.2%)	0.36
Coronary artery disease	2110 (23.3%)	1530 (24.6%)	1307 (25.7%)	0.004
Obstructive sleep apnoea	3369 (37.1%)	2137 (34.3%)	1743 (34.3%)	0.0002
Treatment	2561 (76.9%)	1620 (76.6%)	1295 (74.9%)	0.25
Cardiomyopathy	2609 (28.8%)	1851 (29.8%)	1448 (28.5%)	0.26
Non-ischaemic	1668 (18.4%)	1178 (18.9%)	897 (17.6%)	0.20
Ischaemic	457 (5.0%)	347 (5.6%)	282 (5.5%)	0.25
Restrictive	4 (0.0%)	5 (0.1%)	7 (0.1%)	0.16
Hypertrophic	122 (1.3%)	65 (1.0%)	82 (1.6%)	0.03
Other	497 (5.5%)	339 (5.4%)	245 (4.8%)	0.20
CHA_2DS_2-VASc score	2.7 (1.6)	2.8 (1.6)	3.0 (1.6)	<0.0001
Congestive heart failure	2475 (27.3%)	1765 (28.4%)	1569 (30.8%)	<0.0001
NYHA Class I	696 (7.7%)	417 (6.7%)	364 (7.2%)	0.07
NYHA Class II	1134 (12.5%)	747 (12.0%)	702 (13.8%)	0.01
NYHA Class III	387 (4.3%)	358 (5.8%)	313 (6.2%)	<0.0001
NYHA Class IV	27 (0.3%)	24 (0.4%)	24 (0.5%)	0.25
Left ventricular dysfunction	1230 (13.6%)	941 (15.1%)	770 (15.1%)	0.006
Hypertension	6778 (74.7%)	4579 (73.6%)	3866 (76.0%)	0.01
Diabetes	1978 (21.8%)	1491 (24.0%)	1205 (23.7%)	0.003
Stroke	512 (5.6%)	389 (6.3%)	330 (6.5%)	0.09
Transient ischaemic attack	344 (3.8%)	268 (4.3%)	216 (4.2%)	0.21
Thromboembolic event	465 (5.1%)	385 (6.2%)	249 (4.9%)	0.003
Vascular disease	1552 (17.1%)	1236 (19.9%)	936 (18.4%)	<0.0001
Prior myocardial infarction	774 (8.5%)	593 (9.5%)	469 (9.2%)	0.09
Peripheral arterial disease	313 (3.4%)	238 (3.8%)	214 (4.2%)	0.07
Known aortic plaque	102 (1.1%)	76 (1.2%)	93 (1.8%)	0.0014
HAS-BLED score	1.1 (0.9)	1.2 (0.9)	1.2 (0.9)	<0.0001
Uncontrolled hypertension	737 (8.1%)	523 (8.4%)	495 (9.7%)	0.004
Abnormal renal function	332 (3.7%)	271 (4.4%)	251 (4.9%)	0.001
Abnormal liver function	63 (0.7%)	49 (0.8%)	48 (0.9%)	0.27
Prior stroke	416 (4.6%)	308 (5.0%)	258 (5.1%)	0.36
Prior bleeding	349 (3.8%)	254 (4.1%)	217 (4.3%)	0.46
Labile INR	101 (1.1%)	62 (1.0%)	68 (1.3%)	0.23

Continued

Table 2 *Continued*

	PVI only (*N* = 9076)	PVI + CTI (*N* = 6222)	PVI + adjunctive (*N* = 5088)	*P*-value
Alcohol use	637 (7.0%)	415 (6.7%)	344 (6.8%)	0.68
Anti-platelet medication use	790 (8.7%)	671 (10.8%)	656 (12.9%)	<0.0001
Non-steroidal inflammatory drug use	1825 (20.1%)	1284 (20.7%)	978 (19.2%)	0.17
Physical examination and labs				
Body mass index, mg/m^2	32.5 (10.0)	32.0 (8.2)	32.2 (10.6)	0.004
Systolic blood pressure, mmHg	131.2 (22.9)	131.1 (23.4)	131.2 (23.0)	0.96
Diastolic blood pressure, mmHg	78.3 (15.3)	77.4 (15.0)	78.3 (15.1)	0.0008
Heart rate, beats/min	77.3 (21.0)	79.1 (23.0)	81.2 (22.4)	<0.0001
Body mass index, mg/m^2	32.5 (10.0)	32.0 (8.2)	32.2 (10.6)	0.004
Creatinine	1.1 (0.5)	1.1 (0.5)	1.1 (0.6)	0.005
Bilirubin	0.8 (1.0)	0.8 (0.8)	0.9 (1.5)	0.09
Arrhythmia history				
Symptomatic	8839 (97.4%)	6062 (97.4%)	4972 (97.7%)	0.46
Attempts at AFib termination	7422 (81.8%)	4889 (78.6%)	4104 (80.7%)	<0.0001
Pharmacologic cardioversion	3207 (43.2%)	2070 (42.4%)	1814 (44.2%)	0.21
Direct current cardioversion	6701 (90.3%)	4398 (90.0%)	3666 (89.3%)	0.2
Prior AFL	1212 (13.4%)	2847 (45.8%)	1555 (30.6%)	<0.0001
Typical	895 (73.8%)	2529 (88.8%)	1119 (72.0%)	<0.0001
Pharmacologic cardioversion	228 (2.5%)	458 (7.4%)	320 (6.3%)	<0.0001
Direct current cardioversion	342 (3.8%)	817 (13.1%)	461 (9.1%)	<0.0001
Catheter ablation	584 (6.4%)	176 (2.8%)	327 (6.4%)	<0.0001
Pre-procedure imaging				
Transoesophageal echocardiogram performed	5377 (59.3%)	3682 (59.3%)	3026 (59.6%)	0.96
Left atrial size				
Normal	508 (25.1%)	342 (23.6%)	252 (22.7%)	0.25
Mildly enlarged	615 (30.4%)	435 (30.0%)	364 (32.8%)	0.68
Moderately enlarged	519 (25.7%)	416 (28.7%)	285 (25.7%)	0.02
Severely enlarged	360 (17.8%)	258 (17.8%)	209 (18.8%)	0.83
Computed tomography performed prior	4047 (90.4%)	2575 (85.8%)	2028 (86.5%)	<0.0001
Magnetic resonance imaging performed prior	4463 (49.2%)	2985 (48.0%)	2325 (45.7%)	0.0004
Pre-procedure medications				
Anti-thrombotic therapy				
Warfarin	727 (8.0%)	555 (8.9%)	529 (10.4%)	<0.0001
Direct oral anti-coagulant	4455 (49.1%)	3239 (52.1%)	2521 (49.5%)	0.001
Aspirin	1822 (20.1%)	1309 (21.0%)	1011 (19.9%)	0.23
Rate-control therapy				
Beta-blocker	5427 (59.8%)	3630 (58.3%)	2945 (57.9%)	0.05
Digoxin	417 (4.6%)	296 (4.8%)	274 (5.4%)	0.1
Anti-arrhythmic therapy	6898 (41.2%)	3515 (40.1%)	1536 (30.5%)	<0.0001
Amiodarone	1846 (26.8%)	1391 (39.6%)	851 (55.4%)	<0.0001
Dofetilide	430 (6.2%)	257 (7.3%)	132 (8.6%)	<0.0001
Dronedarone	221 (3.2%)	122 (3.5%)	123 (8.0%)	0.12
Flecainide	459 (6.7%)	378 (10.7%)	198 (12.9%)	<0.0001
Propafenone	170 (2.5%)	93 (2.6%)	60 (3.9%)	0.005
Sotalol	635 (9.2%)	310 (8.8%)	264 (17.2%)	<0.0001
Procedure information				
General	8835 (97.3%)	6071 (97.6%)	5013 (98.5%)	<0.0001

Continued

Table 2 *Continued*

	PVI only (*N* = 9076)	PVI + CTI (*N* = 6222)	PVI + adjunctive (*N* = 5088)	*P*-value
Double transseptal	5126 (30.6%)	3406 (38.8%)	2265 (44.9%)	<0.0001
All veins present able to be isolated by PVI	4871 (95.7%)	8529 (94.0%)	5883 (94.6%)	<0.0001
Assessed with circumferential vein catheter	7793 (91.4%)	5325 (90.7%)	4420 (90.8%)	0.26
Isolation confirmation				
Entrance block	1310 (14.4%)	714 (11.5%)	732 (14.4%)	<0.0001
Exit block	654 (7.2%)	260 (4.2%)	190 (3.7%)	<0.0001
Bidirectional block	5992 (66.0%)	4526 (72.7%)	3472 (68.2%)	<0.0001
Atrial arrhythmia present during procedure	1049 (11.6%)	3330 (53.7%)	2540 (50.0%)	<0.0001
Cardioversion performed during procedure	4912 (54.1%)	2906 (46.7%)	3141 (61.7%)	<0.0001
Hospital characteristics				
Hospital region				
Northeast	1147 (12.6%)	501 (8.1%)	422 (8.3%)	<0.0001
West	1334 (14.7%)	801 (12.9%)	999 (19.6%)	<0.0001
Midwest	3199 (35.2%)	1765 (28.4%)	1357 (26.7%)	<0.0001
South	3396 (37.4%)	3155 (50.7%)	2310 (45.4%)	<0.0001
Location				
Rural	529 (5.8%)	331 (5.3%)	322 (6.3%)	0.07
Suburban	2806 (30.9%)	1706 (27.4%)	1895 (37.2%)	<0.0001
Urban	5741 (63.3%)	4185 (67.3%)	2871 (56.4%)	<0.0001
Hospital type				
Government	324 (3.6%)	365 (5.9%)	25 (0.5%)	<0.0001
Private	7407 (81.6%)	4905 (78.8%)	4260 (83.7%)	<0.0001
University	1345 (14.8%)	952 (15.3%)	803 (15.8%)	0.3003
Teaching	5527 (60.9%)	3097 (49.8%)	2823 (55.5%)	<0.0001
Patient beds	559.4 (265.8)	566.2 (272.9)	516.3 (246.9)	<0.0001
Annual volume	1842.0 (957.2)	1835.1 (874.6)	1769.2 (989.0)	<.0001

CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation; AFL, atrial flutter; INR, international normalized ratio; NYHA, New York Heart Association.

In the multivariable adjusted analysis of the persistent AF cohort, there were no differences in the risk of hospital stay >1 day, any complication, or major complication in PVI plus CTI when compared with PVI only, as shown in *Figure 1*. However, when compared with PVI only, PVI plus adjunctive had a higher risk of any complication (OR 1.30; 95% CI 1.07–1.58; $P = 0.008$) and major complication (OR 1.56; 95% CI 1.10–2.21; $P = 0.014$).

Table 3 Descriptive analysis of adjunctive lesion strategies in the paroxysmal and persistent atrial fibrillation cohorts

	Paroxysmal (*N* = 5041)	Persistent (*N* = 5088)	*P*-value
Superior vena cava isolation	287 (5.7%)	140 (2.8%)	<0.0001
Coronary sinus	126 (2.5%)	128 (2.5%)	0.96
Ligament/vein of Marshall	53 (1.1%)	38 (0.7%)	0.10
Other	1695 (33.6%)	1785 (35.1%)	0.12
Atypical AFL lines	631 (12.5%)	411 (8.1%)	<0.0001
Multiple lesions, including CTI	1846 (36.6%)	2083 (40.9%)	<0.0001
Multiple lesions, non-CTI	403 (8.0%)	503 (9.9%)	0.0009

CTI, cavotricuspid isthmus; AFL, atrial flutter.

Discussion

In this analysis of the largest AF ablation registry including elective outpatient procedures worldwide including 50 937 patients from 2016 to 2020, we observed several important in-hospital findings in patients undergoing PVI with or without adjunctive lesions during first-time ablation. First, 40% of the catheter ablations are being performed in those with persistent AF, and nearly half of the study cohort underwent additional lesions beyond PVI including CTI ablation and other adjunctive lesions. Second, adjunctive lesions were more common in those with persistent AF and a high burden of comorbidities. Third, there was high heterogeneity in the types of adjunctive lesion sets used. Fourth, among those with PAF, those with additional CTI or adjunctive lesions were more likely to experience prolonged hospitalization than PVI only, while there was no increased risk of complications. Lastly, among those with persistent AF, those with PVI plus adjunctive lesions, but not PVI plus CTI alone, were more likely to experience any complications and major complications.

Table 4 Unadjusted prevalence of adverse events among the paroxysmal atrial fibrillation cohort

	PVI only (*N* = 16 735)	PVI + CTI (*N* = 8775)	PVI + adj (*N* = 5041)	*P*-value
In-hospital death	5 (0.0%)	3 (0.0%)	6 (0.1%)	0.03
Hospitalization (>1 vs. ≤1 day)	1366 (8.2%)	885 (10.1%)	711 (14.1%)	<0.0001
Any complication	379 (2.3%)	183 (2.1%)	146 (2.9%)	0.0076
Major complication	133 (0.8%)	64 (0.7%)	53 (1.1%)	0.11
Specific complication				
Bradycardia adverse events	45 (0.3%)	28 (0.3%)	24 (0.5%)	0.07
Cardiac arrest	15 (0.1%)	3 (0.0%)	5 (0.1%)	0.25
Myocardial infarction	8 (0.0%)	2 (0.0%)	4 (0.1%)	0.32
Air embolism	12 (0.1%)	2 (0.0%)	4 (0.1%)	0.25
LA thrombus	5 (0.0%)	2 (0.0%)	0 (0.0%)	0.47
Cardiac thromboembolic event	3 (0.0%)	0 (0.0%)	2 (0.0%)	0.21
TIA/stroke	18 (0.1%)	10 (0.1%)	15 (0.3%)	0.005
Arterial thrombosis	10 (0.1%)	1 (0.0%)	4 (0.1%)	0.14
Deep-vein thrombosis	11 (0.1%)	1 (0.0%)	6 (0.1%)	0.04
Respiratory failure	40 (0.2%)	20 (0.2%)	20 (0.4%)	0.12
Phrenic nerve damage	40 (0.2%)	17 (0.2%)	0 (0.0%)	0.002
Pulmonary embolism	7 (0.0%)	1 (0.0%)	7 (0.1%)	0.004
Pulmonary vein damage/dissection	10 (0.1%)	2 (0.0%)	4 (0.1%)	0.31
Pneumonia	21 (0.1%)	3 (0.0%)	8 (0.2%)	0.04
Sepsis	5 (0.0%)	1 (0.0%)	0 (0.0%)	0.34
Acute renal failure	14 (0.1%)	11 (0.1%)	12 (0.2%)	0.02
GU bleeding	7 (0.0%)	1 (0.0%)	3 (0.1%)	0.30
Heart failure	32 (0.2%)	24 (0.3%)	22 (0.4%)	0.01
Pericardial effusion resulting in cardiac tamponade	42 (0.3%)	24 (0.3%)	19 (0.4%)	0.33
Pericardial effusion requiring cardiac surgery	73 (0.4%)	41 (0.5%)	25 (0.5%)	0.84
Cardiac surgery	17 (0.1%)	6 (0.1%)	6 (0.1%)	0.60
Haemorrhage (non-access site)	15 (0.1%)	11 (0.1%)	5 (0.1%)	0.69
Haematoma at access site	56 (0.3%)	20 (0.2%)	20 (0.4%)	0.18
Bleeding requiring transfusion (access site)	27 (0.2%)	8 (0.1%)	9 (0.2%)	0.29
AV fistula requiring intervention	9 (0.1%)	2 (0.0%)	6 (0.1%)	0.07
Pseudoaneurysm requiring intervention	28 (0.2%)	9 (0.1%)	11 (0.2%)	0.23
Vascular injury	18 (0.1%)	6 (0.1%)	6 (0.1%)	0.56

CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation; AV, arteriovenous; GU, genitourinary; LA, left atrium; TIA, transient ischemic attack.

For over two decades, percutaneous catheter ablation for AF has been shown to be more effective in reducing AF burden than antiarrhythmic drug therapy in several randomized trials.[14,15] Additionally, ablation has also been shown to reduce hospitalizations, improve quality of life, and may improve survival in patients with systolic heart failure.[1–3] Given the superior efficacy, catheter ablation has been strongly endorsed by professional society guidelines, yet approximately one-third of patients with PAF undergoing ablation will have recurrence by 1 year and nearly half of those with persistent AF will have recurrence by 1 year.[5,6,16] Additional ablation strategies targeting arrhythmogenic areas beyond PVI to improve AF-free survival have been evaluated in multiple studies with varying results, although these studies have lacked the power to comprehensively and accurately evaluate procedural complication risk.

In the present study, CTI ablation alone was commonly performed in addition to PVI, including 28.7% of the PAF cohort and 30.5% of the persistent AF cohort. Atrial fibrillation and AFL often coexist and are closely interrelated.[17] Cavotricuspid isthmus ablation combined with PVI in patients with a history of AFL has been shown to reduce recurrence of atrial arrhythmia.[18,19] Although a safe, efficacious, and durable procedure, prophylactic CTI ablation has not been shown to improve freedom from atrial arrhythmia recurrence.[20,21] Therefore, a Class I indication by professional society guidelines exists for concomitant CTI ablation only in those with previously documented or inducible AFL.[5] Over half of the PAF cohort and 46% of the persistent AF cohort had prior documented AFL; however, inducible AFL at the time of the ablation was not captured in the registry. Despite the low procedural risk of CTI ablation with no significant differences across the groups, we found prolonged hospitalization occurred more often with the addition of CTI ablation in those with PAF. While the registry does not capture the reason for prolonged hospitalization, those with PAF undergoing additional CTI ablation may have required ongoing arrhythmia management,

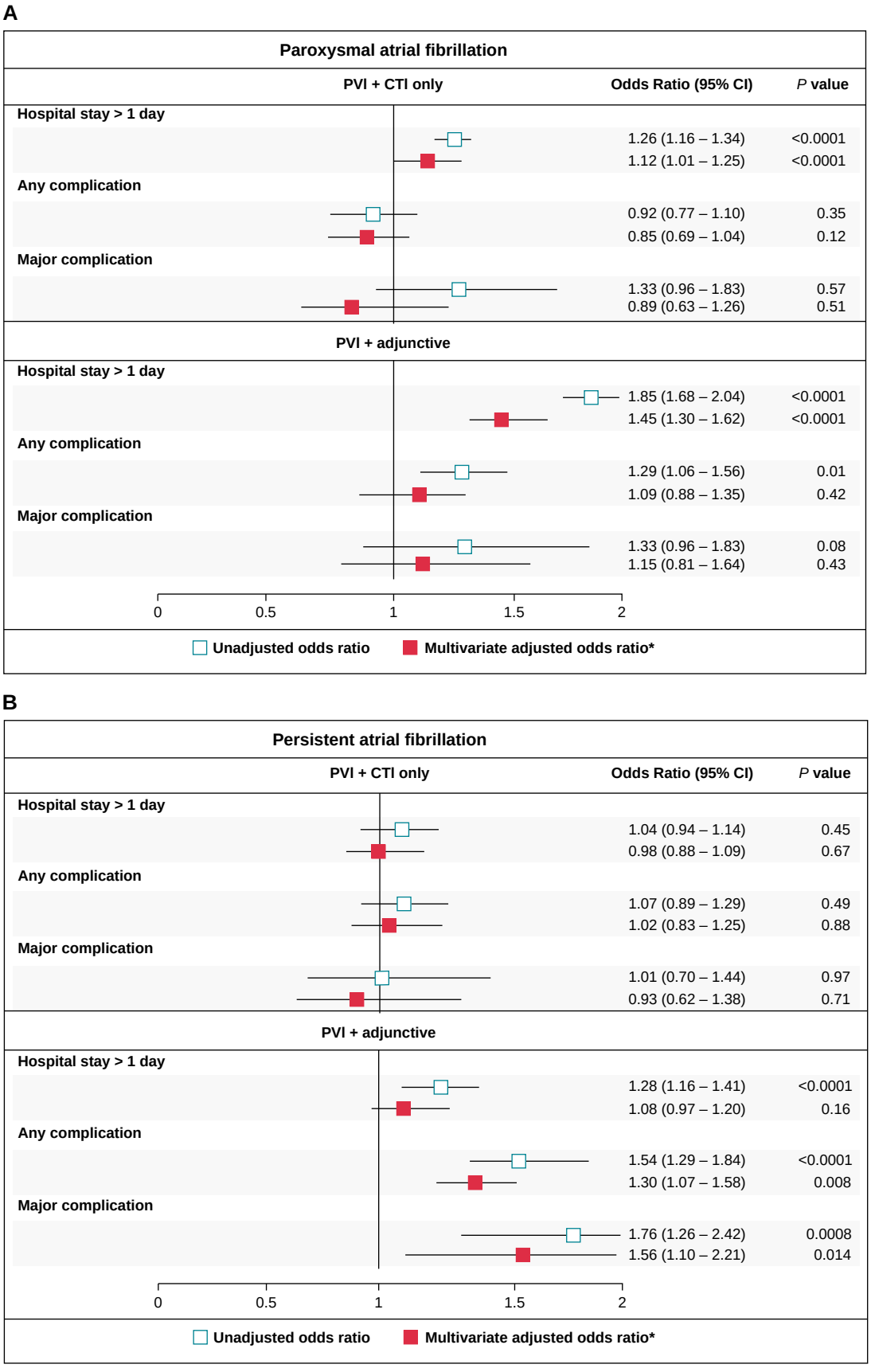


Figure 1 Unadjusted and adjusted outcomes of in-hospital adverse events for those undergoing PVI plus CTI ablation only or adjunctive lesions when compared with PVI only (reference) patients with paroxysmal AF (*A*) and persistent AF (*B*). AF, atrial fibrillation; CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation.

Table 5 Unadjusted prevalence of adverse events among the persistent atrial fibrillation cohort

	PVI only (*N* = 9076)	PVI + CTI (*N* = 6222)	PVI + adj (*N* = 5088)	*P*-value
In-hospital death	3 (0.0%)	3 (0.0%)	7 (0.1%)	0.05
Hospitalization (>1 vs. ≤1 day)	1191 (13.1%)	843 (13.5%)	825 (16.2%)	<0.0001
Any complication	268 (3.0%)	196 (3.2%)	227 (4.5%)	<0.0001
Major complication	74 (0.8%)	51 (0.8%)	72 (1.4%)	0.001
Specific complication				
Bradycardia adverse events	48 (0.5%)	40 (0.6%)	40 (0.8%)	0.17
Cardiac arrest	8 (0.1%)	3 (0.0%)	9 (0.2%)	0.09
Myocardial infarction	1 (0.0%)	2 (0.0%)	2 (0.0%)	0.53
Air embolism	5 (0.1%)	2 (0.0%)	6 (0.1%)	0.18
Left atrial thrombus	3 (0.0%)	1 (0.0%)	0 (0.0%)	0.39
Cardiac thromboembolic event	1 (0.0%)	1 (0.0%)	1 (0.0%)	0.92
TIA/stroke	15 (0.2%)	11 (0.2%)	23 (0.5%)	0.002
Arterial thrombosis	4 (0.0%)	2 (0.0%)	4 (0.1%)	0.52
Deep-vein thrombosis	5 (0.1%)	4 (0.1%)	5 (0.1%)	0.63
Respiratory failure	35 (0.4%)	24 (0.4%)	31 (0.6%)	0.11
Phrenic nerve damage	21 (0.2%)	7 (0.1%)	6 (0.1%)	0.13
Pulmonary embolism	3 (0.0%)	4 (0.1%)	4 (0.1%)	0.49
Pulmonary vein damage/dissection	2 (0.0%)	2 (0.0%)	4 (0.1%)	0.25
Pneumonia	10 (0.1%)	9 (0.1%)	14 (0.3%)	0.06
Sepsis	3 (0.0%)	2 (0.0%)	0 (0.0%)	0.44
Acute renal failure	17 (0.2%)	14 (0.2%)	21 (0.4%)	0.03
GU bleeding	3 (0.0%)	4 (0.1%)	4 (0.1%)	0.49
Heart failure	52 (0.6%)	46 (0.7%)	57 (1.1%)	0.002
Pericardial effusion resulting in cardiac tamponade	21 (0.2%)	15 (0.2%)	18 (0.4%)	0.36
Pericardial effusion requiring cardiac surgery	37 (0.4%)	25 (0.4%)	28 (0.6%)	0.40
Cardiac surgery	7 (0.1%)	9 (0.1%)	8 (0.2%)	0.32
Haemorrhage (non-access site)	6 (0.1%)	9 (0.1%)	10 (0.2%)	0.09
Haematoma at access site	28 (0.3%)	29 (0.5%)	29 (0.6%)	0.06
Bleeding requiring transfusion (access site)	10 (0.1%)	12 (0.2%)	13 (0.3%)	0.12
AV fistula requiring intervention	3 (0.0%)	3 (0.0%)	6 (0.1%)	0.12
Pseudoaneurysm requiring intervention	16 (0.2%)	12 (0.2%)	7 (0.1%)	0.77
Vascular injury	9 (0.1%)	5 (0.1%)	10 (0.2%)	0.16

Major complications included death, stroke, TIA, cardiac arrest, cardiac surgery, vascular injury, access site bleeding, and pericardial effusion.
CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation; AV, arteriovenous; GU, genitourinary; TIA, transient ischemic attack.

including initiation and monitoring of anti-arrhythmic drug therapy, or management of competing comorbidities. As same-day discharge following AF ablation becomes more common, further efforts are warranted to understand the reasons for the prolonged hospitalization in those with PAF requiring additional ablation beyond PVI.[22]

The major finding of the present study was the increased risk of complications observed in those with persistent AF undergoing ablation with adjunctive lesion sets. While PVI remains the cornerstone for AF ablation, recurrence of atrial arrhythmia remains common, often requiring repeat procedures, and further atrial substrate modification, particularly with persistent AF.[23] Strategies including linear ablation, targeting complex fractionated atrial electrogram ablation, or magnetic resonance imaging–guided fibrosis ablation have not demonstrated superiority to PVI in clinical trials.[6,24,25] Although several adjunctive strategies including vein of Marshall ethanol infusion, ablation of non-pulmonary vein (PV) triggers, left atrial appendage isolation, and posterior wall isolation have shown promise in improving AF-free survival in those with persistent AF, no clear consensus exists for guidance of further ablation strategies beyond PVI, leading to debate and uncertainty.[7,8,26,27] As shown in the present study, there was significant heterogeneity in the type of adjunctive lesions performed in both PAF and persistent AF and over a third received multiple lesions. Similarly, in a study of the Get With The Guidelines-Atrial Fibrillation Registry which included 3139 patients from 2016 to 2018, the investigators demonstrated a high use of adjunctive lesions in first-time ablations, including left atrial linear ablations in over a third of patients and posterior wall isolation in nearly a quarter of those with persistent AF, although the rates of procedural complications in those receiving adjunctive lesions were not reported.[10]

While we observed a higher risk in those with persistent AF undergoing adjunctive lesions, this analysis cannot establish a causal

relationship between performing adjunctive ablations and complication risk. The current study is not equipped to determine the underlying cause of complications. Due to the significant heterogeneity in adjunctive lesions performed, often with multiple lesions performed, individual adjunctive lesion outcome analysis was not performed. Furthermore, several factors that may impact the risk relationship remain unknown. The reason for ablation strategy was unavailable in the registry and may be influenced by several factors, including an atrial arrhythmia requiring additional ablation observed before or during the procedure, provider skill and preference for additional lesion type, anatomical factors, or a pre-determined empiric strategy. Furthermore, data on anti-coagulation strategy implementation were limited, including rates of uninterrupted anti-coagulation and the timing of anti-coagulation initiation. While we adjusted for a comprehensive set of comorbidities, those who receive adjunctive may be at inherently higher risk and residual confounding cannot be entirely ruled out. The patients with adjunctive lesions were older and had a higher burden of coronary artery disease, heart failure, hypertension, and diabetes. Indeed, when complications were considered individually, the rates of stroke, acute renal failure, and heart failure were higher in those undergoing adjunctive lesions, although the absolute numbers were small. It is worth noting that phrenic nerve injury was more common in those with PVI only. While it has been shown that phrenic nerve injury is more common with cryoballoon ablation, the current data collection form does not distinguish the ablation modality.[28] Other major complications that may be directly related to vascular access or catheter manipulation, such as pericardial effusion or major bleeding, were not significantly different across the groups. The findings call awareness to optimizing and management of volume status and blood pressure pre-, intra-, and post-procedurally to mitigate risk.

Other factors such as patient selection, ongoing development of safe technology, maintaining adequate volume, and familiarization with newer ablation strategy techniques prior to implementation may also lead to improvement in catheter ablation outcomes in this high-risk cohort. Standardization of ablation strategies beyond PVI to adequately study outcomes in large, randomized trials is also warranted; however, generalizability remains a challenge due to the spectrum of AF burden and the still unknown mechanisms underlying AF initiation and perpetuation. Ultimately, approaches aimed at prevention and delaying progression of AF with lifestyle modification and a paradigm shift to early catheter ablation prior to anti-arrhythmic drug failure and worsening comorbidities may prove instrumental in reducing procedural complications.[29–31]

Limitations

First, the NCDR AFib Ablation Registry is observational data; therefore, causal inferences cannot be made. Although the registry has a large sample size that allows for generalizable data reflecting real-world practice trends and safety data, these findings do not suggest the avoidance of adjunctive lesions during AF ablation. Second, the registry is limited to the index hospitalization. Late complications, such as pulmonary vein stenosis or atrioesophageal fistula, were not captured, nor were long-term atrial arrhythmia recurrence rates. Third, there were several adjunctive lesions likely commonly performed that were not identified on the data collection form, such as posterior wall isolation and left atrial appendage isolation. Lastly, despite adjustment for an extensive list of potential confounders, there may be unmeasured confounders that can influence the risk relationship.

Conclusions

In the largest nationwide cohort of 50 937 patients undergoing first-time AF ablation, those with PAF who underwent PVI plus CTI or adjunctive lesions experienced more prolonged hospitalizations compared with those treated with PVI only, but adjunctive lesion sets otherwise had no impact on adverse outcomes. In patients with persistent AF, those who underwent PVI plus adjunctive lesions were more likely to experience in-hospital complications when compared with those who underwent PVI only, while there was no difference in those who underwent PVI plus CTI. Further strategies are warranted to mitigate the risk of complications in those with persistent AF, including focusing on upstream AF management and further trials to replicate findings, familiarize techniques, and standardize adjunctive lesions.

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Data availability

The data underlying this article were provided by NCDR under funding and permission. Data will be shared on request with the corresponding author with the permission of NCDR.

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