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CLINICAL INVESTIGATIONS

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Catheter ablation and lower risk of incident dementia and mortality in older adults with atrial fibrillation

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Abstract

Background: Atrial fibrillation (AF) has consistently been associated with a higher risk of incident dementia. Observational evidence has suggested catheter ablation may be associated with a lower risk of dementia in patients with AF, but further research is needed. The objectives of this study were to use a global health research network to examine associations between catheter ablation, incident dementia and mortality in older adults with AF, and amongst subgroups by age, sex, co-morbidity status, and oral anticoagulant use.

Methods: The research network primarily included healthcare organizations in the United States. This network was searched on 28th September 2022 for patients aged ≥65 years with a diagnosis of AF received at least 5 years prior to the search date. Cox proportional hazard models were run on propensity-score matched cohorts.

Results: After propensity score matching, 20,746 participants (mean age 68 years; 59% male) were included in each cohort with and without catheter ablation. The cohorts were well balanced for age, sex, ethnicity, co-morbidities, and cardiovascular medications received. The risk of dementia was significantly lower in the catheter ablation cohort (Hazard Ratio 0.52, 95% confidence interval: 0.45–0.61). The catheter ablation cohort also had a lower risk of all-cause mortality (Hazard Ratio 0.58, 95% confidence interval: 0.55–0.61). These associations remained in subgroup analyses in individuals aged 65–79 years, ≥80 years, males, females, participants who received OACs during follow-up, participants with paroxysmal and non-paroxysmal AF, and participants with and without hypertension, diabetes mellitus, ischemic stroke, chronic kidney disease and heart failure, including heart failure with preserved ejection fraction and heart failure with reduced ejection fraction.

Conclusion: The observed lower risk of dementia and mortality with catheter ablation could be an important consideration when determining appropriate patient-centered rhythm control strategies for patients with AF. Further studies including data on the success of ablation are required.

KEYWORDS
atrial fibrillation, catheter ablation, dementia, mortality

INTRODUCTION

The population is aging worldwide, and the expected numbers of people with atrial fibrillation (AF) are predicted to increase from an estimated 2.6 million in 2010 to 12.1 million by 2030 in the United States alone.[1] The numbers of people living with dementia is also predicted to rise to over 9 million people in the United States, and 83 million worldwide by 2030.[2] Observational evidence has consistently demonstrated an association between AF and a higher risk of cognitive impairment and dementia.[3] Furthermore, large population-based cohort studies have suggested the association between AF and higher risk of dementia is independent of the known higher risk of stroke in people with AF.[4,5] In response to the established association between AF and dementia, there is a growing evidence base to determine the potential protective effect of treatments to lower the risk of incident cognitive impairment and dementia for people with AF.

Catheter ablation may be used as part of AF management to restore and maintain sinus rhythm. Randomized controlled trials (RCTs) have shown catheter ablation is a well-tolerated procedure to treat symptomatic AF in patients who have not responded to antiarrhythmic drugs.[6,7] More recently, evidence from RCTs has suggested when compared with antiarrhythmic drugs, catheter ablation as first-line therapy can reduce AF recurrence and hospitalisations.[8,9]

Previous observational research in Korea has suggested catheter ablation in 11,726 people with AF after propensity score matching was associated with a reduced risk of dementia, compared to antiarrhythmic or rate-control drugs alone (Hazard Ratio (HR) 0.73, 95% confidence interval (CI): 0.58, 0.93).[10] Analyses were also performed to determine if the association remained significant in subgroups. For people aged ≥75 years, the association did not remain statistically significant; however, 65% of the cohort were aged <65 years and only 5% were aged ≥75 years. Additional large studies are required to confirm if the association between catheter ablation and risk of dementia remains significant for subgroups including for older individuals.

The main objectives of the current study were to examine the association between catheter ablation and incident dementia in individuals aged ≥65 years and amongst subgroups including by age, sex, co-morbidity status, and oral anticoagulant use. The secondary objective was to examine the association between catheter ablation and mortality in the same cohort.

Key points

- It has not been previously determined if the association between catheter ablation and lower risk of dementia remains significant for different subgroups of patients
- In this large study of over 40,000 individuals with atrial fibrillation after propensity-score matching, catheter ablation was associated with a lower risk of dementia and the association remained significant in all subgroups examined
- Limitations including lack of data on the success of the ablation should be considered when interpreting the findings

Why does this paper matter?

This study confirms the lower risk of dementia and mortality with catheter ablation is upheld irrespective of age, sex, co-morbidities and use of oral anticoagulants. The lower risk of dementia and mortality could be an important consideration when determining appropriate patient-centered rhythm control strategies for patients with atrial fibrillation.

METHODS

Data source

TriNetX is a global federated health research network providing access to anonymized electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information) from participating large healthcare organizations. At the time this study was conducted there were 69 participating healthcare organizations in the TriNetX network. There are healthcare organizations in four participating countries, but these are predominately based in the United States and are a mixture of hospitals, primary care, and specialist providers which contribute data from both insured and uninsured patients. Because of data privacy restrictions, further information about the individual healthcare organizations cannot be provided.

Patient population

The TriNetX network was searched on 28th September 2022 for patients aged ≥65 years with a diagnosis of AF

received at least 5 years prior to the search date (before 28th September 2017) to allow for at least 5 years potential follow-up for all participants. AF was defined according to the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code I48 (atrial fibrillation and flutter). Patients with AF who received antiarrhythmic or rate-control medicines (beta-blockers, calcium channel blockers or cardiac glycosides, Supplementary Table 1) before 28th September 2017 were included. The index date was set as the first recording of antiarrhythmic or rate control drugs. Individuals with dementia (ICD codes: G30 Alzheimer's disease, F01 vascular dementia, F02 dementia in other diseases classified elsewhere or F03 unspecified dementia) or medications for Alzheimer's disease (rivastigmine, galantamine, memantine, or donepezil) recorded in their electronic medical records prior to the first time of receiving antiarrhythmic or rate-control medicines were excluded. This inclusion of these medications in addition to medical codes to define dementia has been used and validated in previous large-scale studies using administrative data.[5,11]

Exposure

Catheter ablation was identified using procedure codes listed in Supplementary Table 2.

Outcomes

The primary outcome for this study was any record of incident dementia (ICD code or dementia medication) in available electronic medical records within 5 years after the index date. The secondary outcome was all-cause mortality within 5 years after the index date.

Statistical analysis

Statistical analyses were completed on the TriNetX online research platform (https://live.trinetx.com). Propensity score matching was used to balance baseline differences between the patients with AF who received catheter ablation and patients who received antiarrhythmic medicines or rate control medicines alone. The TriNetX platform uses logistic regression to generate the propensity scores, through an implementation of the package scikit-learn. Once the system has generated a propensity score for each participant, the system performs greedy nearest neighbor matching with a caliper of 0.1 pooled standard deviations to identify the matched subsets. The following covariates were included in the 1:1 propensity score matching: age, sex, ethnicity and co-morbidities and medications listed in Table 1. The ICD codes used to identify co-morbidities are shown in Supplementary Table 3. Standardized mean differences (SMDs) were reported and SMDs <0.1 were considered well balanced and propensity score density graphs were visually examined.[12] Cox proportional hazard models using R's survival package v3.2–3 within the TriNetX platform were run on the propensity score matched cohorts to examine the association between catheter ablation and dementia (primary outcome) and mortality (secondary outcome). Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported. Subgroup analyses were completed to examine individuals by age, sex, oral anticoagulant (OAC) status during follow-up, atrial fibrillation subtype (paroxysmal or non-paroxysmal) and co-morbidities including hypertension, chronic kidney disease, ischemic stroke, diabetes mellitus and heart failure, including heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).

Ethics statement

As a federated research network, studies using the TriNetX health research network do not require ethical approval as no patient identifiable identification is received. To comply with legal frameworks and ethical guidelines guarding against data re-identification, the identity of participating HCOs and their individual contribution to each dataset are not disclosed. The TriNetX platform only uses aggregated counts and statistical summaries of de-identified information. No protected health information or personal data are made available to the users of the platform.

RESULTS

Patient characteristics

Within the TriNetX network, 20,747 participants were identified with a recording of AF in their electronic medical records from 44 healthcare organizations, and received antiarrhythmic medicines or rate control medicines and catheter ablation. These participants were compared to 767,237 participants within the TriNetX network with a recording of AF in their electronic medical records from 58 healthcare organizations, and received antiarrhythmic medicines or rate control medicines, but had no recording of catheter ablation at any time in their electronic medical records.

TABLE 1 Baseline characteristics of individuals with atrial fibrillation who received catheter ablation or medical therapy (antiarrhythmic or rate control medicines) alone.

	Before propensity score matching			After propensity score matching		
Characteristic	**Catheter ablation ($n = 20,747$)**	**No catheter ablation ($n = 767,237$)**	**SMD**	**Catheter ablation ($n = 20,746$)**	**No catheter ablation ($n = 20,746$)**	**SMD**
Age	68.4 (9.3)	72.3 (9.5)	0.41	68.4 (9.3)	68.4 (9.3)	0.002
Male	59.1 (12,271)	55.4 (424,942)	0.08	59.1 (12,270)	59.3 (12,296)	0.003
Ethnicity						
White	77.5 (16,075)	79.8 (612,264)	0.06	77.5 (16,075)	77.8 (16,136)	0.01
Black/African American	7.1 (1479)	8.4 (64,277)	0.05	7.1 (1479)	7.1 (1469)	0.002
Asian	0.8 (169)	1.0 (7815)	0.02	0.8 (169)	0.7 (145)	0.01
American Indian	0.1 (21)	0.2 (1241)	0.02	0.1 (21)	0.1 (21)	<0.001
Hawaiian/other Pacific	<0.1 (10)	0.1 (551)	0.01	<0.1 (10)	<0.1 (10)	<0.001
Unknown	14.4 (2994)	10.6 (81,089)	0.12	14.4 (2993)	14.3 (2967)	0.004
Co-morbidities						
Hypertension	31.1 (6459)	34.6 (265,445)	0.07	31.1 (6459)	29.6 (6149)	0.03
Ischaemic heart disease	18.9 (3926)	18.0 (138,479)	0.02	18.9 (3926)	18.3 (3794)	0.02
Cerebral infarction	1.9 (396)	2.9 (21,997)	0.06	1.9 (396)	1.7 (357)	0.01
Diabetes mellitus	11.3 (2342)	14.1 (107,830)	0.08	11.3 (2342)	10.8 (2231)	0.02
Chronic kidney disease	6.8 (1405)	9.0 (69,110)	0.08	6.8 (1405)	6.4 (1324)	0.02
Heart failure	13.4 (2770)	11.1 (85,079)	0.07	13.4 (2770)	12.2 (2522)	0.04
PVD	2.8 (571)	3.5 (27,145)	0.05	2.8 (571)	2.3 (482)	0.03
Atherosclerosis	2.3 (472)	2.6 (20,252)	0.02	2.3 (472)	2.0 (409)	0.02
Dyslipidaemia	24.6 (5107)	24.8 (190,025)	0.004	24.6 (5107)	23.4 (4851)	0.03
TIA	1.2 (253)	1.6 (12,344)	0.03	1.2 (253)	1.1 (230)	0.01
Sleep apnoea	6.5 (1355)	4.7 (36,350)	0.08	6.5 (1354)	5.8 (1198)	0.03
Osteoporosis	2.8 (574)	4.2 (32,064)	0.08	2.8 (574)	2.5 (515)	0.02
Hypothyroidism	6.4 (1335)	6.9 (52,829)	0.02	6.4 (1335)	5.9 (1232)	0.02
Hyperthyroidism	0.7 (150)	0.7 (5539)	<0.001	0.7 (150)	0.6 (132)	0.01
Liver disease	1.8 (379)	2.6 (20,099)	0.05	1.8 (379)	1.6 (324)	0.02
COPD	9.7 (2011)	10.4 (79,830)	0.02	9.7 (2011)	9.2 (1903)	0.02
Cancer	13.0 (2694)	16.6 (127,308)	0.10	13.0 (2694)	12.2 (2533)	0.02
Medicines						
Oral anticoagulants	16.6 (3442)	13.1 (100,797)	0.10	16.6 (3441)	15.9 (3307)	0.02
Statins	11.4 (2371)	12.3 (94,508)	0.03	11.4 (2371)	10.6 (2203)	0.03
ACE inhibitors	6.2 (1296)	7.0 (53,403)	0.03	6.2 (1296)	5.9 (1222)	0.02
Diuretics	10.8 (2235)	11.7 (89,775)	0.03	10.8 (2235)	9.8 (2043)	0.03
Antiplatelet agents	11.7 (2422)	10.4 (79,771)	0.04	11.7 (2421)	11.2 (2326)	0.01

Abbreviations: ACE, Angiotensin-converting enzyme; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; TIA, transient ischaemic attack.

Compared with participants who did not receive catheter ablation, participants who received catheter ablation were younger (mean (standard deviation) age 68.4 (9.3) years vs. 72.3 (9.5) years) and had a higher proportion of males (59.1% vs. 55.4%). Participants who received catheter ablation also had a significantly lower prevalence of some co-morbidities including diabetes mellitus, hypertension, cerebral infarction, chronic kidney disease, liver disease, atherosclerosis, hypothyroidism, chronic obstructive pulmonary disease, peripheral vascular disease,

osteoporosis and cancer, but a higher prevalence of ischemic heart disease, heart failure, and sleep apnea. The cohort who received catheter ablation also had a higher proportion of individuals receiving OACs and antiplatelet agents, but a lower proportion of individuals receiving statins, ACE inhibitors and diuretics. After propensity score matching, 20,746 participants were included in each cohort and these were well balanced on all included characteristics (SMD <0.1).

Catheter ablation and risk of dementia

In the propensity score matched cohorts, during the follow-up period there were 253 cases (1.2%) of incident dementia identified in the group of individuals with AF and received catheter ablation, compared with 439 cases (2.1%) identified in the group with AF and did not receive catheter ablation. In the ablation group, 14.2%, 30.8%, and 51.8% of dementia diagnoses were recorded with 12, 24, and 36 months of the ablation procedure, respectively.

Overall, the risk of dementia was lower in the catheter ablation cohort compared to the no catheter ablation cohort (HR 0.52, 95% CI: 0.45–0.61) (Figure 1). When examining the risk by subtype of dementia, the results remained statistically significant for both Alzheimer's disease (0.30, 95% CI: 0.19–0.45) and vascular dementia (0.54, 95% CI: 0.35–0.82).

The association between catheter ablation and lower risk of dementia remained statistically significant in subgroup analyses including only individuals aged 65–79 years, ≥80 years, males, females, participants who received OACs during follow-up, participants with paroxysmal AF and non-paroxysmal AF, and participants with and without hypertension, diabetes mellitus, ischemic stroke, chronic kidney disease and heart failure including HFpEF and HFrEF. Catheter ablation was associated with a non-statistically significant lower risk of dementia for participants who did not receive OACs during follow-up. Supplementary Table 4 shows the characteristics of participants by whether they were prescribed OACs during follow-up. The cohort not prescribed OACs during follow-up had a greater proportion of participants with

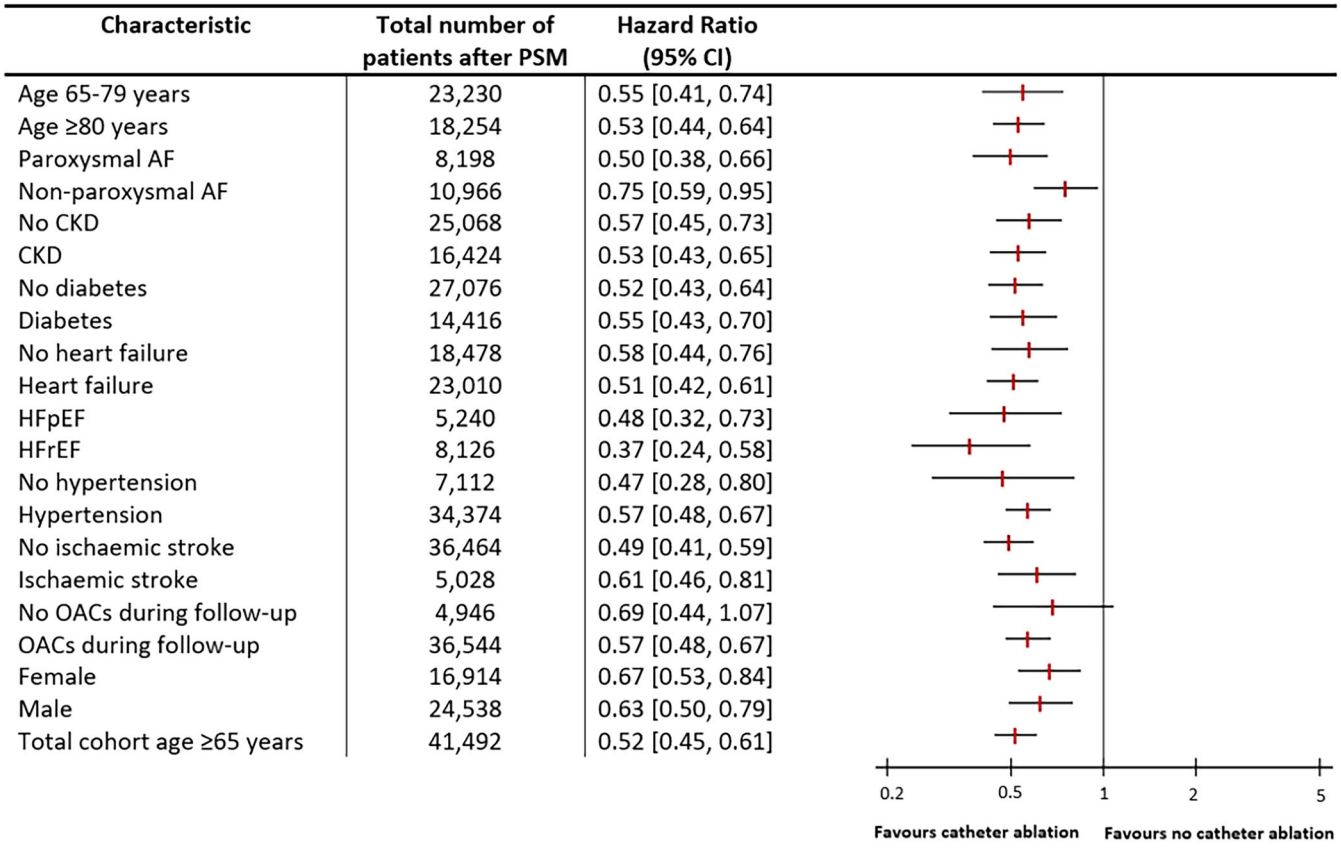

FIGURE 1 Associations between catheter ablation and risk of dementia in 41,492 individuals with atrial fibrillation, and by subgroups. Results are after propensity-score matching for age, sex, co-morbidities and cardiovascular medication use. AF, atrial fibrillation; CKD, chronic kidney disease; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; OAC, oral anticoagulant; PSM, propensity-score matching.

co-morbidities including hypertension, ischemic heart disease, chronic kidney disease, dyslipidemia and cancer.

Catheter ablation and risk of mortality

The catheter ablation cohort had a significantly reduced risk of all-cause mortality compared to the no catheter ablation cohort (2447 deaths (11.8%) compared with 3509 deaths (16.9%), HR 0.58, 95% CI: 0.55–0.61). This association remained statistically significant when examining all subgroups including by age, sex, OAC status during follow-up, AF subtype and co-morbidities including hypertension, diabetes mellitus, ischemic stroke, chronic kidney disease, and heart failure (Figure 2). An overview of the main study findings is shown in Figure 3.

DISCUSSION

This study examined associations between catheter ablation and risk of dementia and mortality in over 41,000 individuals with AF who received antiarrhythmic medicines or rate control medicines. After propensity-score matching for participant characteristics including age, sex, co-morbidities and cardiovascular medication use, catheter ablation was associated with a significantly lower risk of dementia and all-cause mortality over a five-year follow-up period. The associations remained statistically significant in all subgroup analyses, except for dementia in individuals who did not receive OACs during follow-up. However, the sample size for the cohort who did not receive OACs during follow-up was markedly smaller and may not have been sufficient to detect a statistically significant association, but this could not be further explored within the TriNetX online platform. Furthermore, there were notable differences in co-morbidities between the groups who were and were not prescribed OACs during follow-up which may have impacted the results.

The results of this study are in line with previous observational studies which have examined associations between catheter ablation and cognitive impairment or dementia. A relatively smaller study of approximately

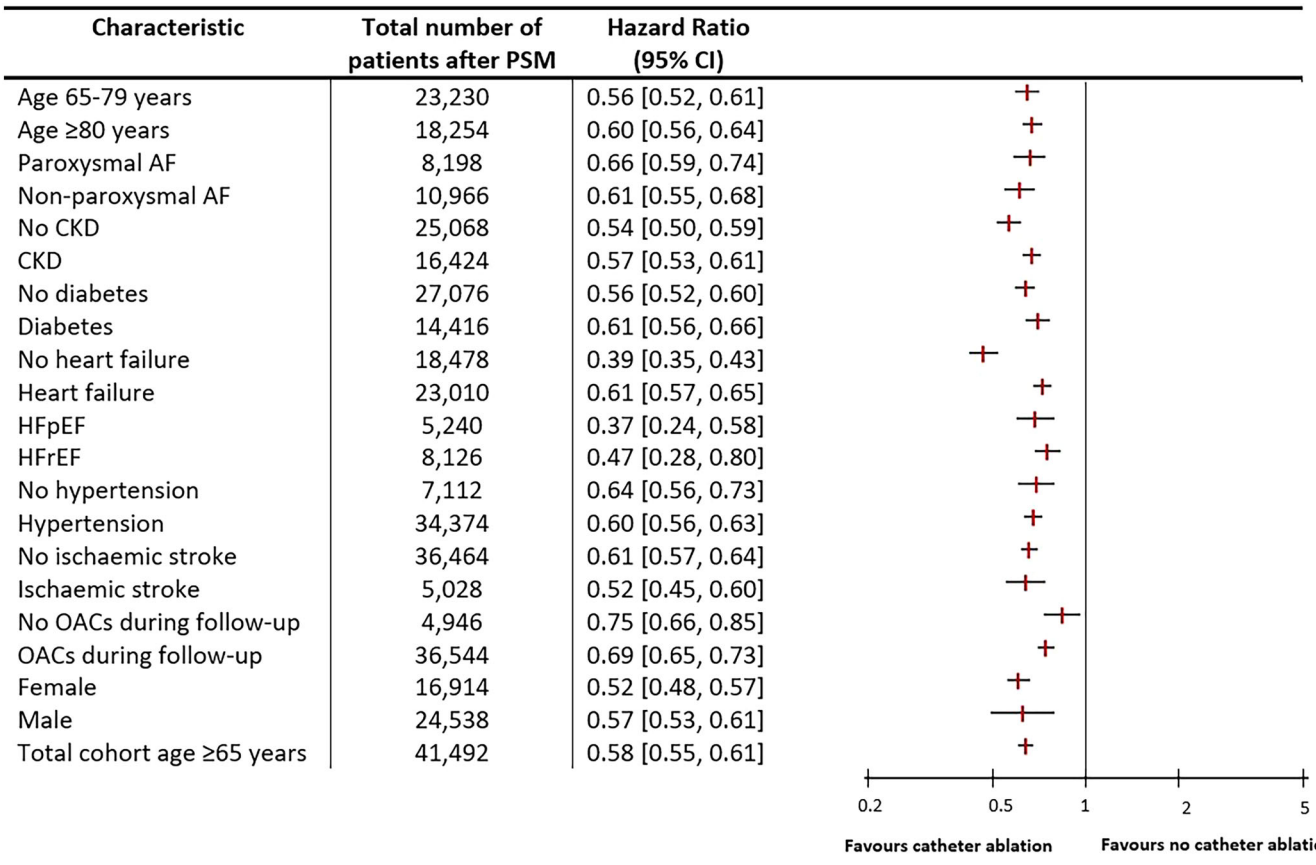

FIGURE 2 Associations between catheter ablation and risk of mortality in 41,492 individuals with atrial fibrillation, and by subgroups. Results are after propensity-score matching for age, sex, co-morbidities and cardiovascular medication use. AF, atrial fibrillation; CKD, chronic kidney disease; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; OAC, oral anticoagulant; PSM, propensity-score matching.

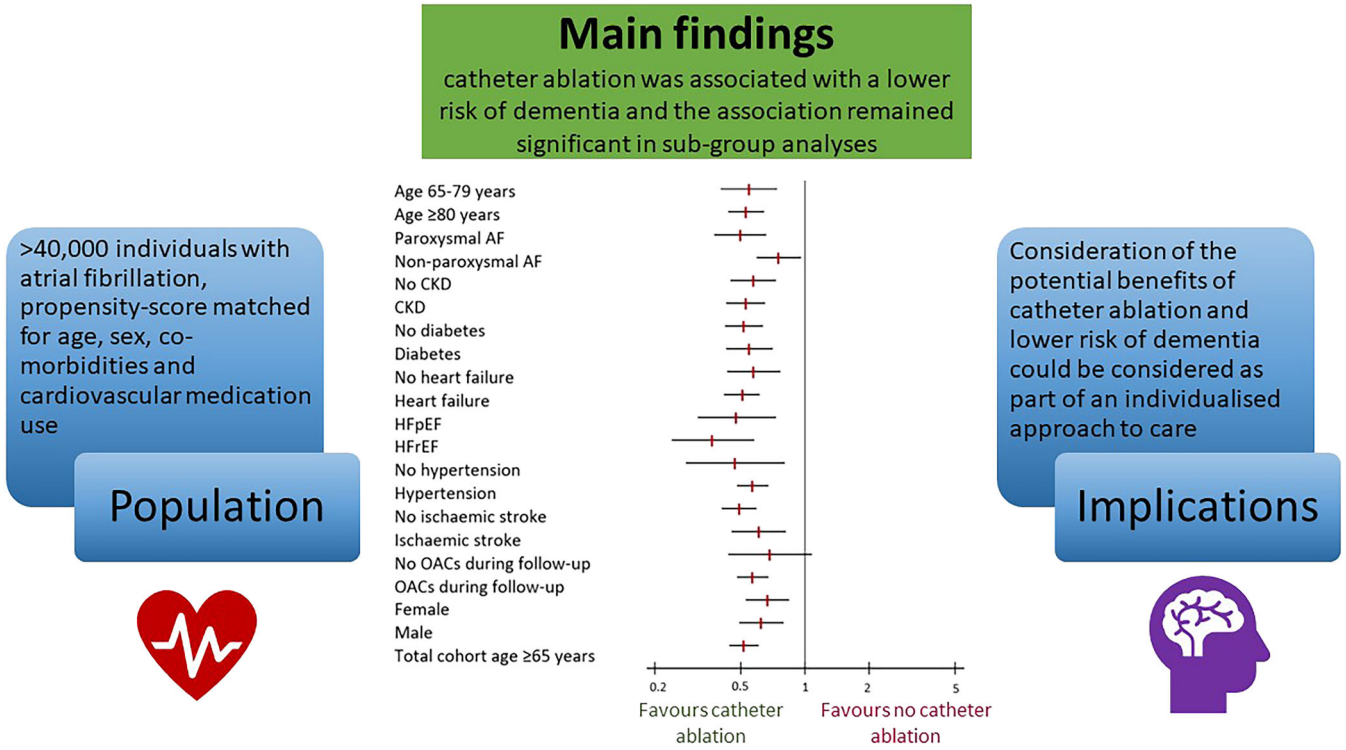

FIGURE 3 Overview of the main study findings.

1500 patients with AF during a longer mean follow-up of 9 years, suggested catheter ablation was associated with lower risk of dementia (HR 0.44, 95% CI: 0.25–0.78).[13] Furthermore, a study of patients with at least 3 years follow-up suggested >4000 patients with AF who received catheter ablation had a comparable risk of dementia to >16,000 patients without AF.[14] A US-based study of 38,176 patients with AF after propensity-score matching suggested catheter ablation was associated with a lower risk of dementia compared to antiarrhythmic drugs, and remained significant for males and females, but no further subgroup analyses were performed.[15]

A previous study in 11,726 patients with AF in Korea also examined subgroups, and the association between catheter ablation and lower risk of dementia persisted when participants were grouped according to the following characteristics: sex, residential area, health care utilization, heart failure or stroke history, estimated stroke risk, and OAC use during follow-up.[10] However, the association was not statistically significant for individuals aged ≥75 years, and individuals without hypertension and with diabetes. In the current study, there were larger numbers of participants and the associations remained statistically significant amongst older individuals, by sex, by AF subtype, and for people with and without all co-morbidities examined. The current study only included people aged ≥65 years as previous studies have suggested younger-onset dementia (<65 years) has different underlying pathologies to dementia developed ≥65 years.[16,17]

In addition to reducing the risk of stroke in people with AF, the use of OACs may also reduce the risk of dementia and all-cause mortality.[5,18] In this study, the association between catheter ablation and lower risk of dementia and mortality persisted amongst those who received OACs during follow-up. This suggests catheter ablation may offer further protective effects on cognitive function and mortality risk, in addition to that seen with OAC use.

The underlying reasons for associations between catheter ablation and reduced risk of dementia are unclear, but potential mechanisms have been proposed. Catheter ablation restores sinus rhythm and previous studies have suggested, compared to rate control, antiarrhythmic drugs are associated with better cognitive performance and lower risk of dementia.[19,20] Lower cerebral perfusion has been observed in patients in AF compared to patients in sinus rhythm.[21] Lower cerebral perfusion may influence multiple pathways which can increase the risk of dementia including oxidative stress and inflammatory pathways.[22,23] Lower cerebral perfusion has also been associated with greater rates of cognitive decline and higher incidence of dementia in a population-based study.[24] Further mechanisms to explain the association between AF and dementia have been proposed including cerebral infarcts, decreased brain volume, and cerebral microbleeds and have been well described previously.[3]

The association observed between catheter ablation and lower risk of mortality in this study is in line with previous results from large observational cohort studies,[14,25,26] and a randomized trial of 363 participants with AF and heart failure [HR for all-cause mortality 0.53 (95% CI: 0.32–0.86)].[27] However, the Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) randomized trial of over 2000 participants with AF reported that catheter ablation did not significantly reduce mortality compared to medical therapy over a median 48.5 months.[28] Differences between observational evidence and randomized trial evidence may be due to residual confounding which could not be addressed in observational research or differences in the characteristics of the study populations.[28]

The 2017 Heart Rhythm Society guidelines state catheter ablation of paroxysmal and persistent AF intolerant to at least one class I or III anti-arrhythmic medication is recommended and reasonable, respectively.[29] Furthermore, the 2019 update of American Heart Association guidelines suggested that catheter ablation may be reasonable for patients with HFrEF and symptomatic paroxysmal AF who have not responded to antiarrhythmic drugs.[30] Consideration of the potential added benefits of catheter ablation and lower risk of dementia and mortality could also be considered when determining which rhythm control strategy should be used. Evidence from RCTs with an adequate follow-up to detect changes in cognitive function and differences in mortality would be needed to establish a causal relationship.

STRENGTHS AND LIMITATIONS

This is the largest study to date to examine the association between catheter ablation and dementia, and multiple subgroup analyses were conducted. The study used propensity-score matching to account for a wide-range of differences between groups including age, sex, ethnicity, co-morbidities and cardiovascular medication use. Due to the study being observational, there remains the possibility of residual confounding. For instance, data were not available to examine if the participants had mild cognitive impairment, and those with mild cognitive impairment may be less likely to be offered catheter ablation. Furthermore, the group who received catheter ablation were more likely to receive all cardiovascular medications investigated. Although cardiovascular medication use was included in the propensity score matching, the cohort who received catheter ablation may have received additional treatments which may not have been fully captured within the dataset. Furthermore, data were not available about whether the participants had DNR orders, received hospice care and whether the participants were discharged to long-term care facilities. Subgroup analyses investigating these participants would be of interest in future research.

Similar to previously conducted research examining the association between catheter ablation and risk of dementia, this study relied on the use of electronic medical records from an administrative database. This has benefits as this has a real-world approach and some groups of people which are often excluded from prospective studies and trials can be included. However, the use of electronic medical records has limitations, such as the reliance on accurate coding of medical conditions by the participating healthcare organizations. The subtypes of atrial fibrillation and heart failure were not available for all participants; therefore, these subgroup analyses were only examined for participants which had an ICD code indicating the subtype. Furthermore, certain known risk factors for dementia such as lifestyle factors and levels of education were not available in the dataset, and events which occur outside of the TriNetX health network may not be captured. The ICD code I48 was used to identify atrial fibrillation in this study which is in line with previous large-scale studies using administrative datasets,[10] but this may also include cases of atrial flutter. The results remained statistically significant when examining associations between catheter ablation and subtypes of dementia. However, these results should be interpreted with caution as the validity of using administrative datasets to identify specific subtypes of dementia is unclear and participants may have mixed underlying pathologies. Because of data privacy restrictions regarding the participating healthcare organizations, it was not possible to examine characteristics regarding the quality of the healthcare organizations which may impact the availability and outcomes of catheter ablation. Within the dataset, it was also not possible to determine if the catheter ablation was successful which may impact the outcomes examined.

CONCLUSION

A large cohort study of individuals with AF who had received rate- or rhythm-control medicines with or without catheter ablation was conducted. Propensity-score matching was used to account for a wide-range for differences in characteristics including age, sex, ethnicity, co-morbidities and cardiovascular medication use. After propensity-score matching, catheter ablation was associated with a significantly lower risk of dementia and mortality compared with receiving rate- or rhythm control medicines alone. The associations persisted upon further

subgroup analysis examining groups by characteristics including age, sex, co-morbidities and for people who received OACs during follow-up. Study limitations including the lack of data on the success of the ablation should be considered and addressed in future studies.

AUTHOR CONTRIBUTIONS

Stephanie L. Harrison was responsible for the conception of the study. Philip Austin was responsible for acquisition of the data. All authors were responsible for interpretation of the data. Stephanie L. Harrison drafted the article and all other authors revised it critically for important intellectual content.

FUNDING INFORMATION

No specific funding was received for this work.

CONFLICT OF INTEREST STATEMENT

Stephanie L Harrison has received funding from Bristol Myers Squibb (BMS). Benjamin JR Buckley has received funding from BMS/Pfizer. Deirdre A Lane has received investigator-initiated educational grants from BMS and Pfizer, has been a speaker for Bayer, Boehringer Ingeheim, and BMS/Pfizer and has consulted for BMS, and Boehringer Ingelheim. Gregory Lip: consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo and speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received to Gregory Lip personally. Philip Austin is an employee for TriNetX LLC.

DATA AVAILABILITY STATEMENT

To gain access to the data in the TriNetX research network, a request can be made to TriNetX (https://live.trinetx.com), but costs may be incurred, a data sharing agreement would be necessary, and no patient identifiable information can be obtained.

SPONSOR'S ROLE

No specific funding was received for this work.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Supplementary Table 1. Codes used to identify rate and rhythm control drugs in the TriNetX network.
Supplementary Table 2. List of procedure codes used to identify catheter ablation.
Supplementary Table 3. ICD-10-CM codes used to identify health conditions in the TriNetX network.
Supplementary Table 4. Characteristics of individuals who received catheter ablation or medical therapy, by oral anticoagulant status during follow-up, after propensity score matching.

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