

Acute pericarditis after atrial fibrillation ablation: Incidence, characteristics, and risk factors



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BACKGROUND Little is known about the incidence and risk factors for the development of acute pericarditis after ablation for atrial fibrillation (AF).

OBJECTIVE The purpose of this retrospective cohort study was to describe the occurrence of and associations with suspected acute pericarditis after AF ablation.

METHODS All patients undergoing AF ablation in our center were enrolled in a prospectively maintained registry. Suspected acute pericarditis was defined as pericardial chest pain treated with disease specific anti-inflammatories within 3 months of AF ablation.

RESULTS Among 2215 patients with AF ablations between January 1, 2018, and December 31, 2019, 226 (10.2%) had suspected acute pericarditis. Treatments included colchicine in 149 patients (65.9%), prednisone in 66 (29.2%), and high-dose ibuprofen in 43 (19.0%). Multiple anti-inflammatory therapies were used in 57 patients (25%). At baseline, a lower CHADS₂VASc score and a higher

body mass index were associated with pericarditis, whereas older patients were less likely to have pericarditis. With multivariable adjustment, age was associated with suspected acute pericarditis (odds ratio 0.95; 95% confidence interval 0.94–0.97; $P < .0001$). Among patients with suspected pericarditis, postprocedure pericardial effusion was present in 9.3% and pericarditis electrocardiographic changes in 19.5%.

CONCLUSION Suspected acute pericarditis is common after AF ablation and is associated with a younger age. Systematic assessments for acute pericarditis after AF ablation should be considered.

KEYWORDS Ablation; Acute Pericarditis; Atrial fibrillation; Inflammation; Pericarditis

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Introduction

The indications for catheter ablation of atrial fibrillation (AF) have increased, and with improved mapping and ablation technology, success rates at 1 year approach 70%–80%. Complications, such as stroke, pulmonary vein stenosis, esophageal injury, and phrenic nerve paralysis, are rare and have also decreased.^{1,2} Acute pericarditis after AF ablation has been described, although primarily through case reports and series,^{3–5} and a broader understanding of postablation pericarditis is lacking. The putative hypothesis of postablation pericarditis relates to transmural injury of the thinner aspects of the left atrial wall resulting in an inflammatory response affecting the pericardium.^{6,7} Given the lack of understanding of acute pericarditis after AF

ablation, the aims of the current study were 2-fold: first, to assess the incidence of suspected acute pericarditis and, second, to evaluate the associations with suspected acute pericarditis.

Methods

Study population and outcomes

Consecutive patients undergoing AF ablation at our institution from January 1, 2018, through December 31, 2019, were included and have been enrolled in a prospective outcomes registry, which includes baseline patient characteristics, procedural information, and data on AF recurrence. This outcomes and quality improvement study was approved by our institutional review board and abides by ethical standards for informed consent according to the Helsinki Declaration. The primary outcome was suspected pericarditis. Suspected acute pericarditis after AF ablation was defined as pericardial chest pain treated with disease-specific anti-inflammatories (ibuprofen at 600–800 mg every 8 hours,

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KEY FINDINGS

- The incidence of acute pericarditis after atrial fibrillation (AF) ablation was 10.2%.
- Suspected acute pericarditis was defined as pericardial chest discomfort necessitating therapy with anti-inflammatory drugs.
- At baseline, a lower CHADS₂VASc score, higher body mass index, and younger age were associated with a higher risk of developing pericarditis after AF ablation.
- In a multivariable logistic regression model, younger age was associated with a higher risk of developing pericarditis after ablation, with a 1-year increase in patient age associated with a 5% decrease in the odds of developing pericarditis.

colchicine, or prednisone) at the time of hospital discharge or within 3 months after AF ablation. Patients were included in the study population if they were prescribed anti-inflammatory drugs after AF ablation as obtained from our institution's pharmacy database. The presence of pericardial chest pain at the time of diagnosis was subsequently confirmed by chart review. Pericardial chest pain was defined as sharp and pleuritic, which typically improved by sitting up and leaning forward.⁷ Clinical information including laboratory values, clinical course, and postprocedural electrocardiographic (ECG) findings were obtained by chart review. Patients were excluded if they had procedural pericardial complications (acute-onset procedural pericardial effusion requiring intervention), if pericardial chest pain could not be verified by chart review, or if patients were prescribed pre-emptive anti-inflammatory drugs in an anticipatory fashion due to extensive ablation. In order to capture a more comprehensive number of patients with postablation suspected acute pericarditis requiring treatment, our study definition for pericarditis was used in lieu of the definition outlined by the European Society of Cardiology (ESC) pericarditis guideline statement. This would have required 2 positive findings of the following: pericardial chest pain, new friction rub, new or worsening effusion, new widespread ST elevation, or PR depression on ECG.⁷

Statistical analysis

Continuous variables are given as mean \pm SD and compared using the Student *t* test if normally distributed, and as median (interquartile range) and compared using the Mann-Whitney test if non-normally distributed. Categorical variables are given as frequencies and were compared using the χ^2 test or the Fisher exact test if expected cell count <5 . To determine important predictors of postprocedure pericarditis, a multivariable logistic regression model was used with a stepwise selection method, with *P* value of .5 cutoff for model entry and cutoff value of .1 to stay in the model. The analysis

was performed using SAS Version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Study population and post-AF ablation pericarditis

During the study period, 2215 patients underwent AF ablation. Overall, patients were generally older, predominantly male, and 1164 (52.6%) had persistent AF (Table 1). In the entire population, 587 (26.5%) presented for a redo ablation. Cryoballoon was used in 236 patients (10.7%), and the remainder were radiofrequency ablations. Among 402 patients treated with anti-inflammatory drugs, 226 (10.2% of the entire cohort) had suspected post-AF ablation acute pericarditis. A total of 5 patients were excluded from the analysis due to pericardial complications at the time of ablation that ultimately required therapy with anti-inflammatory drugs.

Patients diagnosed with suspected post-AF ablation acute pericarditis were younger (mean age 61.4 ± 10.6 years vs 65.9 ± 9.9 years; $P < .01$) and more likely to have paroxysmal AF ($n = 122$ [54.0%] vs $n = 904$ [45.5%]; $P = .02$). Similarly, post-AF ablation pericarditis was less common in patients with hypertension ($n = 122$ [54.0%] vs $n = 1272$ [64.0%]; $P = .003$) and was associated with a lower CHADS₂VASc score (1.8 ± 1.4 vs 2.3 ± 1.5 ; $P < .001$). Patients with post-AF ablation pericarditis had a higher body mass index (BMI) (32 ± 8.0 kg/m² vs 30.7 ± 6.9 kg/m²; $P = .02$) and were more likely to present for an index ablation as opposed to redo procedure ($n = 187$ [82.7%] vs $n = 1441$ [72.4%]; $P = .001$). From a procedural perspective, posterior left atrial wall isolation and additional flutter lines beyond standard AF lesion sets were not associated with developing pericarditis. To identify variables associated with developing post-AF ablation acute pericarditis, a multivariable logistic regression model was used and included patient age, hypertension, diabetes, type of AF, BMI, and posterior wall ablation. Patient age was found to be the sole factor associated with developing post-AF ablation acute pericarditis (odds ratio 0.954; 95% confidence interval 0.937–0.971; $P < .0001$), where a 1-year increase in patient age was associated with a 5% decrease in the odds of developing pericarditis.

Most patients ($n = 149$ [65.9%]) received colchicine monotherapy whereas multiple drugs were given to 25% of patients ($n = 57$) (Table 2). Median time to diagnosis was 1 (1–1) day after AF ablation. Within the pericarditis group, 44 patients (19.5%) were found to have ECG changes consistent with pericarditis at the time of diagnosis, 21 (9.3%) had new pericardial effusions, and 9 (4.0%) had fever. Thus, 59 patients (26%) within the study definition of suspected post-AF ablation acute pericarditis would have met ESC guideline statement diagnostic criteria for acute pericarditis.⁷

Discussion

Our study examined the incidence and risk factors of post-AF ablation acute pericarditis in a large patient population at a quaternary referral center. Our hypothesis is that thermal energy (whether radiofrequency or cryoablation), when

Table 1 Baseline characteristics

Variable	No pericarditis (N = 1989)	Pericarditis (N = 226)	P value
Age (y)	65.9 ± 9.9	61.3 ± 10.6	<.001
Female	606 (30.5)	72 (31.9)	.7
Paroxysmal AF	904 (45.5)	122 (54.0)	.02
Persistent AF	1061 (53.3)	103 (45.6)	.03
Atrial scar	662 (33.3)	56 (24.8)	.01
CAD	415 (20.9)	33 (14.6)	.03
CKD (creatinine >1.2)	330 (16.6)	38 (16.8)	.9
CHF	219 (11.0)	23 (10.2)	.7
CVA	98 (4.9)	6 (2.7)	.1
Diabetes	319 (16.0)	37 (16.4)	.9
Dialysis	7 (0.4)	0.0	.5
Hypertension	1272 (64.0)	122 (54.0)	.003
Pulmonary embolism	44 (2.2)	6 (2.7)	.7
Race			
White	1308 (65.8)	147 (65.0)	.7
Black	41 (2.1)	3 (1.3)	
Other	640 (32.2)	76 (33.6)	
Sleep apnea	355 (17.9)	47 (20.8)	.3
BMI (kg/m ²)	30.7 ± 6.9	32 ± 8.0	.02
EF (%)	55 ± 11	56 ± 9.5	.3
Malignancy	98 (4.9)	15 (6.6)	.3
NYHA functional classification			
No dyspnea	1084 (54.5)	142 (62.8)	.09
Class I	486 (24.4)	52 (23.0)	
Class II	355 (17.9)	29 (12.8)	
Class III/IV	64 (3.2)	3 (1.3)	
PAD	62 (3.1)	4 (1.8)	.3
Creatinine (mg/dL)	1.0 (0.89–1.2)	1.02 (0.86–1.21)	.2
Redo AF ablation	548 (27.6)	39 (17.3)	.001
Atrial flutter ablation	254 (12.8)	21 (9.3)	.1
CHADS ₂ VASc score			
Median	2 (1–3)	2 (1–3)	<.001
Mean	2.3 ± 1.5	1.8 ± 1.4	<.001
Posterior wall ablation	1621 (81.5)	191 (84.5)	.3
Cryoballoon	217 (10.9)	19 (8.4)	.3

Values are given as mean and standard deviation, n (%), or median (interquartile range) unless otherwise indicated.

AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; EF = ejection fraction; NYHA = New York Heart Association; PAD = peripheral artery disease.

transmural, results in pericardial tissue injury, an ensuing inflammatory response, and pericardial chest pain.⁸ Based on our analysis, the incidence of suspected pericarditis after ablation is approximately 10%, and younger age is a risk factor. Except for higher BMI, this is also reflected in the pericarditis patient population having fewer comorbidities.

Pericardial complications due to perforation or reactive effusions in the absence of pericardial pain during catheter ablation of AF have been described. However, pericarditis after AF ablation has only been reported, and we believe underreported, as a complication in studies evaluating catheter ablation outcomes and not as a primary objective.^{2,4} In the CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial, a 1.1% incidence (n = 11) of severe pericardial chest pain after ablation was found. Likely due to a low event rate, there is no information as to risk factors for developing pericarditis in this study or how it was managed. Furthermore, although the definition of severe pericardial chest pain in the trial is unclear, pain that is not

severe is clinically meaningful as it should require treatment and does present a risk of recurrent episodes after an initial course of therapy. Mugnai et al³ described their series of 450 patients undergoing second-generation cryoballoon ablation for paroxysmal AF. In their analysis, 4% of patients developed acute pericarditis. Patients who went on to develop pericarditis required more cryo-applications and

Table 2 Post-AF ablation acute pericarditis (N = 226)

ECG changes	44 (19.5)
Pericardial effusion	21 (9.3)
Fever	9 (4.0)
Drug choice	
Colchicine	149 (65.9)
Prednisone	66 (29.2)
Ibuprofen	43 (19.0)
Multiple drugs	57 (25)

Values are given as n (%).

AF = atrial fibrillation; ECG = electrocardiography.

longer freeze durations, particularly along the right inferior pulmonary vein. There were no patient specific clinical parameters that were associated with developing acute pericarditis. Darmoch et al⁹ evaluated the incidence of acute pericarditis after AF ablation using the National Inpatient Sample and found an incidence of 0.8%. Female sex and BMI >30 were risk factors associated with developing pericarditis. Of note, the diagnosis of acute pericarditis in this sample had to be billed at discharge and likely was underreported.

Acute pericarditis after cardiac surgery has been recognized and well studied over time. In an analysis by Imazio et al,⁶ postpericardiotomy syndrome was diagnosed in 15% and was associated with female sex. Narasimhan et al¹⁰ evaluated the efficacy of methotrexate in patients with refractory postprocedure pericarditis and identified 408 patients with treatment-refractory pericarditis after epicardial ablations, LARIAT suture delivery (SentreHeart, Pleasanton, CA), and open cardiac surgery; 6.1% went on to receive methotrexate for symptom resolution. Furthermore, acute pericarditis after implantable cardiac devices has been well reported to have an incidence between 1% and 5%.¹¹ Some studies have implicated active fixation atrial leads in this phenomenon, resulting in microperforation along the thinner atrial walls.^{12–14} In both these circumstances, as well as the premise of our current analysis, trauma to the pericardium is thought to trigger the inflammatory response responsible for pericardial symptoms.

Study Limitations

Our analysis has the inherent limitations of a retrospective cohort study. A practical definition for suspected acute pericarditis was used, and fewer patients met the ESC guideline definition for acute pericarditis, although this definition has not been evaluated in patients after AF ablation.⁷ The amount of ablation delivered, mean lesion duration, and energy delivery per lesion were not obtained and may have a contributing role in developing pericardial inflammation. Finally, related to the retrospective design of our study, assessments were not systematic, and C-reactive protein measurements were not obtained routinely.

Conclusion

Acute pericarditis after AF ablation has been observed but is poorly defined. Our study demonstrated that post-AF ablation pericarditis has an incidence of 10.2%, which is higher than previously reported. Younger patients with a higher

BMI but otherwise fewer comorbidities seem to be most at risk. Future studies should further delineate the mechanisms of injury and assess the efficacy of prophylactic therapies in patients at risk for post-AF ablation pericarditis.

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Ethics Statement: This outcomes and quality improvement study was approved by our institutional review board and abides by ethical standards for informed consent according to the Helsinki Declaration.

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