Acute and long-term results of radiofrequency ablation of common atrial flutter and the influence of the right atrial isthmus ablation on the occurrence of atrial fibrillation

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Aims The purpose of this study was to evaluate the acute success rate and long-term efficacy of radiofrequency ablation of common type atrial flutter (AFL) by using a standardised anatomical approach in a large series of patients and to assess the influence of right atrial isthmus ablation on the occurrence of atrial fibrillation. There are no large scale prospective or retrospective multicentre studies for radiofrequency ablation of AFL.

Methods and results The study population consisted of 363 consecutive patients with AFL (mean age 58±16 years, 265 men) who underwent radiofrequency ablation at the inferior vena cava-tricuspid annulus (IVC-TA) isthmus using a standardised anatomic approach. Bidirectional isthmus block at the IVC-TA was achieved in 328 patients (90%). Following radiofrequency ablation, 343 patients (95%) were followed for a mean of 496±335 days. During the follow-up period, 310 patients (90%) remained free of AFL recurrences. Multivariate analysis identified five independent predictors of AFL recurrence: fluoroscopy time (p<0.001), atrial fibrillation after AFL ablation (p=0.01), lack of bidirectional block (p=0.02), reduced left ventricular function (p=0.035) and right atrial dimensions (p=0.046). Atrial fibrillation occurrence was significantly reduced after AFL ablation (112 in 343 patients, 33%) as compared to occurrence of atrial fibrillation before radiofrequency ablation (198 in 363 patients, 55%, p<0.001).

Conclusion The current anatomical ablation approach for AFL and criteria for evaluation of the IVC-TA isthmus block is associated with an acute success rate of 90% and a long-term recurrence rate of 10%. Radiofrequency ablation of common AFL results in a significant reduction in the occurrence of atrial fibrillation.

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KEYWORDS
Atrial flutter; Atrial fibrillation; Radiofrequency ablation

Introduction
Typical atrial flutter (AFL) is a macroreentrant supraventricular tachycardia whose reentry circuit is entirely located in the right atrium.1,2 A recent
population-based study have suggested that the overall incidence of AFL is 88/100 000 person-years or 200 000 new cases in the US population annually.\(^3\) AFL is highly symptomatic in the majority of patients\(^4\) and is associated with morbid events such as tachycardic cardiomyopathy,\(^5\) thromboembolism,\(^6\)–\(^8\) atrial stunning after therapeutic termination,\(^9\)\(^,\)\(^10\) inappropiate heart rate during effort\(^11\) and marked reduction of exercise tolerance especially in patients with advanced structural heart disease.\(^12\) Radiofrequency current application at the inferior vena cava-tricuspid annulus (IVC-TA) isthmus evolved from an experimental technique to the therapy of choice for the treatment of AFL. Earlier single centre radiofrequency studies reported a high initial success rate but, on the other hand a relatively high recurrence rate of 11–25%.\(^1,\)\(^13,\)\(^14\) Clinical application of the anatomical approach of radiofrequency ablation\(^15\) and development of criteria for evaluation of bidirectional isthmus block\(^16,\)\(^17\) transformed the technique of ablation of AFL into a safe and effective means of therapy and improved substantially the long-term results. However, the NASPE Prospective Catheter Ablation Registry for year 1998 reported an acute success of AFL ablation of 85.8% and recurrence rates of 14.7%.\(^18\) Reasons for these less favourable results as compared to the aforementioned studies were not known. On the other hand, there are no large scale prospective or retrospective multicentre studies for radiofrequency ablation of AFL.\(^18\)

Thus, the purpose of this study was to evaluate the acute success rate and long-term efficacy of radiofrequency ablation of common type AFL by using a standardised anatomical approach in a large series of patients. A second objective of the study was to assess the influence of isthmus ablation on the occurrence of atrial fibrillation.

**Methods**

**Study population**

From October 1998 till June 2002, 363 consecutive patients (mean age 58±16 years, range 2–86 years, 265 men) with common AFL who underwent radiofrequency ablation at our hospital were included in this study. All patients had spontaneous AFL episodes documented with 12-lead surface electrocardiogram (counterclockwise flutter in 298 patients, 82% and clockwise flutter in 52 patients, 14% and both types in 14 patients 4%). One hundred and eighty-nine patients (55%) had a documented history of atrial fibrillation. Atrial fibrillation was paroxysmal in 176 patients and persistent in 22 patients. The first episodes suggestive of atrial fibrillation were reported 50±49 months before the ablation procedure. In 261 patients (72%) a structural heart disease was found. Clinical characteristics of the patients are shown in Table 1.

Antiarrhythmic medications were withheld at least five plasma half-lives before electrophysiologic study except for amiodarone (23 patients). Coumadine derivatives were stopped 2 days before the procedure.

All patients underwent an initial clinical evaluation that included history, physical examination, 12-lead surface electrocardiogram, 24-h electrocardiographic monitoring, X-ray examination, blood chemistry tests and two-dimensional echocardiography with colour flow Doppler measurements.

**Definition of arrhythmia**

Electrocardiographic/electrophysiologic criteria of common type AFL were as follows: (1) typical surface electrocardiographic appearance for counterclockwise and clockwise AFL, (2) counterclockwise or clockwise activation around the tricuspid annulus and (3) concealed entrainment during pacing from the IVC-TA isthmus.\(^2,\)\(^19\) Patients with intra-atrial reentrant tachycardia following reparative surgery for complex congenital heart disease were excluded from this study.
Electrophysiological study

Before undergoing mapping/ablation procedure, patients gave written informed consent. Three electrode catheters were inserted from one or both femoral veins and positioned in the right atrium and the coronary sinus: one 20-polar catheter was positioned around the tricuspid annulus with the electrode pair 1/2 located in the low portion of the lateral wall near the lateral entry of the IVC-TA isthmus; one eight-polar mapping catheter was inserted in the coronary sinus and a third catheter was the ablation catheter. In 18 patients (5%), a 4-mm tip ablation catheter was used. In the remaining patients, either an 8-mm tip (n=290, 85%) or cooled-tip ablation (n=55, 15%) catheters were used. In the 2-year-old patient, 2.5 F mapping catheters were used.

In those subjects who were not in AFL at the time of electrophysiologic testing, programmed atrial stimulation from the coronary sinus and high right atrium was performed. During sustained AFL, activation sequence mapping was performed to define the nature of arrhythmia. Entrainment mapping was performed by pacing at the IVC-TA isthmus with paced cycle length of 20–40 ms shorter than the arrhythmia cycle lengths.

Radiofrequency ablation and isthmus block evaluation

The anatomical approach with a goal of producing a line of block between the tricuspid annulus and the inferior vena cava was used for radiofrequency ablation. The ablation catheter was steered under fluoroscopic control and placed in the isthmus region. The catheter was manoeuvred to approach the tricuspid annulus (local electrogram reflecting equally the atrial and ventricular signals) and then withdrawn gradually from the tricuspid annulus towards the inferior vena cava. If radiofrequency ablation was performed during AFL episodes, coincidence of local electrogram with the middle of plateau (in counterclockwise flutter) or the down-sloping part of the P waves (clockwise flutter) in the inferior electrocardiographic leads served as criteria for correct mid-isthmus positioning of the ablation catheter.20 Radiofrequency energy was delivered as a nonmodulated radiofrequency current at a frequency of 550 kHz between the tip of the catheter and a skin patch placed under the left shoulder for up to 60 s at a preset temperature mode (60 °C). Ablation was considered successful when the arrhythmia was no longer inducible and the criteria for bidirectional isthmus conduction block were observed.6,17 Provocative pacing and isthmus conduction testing were performed immediately after and at 30–45 min after the last radiofrequency delivery that resulted in isthmus block. In the first series of the patients (120 patients) sequence activation criteria of the lateral and posterior wall of the right atrium during pacing from the coronary sinus and the low lateral wall were used to test conduction in the post-ablation isthmus. In patients ablated during the last 2 years, sequence and local criteria (double potentials in the isthmus region during pacing from the coronary sinus and low lateral wall of the right atrium) for isthmus block were applied. Transthoracic echocardiography was performed immediately following ablation procedure to seek for eventual pericardial effusion.

Post-ablation management and follow-up

Patients were discharged from hospital on treatment for the underlying heart disease. All patients were discharged on oral anticoagulants for 2 months. In patients with concomitant atrial fibrillation oral anticoagulants were maintained. Follow-up information was obtained at the time of revisits at the ambulatory arrhythmia clinic or by telephone contact with the patients or the patients’ private physicians at 3 months, 6 months, 1 year and then yearly after the ablation procedure. Whenever the patients had symptoms suggestive of arrhythmia they were advised to seek consultation from the ambulatory arrhythmia clinic or contact their physicians to evidence the eventual arrhythmia relapse. In case of AFL recurrence, the patients were hospitalised and reablation was offered.

Statistical analysis

Data are presented as mean±SD, percentage or range. Univariate comparisons between variables were made by chi-square test for categorical variables and unpaired t-test for continuous variables. Cumulative probability of freedom from AFL recurrence was calculated with the Kaplan–Meier method. Multivariate analysis was performed with a Cox proportional hazards model with stepwise backward selection to identify independent factors for AFL recurrence. Clinical and procedural variables that were subjected to the model were: age, sex, left atrial dimensions, right atrial dimensions, structural heart disease, left ventricular ejection fraction, atrial fibrillation before ablation, atrial fibrillation after ablation, achievement of bidirectional isthmus block, type of the ablation catheter,
fluoroscopy time and number of radiofrequency current applications. A \( p < 0.05 \) was considered statistically significant.

**Results**

**Patient characteristics**

Clinical characteristics of the patients are shown in Table 1. Included in the study were patients with ages from 2 to 86 years old. AFL was more frequent in the age group of 55–75 years (225 patients, 62%). Male patients predominated. Male-to-female ratio was found to be 2.7:1. The most common structural heart disease was arterial hypertension (188 patients, 52%) followed by coronary artery disease (93 patients, 26%). In 102 patients no clinically detectable structural heart disease was found. In 198 patients (55%) besides AFL, atrial fibrillation episodes were documented before radiofrequency ablation.

**Electrophysiological data and acute ablation results**

At the time of electrophysiologic testing, 175 patients (48%) were in AFL and 162 patients presented with sinus rhythm (45%). In 70 of the patients with sinus rhythm at the time of the electrophysiological procedure atrial pacing induced AFL whereas in 93 patients (all of them with electrocardiographical documentation of spontaneous episodes of sustained typical AFL) radiofrequency ablation and testing of completeness of the isthmus block were performed during coronary sinus pacing. In 22 patients with persistent atrial fibrillation, internal cardioversion was performed before the ablation procedure. In patients with spontaneous or induced counterclockwise and clockwise AFL the cycle lengths were 239±27 and 241±42 ms \( (p=0.80) \), respectively.

Radiofrequency ablation at the IVC-TA was attempted in all patients. Criteria for bidirectional block were achieved in 328 patients (90%). Mean fluoroscopy time was 28±21 min. Mean number of radiofrequency applications was 22±17 deliveries. In 35 patients (10%), despite more radiofrequency applications \( (40±20 \text{ vs. } 21±17, \ p<0.001) \) or longer fluoroscopy times \( (56±34 \text{ vs. } 27±20 \text{ min}, \ p<0.001) \) as compared to successfully ablated patients, criteria for bidirectional block could not be achieved.

**Complications**

In nine patients (nearly 3%) procedure-related complications were observed. In four patients, femoral artery-to-femoral vein fistulas were documented. In two patients, acute complete atrioventricular conduction block was produced during isthmus ablation for which dual-chamber pacemakers were implanted. One patient collapsed 10 days after ablation procedure and complete atrioventricular conduction block was documented. The patient was resuscitated and a VVI pacemaker was implanted. The patient died 3 months later due to progression of congestive heart failure. In two patients slight pericardial effusion was detected by transthoracic echocardiography. No pericardial puncture was applied and no other clinical events were observed.

**Medications at discharge**

Following the radiofrequency ablation patients were discharged on the following antiarrhythmic regimen: beta blockers (291 patients), amiodarone (10 patients) and flecainide (one patient). No statistical differences were observed between antiarrhythmic therapy before (288 patients, 79%) and after ablation (302 patients, 83%, \( p=0.18 \)). All patients were discharged on coumadine derivatives. In patients without AFL recurrences, coumadine derivatives were stopped after 2 months of follow-up. In patients with atrial fibrillation episodes (112 patients, see below) coumadine derivatives were maintained. Angiotensin-converting enzyme inhibitors, diuretics and digitalis were prescribed in 166, 118 and 20 patients, respectively. Aspirin was prescribed in 85 patients after discontinuation of coumadine derivatives.

**Follow-up results**

Three hundred and forty-three patients (95% of the study population) were followed for a mean of 496±335 days. Twenty patients were lost during follow-up. During this time interval six patients died. Two patients died due to malignancies (one breast cancer and one lung cancer). Three patients with advance heart disease died due to progression of congestive heart failure including one patient with an implanted internal cardioverter-defibrillator. One patient with pemphigus vulgaris died due to multi-organ failure. During the follow-up period, 310 patients (90%) were free of AFL recurrences. In 33 patients (10%) recurrences of typical AFL occurred and were reablated. Four patients underwent a third ablation procedure. Recurrences occurred in nine of 35 patients (26%) in whom no criteria for bidirectional isthmus block were achieved and 24 of 328 patients (7%)
with bidirectional isthmus block \((p=0.002)\). Kaplan–Meyer analysis revealed that the majority of recurrences occurred in the first months following the ablation procedure (Fig. 1). Multivariate analysis identified five independent predictors of AFL recurrence: fluoroscopy time \((p<0.001)\), atrial fibrillation after ablation \((p=0.01)\), lack of bidirectional block \((p=0.02)\), reduced left ventricular function \((p=0.035)\) and right atrial dimensions \((p=0.046)\).

Atrial fibrillation after AFL ablation

As compared with atrial fibrillation episodes before the radiofrequency ablation, the incidence of atrial fibrillation after the flutter ablation was reduced significantly (112 patients, 33%) as compared to occurrence of atrial fibrillation before radiofrequency ablation (198 in 363 patients, 55%, \(p<0.001\)). Proportions of the patients with atrial fibrillation before and after radiofrequency ablation are shown in Fig. 2.

Discussion

This study evaluated the efficacy of radiofrequency ablation for treatment of AFL in a large series of patients analysed retrospectively. Since, a standard anatomical approach and criteria for evaluation of isthmus block were used in all patients, results of this study reflect the therapeutic power of a mature and standardised radiofrequency ablation approach for this arrhythmia.

Acute results of radiofrequency ablation of AFL

Our study showed that radiofrequency ablation at the IVC-TA isthmus results in a high acute success rate of 90%. In 10% of patients, despite more radiofrequency current deliveries, we were unable to achieve a complete isthmus block. These data coincide with a recent study by Jais et al. who found that in 7.6% of the patients conventional radiofrequency ablation failed to create a complete isthmus block.21 Reasons for failure to produce a complete isthmus block are unclear. However, several factors might be responsible. First, anatomic factors (thicker isthmus myocardium or an isthmus geometry which prevents a close catheter tissue contact throughout the isthmus entirety) should be considered.21,22 The fact that Jais et al. succeeded in producing complete isthmus block using an irrigated-tip catheter which results in deeper lesions supports the importance of this factor.21 Second, with the use of conventional mapping technique the possibility of rapid conduction around the posterior aspect of the inferior vena cava23 cannot be excluded. In the latter situation, the completeness of the isthmus block cannot be evaluated.

Long-term results of radiofrequency ablation of AFL

During a mean follow-up of 496±335 days, 10% of the patients developed recurrences of AFL. Interestingly, these data coincide with two recent studies which included a relatively large number of
patients. In a series of 200 patients with common AFL Fischer et al. reported a recurrence rate of AFL of 15.5% after a mean of follow-up of 24±9 months. In the 1998 NASPE Prospective Catheter Ablation Registry, Scheinman and Huang reported a similar recurrence rate of 14.8%. Several other studies, in which conduction through the isthmus region was verified with electroanatomic mapping, have demonstrated resumption of the trans-isthmus conduction following radiofrequency ablation for cure of AFL. From these studies and the present one, it seems that isthmus conduction resumed in nearly 7% of patients with AFL in whom an acute isthmus bidirectional block has been evidenced by the current criteria. Although, the exact factors that favour the resumption of the conduction through acutely ablated isthmus are not clear, the possible role of acute ischaemia and oedema caused by radiofrequency ablation might be considered as factors that participate in acute interruption of the trans-isthmus conduction, masking the presence of still viable isthmus myocardium. Since these factors fade gradually after acute damage, viable myocardium at the isthmus might restore capacity for conduction. Improvement of isthmus conduction with isoproterenol underscores the importance of these factors. Furthermore, details of isthmus remodelling following radiofrequency ablation for AFL are obscure. Our study showed that multiple factors like those that reflect the severity of the structural heart disease (left ventricular function and atrial dimensions), trigger factors (atrial fibrillation after ablation) and procedural parameters (longer procedures and failure to achieve bidirectional isthmus block) were independent predictors for AFL recurrences following radiofrequency ablation.

Incidence of atrial fibrillation before and after ablation

A close link between AFL and fibrillation has been demonstrated from Holter monitoring and electrophysiologic studies. In patients with AFL a high incidence of atrial fibrillation has been reported which might be explained with more advanced heart disease as compared with patients with flutter episodes only. However, the impact of AFL ablation on the incidence of atrial fibrillation is complex and still an issue of debate. Previous studies have suggested the importance of right AFL for induction of atrial fibrillation. A possible reduction in the atrial fibrillation episodes after radiofrequency ablation of AFL have been suggested by small-number studies. Our data gathered from a large number of patients show that radiofrequency ablation of AFL reduces significantly the incidence of atrial fibrillation and stress the fact that regular supraventricular rhythms do play a role in precipitation of atrial fibrillation.

Conclusions

The current anatomical ablation approach and set of criteria to assess post-ablation isthmus block is associated with an acute success rate of 90% and long-term recurrence rate of 10%. Radiofrequency ablation of common AFL results in a significant reduction of incidence of atrial fibrillation.

References