









# The effect of patient characteristics to the acute procedural success and long term outcome of atrial tachycardia and atrial flutter cases undergoing catheter ablation

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## ABSTRACT

**Objective:** In the present study we aimed to demonstrate clinical characteristics, predictors of procedural success and long term recurrence of atrial tachyarrhythmia patients undergoing catheter ablation (CA).

**Patients and Methods:** Consecutive patients who had undergone CA due to an atrial tachyarrhythmia in a single centre arrhythmia unit between 2012 – 2020 were screened. Predictors of procedural success and recurrence were analysed by logistic regression.

**Results:** Study population consisted of 299 consecutive patients (95 [31.8 %] atrial tachycardia, 204 [68.2 %] atrial flutter cases); 163 (54.5 %) were male; median age was 54 (IQR; 42-64). Median follow up was 330 (IQR; 90 – 810) days. Atrial flutter patients were older and had more co-morbidities. Acute procedural success rate was 82.1 % vs. 77.0 % (p= 0.313) and recurrence was 9.3 % vs. 21.6 % (p=0.022) in atrial tachycardia (AT) and atrial flutter (AFL) cases respectively. History of valvular or congenital heart disease surgery, left atrium diameter and age were found to be independent predictors of failed ablation, recurrence and post-procedural atrial fibrillation.

**Conclusion:** Age, left atrium diameter, valvular or congenital heart disease surgery are independent predictors for acute procedural success, recurrence and post-procedural atrial fibrillation in AT and AFL patients who undergo catheter ablation.

**Keywords:** Atrial arrhythmia, Atrial tachycardia, Atrial flutter, Catheter ablation

## 1. INTRODUCTION

Atrial arrhythmias including frequent atrial extrasystoles, atrial tachycardia (AT) and atrial flutter (AFL) are seen less commonly in the clinical practice compared to other types of supraventricular tachyarrhythmias. However, in some cases, these arrhythmias may cause tachycardiomyopathy and severe symptoms. In addition, AT and AFL may precipitate atrial fibrillation. Focal automaticity, triggered activity, micro or macro re-entry may be underlying mechanism of ATs, whereas macro re-entry is the only mechanism of atrial flutter [1-5]. Liu et al., showed that unresponsiveness of focal AT to adenosine is a sign of micro re-entry mechanism rather than automaticity or triggered activity [6]. Although, focal ATs are mostly observed in patients with structurally normal heart, those may also be seen in patients with structural heart disease. Fibrosis in the atria

causes slow conduction areas and focal conduction block. These areas with conduction disturbance constitute the underlying mechanism of micro or macro-re-entry. Aging, heart failure, hypertension, diabetes mellitus, coronary and valvular heart disease can cause fibrosis in the atria by using different pathways [7,8]. Atriotomy scar in patients with prior open-heart surgery is also a common source of re-entrant atrial arrhythmias [9,10]. Antiarrhythmic drugs may fail to control heart rate in most AT and AFL cases. Catheter ablation (CA) of those arrhythmias can effectively be performed, and satisfactory results have been reported in the current literature [1-4]. There is a wide range of variation with respect to clinical characteristics in patients with AT and/or AFL. Patients with AT who have micro or

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macro re-entry as underlying mechanism may display similar clinical characteristics and CA outcomes, when compared to patients with AFL. There is limited data in the current literature regarding the comparison of clinical characteristics and CA outcomes of patient population with AT and AFL.

In the present study, we aimed to comparatively investigate the clinical characteristics of patients with AT and AFL by retrospectively evaluating the data of patients who had undergone CA for these arrhythmias in a single centre. We also aimed to investigate the potential variables that might have predictive values for the outcomes of CA and long-term recurrence in these patients.

## 2. PATIENTS and METHODS

### Study design, patient population and data collection

This study was designed to be conducted in a retrospective observational manner. Patients who had undergone CA because of AT and AFL between December 2012 and September 2020 in a single centre arrhythmia unit were screened. Electronic archive files were used to obtain patients' data. Demographic characteristics of patients, history of prior cardiac surgery, history of coronary artery disease, hypertension and diabetes mellitus were noted. Left atrium (LA) diameter and left ventricle ejection fraction data were extracted from pre-procedural echocardiography reports. Follow-up echocardiography parameters of patients with low pre-procedural ejection fraction were also recorded to evaluate the recovery of left ventricular function after the ablation. Patients whose data could not be achieved were excluded from the study. The study protocol was approved by the Kartal Kosuyolu Training and Research Hospital Ethics Committee (approval number: 2019.7/15-231).

### Catheter ablation procedure and follow-up

Catheter ablation was performed in accordance with the standard protocols. All of the antiarrhythmic drugs were stopped at least five half-live times before the procedure. Tachycardia was induced with programmed electrical stimulation and/or isoproterenol infusion in patients with sinus rhythm. Ablation was not performed if the tachycardia could not be induced except for the cases who had surface electrocardiogram (ECG) tracing of the tachycardia suggestive of typical AFL. After the tachycardia was induced, the diagnosis of AT was confirmed with diagnostic maneuvers. Atrial flutter was diagnosed if the isoelectric line was displaced by flutter waves on surface ECG. However, in some cases, the definitive distinction of AFL and AT could only be made by electro-anatomical mapping. Conventional radiofrequency (RF) ablation or electro-anatomic mapping system was employed depending on complexity of the case or eligibility of equipment. Electro-anatomic mapping system was used in most of AT and atypical AFL cases. Ablation was performed during sinus rhythm in some patients whose arrhythmia was assumed to be cavotricuspid isthmus (CTI) dependent AFL. In remaining AFL and AT cases, ablation was performed during tachycardia. Activation mapping and

entrainment maneuvers were used to detect critical isthmus of tachycardia in AFL cases. All the left sided ablations were performed via transseptal approach. Non-coronary aortic cusp was mapped initially in case of right sided parahisian localisation. Non inducibility with aggressive programmed electrical stimulation or burst pacing for AFL and AT cases was accepted as procedural success after ablation. In addition, isoproterenol infusion was used to check inducibility of arrhythmia for AT patients. Post-procedural follow-up data were obtained from polyclinic visits or emergency admission records. Recurrence was diagnosed if the patient had presented with the same tachycardia that was confirmed by 12-derivation surface ECG. Recurrence was also accepted to be present in patients with tachycardia episodes on 24-hour rhythm Holter monitoring during follow-up and in whom pre-ablation tachycardia was induced during electrophysiological study. Patients who had presented with atrial fibrillation (AF) after the procedure were also noted.

### Statistical Analysis

All statistical analyses were performed by using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Data distribution was evaluated by using Kolmogorov-Smirnov test and histogram. Categorical variables were expressed with percentages, continuous variables were expressed as mean or median depended on distribution of the data. Two-sided t-test or Mann-Whitney U test was used to compare continuous variables and Chi-square was used for categorical data. Binary logistic regression analysis was performed to estimate predictors of study outcome (composite of failed ablation, recurrence, post ablation AF). Predictors that were found to be statistically significant in uni-variable analysis and those with potential that may predict study outcome based on reported data in previous studies were included in the multivariable model. Statistical power of logistic regression was estimated to be 0.90 for an Odds ratio of 1.5 for a sample size of 283 patients. Kaplan-Meier analysis with Log-rank test was used to compare event-free survival between AT and AFL patients. A p value < 0.05 was accepted as statistically significant.

## 3. RESULTS

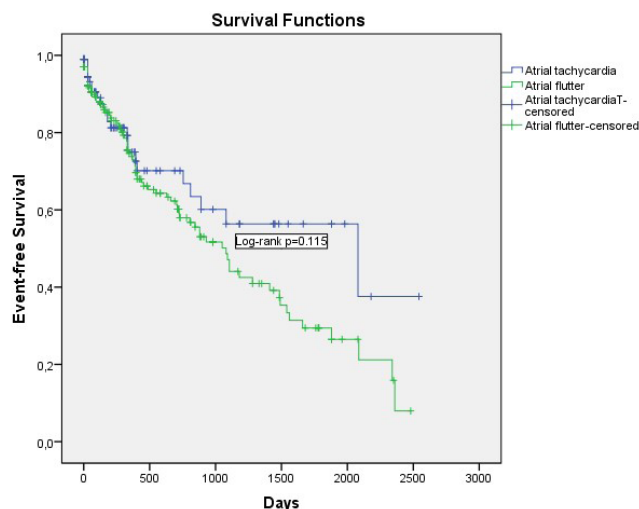
A total of 339 consecutive patients were evaluated. Of those; 32 patients were excluded due to inadequate data, 8 patients were excluded because ablation was not performed and procedure remained as a diagnostic EP study. Final study population consisted of 299 patients (95 [ 31.8 %] AT, 204 [ 68.2 %] AFL cases); 163 ( 54.5 % ) were male and median age was 54 (IQR; 42-64). Median follow up was 330 (IQR;90-180) days (range between 30-2543 days). Characteristics of study patients grouped as AT and AFL are displayed on Table I. None of the patients had a prior history of AF ablation procedure. Atrial tachycardia originated from the left atria (LA) in 13 patients including 4 patients from pulmonary veins. In the remaining 82 patients AT originated from the right atrium. Atrial flutter cases were older, had more co-morbidities and more frequently had history of open heart surgery. In addition, there were more

male patients in AFL group. Patients in AFL group had larger LA diameter and lower left ventricle ejection fraction values compared with patients in AT group. Acute procedural success rate was 82.1 % in AT group while it was 77.0 % in AFL group ( $p = 0.313$ ). Recurrence rate was 9.3 % and 21.6 % in AT and AFL patients respectively ( $p = 0.022$ ). Among patients with failed ablation or recurrence, 2 patients in AT and 22 patients in AFL group presented with paroxysmal or persistent AF during follow-up. There were 16 patients who displayed improvement in left ventricle ejection fraction after CA (4 patients in AT group, 12 patients in AFL group). Multivariable logistic regression analyses showed ; age (OR 1.023 [1.004-1.041]  $p = 0.015$ ), history of valvular or congenital heart disease (CHD) surgery (OR 2.020 [0.987-4.136]  $p = 0.05$ ) and LA diameter (OR 2.549 [1.487-4.368]  $p = 0.001$ ) had emerged as independent predictors of failed ablation, recurrence and AF occurrence in patients with AT and AFL ( Table II). Age, history of valvular or CHD surgery and LA diameter also independently predicted composite endpoint including failed ablation, recurrence and AF occurrence in patients with AFL (Table III). Multivariate analysis could not be performed for AT patients separately due to low number of patients who exhibited study outcome. Kaplan Meier analysis with Log-rank test demonstrated that there was a non-significant trend for higher event-free survival in AT patients compared to AFL patients (Log-rank  $p = 0.115$ ) (Figure 1).

**Table I.** Characteristics of study patients with comparison of atrial tachycardia and atrial flutter cases

	Atrial tachycardia (n= 95)	Atrial flutter (n= 204)	P value
* Age ( years )	51 (29-59)	57 (45-66)	<0.001
Female ( n%)	62 (65.3)	74 ( 36.3)	<0.001
HT ( n%)	22 (23.2)	69 ( 33.8)	0.06
DM ( n%)	4 ( 4.2)	17 ( 8.3)	0.194
CAD (n%)	5 ( 5.3)	37 ( 18.1)	<0.001
<b>Cardiac Surgery ( n%)</b>	7 ( 7.2)	52 ( 25.5)	<0.001
CABG ( n%)	1 (1.1)	13 (6.4)	
Valve replacement (n%)	1( 1.1)	26 ( 12.7)	
Congenital (n%)	5 ( 5.3)	13(6.4)	
<b>Echocardiography</b>	61.1 (± 7.6)	56.5 (± 10.7)	< 0.001
LV Ejection Fraction (%)	3.5 (± 0.44)	4.1 (± 0.53)	< 0.001
LA diameter ( mm)			
Tachycardiomyopathy (n,%)	4 ( 4.2)	12 ( 5.9)	0.783
Acute procedural success (n,%)	78 (82.1)	157 ( 77)	0,313
** Recurrence ( n%)	7/75 ( 9.3)	33/153 ( 21.6)	0.022

\*Age was expressed as median and 25-75 interquartile range, remaining continuous data were expressed as mean ± standard deviation. HT: Hypertension; DM: Diabetes mellitus; HT: Hypertension; CAD: Coronary artery disease; CABG: Coronary artery by-pass graft; LV: Left ventricle; LA: Left atrium. \*\*Patients with failed ablation and lost to follow-up were extracted.



**Figure 1.** Kaplan-Meier curve showing the event free survival after catheter ablation

**Table II.** Univariable and multivariable regression analysis of study patients for composite endpoint ( failed ablation, recurrence and post-procedural AF )

	Univariable OR (%95 CI)	P value	Multivariable OR (% 95 CI)	P value
Female gender	0.982 ( 0.689-1.584)	0.941		
Age	1.028( 1.011-1.044)	0.001	1.023( 1.004-1.041)	0.015
DM	1.445 ( 0.588-3.550)	0.423		
HT	1.024 ( 0.611-1.717)	0.927		
CAD	1.672 ( 0.863-3.237)	0.128		
CABG	1.938 ( 0.661-5.684)	0.228		
Heart valve or Congenital heart disease surgery	2.486 ( 1.307-4.727)	0.005	2.020(0.987-4.136)	0.05
Atrial flutter vs AT	1.909 ( 1.111-3.280)	0.019	0.935 ( 0.500-1.750)	0.834
LV Ejection fraction	0.995 ( 0.972-1.019)	0.706		
LA diameter	3.226 ( 2.017-5.161)	<0.001	2.549 (1.487-4.368)	0.001

DM: Diabetes mellitus; HT: Hypertension; CAD: Coronary artery disease; CABG: Coronary artery by-pass graft; LV: Left ventricle; LA: Left atrium

**Table III.** Predictors of failed ablation, recurrence and post-procedural AF in atrial flutter patients

	Univariable OR ( 95 % CI)	P value	Multivariable OR (95%CI)	P value
Age	1.017(0.997-1.038)	0.092	1.025(1.006-1.043)	0.009
Female Gender	1.552(0.868-2.777)	0.138		
DM	1.838(0.678-4.982)	0.232		
HT	0.907(0,500-1.647)	0.748		
CAD	1.672(0.863-3.237)	0.128		
CABG operation	1.886(0.610-5.831)	0.271		
Heart valve or CHD operation	2.734(1.333-5.563)	0.006	1.534(0.716-3.290)	0.049
LA diameter	3.226 (2.017-5.161)	<0.001	2.489(1.501-4.127)	<0.001
LV EF	0.995(0.972-1.019)	0.706		
Atypical AFL vs CTI dependent AFL	3.339(1.337-8.343)	0.01	1.534(0.716-3.290)	0.271

DM: Diabetes mellitus; HT: Hypertension; CAD: Coronary artery disease; CABG: Coronary artery bypass graft; CHD: Congenital heart disease; LA: Left atrium; LV EF: Left ventricle ejection fraction; AFL: Atrial flutter; CTI: Cavo-tricuspid isthmus

#### 4. DISCUSSION

Main findings of the present study are; (i) patients who had AT and had undergone CA were younger, mostly female and had less frequent co-morbidities compared to patients who had undergone CA due to AFL (ii) older age, history of valvular or CHD surgery and LA diameter were independent predictors of failed ablation, recurrence of index arrhythmia and occurrence of AF (iii) same variables predicted same outcomes when AFL

patients were analysed separately. We have observed significant differences regarding some clinical characteristics and recurrence rates between patients with AT and AFL who had undergone CA in this single centre study. Although, focal automaticity has been suggested to be underlying mechanism for majority of ATs, macro re-entry has also been demonstrated as underlying mechanism in a growing number of AT patients undergoing CA. Fibrosis in the atria causes electrical heterogeneity and focal conduction alterations. Degeneration in the atria causes fibrosis and scar formation. Aging, coronary artery disease, hypertension are all contributing factors for development and progression of atrial fibrosis. Atriotomy scar, sutures, prosthetic valves, patches and baffles can serve as a ground for both AT and AFL. In addition, CA itself can create functional block and slow conduction areas in the atria. Currently, as the number of atrial fibrillation ablation procedures increase, electrophysiologists face with left sided AT and AFL more frequently [11,12]. On the other hand, the mechanism of AT may have automaticity; triggered activity or micro-re-entry in a restricted area of atrium and those patients generally have healthy myocardium in the remaining atria. Young age is a predictor for automaticity mechanism of focal AT [6]. In some type of focal ATs, the mechanism of tachycardia is micro re-entry. For instance, confined slow conduction area and micro re-entry have been demonstrated to have an underlying pathology in crista terminalis ATs [12]. In accordance to that finding, patients with crista terminalis AT are older than the other focal AT patients. Our findings showed that the older age and larger LA diameter are both emerging factors for failed ablation, recurrence, and post – procedural AF in atrial tachyarrhythmia patients. In most studies, it has been shown that larger LA diameter is related with recurrence after CA of AF. [13]. Voight et al., demonstrated that LA diameter is an independent predictor for new onset AF after CTI dependent AFL ablation [14]. In our study, 2 patients in AT group and 22 patients in AFL group presented with AF. Among the study population with post procedural AF; CA had been unsuccessful in 10 patients and recurrence of index arrhythmia had been detected before the AF in 6 patients. Remaining 8 patients presented with AF following the successful ablation. Larger LA diameter is related with advanced fibrosis, scar formation and inflammation in both atrial myocardial tissues. Therefore, LA diameter may predict CA results not only for left sided arrhythmias but also for the tachyarrhythmias that is confined to the right atrium. In addition, it is also relevant to say that altered electrical activity due to unhealthy atrial substrate can precipitate both AFL and AF. Kaneshiro et al., demonstrated that pulmonary vein firing may initiate AFL in patients with prior AF diagnosis [15]. Hence, it is common to observe AF following atrial tachyarrhythmia ablation or vice versa particularly in cases with diseased atrial substrate. Patients with more complex electrical characteristics in atria including functional blocks, slow conduction areas and low amplitude fractionated local electrograms comprise more difficulties for mapping and ablation [16]. In addition, due to progressive nature of fibrosis, arrhythmia recurrence and incidence of post ablation AF are both more common in those patients.



Older age has emerged as an independent predictor of our study outcome. In a study by Brunch et al., it was reported that older age is related with AFL/AF recurrence and increased mortality after AF ablation [17]. In contrast, patients older than 70 years of age had lower recurrence rates after AFL ablation in another study which focused on relationship between age and AFL ablation outcomes [18]. However, patients older than 70 years of age had higher incidence of AF after CA of AFL in the same study. In a study by Huo et al., it was suggested that presence of low voltage zone in LA was related with older age in AF patients who had undergone CA [19]. Hence, poor outcome of elderly patients in our study might be explained with increased atrial fibrosis.

Early diagnosis and technical improvements in the surgical procedures have led to increased survival through older ages for patients with CHD and valvular heart disease. However, atrial arrhythmias are commonly seen in those patients. It has been shown that CA ablation procedures for CHD patients that present with ATs and AFL are more challenging with high recurrence rates [20,21]. Occurrence of more than one tachycardia mechanism (biatrial re-entry, AFL, AF, focal micro re-entry), complexity of cardiac abnormality, dilatation in heart chambers, complexity of corrective surgery, prosthetic heart valves, conduits and patches are all contributing factors of failed ablation and arrhythmia recurrence. In accordance with prior data, prior history of CHD and heart valve operation emerged as an independent predictor of failed ablation and arrhythmia recurrence in our study population.

### Limitations

This study has several limitations: (i) Our study was a retrospective study, and we could not obtain rhythm Holter recordings after ablation for evaluation of recurrence in each patient. Given the fact that Holter monitoring had been performed only in symptomatic patients, recurrence of index arrhythmia or asymptomatic AF attacks might have been undiagnosed in some patients. (ii) Pooled analyses of patients that exhibit large variety of clinical conditions (iii) Cumulative study outcome including failed ablation, recurrence of index arrhythmia and post-procedural AF. We used pooled patient analysis by combining AT and AFL population because we think that it would define the characteristics of these patients more precisely as both may have similar arrhythmia mechanisms. We preferred to evaluate cumulative outcome, because statistical power of analysis would have been reduced if the outcomes had been evaluated separately.

### Conclusion

Atrial tachycardia patients were younger and more frequently female compared to AFL patients in our study. Recurrence was more common in AFL patients compared to AT after CA. Age, LA diameter, history of CHD or heart valve operation were independent predictors of failed ablation, recurrence and post-procedural AF in both pooled patient population and AFL patients.

### Compliance with Ethical Standards

**Ethical approval:** The study protocol was approved by the Kartal Kosuyolu Training and Research Hospital Ethics Committee (approval number: 2019.7/15-231).

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**Conflict of interest:** The authors have no potential conflicts to declare.

**Authors' contributions:** Literature search: MC and AK, Study design: KG, AK and SD, Legislative applications: KG and SD, Data collection: KG, AU, GBK and TA, Supervision and quality control: AK, Statistical advice: AK, Statistical data analysis: AK and KG, Data interpretation: SA and TA, Drafting the manuscript: KG. All authors read and approved the final version of the article.

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