

Received: 2018.08.25

Accepted: 2018.10.18

Published: 2019.05.05

# A Retrospective Study of Atrial Fibrillation Following Cavotricuspid Isthmus Ablation for Atrial Flutter

Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ACDE **Izabela Warchoł**  
ABD **Bartłomiej Jacek Bińkowski**  
ABD **Tomasz Kucejko**  
ACF **Joanna Sobiczewska**  
ADF **Andrzej Lubiński**

Department of Interventional Cardiology and Cardiac Arrhythmias, Medical University of Łódź, Łódź, Poland

**Corresponding Author:** Izabela Warchoł, e-mail: [izabelaritawarchol@gmail.com](mailto:izabelaritawarchol@gmail.com)

**Source of support:** Departmental sources

**Background:** Catheter radiofrequency ablation for typical atrial flutter is considered to be safe and effective. However, atrial fibrillation (AF) following cavotricuspid isthmus ablation for atrial flutter has been reported in patients without a previous history of AF, which has implications for the decision to use oral anticoagulation. This retrospective study at a single center aimed to evaluate the occurrence of AF in patients after successful cavotricuspid isthmus ablation of typical atrial flutter and to determine the incidence and associations with AF during follow-up.

**Material/Methods:** Between January 2011 and July 2017, of 110 consecutive patients who underwent cavotricuspid isthmus ablation for typical atrial flutter, 67 patients had no previous history of AF, of which 40 patients underwent follow-up. The 40 patients included in this retrospective clinical study included 34 men and 6 women, with a mean age of  $67 \pm 10$  years.

**Results:** Forty patients underwent post-ablation follow-up for  $46 \pm 23$  months, and 12 patients (30%) developed AF; six patients (15%) experienced recurrent of atrial flutter. More than half of the patients with post-ablation AF were asymptomatic with a European Heart Rhythm Association (EHRA) score of 1, and univariate analysis showed the absence of variables associated with the prevalence of AF.

**Conclusions:** Following cavotricuspid isthmus ablation for atrial flutter, recurrence of atrial flutter was found in 15% of cases, and asymptomatic AF occurred in 30%. These findings have implications for the use of post-ablation oral anticoagulation treatment, which is often discontinued following ablation therapy and before patient follow-up.

**MeSH Keywords:** **Anticoagulants • Atrial Fibrillation • Atrial Flutter • Catheter Ablation**

**Full-text PDF:** <https://www.medscimonit.com/abstract/index/idArt/912918>



2023



1



1



17



## Background

Episodes of atrial flutter and atrial fibrillation (AF) often occur in the same patients, although these conditions differ mechanistically and have different therapeutic strategies. In atrial flutter, a macroreentrant circuit is localized in the upper portion of the right atrium between the tricuspid valve and the crista terminalis [1]. The main triggers that cause AF originate from the pulmonary veins [2], although for some time there has been recognized to be a pathophysiologic association between both atrial flutter and AF [3].

Ablation therapy for atrial flutter is often offered as a first-line treatment for symptomatic and recurrent typical atrial flutter, and due to the high procedural success rate (95%) and the low annual recurrence rate (5–10%) ablation is often considered to be a curative treatment [4], established by current guidelines as class I indication, with a B level of evidence [5]. However, the benefit of ablation therapy for atrial flutter is negated by the onset of subsequent AF [6]. The reported incidence of AF after ablation for atrial flutter varies from 16–82% [6–8].

Therefore, patients with atrial flutter have been reported to have an increased all-cause mortality rate when compared with patients who undergo ablation therapy for AF, but there is a similar trend for thromboembolic risk [9]. Although the interrelationship between AF and atrial flutter is complex [10], an important clinical question remains regarding the use of oral anticoagulation following a successful ablation procedure in patients with documented isolated atrial flutter.

Therefore, this retrospective study was conducted at a single center and aimed to evaluate the occurrence of AF in patients after successful cavotricuspid isthmus ablation of typical atrial flutter and to determine the incidence and associations with AF during follow-up.

## Material and Methods

### Patients

Between January 2011 and July 2017, 110 consecutive patients underwent cavotricuspid isthmus ablation for typical documented atrial flutter. Sixty-seven patients had no prior history of atrial fibrillation (AF) documented or suspected before ablation. Sufficient data were available for 40 patients who were enrolled in this retrospective clinical study and included 34 men and 6 women, with a mean age of  $67 \pm 10$  years. The remaining patients were excluded from the study due to lack of clinical follow-up data (Figure 1).

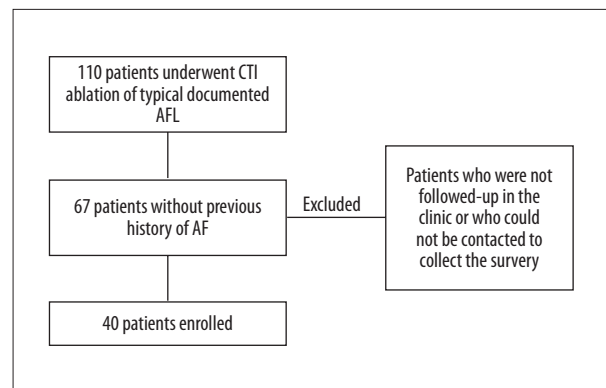


Figure 1. Selection of study participants.

### Radiofrequency cavotricuspid isthmus ablation

All patients underwent a standard radiofrequency cavotricuspid isthmus ablation procedure. The endpoint of ablation was the achievement of bidirectional cavotricuspid isthmus ablation block determined by electrophysiologic study.

### Clinical follow-up

The patients were followed for  $46 \pm 23$  months. Data on previous medical history was obtained from a nine-question telephone interview and any incomplete data were collected from the clinical records of each patient.

The occurrence of arrhythmia was detected using a 12-lead electrocardiogram (ECG) and 24-hour Holter recordings taken on follow-up visits, performed if the patient reported palpitations or symptoms suspected to be the consequence of atrial fibrillation (AF) or atrial flutter occurrence/recurrence.

Symptom severity was determined using the telephone survey, which was used to identify factors related to the subsequent risk for the occurrence of AF. Age, gender, the presence of hypertension, heart failure, diabetes mellitus, left ventricular ejection fraction (LVEF), left ventricular hypertrophy (LVH), left atrial (LA) enlargement, right ventricular (RV) enlargement, and mitral regurgitation (MR) were noted.

### Statistical analysis

Univariate analysis of clinical variables related to the post-ablation occurrence of AF was conducted using binary logistic regression with robust standard errors (due to the small sample size). A P-value  $< 0.05$  was considered to be statistically significant.

**Table 1.** Clinical and follow-up data in patients with and without atrial fibrillation after catheter ablation of atrial flutter.

Investigated trait	Overall (n=40)	AF after procedure (n=12)	No AF after procedure (n=28)	OR (95% CI)	p-Value
	Mean ( $\pm$ SD) or n (%)	Mean ( $\pm$ SD) or n (%)	Mean ( $\pm$ SD) or n (%)*		
Gender (men)	34 (85.0)	9 (75.0)	25 (89.3)	0.36 (0.06–2.17)	P=0.27
Age (years)	66.6 $\pm$ 11.4	65.3 $\pm$ 12.0	67.1 $\pm$ 11.2	0.99 (0.93–1.05)	P=0.66
Age $\geq$ 70 years	19 (47.5)	4 (33.3)	15 (53.6)	0.43 (0.10–1.81)	P=0.25
BMI (kg/m <sup>2</sup> )	30.83 $\pm$ 4.56	29.18 $\pm$ 2.56	31.77 $\pm$ 5.21	0.86 (0.73–1.01)	P=0.07
Obese (BMI >30 kg/m <sup>2</sup> )	19 (57.6)	6 (50.0)	13 (61.9)	0.61 (0.14–2.64)	P=0.51
LA diameter (cm)	4.27 $\pm$ 0.55	4.26 $\pm$ 0.54	4.28 $\pm$ 0.56	0.92 (0.27–3.19)	P=0.90
LA enlargement ( $\geq$ 4.2 cm)	23 $\pm$ 57.5	8 $\pm$ 66.7	15 $\pm$ 53.6	1.73 (0.41–7.24)	P=0.45
LVEF (%)	51.05 $\pm$ 11.56	54.50 $\pm$ 7.70	49.52 $\pm$ 12.74	1.04 (0.99–1.10)	P=0.14
LVEF <50%	13 (33.3)	2 (16.7)	11 (40.7)	0.29 (0.05–1.63)	P=0.16
IVSd (cm)	1.16 $\pm$ 0.18	1.11 $\pm$ 0.11	1.18 $\pm$ 0.21	0.09 (0.01–4.01)	P=0.21
LV hypertrophy (IVSd $\geq$ 1.2 cm)	13 (34.2)	2 (16.7)	11 (42.3)	0.27 (0.05–1.54)	P=0.14
RVDd (cm)	3.09 $\pm$ 0.43	3.03 $\pm$ 0.44	3.13 $\pm$ 0.42	0.56 (0.11–2.88)	P=0.49
RV enlargement (RVDd >2.6 cm)	30 (76.9)	10 (83.3)	20 (74.1)	1.75(0.30–10.25)	P=0.54
Arterial hypertension	33 (82.5)	9 (75.0)	24 (85.7)	0.51 (0.07–2.74)	P=0.43
Heart failure	14 (35.0)	4 (33.3)	10 (35.7)	0.90 (0.21–3.82)	P=0.89
Diabetes mellitus	15 (37.5)	2 (16.7)	13 (46.4)	0.23 (0.04–1.28)	P=0.09
Mitral regurgitation	34 (87.2)	11 (91.7)	23 (85.2)	1.91(0.18–19.78)	P=0.59
TIA/stroke	4 (10)	2 (17)	2 (7)	2.60(0.32–21.05)	P=0.57
OAC	11 (33)	4 (33)	7 (33)	1.00 (0.22–4.50)	P=1.00
Fluoroscopy time (min.)	8.86 $\pm$ 4.98	9.19 $\pm$ 4.38	8.93 $\pm$ 5.35	0.26(–3.75–4.27)	P=0.89

M $\pm$ SD – mean  $\pm$  standard deviation values for numerical traits; n (%) – absolute number and percentage for discrete traits; OR – odds ratio; CI – confidence interval; BMI – body mass index; IVSd – interventricular septal end diastolic dimension; LA – left atrium; LV – left ventricle; LVEF – left ventricular ejection fraction; RV – right ventricle; RVDd – right ventricular end-diastolic dimension; OAC – oral anticoagulation; TIA – transient ischemic attack.

## Results

The clinical and echocardiographic characteristics of the 40 patients included in this retrospective study who underwent cavotricuspid isthmus ablation with follow-up are summarized in Table 1. During follow-up of (mean, 46 $\pm$ 23 months), AF developed in 12 patients (30%), four patients (10%) had a recurrence of isolated atrial flutter, and two patients (5%) patients had a recurrence of atrial flutter and subsequent AF. Twenty-four patients (60%) remained free from any recurrent atrial arrhythmias during follow-up.

More than half of the patients with post-ablation AF were asymptomatic with a European Heart Rhythm Association (EHRA) score of 1, and univariate analysis showed the absence of variables associated with the prevalence of AF. There were 27% of patients who presented with mild symptoms (EHRA 2), while normal daily activity was affected in 18% of patients (EHRA 3). None of the patients presented disabling symptoms that would discontinue daily activity (EHRA 4).

The most common clinical symptoms in patients with AF were fatigue (75%) and palpitation (67%), followed by dyspnea (42%), chest pain (42%), and ankle edema (25%). The mean

left ventricular ejection fraction (LVEF) was  $51\pm 11\%$  and the mean body mass index (BMI) was  $30.83\pm 4.56$ . The prevalence of obesity in the study population was found to be  $>57\%$ . There was no clinical variable associated with the occurrence of AF following successful cavotricuspid isthmus ablation of typical atrial flutter. There was a nonsignificant trend towards the association between the incidence of AF and BMI (OR, 0.86; 95% CI, 0.73–1.01;  $p=0.07$ ) and LVEF (OR, 1.04; 95% CI, 0.99–1.10;  $p=0.14$ ).

During the ablation procedure, only one patient experienced AF induced by the procedure. Compared with the group without post-ablation AF, patients who experienced post-ablation AF had an increased fluoroscopy time ( $8.93\pm 5.35$  min vs.  $9.19\pm 4.38$  min). Four patients with subsequent AF after cavotricuspid isthmus ablation for atrial flutter ablation were treated with oral anticoagulants. During follow-up, transient ischemic attacks or stroke occurred in 4 (10%) of the patients who underwent cavotricuspid isthmus ablation for atrial flutter ablation.

## Discussion

Radiofrequency ablation is considered to be a first-line treatment for recurrent cavotricuspid isthmus-dependent atrial flutter due to its high success rate and low risk of complications [11]. In the present study, the long-term recurrence of isolated atrial flutter was approximately 10%, which was higher than previously reported. When patients with concomitant atrial fibrillation (AF) are included, the recurrence of atrial flutter following cavotricuspid isthmus ablation has been reported to be 15% [6]. The differences between the findings of the present study and those of previously published studies may reflect the difference in the study population size, which was relatively small in this study, as well as the duration of post-ablation follow-up, which was almost four years in the present study. However, it has previously been reported that patients with typical atrial flutter undergoing cavotricuspid isthmus ablation for atrial flutter are at a significantly increased risk of developing new-onset AF following ablation [1,2,6–10].

Pérez et al. reported the findings from a meta-analysis of 99 published studies that included 7328 patients on the long-term outcomes following catheter ablation of cavotricuspid isthmus-dependent atrial flutter and reported new-onset episode of AF in between 16–82% of the patients [7]. In the present study, the findings supported some of the findings from previous studies as 30% of patients in the present study population who received cavotricuspid isthmus ablation for atrial flutter experienced new-onset AF during a mean follow-up of  $46\pm 23$  months. This finding is supported by data from the study by Celikyurt et al. [12], who reported a prevalence of AF (22%) during a two-year follow-up period, but was lower than that

reported in a previous study by Mittal et al. who studied 20 patients and observed AF onset in almost 50% during a follow-up period of one year [13]. In the study by Mittal et al., the use of implanted loop recorders allowed continuous rhythm monitoring after cavotricuspid isthmus ablation [13]. In the present study, the effectiveness of cavotricuspid isthmus ablation for atrial flutter was greater than that previously reported by Ellis et al. [6], despite a similar duration of follow-up.

However, in contrast to previously reported studies, univariate analysis in the present study showed that there was no significant difference between patients who developed new-onset AF following ablation therapy and those who did not. Pérez et al. showed that one of the independent predictors of AF was left ventricular ejection fraction (LVEF) [7], while Costa et al. reported that the occurrence of mitral regurgitation was the only independent predictor of AF in patients with new-onset AF [14]. Celikyurt et al. [12] identified the size of the left atrium as an independent predictor for subsequent AF in patients without pre-ablation AF, whereas, BMI was a predictor of AF for the whole group of 364 patients, in patients with atrial flutter alone and with atrial flutter and pre-ablation AF [12]. Similarly, the findings of the present study that included a smaller population size also showed the emerging tendency towards an association between BMI and AF in patients without a previous history of AF.

Catheter-based ablation treatment of atrial flutter is feasibility, and effective, with low procedural risk and for these reasons, it is recommended as a first-line treatment of atrial flutter [14,15]. However, patients remain at risk for developing post-procedural AF, which may suggest that both arrhythmias share the same electrophysiologic triggers and anatomic substrate [16]. According to Schneider et al., atrial flutter is an early indicator of AF [2]. Schneider et al. have also suggested that the pulmonary veins and AF are the true trigger mechanisms for the initiation of atrial flutter [2]. In their study, Schneider et al. emphasized that even if pulmonary vein isolation is performed for patients with typical atrial flutter, it is also recommended that cavotricuspid isthmus ablation for atrial flutter is performed because pulmonary vein reconnection may occur, resulting in recurrent atrial flutter [2]. Navarrete et al., have highlighted the importance of the interrelationship between atrial flutter and AF, indicating that besides cavotricuspid isthmus ablation for isolated atrial flutter, additional pulmonary veins isolation may be necessary to eradicate AF and to reduce the high thromboembolic risk, even if AF is not initially clinically present [1].

The CHADS<sub>2</sub> score (congestive heart failure, hypertension, age  $\geq 75$  years, diabetes mellitus, and stroke [double-weighting]) was developed to accurately predict the risk of stroke in patients with AF [17]. CHADS<sub>2</sub> was extended to include the additional

independent risk factors of vascular disease (coronary artery disease, peripheral artery disease, and aortic atherosclerosis), age 65–74 years, and female gender [17]. For patients with a  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score  $\geq 2$ , the current treatment recommendations are for oral anticoagulant therapy, which should be given to patients after ablation of isolated atrial flutter, because of the high risk of AF [17].

This study had several limitations. This was a retrospective study conducted at a single center that was of relatively small size and relied upon accurate, detailed and available patient data. The study included a non-question telephone survey and the data obtained relied upon the subjective information acquired from patients and their families. The study was limited by too little of empirical data to draw meaningful and reliable conclusions. Therefore, exact tests for small samples were used in the data analysis. However, the outcomes should be interpreted with caution. In this study, the number of individuals with asymptomatic arrhythmia events may have been underestimated. Because not all of the patients were followed-up in the clinic, some follow-up data was inaccessible or difficult to obtain. In this study, the  $\text{CHA}_2\text{DS}_2\text{-VASc}$  scores were not documented or analyzed for each patient. However, the finding from this study have important implications and warrant further large-scale, multicenter, prospective studies.

## References:

- Navarrete A, Conte F, Moran M et al: Ablation of atrial fibrillation at the time of cavotricuspid isthmus ablation in patients with atrial flutter without documented atrial fibrillation derives a better long-term benefit. *J Cardiovasc Electrophysiol*, 2011; 22(1): 34–38
- Schneider R, Lauschke J, Tischer T et al: Pulmonary vein triggers play an important role in the initiation of atrial flutter: Initial results from the prospective randomized Atrial Fibrillation Ablation in Atrial Flutter (Triple A) trial. *Heart Rhythm*, 2015; 12(5): 865–71
- Waldo AL: More musing about the inter-relationships of atrial fibrillation and atrial flutter and their clinical implications. *Circ Arrhythm Electrophysiol*, 2013; 6(3): 453–54
- Lee G, Sanders P, Kalman JM: Catheter ablation of atrial arrhythmias: State of the art. *Lancet*, 2012; 380(9852): 1509–19
- Katritsis DG, Boriani G, Cosio FG et al: European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latino Americana de Estimulación Cardíaca y Electrofisiología (SOLAEC). *Europace*. 2017; 19(3): 465–511
- Ellis K, Wazni O, Marrouche N et al: Incidence of atrial fibrillation post-cavotricuspid isthmus ablation in patients with typical atrial flutter: Left-atrial size as an independent predictor of atrial fibrillation recurrence. *J Cardiovasc Electrophysiol*, 2007; 18(8): 799–802
- Pérez FJ, Schubert CM, Parvez B et al: Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter a meta-analysis. *Circ Arrhythm Electrophysiol*, 2009; 2(4): 393–401
- Haghjoo M, Salem N, Rafati M, Fazelifar A: Predictors of the atrial fibrillation following catheter ablation of typical atrial flutter. *Res Cardiovasc Med*, 2013; 2(2): 90–94
- Vadmann H, Gorst-Rasmussen A, Hjørtshøj SP et al: Death and thromboembolic risk after ablation of atrial flutter compared with atrial fibrillation: A nationwide cohort study. *Europace*, 2017; 19(5): 838–42
- Waldo AL: Atrial fibrillation-atrial flutter interactions: Clinical implications for ablation. *Circulation*, 2007; 116(24): 2774–75
- Wellens HJ: Contemporary management of atrial flutter. *Circulation*, 2002; 106(6): 649–52
- Celikyurt U, Knecht S, Kuehne M et al: Incidence of new-onset atrial fibrillation after cavotricuspid isthmus ablation for atrial flutter. *Europace*, 2017; 19: 1776–80
- Mittal S, Pokushalov E, Romanov A et al: Long-term ECG monitoring using an implantable loop recorder for the detection of atrial fibrillation after cavotricuspid isthmus ablation in patients with atrial flutter. *Heart Rhythm*, 2013; 10(11): 1598–604
- Da Costa A, Romeyer C, Mourot S et al: Factors associated with early atrial fibrillation after ablation of common atrial flutter. *Eur Heart J*, 2002; 23(6): 498–506
- Da Costa A, Zarganeh-Sliman N, Romeyer-Bouchard C et al: Safety and efficacy of radiofrequency ablation of common atrial flutter in elderly patients: A single center prospective study. *Pacing Clin Electrophysiol*, 2003; 26(8): 1729–34
- Mohanty S, Natale A, Mohanty P et al: Pulmonary vein isolation to reduce future risk of atrial fibrillation in patients undergoing typical flutter ablation: Results from a randomized pilot study (REDUCE AF). *J Cardiovasc Electrophysiol*, 2015; 26(8): 819–25
- Camm AJ, Lip GY, De Caterina R et al: 2012 focused update of the ESC guidelines for the management of atrial fibrillation: An update of the 2010 ESC guidelines for the management of atrial fibrillation. Developed with the Special Contribution of the European Heart Rhythm Association. *Eur Heart J*, 2012; 33(21): 2719–47

## Conclusions

A retrospective clinical study conducted at a single center evaluated 40 patients who underwent cavotricuspid isthmus ablation for atrial flutter. This study included a post-ablation follow-up period of  $46 \pm 23$  months, which was longer than previous studies. Following ablation therapy, recurrence of atrial flutter was found in 15% of cases, and asymptomatic AF occurred in 30%. These findings have implications for the use of post-ablation oral anticoagulation treatment, which is often discontinued following ablation therapy and before patient follow-up. Therefore, withdrawal of oral anticoagulants after cavotricuspid isthmus ablation of typical atrial flutter in patients with no previous history of AF history before the procedure may put patients at risk. There remains a need to develop consensus guidelines for the long-term follow-up of patients after cavotricuspid isthmus ablation for atrial flutter ablation. It is the view of the authors that a subset of patients who have had ablation of isolated atrial flutter and who have a  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score  $\geq 2$  should continue oral anticoagulants because of the high risk of developing subsequent AF.

## Conflict of interest

None.