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Original research

# Association between catheter ablation of atrial fibrillation and mortality or stroke

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## ABSTRACT

**Objective** Catheter ablation of atrial fibrillation effectively reduces symptomatic burden. However, its long-term effect on mortality and stroke is unclear. We investigated if patients with atrial fibrillation who undergo catheter ablation have lower risk for all-cause mortality or stroke than patients who are managed medically.

**Methods** We retrospectively included 5628 consecutive patients who underwent first-time catheter ablation for atrial fibrillation between 2008 and 2018 at three major Swedish electrophysiology units. Control individuals with an atrial fibrillation diagnosis but without previous stroke were selected from the Swedish National Patient Register, resulting in a control group of 48 676 patients. Propensity score matching was performed to produce two cohorts of equal size (n=3955) with similar baseline characteristics. The primary endpoint was a composite of all-cause mortality or stroke.

**Results** Patients who underwent catheter ablation were healthier (mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score 1.4±1.4 vs 1.6±1.5, p<0.001), had a higher median income (288 vs 212 1000 Swedish krona [KSEK]/year, p<0.001) and had more frequently received university education (45.1% vs 28.9%, p<0.001). Mean follow-up was 4.5±2.8 years. After propensity score matching, catheter ablation was associated with lower risk for the combined primary endpoint (HR 0.58, 95% CI 0.48 to 0.69). The result was mainly driven by a decrease in all-cause mortality (HR 0.51, 95% CI 0.41 to 0.63), with stroke reduction showing a trend in favour of catheter ablation (HR 0.75, 95% CI 0.53 to 1.07).

**Conclusions** Catheter ablation of atrial fibrillation was associated with a reduction in the primary endpoint of all-cause mortality or stroke. This result was driven by a marked reduction in all-cause mortality.

## INTRODUCTION

Atrial fibrillation (AF) is the most frequent sustained arrhythmia with an estimated prevalence in adults of between 2% and 4%, which is expected to further increase due to extended longevity and improved screening.<sup>1,2</sup> AF is associated with an increased risk of mortality and morbidity related to stroke, heart failure and dementia. Moreover, AF is typically

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Catheter ablation of atrial fibrillation is effective in reducing symptomatic burden; however, several studies on its long-term effect on mortality and stroke show conflicting results.

## WHAT THIS STUDY ADDS

⇒ In this large real-world population study of consecutive patients who underwent catheter ablation at three major Swedish electrophysiology units between 2008 and 2018, we found a significant reduction in mortality or stroke in ablated patients and this was driven by a marked reduction in mortality.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study results should encourage future randomised controlled trials to be conducted on the same topic, and if our findings are corroborated indication for catheter ablation will be strengthened for this patient group.

linked to impaired quality of life and has substantial socioeconomic implications.<sup>3,4</sup> Catheter ablation for AF is more effective than antiarrhythmic drug therapy in restoring sinus rhythm,<sup>5,6</sup> including in therapy-naïve patients, and has been associated with a significant improvement in quality of life.<sup>7</sup> Furthermore, in selected patients with heart failure, three randomised clinical trials (RCTs) found that AF ablation reduces mortality and hospital admissions.<sup>8–10</sup> However, whether ablation also improves clinical outcomes such as stroke and mortality in a general AF population has not been established. The CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial failed to show a reduction in the primary composite endpoint of death, stroke, serious bleeding or cardiac arrest when compared with medical therapy.<sup>11</sup> Several observational and registry studies have attempted to evaluate the effect of AF ablation on stroke and mortality risk with mixed results.<sup>12–16</sup> In addition, two meta-analyses of AF ablation RCTs showed contradictory results on clinical outcomes.<sup>17,18</sup>

Our aim was to evaluate the long-term effects of catheter ablation on the risk of all-cause mortality or stroke in patients with AF in a large real-world cohort followed up by national registries.

## METHODS

### Ablation patients

We included all consecutive patients who underwent first-time AF ablation between 1 January 2008 and 31 December 2018 at three high-volume electrophysiology centres (>300 AF ablations/year) in Sweden (Karolinska University Hospital, Stockholm; Arrhythmia Center, Stockholm; and Linköping University Hospital, Linköping). Patients were prospectively entered into local databases at the time of ablation, together with pertinent information and details about the procedure. Catheter ablation was indicated according to current national and international guidelines, and the electrophysiology procedures followed conventional and local standards as described previously.<sup>19</sup> All patients were on oral anticoagulants (OACs) (warfarin or novel OACs) for at least 3–4 weeks prior to the procedure and intraprocedural heparin was used to maintain activated clotting time (ACT) levels >300 s. Routine transoesophageal echocardiography was performed prior to the ablation to exclude intra-atrial thrombosis. In all cases, pulmonary vein isolation (PVI) was either performed with a radiofrequency (RF) catheter (point-by-point technique) or with a cryoballoon. Ablation in addition to PVI was carried out according to the operator's discretion and consisted of empirical lines, complex fractionated electrograms and substrate ablation. Major complications were defined as tamponade, vascular (requiring invasive treatment or blood transfusion), phrenic paralysis, stroke and death. Given the nature of the study (large sample registry study), we have limited detailed information on follow-up visits, arrhythmia monitoring and arrhythmia status. The patients were followed up according to standard of care, which in general consisted of regular cardiology clinics with 12-lead ECG and 24-hour Holter recordings 3, 6, 12 and 24 months following catheter ablation. For non-ablated patients, follow-up usually consisted of 6–12 months of follow-up with 12-lead ECG and 24-hour Holter recordings.

### Control patients

The control group was selected from the Swedish National Patient Register, which is based on civic registration numbers given to all residents in Sweden irrespective of citizenship, which are used by all authorities, hospitals, open care clinics and pharmacies. The present study used codes according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10 SE). A validation study found the positive predictive value for a diagnosis of stroke (I63) to be 98.6% and for AF (I48) 97%.<sup>20</sup> The civic registration numbers make it possible to follow every patient's medical history as well as purchases of prescribed drugs. The control group consisted of patients with a registered AF diagnosis (I48) at a hospital admission or outpatient clinic visit between 2008 and 2018. Patients with a previous diagnosis of catheter ablation (Nordic Medico-Statistical Committee (NOMESCO) code beginning with FPB or Swedish procedure code DF003) were excluded, as well as patients who had lived less than a year in Sweden prior to study inclusion.

### Patient and public involvement

This research was conducted without patient involvement.

### Matching

A total of 10 control patients per case were selected, matched by age and sex. For all patients in the ablation and control group, baseline characteristics including comorbidities, socioeconomic status and medications at baseline were collected from the Swedish National Patient Register, Statistics Sweden and Swedish Drug Register, respectively. Medication at baseline was defined as a filled prescription within 6 months before study inclusion. Information about medical events during follow-up was obtained from the Swedish National Patient Register and the Cause of Death Register. Baseline characteristics variables known to have a potential impact on the primary combined endpoint (all-cause mortality or stroke) and available from the registry databases were selected for propensity score matching. A total of 29 variables were included in the propensity score matching (online supplemental table 1).

The CHA<sub>2</sub>DS<sub>2</sub>-VASc (heart failure, hypertension, age, diabetes, stroke, vascular disease and gender) scores were calculated based on patient characteristics. The primary endpoint was a composite of all-cause mortality or stroke. Secondary endpoints were all-cause mortality, stroke, cardiovascular mortality and heart failure. The only variable with missing data was classification of level of education and those patients (n=410) were classified as having 'unknown' level of education.

### Statistical analysis

Continuous variables are expressed as mean±SD or as median with IQR for skewed or non-normal data. Comparisons of means were made using Student's t-test for independent samples or Mann-Whitney U test for non-normal distributions. Categorical variables are expressed as absolute frequencies and percentages and compared with Pearson's X<sup>2</sup> test. Propensity scores were obtained for the likelihood of AF ablation through logistic regression. Matching of scores for cases and controls was made to the nearest neighbour in a 1:1 fashion with a calliper of 0.1. No replacements were used. Cox regression was used to evaluate the association between outcomes and AF ablation.

A falsification endpoint (the incidence of a new diagnosis of cancer) was used to detect the prognostically important differences in background risk factors between the cohorts that we were not able to detect from registry data and hence could not adjust for. A p value of <0.05 and a standardised difference of >0.1 were considered significant for all statistical tests. CIs are given as 95%. The statistical analyses were performed using Stata V.17.0.

## RESULTS

### Baseline characteristics

Over an 11-year study period, we included 5628 patients who underwent a first-time AF ablation at three EP sites. The ablation techniques were PVI only by RF point-by-point ablation (66.1%), cryoballoon PVI (23.8%) and PVI plus additional atrial ablation (10.1%). Major complications occurred in 1.9% of the patients. There were no deaths related to the procedures. One or more redo procedures were made among 30.9% of the patients during follow-up (table 1). Changes in ablation techniques over the study period included a larger proportion of cryoballoon being performed during the first half of the study period (32% in 2008–2013 vs 24% in 2014–2018) and the introduction of contact-force RF ablation catheters from 2014 and onwards. Throughout the whole study, ablation catheters and three-dimensional mapping system from Biosense Webster (Diamond Bar, California) were used in the vast majority (94%) of all RF

**Table 1** Procedural characteristics (N=5628)

		n (%)
Hospital site	Karolinska University Hospital	2466 (43.8)
	Arrhythmia Center	1690 (30.0)
	Linköping University Hospital	1472 (26.2)
BMI	26.8 (24.5–29.9)	
Structural heart disease		627 (11.3)
AF type	Paroxysmal	3559 (66)
	Persistent	1282 (23.8)
	Long-standing persistent	547 (10.1)
Type of ablation	RF PVI only	2684 (64.7)
	Cryoballoon PVI only	1121 (27.0)
	RF PVI+additional ablation	345 (8.3)
Procedural duration (min)	171 (136–207)	
Major complications	Tamponade	34 (0.8)
	Vascular (requiring invasive treatment or blood transfusion)	9 (0.2)
	Phrenic paralysis	15 (0.4)
	Stroke	20 (0.5)

AF, atrial fibrillation; BMI, body mass index; PVI, pulmonary vein isolation; RF, radiofrequency.

ablation cases. The control group consisted of 48 676 patients with AF who had not undergone AF ablation, matched by age and sex to the study patients.

Compared with the control group, patients in the study group were healthier with less comorbidities, were more likely to be on an antiarrhythmic medication, had used healthcare resources to a greater extent and had a different socioeconomic status, characterised by a higher median disposable income and higher level of education. Propensity score matching resulted in two cohorts of equal size (n=3955) and similar characteristics (table 2 and online supplemental table 1). The proportion of patients on an OAC, as per pharmacy dispense records, throughout the study period showed a lower proportion of ablated patient on an OAC when compared with the control group (online supplemental table 2).

The falsification endpoint newly detected cancer disease occurred equally often among cases and controls (HR 1.06, 95% CI 0.92 to 1.23), indicating that any major residual confounding due to unaccounted comorbidity was unlikely. The mean follow-up was 4.5±2.8 years and there were no losses during follow-up due to the registry nature of the study. In the following, all comparisons refer to the propensity score-matched cohorts.

### Study endpoint comparison

The primary combined endpoint of stroke or all-cause mortality occurred in fewer patients in the ablation group than in the control group (174 vs 293 patients), with an HR of 0.58 (95% CI 0.48 to 0.69) (figure 1). This was driven by all-cause mortality (HR 0.51, 95% CI 0.41 to 0.64) (figure 2), whereas a statistically non-significant trend in favour of catheter ablation was observed for stroke, with 56 patients with stroke in the ablated vs 72 patients in the control group (HR 0.75, 95% CI 0.53 to 1.06) (figure 3). When excluding strokes <30 days postablation, the trend in favour of catheter ablation remained statistically non-significant (121 events; HR 0.83, 95% CI 0.51 to 1.04). Cardiovascular death was common, but in patients who underwent catheter ablation cardiovascular death was significantly reduced (55 patients in the ablated vs 122 patients in the control group), with an HR of 0.44 (95% CI 0.32 to 0.60). The primary combined endpoints for the first (2008–2013) and

second (2014–2018) half of the study period had an HR of 0.62 (CI 0.50 to 0.77) and 0.51 (95% CI 0.37 to 0.72), respectively. A summary of the primary and secondary outcomes can be found in table 3. A separate outcome assessment considering significant covariates in the Cox regression analysis and using death as a confounding competing risk to stroke showed similar results (online supplemental table 3).

In a sensitivity analysis, only regarding patients with heart failure, the apparent benefit of catheter ablation was greater than in the overall cohort (HR 0.41, CI 0.28 to 0.61) for the primary combined endpoint of all-cause mortality or stroke. After exclusion of patients with a heart failure diagnosis prior to inclusion (full cohort n=45 402 and propensity score-matched cohort n=6544), there was a reduction in the incidence of de novo heart failure diagnoses among those who underwent catheter ablation than among those in the control group (HR 0.77, CI 0.61 to 0.98) (figure 4). During follow-up, almost twice as many ablated patients underwent direct-current cardioversions (DCCV) (following the 3-month blanking period) when compared with the control group (419 vs 269, p<0.001).

Of the 128 patients with stroke, 36 (28.1%) were not on an OAC at the time of stroke diagnosis (20 and 16 patients in the ablation and control group, respectively). However, some of these patients had no indication for OAC (CHA<sub>2</sub>DS<sub>2</sub>-VASc score=0), leaving a final of 24 (18.8%) patients with stroke (16 and 8 patients in the ablation and control group, respectively), not receiving an OAC despite treatment indication.

### DISCUSSION

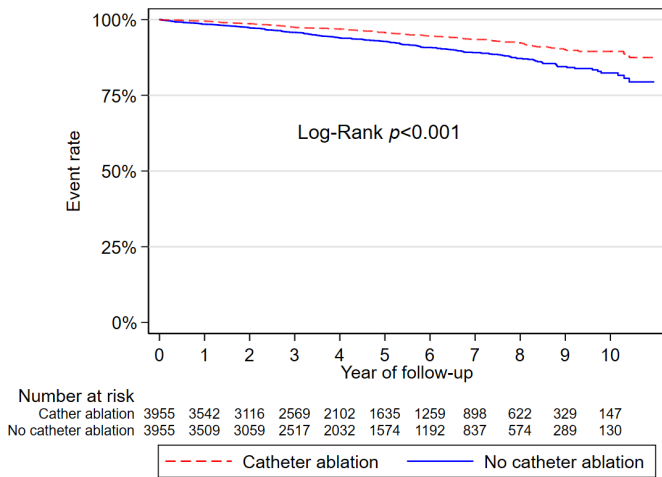
The main finding of this propensity matched case-control study was that AF ablation was associated with reduction in the primary endpoint of all-cause mortality or stroke. This result was driven by a marked decrease in all-cause mortality, in particular cardiovascular death, with stroke reduction showing a trend in favour of catheter ablation. The clinical benefit of ablation was greater in those with a previous diagnosis of heart failure, and the incidence of a de novo heart failure diagnosis was reduced in ablated patients.

During the last decade, several studies have evaluated whether catheter ablation can reduce mortality in patients with AF, both in RCTs and observational real-life cohorts, with conflicting

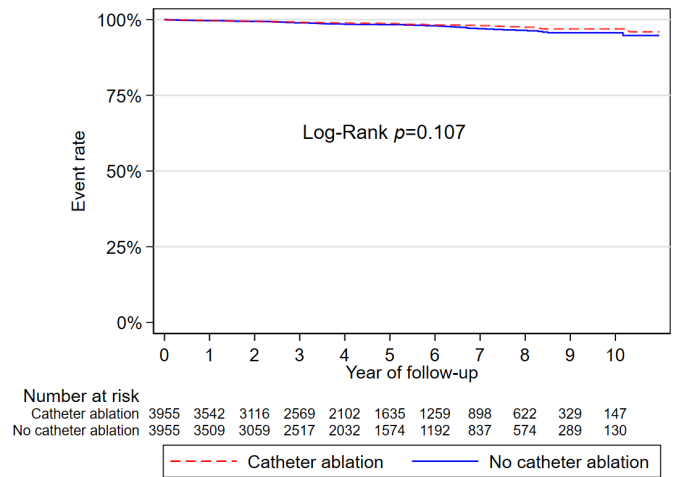
**Table 2** Baseline characteristics before and after propensity score matching

	Full cohort (before PS score matching)			PS-matched cohorts			
	Controls (n=48 676)	Cases (N=5628)	P value	Controls (n=3955)	Cases (n=3955)	P value	Std diff
Demographic characteristics on index date							
Age, years	Mean (SD)	61.1 (10.0)	59.9 (10.0)	<0.001	61.7 (9.5)	60.9 (9.7)	<0.001
	Median (IQR)	63 (56–68)	61 (54–67)		64 (57–68)	62 (55–68)	
Female	n (%)	14 902 (30.6)	1 564 (27.8)	<0.001	11 82 (29.9)	1 168 (29.5)	0.731
Education	Elementary, n (%)	12 198 (25.1)	822 (14.6)	<0.001	652 (16.5)	657 (16.6)	0.952
	High school, n (%)	22 030 (45.3)	2 243 (39.9)		16 40 (41.5)	1 617 (40.9)	
	University, n (%)	14 063 (28.9)	2 538 (45.1)		16 41 (41.5)	1 661 (42.0)	
	Unknown, n (%)	385 (0.8)	25 (0.4)		22 (0.6)	20 (0.5)	
Income (KSEK/year)	Mean (SD)	273.2 (1418.6)	415.2 (934.1)	<0.001*	469.3 (4842.9)	363.7 (649.8)	0.014*
	Median (IQR)	211.7 (143.9–305.8)	287.9 (192.8–419.7)		261.3 (178.2–362.8)	269 (179.3–394.5)	
Civil status	Alone, n (%)	21 863 (44.9)	2 004 (35.6)	<0.001	1402 (35.4)	1 435 (36.3)	0.439
Born abroad	n (%)	6 586 (13.5)	480 (8.5)	<0.001	352 (8.9)	367 (9.3)	0.557
Healthcare utilisation during 10 years prior to index date							
Outpatient visits	Mean (SD)	8.1 (22.6)	12.1 (11.1)	<0.001*	12.2 (43.2)	12.0 (10.2)	0.347*
	Median (IQR)	4 (1–10)	10 (6–15)		8 (4–14)	10 (5–15)	
Hospitalisation	Mean (SD)	2.9 (4.3)	4.4 (5.0)	<0.001*	4.0 (5.2)	4.0 (4.5)	0.347
Comorbidities prior to index date, n (%)							
Hypertension		21 002 (43.2)	2 409 (42.8)	0.623	1927 (48.7)	1 801 (45.5)	0.005
Heart failure		8 166 (16.8)	738 (13.1)	<0.001	619 (15.7)	580 (14.7)	0.221
Ischaemic heart disease		6 195 (12.7)	396 (7.0)	<0.001	322 (8.1)	316 (8.0)	0.804
Chronic kidney disease		1 922 (4.0)	82 (1.5)	<0.001	75 (1.9)	67 (1.7)	0.498
Diabetes (type 1 and 2)		6 804 (14.0)	396 (7.0)	<0.001	326 (8.2)	331 (8.4)	0.839
Drug prescriptions 6 months prior to index date, n (%)							
Amiodarone		721 (1.5)	887 (15.8)	<0.001	432 (10.9)	423 (10.7)	0.744
Flecainide		1 887 (3.9)	1 220 (21.7)	<0.001	678 (17.4)	653 (16.5)	0.452
Dronedarone		774 (1.6)	1 104 (19.6)	<0.001	500 (12.6)	540 (13.7)	0.183
NOAC		4 299 (8.8)	1 982 (35.2)	<0.001	1 351 (34.2)	1 269 (32.1)	0.050
Warfarin		4 488 (9.3)	3 750 (66.6)	<0.001	2 562 (64.8)	2 556 (64.6)	0.888
Digoxin		3 965 (8.2)	328 (5.8)	<0.001	295 (7.5)	272 (6.9)	0.316

\*Mann-Whitney U test.  
KSEK, 1000 Swedish krona; NOAC, non-vitamin K antagonist oral anticoagulants; PS, propensity score; Std diff, standardised differences.



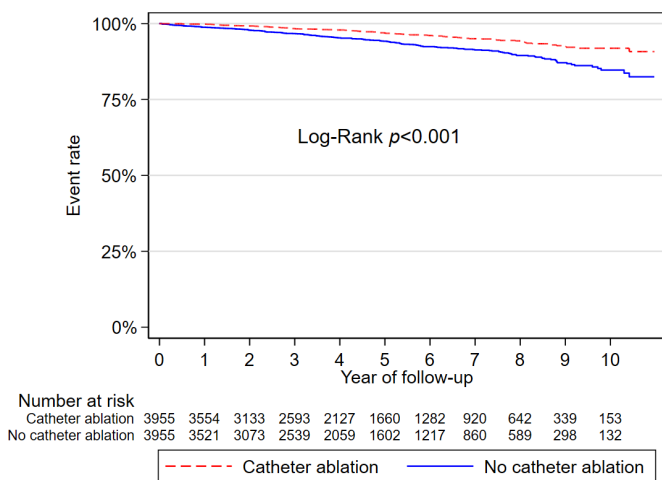
**Figure 1** Combined primary endpoint of all-cause mortality or stroke after propensity score matching in patients with atrial fibrillation treated medically or with catheter ablation.



**Figure 3** Stroke in the propensity score-matched cohorts in patients with atrial fibrillation treated medically or with catheter ablation.

results.<sup>11–16</sup> To date, the CABANA trial is the only large RCT to include a general AF population randomised to catheter ablation or medical therapy.<sup>11</sup> The trial failed to show a significant benefit of catheter ablation (HR 0.86, CI 0.65 to 1.15) for the composite primary endpoint of death, disabling stroke, serious bleeding or cardiac arrest. However, in the on-treatment analysis, there was a clear benefit for catheter ablation on all-cause mortality (HR 0.67, CI 0.50 to 0.89) and stroke (HR 0.60, CI 0.42 to 0.86).

In published observational case–control studies, majority have found that catheter ablation is associated with a reduction in mortality and stroke. For instance, Noseworthy *et al*<sup>21</sup> used a large administrative database to identify 183 760 patients who would fit the CABANA enrolment period and estimated that, for the 73.8% who were potentially trial-eligible, there was a significant reduction in the CABANA composite endpoint (HR 0.70, CI 0.63 to 0.77). Another study using discharge and surgical records from California non-federal hospitals reported a significantly lower mortality (HR 0.59, CI 0.45 to 0.77) and ischaemic stroke (HR 0.68, CI 0.47 to 0.95). On the contrary, a propensity score-matched cohort study based on the outcome registry



**Figure 2** All-cause mortality in the propensity score-matched cohorts in patients with atrial fibrillation treated medically or with catheter ablation.

for better informed treatment of atrial fibrillation (ORBIT-AF) found no difference in all-cause and cardiovascular deaths nor neurological events during 1 year of follow-up.<sup>13</sup> Similarly, a Taiwanese cohort study of 846 patients who underwent AF ablation between 2003 and 2009 matched with 11 324 AF controls found no difference in mortality, hospitalisation for heart failure or stroke during a 3.5-year follow-up.<sup>12</sup>

Our results in consecutive real-world patients are in line with the on-treatment CABANA results and are strengthened by the large number of patients, the long duration and completeness of follow-up, and the lack of endpoint adjudication bias due to the use of data from national registries. In our study, ablated patients with heart failure obtained a particularly large reduction in the primary endpoint and the development of de novo heart failure was significantly reduced in the catheter ablation group. This AF–heart failure interaction is a possible explanation for the observed reduction in all-cause mortality and is in line with previous findings from three RCTs.<sup>8–10</sup> While a decreased stroke risk may offer another possible explanation for better survival, we did not find a significant difference in stroke between the study groups. However, for reasons not known, there was a significant proportion of patients (18.8%) who were not on an OAC at the time of stroke diagnosis despite a CHA<sub>2</sub>DS<sub>2</sub>-VASc score ≥ 1, the majority being ablated patients. Furthermore, the proportion of patients on an OAC was lower in the ablated patients compared with the control group (67.2% vs 82.6% at the end of follow-up) (online supplemental table 2). One may speculate that the physician and/or patient misbelief that OAC is no longer needed after AF ablation led to drug discontinuation in some of these cases and may explain why there was no significant stroke reduction in the ablation group.

In our study, the ablation group represents consecutive first-time AF ablations from three major EP centres in Sweden and not from a national health registry, which makes this study different from the other previously published case–control registry studies. The positive results may therefore have been influenced by the inclusion of only high-volume centres. Studies have shown that high-volume centres have a lower complication rate and recent clinical trials have largely involved high-volume academic centres.<sup>22</sup> Our study period (2008–2018) covers a period of several technological advances in AF catheter ablation, such as contact-force sensing catheters (used in approximately half of the ablation group) and one-shot devices

**Table 3** Primary and secondary clinical outcomes in patients with atrial fibrillation receiving catheter ablation versus controls

	Full cohort before propensity score matching (n=54 311)			Propensity score-matched cohorts (n=7910)		
	Events (n)	HR* (95% CI)	P value	Events (n)	HR* (95% CI)	P value
<b>Primary outcome</b>						
Combined all cause-mortality or stroke	6728	0.30 (0.26 to 0.34)	<0.001	466	0.58 (0.48 to 0.69)	<0.001
<b>Secondary outcomes</b>						
All-cause mortality	5503	0.27 (0.23 to 0.31)	<0.001	363	0.51 (0.41 to 0.64)	<0.001
CV mortality	2583	0.25 (0.20 to 0.32)	<0.001	177	0.44 (0.32 to 0.60)	<0.001
Stroke	1670	0.38 (0.30 to 0.48)	<0.001	128	0.75 (0.53 to 1.07)	0.107
Heart failure†	3456	0.47 (0.41 to 0.55)	<0.001	280	0.77 (0.61 to 0.98)	0.032

\*HR using non-catheter ablation as the reference.  
 †Excludes patients with a heart failure diagnosis prior to inclusion (full cohort n=45 402 and propensity score-matched cohort n=6544).  
 CV, cardiovascular.

such as cryoballoon. This may also explain our positive results in comparison with some older case-control studies<sup>12 13</sup> as well as the CABANA study with an earlier inclusion period.<sup>11</sup>

An interesting finding was that almost twice as many patients in the catheter ablation group underwent DCCV. Most likely this reflects a dedication to sinus rhythm maintenance in this patient group, although we do not have data on rhythm status during follow-up. Therefore, our results may be interpreted as a rhythm versus rate strategy comparison, showing a clear benefit for rhythm control. This is in line with the recent EAST-AFNET 4 (Early Rhythm-Control Therapy in Patients with Atrial Fibrillation) trial which demonstrated that early rhythm control therapy was associated with reduction in the composite endpoint of death from cardiovascular causes, stroke or hospitalisation with worsening heart failure or acute coronary syndrome.<sup>23</sup> Nevertheless, our study aimed to compare therapeutic strategies, that is, ablation or no ablation, which is a more relevant clinical question than the effectiveness in sinus rhythm restoration by catheter ablation per se.

**Limitations**

This is a retrospective registry-based study which shows associations but cannot establish causal relationships. Moreover, given the study design, it cannot eliminate all potential differences between the treatment groups. Before propensity score matching, the two study groups differed in almost all baseline characteristics

analysed, and despite adjustments possible unknown confounders may exist which may boost the effect of catheter ablation. Nonetheless, using cancer diagnosis as a falsification endpoint, without any clear relationship to the type of treatment studied, we could not show a significant difference between the groups. Another limitation is the incompleteness of medical records, which commonly leads to underestimation of comorbidities, although in theory balanced across both treatment groups. Also, one may speculate that more specialised and continuous medical attention was given to ablated patients, which in turn may lead to both an overall improved healthcare but also higher registration of medical events, which may have affected the observed ablation benefit in both directions. Furthermore, AF subtype is not commonly coded in the medical records and could not be included in the study subanalysis and we can therefore not make any conclusions on the benefits of catheter ablation on specific AF subtypes.

Finally, there have arguably been significant advancements in catheter ablation during the study period which may have affected the outcomes. However, when we analysed the first and second half of the study period, the primary combined endpoint showed similar positive results for catheter ablation.

**CONCLUSIONS**

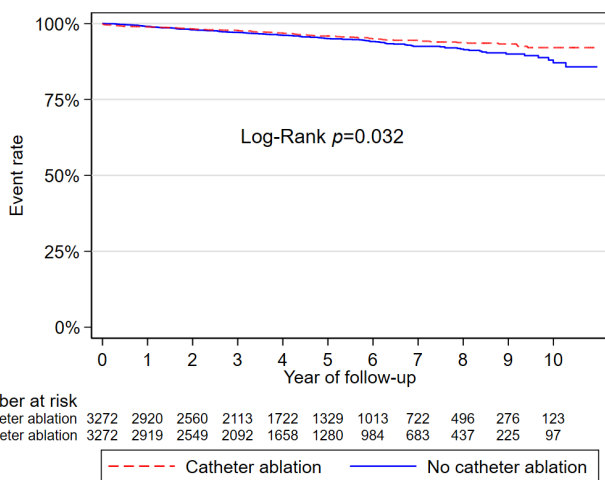
Catheter ablation of AF was associated with reduced all-cause mortality or stroke when compared with medical therapy in real-world Swedish patients. This result was driven by a marked decrease in all-cause mortality, with stroke reduction showing a trend in favour of catheter ablation.

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**Contributors** FAK, JH, MJ-U, PI, FB and ND designed the study. FAK, JH, EC and FT acquired the data. FAK, LF and EC performed the statistical analysis. FAK, MJ-U, ND, LF, JS, ES and FB were involved in the data interpretation. FAK drafted the manuscript, approved its final version and is guarantor for the content of the manuscript. JH, EC, FT, FAs, HB, TB, FB, ND, AE, LF, PI, AHJ, GK, AP-N, BS, OS, SS, JS, ES, JT, YT and MJ-U provided critical revision, editing and approval of the final manuscript.



**Figure 4** Heart failure in the propensity score-matched cohorts in patients with atrial fibrillation treated medically or with catheter ablation.

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**Patient consent for publication** Not required.

**Ethics approval** This study involves human participants and was approved by Stockholm (Sweden) regional ethical review board (ID: 2016/147-31). This was a retrospective study where informed consent was not mandatory.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Requests should be made to FAK.

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