

## Predictors of Atrial Fibrillation after Ablation of Typical Atrial Flutter

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### Summary

**Background:** The occurrence of atrial fibrillation (AF) after successful ablation of cavotricuspid isthmus-dependent atrial flutter (CTI-AFL) is an important medical event, but predictors of this event are still controversial.

**Objective:** To determine the incidence of AF and its predictors in patients undergoing ablation of cavotricuspid isthmus-dependent atrial flutter (CTI-AFL).

**Methods:** Fifty two patients with CTI-AFL underwent ablation from January 2003 to March 2004, in Instituto do Coração (InCor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo.

**Results:** During the mean follow-up period of  $26.2 \pm 9.2$  months, 16 (30.8%) patients presented AF. The univariate analysis revealed two clinical variables as predictive of the occurrence of AF after ablation of CTI-AFL for three years or longer (RR: 3.00;  $p = 0.020$ ). In the multivariate analysis, these factors were independent variables associated with the occurrence of AF after ablation of CTI-AFL.

**Conclusion:** AF is frequently observed during the follow-up of patients undergoing ablation of CTI-AFL. Persistent CTI-AFL and history of arrhythmia for more than three years are predictors of the occurrence of AF during the clinical follow-up. (*Arq Bras Cardiol* 2009; 93(5):448-453)

**Keywords:** Atrial Flutter; Atrial Fibrillation; Catheter Ablation.

### Introduction

Atrial fibrillation (AF) occurring after radiofrequency (RF) catheter ablation of cavotricuspid isthmus-dependent atrial flutter (CTI-AFL)<sup>1-9</sup> is an important medical event because, despite the high success rate of CTI ablation, some patients still require antiarrhythmic drugs or new interventions for its control. Although several studies on this issue have been conducted<sup>1-9</sup>, information on predictors of the occurrence of AF after ablation of CTI-AFL is still controversial. The objective of this study was to determine the incidence of AF and its predictors in a selected sample of patients undergoing ablation of CTI-AFL.

### Methods

#### Patients

From January 2003 to March 2004, 52 patients with CTI-AFL referred for ablation in the Laboratory of Electrophysiology of the Clinical Unit of Arrhythmias and Pacemaker of Instituto do Coração (InCor) of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo were selected.

Patients who had electrocardiographic record of recurrent spontaneous atrial flutter with participation of the CTI in the arrhythmia circuit, as confirmed by electrophysiological study, were included. Patients who had previously undergone ablation procedures were excluded.

The clinical characteristics of the population studied are summarized in Table 1. Rare episodes of paroxysmal AF prior to the ablation of CTI-AFL had been documented in 10 patients, and therefore that was not the patient's main arrhythmia. The 32 patients with AFL rhythm underwent transesophageal echocardiography on the day of the procedure to rule out the presence of intracardiac thrombi<sup>10,11</sup>. Antiarrhythmic drugs were discontinued for five half-lives prior to the procedure, except for amiodarone (61.5% of the patients) which was discontinued for five days.

#### Electrophysiological study and RF ablation

The ablation procedure was performed by one single operator and has been described elsewhere<sup>12</sup>. The studies were performed with the patients fasted and under deep sedation with midazolam and propofol, and analgesia with fentanyl controlled by an anesthesiologist.

Three electrode catheters were introduced via right femoral venipuncture (and left, if necessary) and positioned under direct fluoroscopic guidance around the tricuspid annulus, in the coronary sinus, and in the CTI region for recording of intracavitary potentials, programmed atrial pacing and

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Table 1 – Characteristics of the study population

Nº of patients (n)	No AF 36	With AF 16	P
Male gender, n	31 (86.1%)	13 (81.2%)	NS
Age, years ± SD	57.4 ± 13.5	54.5±11.7	NS
Persistent CTI-AFL n	18 (50%)	13 (81.2%)	0.06
CTI-AFL cycle, ms	278.1± 32.1	300.9±58.8	0.08
Associated paroxysmal AF, n	7 (19.4%)	3 (18.7%)	1
Dilated cardiomyopathy, n	9 (25%)	4 (25%)	NS
Heart valve disease, n	1 (2.8%)	0 (0%)	NS
Ischemic coronary disease, n	5 (13.9%)	1 (6.25%)	NS
COPD, n	1 (2.8%)	1 (6%)	NS
Cardiac Surgery*, n	4 (11.1%)	2 (12.5%)	NS
LA	40.8±5.6	41.3±5.7	0.75
LVEF	60.9±14.4	62.7±13.8	0.68
CHADS 2 0	22 (61.1%)	9 (56.2%)	NS
CHADS 2 ≥ 2	1 (2.8%)	1 (6.25)	NS

\* CABG (4), surgical ASD correction (1) and heart valve replacement (1)  
COPD: chronic obstructive pulmonary disease, LA: Left Atrium, LVEF: left ventricular ejection fraction.

RF ablation. The distal electrode of the catheter around the tricuspid valve annulus (5-French, 2/8/2 mm, decapolar, St Jude Medical, Inc., MN, USA) was positioned adjacent to the lateral region of the ablation line, posterior to the tricuspid annulus, and anterior to the *crista terminalis*. The coronary sinus catheter (5-French, 2/5/2 mm, decapolar, Irvine Biomedical, Inc., CA, USA) was introduced in such a way that the proximal pair was located in the ostial region.

The intracavitary potentials were recorded in a digital system (Electrophysiologic Measurement System – EMS – University of Limburg – The Netherlands) with up to 32 simultaneous electrophysiological channels (12 peripheral and 24 intracavitary) with frequency cut-off between 50 and 500 HZ and recording speed of up to 200 mm/s.

In patients who had atrial flutter rhythm at the beginning of the procedure (32 patients), the CTI participation was demonstrated by the entrainment technique<sup>13</sup>. When the patient presented sinus rhythm, this participation was demonstrated after induction of atrial flutter. The protocol for induction of atrial flutter included pacing of the lateral right atrium and/or proximal coronary sinus with regular cycles (S1-S1) of 600 to 200ms, or up to the atrial refractory period, applied in pulses of 10 to 30 beats, or with up to three extra stimuli applied during basic 430-millisecond cycles. In four patients, the induced atrial flutter was not sustained and the cavotricuspid isthmus participation in the spontaneous atrial flutter was empirically presumed based on the aspect of the flutter wave on conventional ECG<sup>14</sup>.

The RF ablation was started during the CTI-AFL rhythm in 48 patients (92.3%) or during coronary sinus pacing in four patients (7.7%). Application of RF pulses was started close to the tricuspid annulus with stable electrograms (atrial electrogram smaller than the ventricular electrogram). During RF application, the position of the catheter was controlled by fluoroscopic guidance in the left anterior oblique (LAO) view at 45°C, ensuring that the tip of the catheter was in contact with the isthmus tissue. The RF pulses were applied point by point for 60 seconds, following a line corresponding to 6 o'clock in the tricuspid annulus in LAO view up to the inferior vena cava ring. RF energy release and duration of application were performed using 8-mm-tip catheters (7 French Steerable Curve – Dual Thermister Ablation Catheter Quadripolar – Irvine Biomedical; CA, USA) or closed irrigation (7-French, 4-mm-tip, Chilli Cooled Ablation System, Cardiac Pathways Corporation, Sunnyvale, CA, USA), following the technique described elsewhere<sup>12</sup>.

The procedure was considered completed when bidirectional CTI block was achieved. This bidirectional block was considered to be present when: a) an inversion in the sequence of atrial depolarization recorded in the catheter around the tricuspid annulus occurred during pacing of the coronary sinus<sup>12,15</sup>; and b) when the presence of a double low-amplitude (<80%) potential separated by an isoelectric line with more than 100 milisecc duration was demonstrated along the line of RF application both clockwise and counterclockwise<sup>12,16</sup>. These criteria were reassessed

after infusion of 1 to 5  $\mu\text{g}/\text{min}$  of isoproterenol<sup>17</sup> and after 20 minutes of the last RF application.

### Follow-up

Clinical evaluation was performed at one month and then every three months after RF ablation. 12-lead ECG was performed in every visit, and 24-hour Holter monitoring at the first, third, twelfth and twenty fourth months after ablation. If the patient reported palpitations, a 24-Holter monitor and/or an event monitor was placed for seven days (loop recorder). Antiarrhythmic drugs were discontinued after successful RF ablation.

### Definition of terms

Paroxysmal CTI-AFL: recurrent CTI-AFL ( $\geq 2$  episodes) that terminates spontaneously within seven days<sup>18</sup>.

Persistent CTI-AFL: (according to the standardization of the literature, we chose to use the term persistent) sustained CTI-AFL beyond seven days or lasting less than seven days, but requiring electric or pharmacological cardioversion<sup>18</sup>.

### Statistical analysis

The variables analyzed were: gender; presence of heart disease; left atrial size; mitral regurgitation; left ventricular (LV) ejection fraction; presence of paroxysmal AF before AFL ablation; age greater than 60 years; time of onset of CTI-AFL; and classification of CTI-AFL as paroxysmal or persistent. Descriptive data are expressed as mean  $\pm$  standard deviation (SD). The Kaplan-Meier analysis and the log rank test (Mantel-Cox) were used to determine the variables associated with a higher incidence of AF. The logistic regression analysis, Cox model, was carried out to determine the predictors of AF after ablation of CTI-AFL, using the previously mentioned covariables. P values  $< 0.05$  were considered significant.

Variables with statistical significance for a higher incidence of AF in the multivariate analysis were considered as risk factors for the occurrence of AF.

### Results

During the mean follow-up of  $26.2 \pm 9.2$  months, three (5.8%) patients experienced recurrent atrial flutter. A second procedure was successfully performed in two patients. The third patient chose drug therapy under his physician's supervision.

### Occurrence of AF

AF occurred in 16 (30.8%) of the 52 patients undergoing CTI ablation (the moment at which the event occurred can be observed in the curve – Figure 1). The AF episodes were diagnosed in seven (43.75%) patients using 12-lead ECG and in nine (56.25%) using 24-h Holter monitoring. All patients experienced paroxysmal AF. Of the ten patients who had presented AF before ablation of CTI-AFL, only three (30%) presented AF in the follow-up period. The univariate analysis revealed that two clinical variables were

predictive of the occurrence of AF after ablation of CTI-AFL: 1) the presence of persistent CTI-AFL (RR: 2.94; P = 0.053); 2) CTI-AFL for three years or longer (RR: 3.00; P = 0.020) (Figure 2).

Among the 31 patients with persistent CTI-AFL, AF was observed (as recorded during clinical investigation for palpitation) in 13 patients (41.9%); among the 21 patients with paroxysmal CTI-AFL, AF occurred in three (14.3%).

In the multivariate analysis, the presence of persistent CTI-AFL and history of CTI-AFL for three years or longer proved to be independent variables associated with the occurrence of AF after ablation of CTI-AFL (Figure 3).

Patients with two risk factors for AF had a significantly higher risk for the occurrence of AF in the late follow-up ( $p = 0.048$  in relation to one risk factor, and  $p = 0.023$  in relation to the absence of risk factors) (Figure 4).

Patients who presented AF episodes were treated with amiodarone (56.3%) or propafenone (25%); 18.7% of the patients did not receive antiarrhythmic drugs. Of these patients, four underwent AF ablation because they were refractory to the antiarrhythmic drugs.

### Discussion

Previous studies have demonstrated an interrelation between CTI-AFL and AF<sup>19-20</sup>. Patients who primarily present AFL usually also present AF and vice versa. RF ablation is known to be the treatment of choice for recurrent CTI-AFL thanks to its high success rate and low risk of complications<sup>21,22</sup>. However, AF episodes are described in 25% to 36% of the patients undergoing ablation of CTI-AFL<sup>5-9</sup>. Ellis et al<sup>23</sup> reported an 82% incidence of AF refractory to antiarrhythmic drugs in the late follow-up of patients undergoing ablation of CTI-AFL; in their case series, the predictor of this condition was the left atrial size. Other studies described previous history of AF and ventricular dysfunction lower than 50% as predictive of AF in the follow-up<sup>24</sup>. Da Costa et al<sup>25</sup> reported mitral regurgitation as predictive of AF.

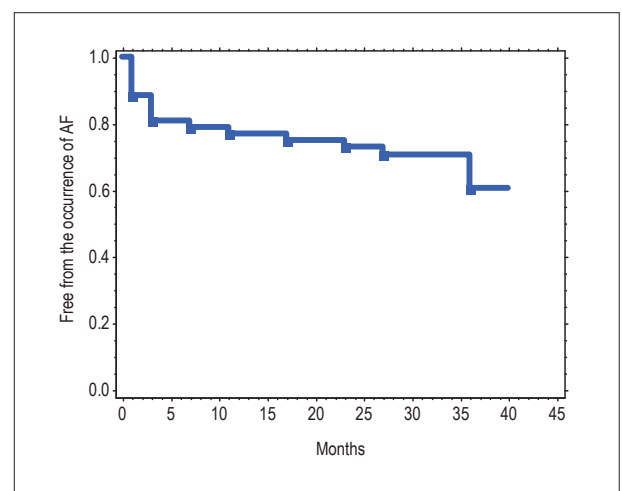


Fig. 1 - Kaplan-Meier curve for the occurrence of AF after ablation of CTI-AFL (n=52).

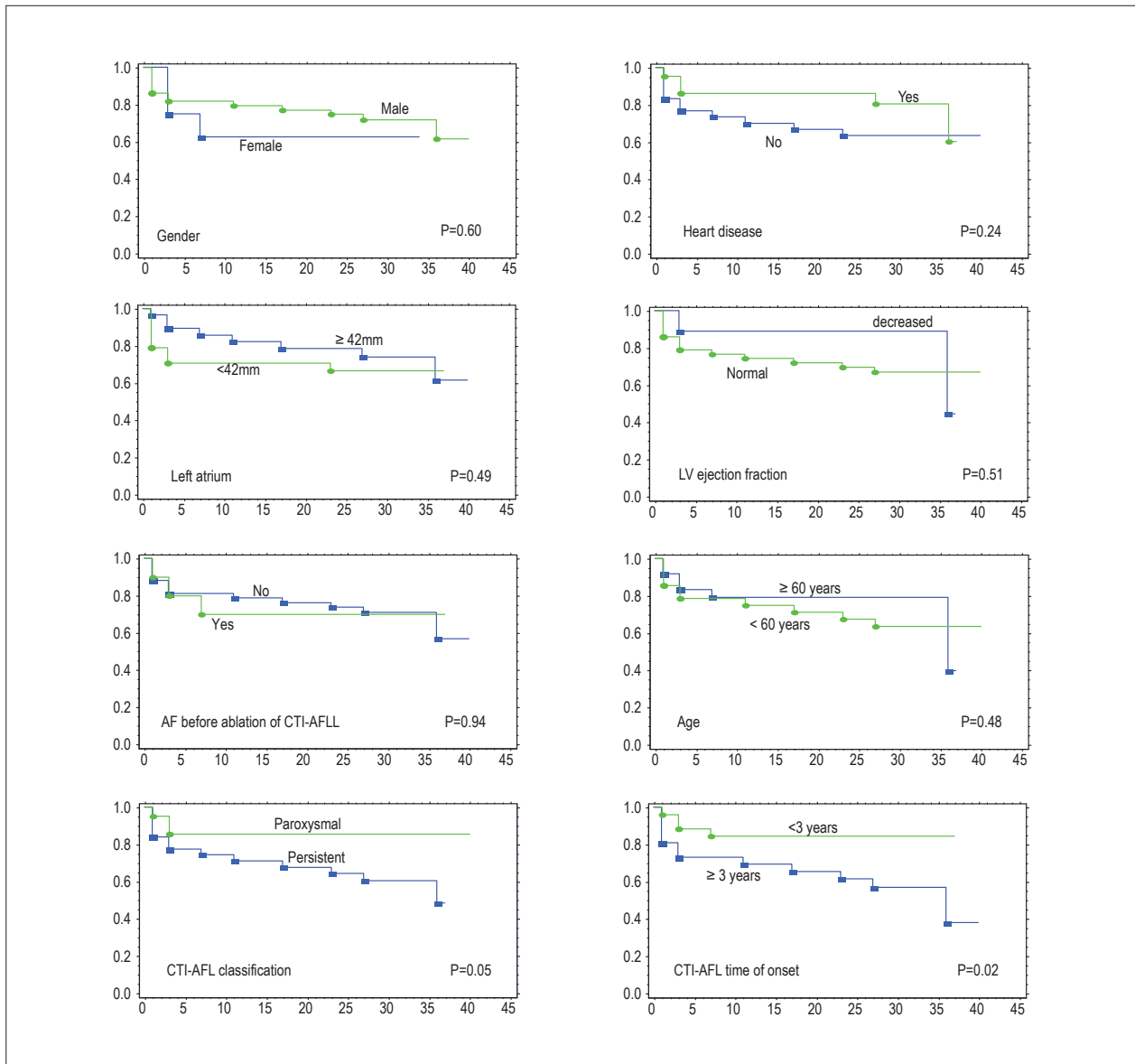


Fig. 2 - Kaplan-Meier curve for follow-up free from the occurrence of AF after ablation of CTI-AFL (n = 52)

In our case series, we found other predictors of AF: history of CTI-AFL for more than three years and the presence of persistent CTI-AFL.

Recent studies suggested pulmonary vein triggers could initiate both AF and AFL<sup>26</sup>. Pulmonary vein isolation is currently the treatment proposed for patients with AF refractory to medical treatment<sup>27</sup>. Given the high incidence of concurrent AF and AFL, this hybrid technique represents an acceptable initial approach for the treatment of CTI-AFL, at least in patients at a high risk of developing AF<sup>26</sup>.

### Clinical implications

Patients with persistent or long-standing flutter should be warned about the risk of recurrence of symptoms due to the occurrence of AF after CTI ablation. The need for the use of

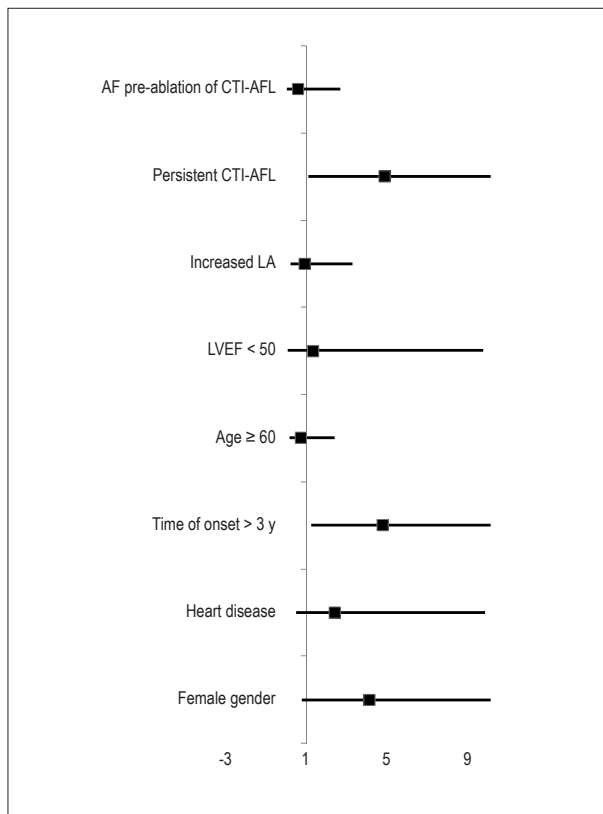
antiarrhythmic drugs as well as of systemic anticoagulation is also worth of consideration in patients with risk factors for embolic events.

### Study limitations

The major limitations of this study are the small number of patients included and the technique of AF documentation before and after ablation of AFL, which may have caused this condition to be underdiagnosed.

### Conclusion

AF is commonly observed after ablation of CTI-AFL. Documentation of persistent AFL and history of arrhythmia for more than three years identify patients at a higher risk for its occurrence. These findings are clinically important, especially

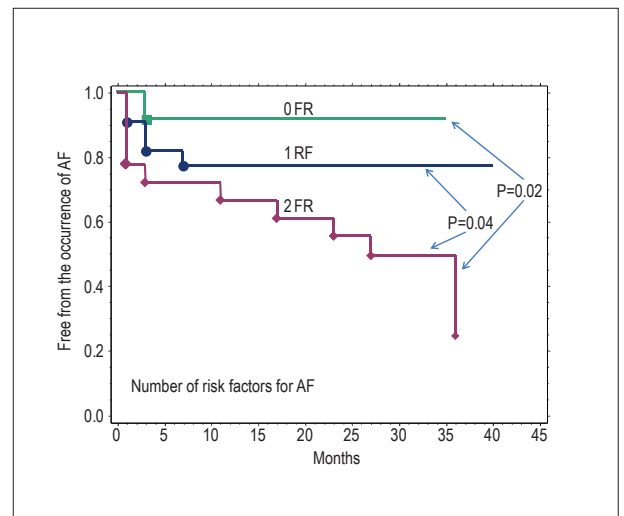


**Fig. 3 -** Multivariate analysis for the occurrence of AF after ablation of atrial flutter (\*  $p < 0.005$ )

in patients at a high risk for thromboembolic events. Thus, a more judicious assessment is recommended, especially before systemic anticoagulation is discontinued.

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**Fig. 4 -** Freedom from occurrence of AF curve in patients with two, one or no risk factors (persistent CTI-AFL or for more than 3 years) for the occurrence of AF

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

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