BRIEF REPORT

Associations between atrial fibrillation symptom clusters and major adverse cardiovascular events following catheter ablation

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Introduction

Atrial fibrillation (AF) is associated with a heavy burden of symptoms, but they are poorly understood.[1] In addition to cardiac symptoms including chest pain, dyspnea, and palpitations,[2] patients with AF may experience nonspecific symptoms including anxiety, malaise, dizziness, and weakness.[3] Many patients may be asymptomatic. AF symptoms may be under-recognized in about one-third of patients.[4] Recognition of AF symptoms is important because they have been correlated with cardiac function, socioeconomic status, and comorbidities.[5] To better understand symptom presentations in clinical practice, prior work has identified distinct clusters of AF symptoms that co-occur and correlate with sex and race.[3] The clinical relevance of these symptom clusters has not been determined. Although AF is a known major risk factor for stroke, morbidity, mortality, and increased healthcare utilization and costs,[6] it is unclear whether AF symptom clusters are prognostic of these outcomes. This study aimed to determine associations between 6 distinct AF symptom clusters our team previously identified[3] and AF-related major adverse cardiovascular events (MACE) 1 year following de novo catheter ablation.

KEY FINDINGS

- In our sample, approximately one-third of patients undergoing catheter ablation experienced atrial fibrillation–related major adverse cardiovascular events (MACE) 1 year postablation.
- Two preablation symptom clusters characterized by a high prevalence of patients with (1) anxiety and (2) fatigue/palpitations correlate with postablation MACE.
- It is possible that patients with specific symptoms preablation may be at increased risk for atrial fibrillation–related MACE.

Methods

Study design and sample

We conducted a retrospective secondary analysis of electronic health record (EHR) data for adults with AF who underwent catheter ablation (N = 1292) at 1 large academic medical center in New York City from 2010 to 2020. Patients were included if they had a diagnosis of AF determined by International Classification of Diseases–Ninth Revision and International Classification of Diseases–Tenth Revision codes, underwent catheter ablation determined by billing codes, and were ≥18 years of age. Data from the time of the ablation through 1-year postprocedure were included in the analysis. This study was approved with a patient consent waiver by the Weill Cornell Medicine and Columbia University Irving Medical Center Institutional Review Boards, and was conducted in accordance with the guidelines outlined in the Declaration of Helsinki.

Measurement

Our dataset consisted of structured and unstructured data elements from the EHRs. Structured elements included demographic characteristics (age, sex, and race), and postablation encounters (emergency department [ED] visits, hospitalizations), stroke, and death. We created a composite binary outcome variable to reflect AF-related MACE including AF-specific ED visit, hospitalization, stroke, and/or death within 1 year postablation.

Unstructured data elements included AF symptoms documented in free-text clinical notes at the time of the ablation. In previous work, we used natural language

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Table 1 Characteristics of adults with AF who underwent catheter ablation

	No AF-related MACE (n = 920)	AF-related MACE (n = 372)	Overall (N = 1292)
Age, y	64.6 ± 12.5	67.7 ± 12.4	65.5 ± 12.6
Race			
Asian	43 (4.7)	16 (4.3)	59 (4.6)
Black	39 (42)	29 (7.8)	68 (5.3)
White	528 (57.4)	222 (59.7)	750 (58)
Other	75 (8.2)	38 (10.2)	113 (8.7)
Missing	235 (25.5)	67 (18)	302 (23.4)
Sex			
Female	301 (32.7)	154 (41.4)	455 (35.2)
Male	619 (67.3)	218 (58.6)	837 (64.8)
Symptom cluster			
1. Generally symptomatic	516 (56.1)	235 (63.2)	751 (58.1)
2. Dyspnea/edema	82 (8.9)	37 (9.9)	119 (9.2)
3. Chest pain	77 (8.4)	36 (9.7)	113 (8.7)
4. Anxiety	108 (11.7)	30 (8.1)	138 (10.7)
5. Asymptomatic	37 (4.0)	10 (2.7)	47 (3.6)
6. Fatigue/palpitations	100 (10.9)	24 (6.5)	124 (9.6)

Values are mean ± SD or n (%).
AF = atrial fibrillation; MACE = major adverse cardiovascular events.

processing applied to clinical notes to extract 10 symptoms experienced by AF patients: anxiety, chest pain, dizziness, dyspnea, edema, fatigue, malaise, palpitations, syncope, and weakness.[7] We previously identified 6 mutually exclusive clusters of these extracted symptoms using machine learning hierarchical clustering techniques, representing clusters of patients with similar symptom profiles.[3] These clusters were labeled using the most prevalent symptoms in the cluster: generally symptomatic (cluster 1), dyspnea/edema (cluster 2), chest pain (cluster 3), anxiety (cluster 4), asymptomatic (cluster 5), and fatigue/palpitations (cluster 6).[3] These 6 clusters formed the basis of our symptom measurement in the present study.

Data analysis

Descriptive statistics (mean and percentage) were calculated to describe the sample. We used logistic regression models to examine associations between the 6 previously defined symptom clusters[3] and AF-related MACE adjusting for age, sex, and race. Analyses were performed using R software version 4.2.2 (R Foundation for Statistical Computing).

Results

Sample characteristics and differences by AF-related MACE are provided in Table 1. Among 1292 patients, 372 (28.8%) had AF-related MACE within 1 year. Frequencies of each MACE for the overall sample and by symptom cluster are provided in Supplementary Table 1.

Table 2 shows a significant group difference in the odds of having AF-related MACE within 1 year postablation (P = .037). Compared with generally symptomatic patients (ie, cluster 1) and adjusting for age, sex, and race, patients in the anxiety cluster (ie, cluster 4) and fatigue/palpitations cluster (ie, cluster 6) were 39% (adjusted odds ratio 0.61, 95% confidence interval 0.39–0.95, P = .03) and 41% (adjusted odds ratio 0.59, 95% confidence interval 0.37–0.98, P = .03) less likely to have AF-related MACE within 1 year postablation, respectively.

Discussion

Among almost 1300 patients with AF who underwent catheter ablation, we found that approximately one-third experienced AF-related MACE 1 year postablation, and this was correlated with specific symptom clusters preablation. Existing evidence suggests that, broadly, AF symptom severity is associated with higher hospitalization rates.[2,8] Although confirmation is warranted in future studies, these findings are clinically relevant by drawing attention to the possibility that patients with specific symptoms preablation may be at increased risk for AF-related MACE.

Table 2 Logistic regression models examining associations between symptom clusters and AF-related MACE for adults who underwent catheter ablation (N = 1292)

Symptom cluster	OR	95% CI
1. Generally symptomatic	Reference	Reference
2. Dyspnea/edema	1.05	0.69–1.61
3. Chest pain	1.14	0.74–1.76
4. Anxiety	0.61	0.39–0.95
5. Asymptomatic	0.63	0.30–1.30*
6. Fatigue/palpitations	0.59	0.37–0.96*

Models were adjusted for age, sex, and race.
AF = atrial fibrillation; CI = confidence interval; MACE = major adverse cardiovascular events; OR = odds ratio.
*P <.05

Our findings are discordant with prior AF symptom cluster and outcomes research suggesting increased odds of acute care utilization for patients in a cluster with fatigue and palpitations.[9] However, in this prior study, fatigue and palpitations co-occurred with more emergent cardiac symptoms (ie, chest pain, shortness of breath, and dizziness), and acute care utilization was determined per patient self-report.[9] Additionally, this study did not include any psychological symptoms (eg, anxiety) and focused on patients with chronic AF,[9] whereas we included patients postablation.

Our findings may be explained by differences in AF severity or prompt healthcare-seeking behavior in outpatient contexts among patients with cardiac-specific but nonemergent symptoms (eg, palpitations)[10] and anxiety,[11] promoting timely symptom management to prevent AF-related MACE. Prior work identified illness perceptions and the burden of chronic symptoms that inform one's illness perceptions as a predictor of health-related quality of life[12] and healthcare seeking,[13] which may also contribute to the relationship between AF-related symptoms and MACE. Conversely, patients with emergent symptoms (ie, chest pain warranting a further workup to rule out myocardial infarction) may have been directed to an ED. Additionally, prior research suggests increased symptom perception among females, which may lead to proactive care seeking and treatment adherence,[14] explaining differences by sex that we observed. Further research is needed to develop and test interventions that address multidimensional symptoms experienced by patients with AF postablation.

Strengths of this study include the large cohort (nearly 1300 patients) and time frame (10 years) of data, and the use of natural language processing to extract symptoms from "real world" contexts using EHRs. EHR-documented symptoms correlate with self-reported symptoms.[3] Limitations include the potential for missed MACE outcomes if they occurred outside of our health system. We did not examine AF recurrence postablation due to the high prevalence of missed recurrence in clinical care, translating to limited documentation in EHRs. We analyzed symptoms documented by clinicians, which may have resulted in missing symptoms reported by patients but not documented. Additionally, analyzing symptoms documented by clinicians may have resulted in selection or misclassification bias, as anxiety and fatigue are nonspecific symptoms that may be less likely to be documented. Future research should employ prospective study designs with systematic assessment of these symptoms to draw definitive conclusions.

Conclusion

Patients who experience anxiety and fatigue/palpitations preablation may be less likely to have an AF-related MACE within 1 year postablation. Findings highlight the potential that patients with certain symptoms preablation may be at increased risk for AF-related MACE.

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Disclosures: Meghan Reading Turchioe has served as a consultant for Boston Scientific; and is a co-founder of and owns equity in Iris OB Health. The remaining authors have no conflicts to disclose.

Patient Consent: Because this is a secondary use of electronic health records, we received an Institutional Review Board exemption for patient consent and a Health Information Portability and Accountability Act waiver of consent.

Ethics Statement: This research was approved by the Weill Cornell Medicine and Columbia University Irving Medical Center Institutional Review Boards. This study was conducted in accordance with the guidelines outlined in the Declaration of Helsinki.

Data Availability: Data are available upon reasonable request. De-identified data used in this study will be made available upon reasonable request to the corresponding authors, following completion of an institutional data sharing agreement.

Appendix

Supplementary Data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2024.08.013.

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