Acute myocardial infarction treatment : from prehospital care to secondary prevention

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Chapter 12

Long-term clinical outcome after radiofrequency ablation of cavotricuspid isthmus dependent atrial flutter and risks of atrial fibrillation occurrence.

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ABSTRACT

Objective

To assess long-term (median 40 months) outcome of cavotricuspid isthmus ablation in terms of atrial flutter (AFL) recurrence and particularly in terms of atrial fibrillation (AF) occurrence in a clinical population with electrocardiographically documented isthmus dependent AFL with or without a history of AF.

Methods

From 1995 to 2006 149 patients underwent radiofrequency ablation procedures for AFL. Of these patients, 87 patients had a known history of paroxysmal AF (87/149, 58%) and were assigned to group 1. The remaining patients were defined as group 2.

Results

A total of 133/149 patients had an initially successful AFL ablation. In 85% (113/133) of procedures bidirectional isthmus block was achieved (others were defined as successful due to noninducibility). Patients in group 1 had a significantly higher cumulative incidence rate of AF occurrence than patients in group 2 (p=0.0007): The cumulative incidence of AF occurrence was 60% at 1 year (95%CI 48%-72%) and 81% at 5 years (95%CI 71%-92%). AF occurrence in group 2 at 1 year was 28% (95%CI 14%-43%) and at 5 years 57% (95%CI 39%-75%). However, the large difference between groups 1 and 2 reflected primarily the much higher rate of AF occurrences in group 1 during the first 1.5 year post-ablation.

Conclusion

Despite the efficacy of cavotricuspid isthmus RF ablation in the treatment of AFL, most patients cannot be considered completely cured, particularly with regard to AF occurrences. Patients with a preablation history of AF and high diastolic blood pressure were at significantly higher risk and should be monitored more closely and treated more aggressively for hypertension. However, preablation AF did not lead to an increased long-term (>1.5 year) risk after AFL ablation. Patients in this subgroup therefore may expect the same long-term risk of AF as patients without pre-existing AF.

INTRODUCTION

Catheter ablation of the inferior vena cava–tricuspid isthmus is an established treatment modality for typical atrial flutter (AFL). Though ablative therapy of AFL has proven to be efficacious, long-term outcome of ablation may be complicated by the occurrence of atrial fibrillation (AF), either preexisting or developing de novo[1-3]. Studies investigating factors predictive of AF arising after ablation of AFL showed that there is a high risk of developing AF particularly in a subgroup of patients with a history of paroxysmal AF[1-6]. Despite the seemingly pessimistic outlook for this patient subgroup, several follow-up studies including patients with both AFL and AF, showed that ablation of the right atrial isthmus for typical AFL in combination with previously ineffective antiarrhythmic drug (AAD) therapy was found to result in longer arrhythmia-free intervals in a large proportion of patients[7;8]. It has therefore been suggested that patients with preexisting AF may benefit from isthmus ablation of AFL in terms of less recurrences of AF and better effect of medication on previously therapy-resistant AF [7;8]. The purpose of this retrospective study was to assess the long-term (median 40 months) outcome of cavotricuspid isthmus ablation in terms of AFL recurrence and particularly in terms of AF occurrence in a population of "real-practice" patients with electrocardiographically documented isthmus dependent AFL with or without a preablation history of AF.

METHODS

Patient population

Consecutive patients referred between June 1995 and Aug 2003 for ablative therapy of electrocardiographically documented isthmus dependent atrial flutter were included in the current retrospective study. Patients were divided into 2 groups: Group 1 were patients with isthmus dependent AFL and documented coexisting paroxysmal AF and group 2 consisted of patients with AFL who had no history of AF. Patients with congenital heart disease were excluded from this study.

Electrophysiology study and ablation procedure

Linear ablation of the right atrial isthmus was guided by either fluoroscopy only or with 3-D electro-anatomical mapping techniques. In case of conventional mapping, the right atrial pattern of activation was studied with a 7F 20-electrode steerable catheter (Halo catheter, Cordis-Webster, Diamond Bar, California, USA) or a 8F 64-electrode collapsible Basket catheter (Cardiac Pathways, Sunnyvale, California, USA).

Three-dimensional electro-anatomical mapping techniques used included the CARTO™ (Biosense-Webster, Diamond Bar, California, USA), the Real time position management system (RPM, Cardiac Pathways, Sunnyvale, California, USA) or the Ensite system (Endocardial Solutions Inc., St. Paul, Minnesota, USA). Detailed description of the underlying technology and use of these various electro-anatomical mapping techniques has been given previously by others.[9-11]

For induction of AFL, programmed electrical stimulation applying up to three extrastimuli or burstpacing at 2 times diastolic threshold (pulse width 2 ms) was performed with a constant current stimulator (Medtronic, Minneapolis, MN, USA). Ablation was performed with either a non-cooled or cooled 7F 4 mm Navi-star catheter (Biosense-Webster, Diamond Bar, California, USA), a 7F 4mm tip steerable cooled ablation catheter (Cardiac Pathways, Sunnyvale, California, USA) or a standard 7F 4 mm steerable ablation catheter.

At each site, radiofrequency current was applied for 60 seconds. In case of non-cooled ablation, tip temperature was set at 70°C and the maximum output at 50W. During ablation using an irrigated-tip catheter, temperature was limited to 50°C and power to 45W with saline flow of 17 ml/hour (4 ml/min). Each lesion was tagged on the electro-anatomical right atrial map when using a 3-D electro-anatomical mapping system.

During the procedure, heparin was administered intravenously to maintain an anti-clotting time of 2.5-3 times the control value for adequate anti-coagulation. If necessary, patients were intravenously sedated with midazolam and fentanyl. Acute procedural success was initially defined as termination of AFL during ablation and non-inducibility, and later in time as establishing bidirectional conduction block over the cavo-tricuspid isthmus.[3;12]

Definitions

Some patients underwent more than one AFL ablation procedure. The first successful AFL ablation procedure is defined as the first of several AFL ablation procedures during which acute procedural success was achieved. The last successful AFL ablation procedure is defined as the last of several AFL ablation procedures during which acute procedural success was achieved.

AFL or AF episodes at follow-up were documented by either electrocardiographic or 24-hour Holter recordings and by repeat electrophysiology study if repeat ablation was clinically indicated.

Follow-up

Follow-up was conducted at the out patient clinic initially at 3 months post-ablation and subsequently continued at the arrhythmia clinic or at the patients' referring physician at 6 month intervals except when patients remained entirely free of symptoms. In the event of a recurrence, symptomatic or documented, patients were referred back to the arrhythmia clinic for re-analysis.

Statistical Analysis

Continuous data are expressed as mean (±standard deviation [SD]), or as median (interquartile range [IQR]), and dichotomous data are presented as numbers and percentages. Differences between categorical data were tested for statistical significance using a Pearson chi-square test using continuity correction where appropriate. Continuous normally distributed data were tested by student t-tests or in the case of a non-Gaussian distribution by a nonparametric test for independent samples. One way analysis of variance (ANOVA) was performed when comparing normally distributed data between more than two independent groups. Normal distribution was tested using the Kolmogorov-Smirnov test. Survival was analyzed by method of Kaplan-Meier with corresponding log-rank test for differences in distribution between the curves. Univariate and multivariate Cox regression analysis was performed to determine a relation between potential risk factors at baseline and the occurrence of AF. All variables with an unadjusted p value of <0.10 entered the multivariate regression model. Adjusted Hazard Ratio (HR) is reported in the text with the corresponding 95% confidence interval (CI). All tests were two-sided, a p-value of <0.05 was considered significant.

RESULTS

Patients

Between June 1995 and July 2006 149 patients underwent a total of 210 radiofrequency ablation procedures for isthmus dependent atrial flutter. Baseline characteristics are shown in table 1 for the total patient population and for group 1 and 2 separately. Of the total patient population, 87 patients had a known history of paroxysmal AF (87/149, 58%) and were therefore assigned to group 1.

Patients in group 2 were younger than patients in group 1 (61 ± 13 years vs. 66 ± 11 years, p=0.015) and used more Class 1C antiarrhythmic drugs (20% vs. 5%, respectively, p=0.009). Eighty patients (80/149, 54%) had at least one kind of structural heart disease, the majority being valvular heart disease (n=63), which was in most cases mitral valve insufficiency (54/63, 86%). The incidence of structural heart disease was similar between the two patient groups as well as the cardiovascular risk profile.

Figure 1 illustrates the distribution of symptoms reported by patients in group 1 and 2. Overall, symptoms reported by patients were similar. Palpitations was the most frequently reported complaint (>70%) in both groups. Ten percent of all patients were asymptomatic at the time of enrolment. Significantly fewer patients in group 2 had complaints of dyspnea when compared to patients in group 1 (24% vs. 40%, p=0.041; Figure 1).

Table 1. Baseline characteristics.

	Total (n=149)	Group 1 (n=87)	Group 2 (n=62)	p-value
Men	116 (78%)	72 (83%)	44 (71%)	0.09
Age (years ± SD)	64 ± 12	66 ± 11	61 ± 13	0.015*
Structural heart disease				
Dilating cardiomyopathy	16 (11%)	9 (10%)	7 (11%)	0.85
Hypertrophic cardiomyopathy	6 (4%)	4 (5%)	2 (3%)	1.00
Valvular heart disease	63 (42%)	41 (47%)	22 (36%)	0.16
Coronary artery disease	16 (11%)	11 (13%)	5 (8%)	0.37
Coronary bypass surgery	12 (8%)	9 (10%)	3 (5%)	0.36
Congenital heart disease	-	-	-	-
Body Mass Index (± SD)	26.0 ± 3.9	26.1 ± 4.8	25.9 ± 3.0	0.80
Hypertension	37 (25%)	24 (28%)	13 (21%)	0.36
Diabetes	13 (9%)	7 (8%)	6 (10%)	0.73
Hypercholesterolemia	29 (20%)	21 (24%)	8 (13%)	0.09
Thyroid disease	13 (9%)	8 (9%)	5 (8%)	0.81
Antiarrhythmic drugs				
Class IA	1 (0.7%)	1 (1.6%)	0	0.86
Class IB	1 (0.7%)	1 (1.6%)	0	0.86
Class IC	20 (13%)	3 (5%)	17 (20%)	0.009*
Class II	19 (13%)	14 (16%)	5 (8%)	0.15
Class III	80 (54%)	49 (56%)	31 (50%)	0.45
Class IV	21 (14%)	13 (15%)	8 (13%)	0.72
Lanoxin	29 (20%)	18 (21%)	11 (18%)	0.65
Left atrial size (mm ± SD)	44.1 ± 0.8	45.5 ± 0.8	42.4 ± 0.7	0.055

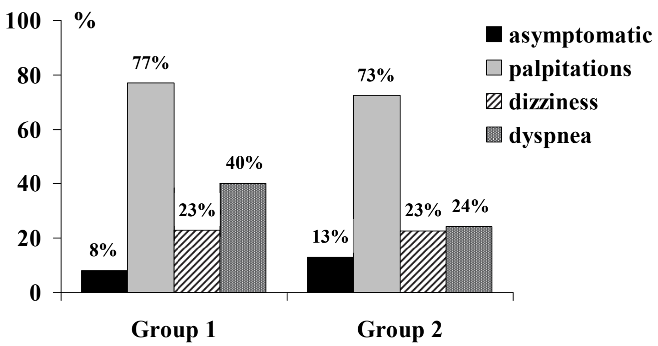


Figure 1. Symptom characteristics.

Procedure

Procedural characteristics are summarized in table 2. Of the 210 AFL ablation procedures 173 (83%) were considered acutely successful, either by achieving termination of AFL with noninducibility (13%) or by the confirmation of a line of conduction block (87%). The proportion of patients with procedural success was not significantly different between the groups. In terms of patients, 133 of 149 patients (89%) underwent at least one ablation procedure that was considered acutely successful. Eleven patients required more than one ablation procedure (11/133, 8%) to achieve this result. In the remaining patients, a bidirectional conduction block was not achieved despite extensive ablation.

Patients in group 2 had a shorter AFL cycle length than patients in group 1 (240 ± 45ms vs 259 ± 42ms, p=0.013) and acute success was more often defined by noninducibility than by bidirectional isthmus block when compared to patients in group 1 (19% vs 9%, p=0.042).

Table 2. Procedure characteristics.

	Total (n=149)	Group 1 (n=87)	Group 2 (n=62)	p-value
Procedures (n)	210	123	87	
Patients with >1 RFA of AFL (n)	47/149 (32%)	30/87 (35%)	17/62 (27%)	0.36
Acute procedural success achieved	133/149 (89%)	80/87 (92%)	53/62 (86%)	0.21
Acute success after 1st RFA	122/149 (82%)	74/87 (85%)	48/62 (77%)	0.23
Initial rhythm during study				
Sinus	110/210 (52%)	59/123 (48%)	51/87 (59%)	
AFL	71/210 (34%)	36/123 (29%)	35/87 (40%)	<0.001*
AF	29/210 (14%)	28/123 (23%)	1/87 (1%)	
AFL cycle length (ms ± SD)	249 ± 44	259 ± 42	240 ± 45	0.013*
Acute success of RFA of AFL	173/210 (83%)	105/123 (85%)	68/87 (78%)	0.18
Criteria of successful RFA				
Noninducibility	22/173 (13%)	9/105 (9%)	13/68 (19%)	
Bidirectional conduction block	151/173 (87%)	96/105 (91%)	55/68 (81%)	0.042*
Rhythm at procedure end				
Sinus rhythm	176/210 (84%)	105/123 (85%)	71/87 (82%)	
Conversion to AF	30/210 (14%)	17/123 (14%)	13/87 (15%)	0.37
AFL	4/210 (2%)	1/123 (1%)	3/87 (3%)	
Procedure time (min ± SD)	201 ± 72	199 ± 70	203 ± 75	0.82
Fluoroscopy time (min ± SD)	34 ± 19	34 ± 17	35 ± 21	0.97
RFA guiding technique				
Conventional	51/210 (24%)	27/123 (22%)	24/87 (28%)	
CARTO	134/210 (64%)	79/123 (64%)	55/87 (63%)	
Ensite	14/210 (7%)	9/123 (7%)	5/87 (6%)	
RPM	11/210 (5%)	8/123 (7%)	3/87 (3%)	0.62

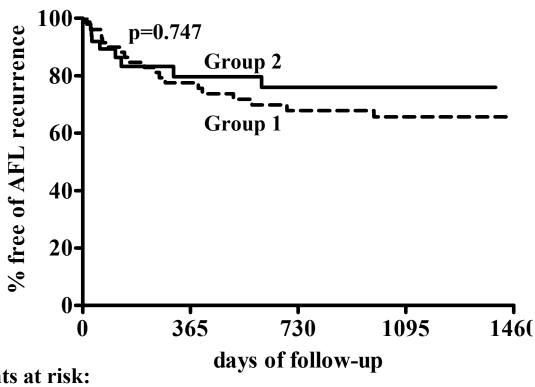
Ablation techniques

Ablation procedures were guided with conventional techniques (24%), or the CARTO™ (64%), the RPM (5%) or ENSITE (7%) system (Table 2). Overall, procedure time did not differ significantly between the 4 ablation techniques (overall mean procedure time: 201 ± 72 minutes, one-way ANOVA test: p=0.52). Fluoroscopy time was for the most part similar between the different ablation techniques (overall mean fluoroscopy time: 34 ± 19 min), but a significant difference in fluoroscopy times was found between the 4 techniques due to the shorter fluoroscopy times in the subgroup guided with the CARTO™ system (32 ± 18min) when compared to the Ensite system (47 ± 22min, one-way ANOVA test: p=0.005). No significant differences were observed in procedure-, or fluoroscopy time between consecutive ablation procedures.

Follow-up: AFL recurrence rate

Figure 2 illustrates the estimated cumulative rate of freedom from AFL recurrence in patients with and without a history of AF from the moment of the last successful AFL ablation procedure (median follow-up: 34 months, IQR 2-62 months). As mentioned earlier, this was achieved in 133 patients (table 2). Of these patients, 43 (32%) underwent >1 AFL ablation procedure (26/80, 33% in group 1 and 17/53, 32% in group 2). As initial success was not yet based on bidirectional isthmus block in the earliest procedures performed in this study, the last successful AFL ablation procedure was chosen as starting point from which AFL recurrence rate was evaluated (Figure 2). In 89% (119/133) of these last procedures immediate success was defined by bidirectional isthmus block.

The cumulative incidence rate of AFL recurrence in patients of group 1 at 1 year was 23% (95%CI 12%-33%) and at 4 years 34% (95%CI 22%-47%). For patients in group 2



Patients at risk:					
Group 1:	**80**	**42**	**34**	**29**	**23**
Group 2:	**53**	**23**	**22**	**20**	**14**

Figure 2. Recurrence of atrial flutter after the last successful AFL ablation procedure (32% of these patients underwent >1 AFL ablation procedure).

the cumulative incidence of AFL recurrence was similar: At 1 year 20% (95%CI 7%–34%) and at 4 years 24% (95%CI 9.7%–38%).

Follow-up: AF occurrence rate

Figure 3 demonstrates the estimated cumulative rate of freedom from AF in patients in groups 1 and 2 from the moment of the first successful AFL ablation procedure (n=133, median follow-up: 40 months, IQR 5-70 months). In 85% (113/133) of these early initially successful procedures bidirectional isthmus block was achieved (the rest was defined as successful due to noninducibility of AFL). Not surprisingly, patients with a known history of AF (group 1) had a significantly higher cumulative incidence rate of AF occurrence than patients in group 2 (log-rank test: p=0.0007). The cumulative incidence rate of AF occurrence in group 2 at 1 year was 28% (95%CI 14%-43%) and at 5 years 57% (95%CI 39%-75%). For patients in group 1 the cumulative incidence of AF occurrence was 60% at 1 year (95%CI 48%-72%) and 81% at 5 years (95%CI 71%-92%). However, figure 4 demonstrates that the large difference between groups 1 and 2 reflects primarily the much higher rate of AF occurrences in group 1 during the first 1.5 year post-ablation. This difference was highly significant (log-rank p=0.0006). After 1.5 year the cumulative incidence of first AF episodes in the group of patients with a history of AF was similar to the group of patients without a history of AF.

Multivariate Cox regression analysis (table 3) revealed that a known history of AF and a diastolic blood pressure ≥90 mmHg (measured at hospital admission for the ablation procedure) were independently associated with a 2-fold increased risk of AF occurrence at follow-up.

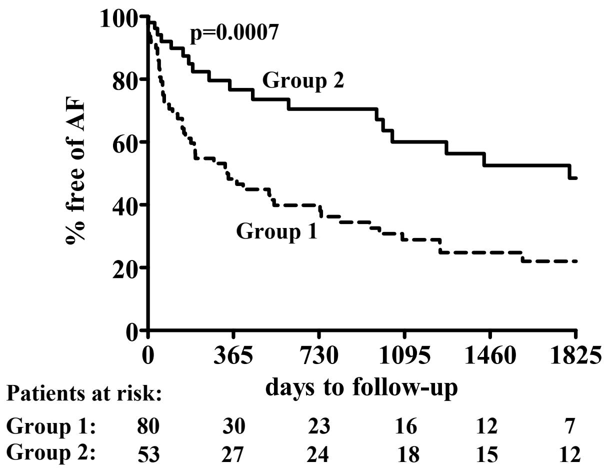


Figure 3. Occurrence of atrial fibrillation after initially successful ablation of typical AFL.

Table 3. Multivariable Cox Regression Analysis.

	AF occurrence after successful AFL ablation			
	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age †	1.02 (1.00-1.04)	0.036*	1.01 (0.99-1.03)	0.456
Sex (male)	1.03 (0.59-1.80)	0.919		
Preablation AF †	2.24 (1.33-3.77)	0.002*	2.17 (1.24-3.79)	0.006*
Syst. blood pressure ≥140 mmHg	0.98 (0.61-1.58)	0.932		
Diast. blood pressure ≥90 mmHg †	2.02 (1.23-3.33)	0.006*	2.00 (1.21-3.31)	0.007*
Coronary artery disease	1.71 (0.69-4.26)	0.248		
Diabetes Mellitus	0.55 (0.25-1.20)	0.134		
Thyroid disease	0.77 (0.31-1.94)	0.579		
Bidirectional isthmus block †	0.41 (0.17-1.03)	0.058	0.66 (0.24-1.86)	0.435
ACE-inh/AT2-antag. at discharge	0.75 (0.46-1.21)	0.237		
Sotacor at discharge	0.91 (0.53-1.56)	0.743		
Flecainide at discharge	0.68 (0.38-1.20)	0.184		
Amiodarone at discharge	0.84 (0.45-1.58)	0.596		
Verapamil at discharge	0.86 (0.43-1.74)	0.678		
Statin at discharge	0.80 (0.45-1.41)	0.432		
Recurrence of AFL	1.21 (0.72-2.04)	0.474		
Left atrial diameter	1.02 (0.98-1.06)	0.340		
AF at procedure end	0.60 (0.26-1.40)	0.240		
RFA without use of 3D-electroanatomical mapping †	2.08 (1.08-3.99)	0.028*	1.90 (0.92-3.96)	0.085

Only variables with an unadjusted p-value of <0.10 were included in multivariable analysis (indicated with †). Unadjusted and adjusted Hazard Ratio (HR) is reported with the corresponding 95% confidence interval (CI). * p<0.05

Long-term treatment course

Figure 4 shows prevalence of AAD treatment in patients who underwent a successful AFL ablation procedure (n=133). The percentage of patients on AAD therapy at baseline is shown next to the percentage of patients on AAD treatment by the end of follow-up (median 40 months). There was no significant change in AAD use for patients in group 1 when compared to baseline AAD use: Fifteen percent (n=12/80) of patients in group 1 used no AAD at all at the end of follow-up versus 11% (9/80) at baseline (p=0.48)

Similarly, in group 2 the proportion of patients that did not require AAD treatment by the end of follow-up was comparable to the percentage of patients without AAD therapy at baseline (baseline: 26%, 14/53, versus follow-up: 36%, 19/53; p=0.29). However, there was a significant change in AAD treatment class. Significantly fewer patients in group 2 were on Class III AAD treatment at follow-up (baseline: 49%, 26/53, vs follow-up: 30%, 16/53; p=0.047). Of the 26 patients who were on Class III AAD's at baseline, seven patients needed no AAD treatment by the end of follow-up, 3 patients were treated with only rate-control

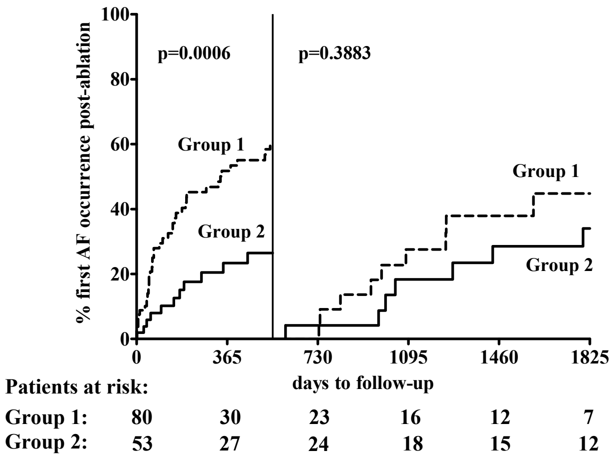


Figure 4. Landmark incidence estimates for AF occurrence after successful AFL ablation.

(beta-blockers) at follow-up and 3 patients were switched to a Class IC AAD. Slightly more patients in group 2 appeared to be on Class IC AAD therapy by the end of follow-up when compared to baseline (baseline: 6%, 3/53, vs follow-up: 17%, 9/53; p=0.066), but this was not statistically significant.

Ten patients (10/80, 13%) in group 1 underwent pulmonary vein isolation for AF during follow-up. In group 2 only one patient (1/53, 2%, p=0.049) was treated for AF with pulmonary vein isolation during follow-up. His bundle ablation was performed in 11% of patients of group 1 (n=9/80) versus 6% of patients in group 2 (3/53, p=0.43).

DISCUSSION

Key findings of this study are that: (1) The cumulative incidence of AF after successful AFL ablation procedures was high, with 57% during 5 year follow-up even in the patient group without preexisting AF (group 2), (2) that after 1.5 year post-AFL ablation patients with a history of AF had a similar AF occurrence rate compared to patients without a history of AF, and (2) a twofold and highly significant risk of AF occurrence was observed for patients with a diastolic blood pressure ≥90mmHg, independent of a pre-ablation history of AF.

AFL recurrence

Earlier studies of RF ablation of the cavotricuspid isthmus for typical AFL yielded disappointing results with immediate procedural success rates as low as 78% and short-term recurrence rates as high as 41%.[13] Since the introduction of complete bidirectional isthmus block as a procedural end-point, the success rate has risen to ≥90%.[6;14-16] In accordance, acute ablation success in this study was achieved in 89% (133/149) of patients, in >80% of patients by means of bidirectional conduction block as confirmation of success. With a 1-year recurrence rate of 22% (average of group 1 and 2) and a 4-year rate of 29% (average), recurrence of typical AFL was a relatively common problem in this series. In the early part of this series, conduction block in the isthmus was not tested as an endpoint after ablation and predominantly non-cooled catheter tips were used for ablation. It is possible that therefore analysis of recurrence is limited compared to other series where bidirectional block was used as endpoint and cooled catheter tips were used for isthmus ablation in all patients. Results are relatively comparable to other early observational studies with similar time period related experience, and procedural conditions.[4;17]

Coexistence between AFL and AF

Atrial flutter and atrial fibrillation, which are both intra-atrial reentrant arrhythmias with differing complexity in their activation pattern and mechanisms, are frequently seen to cooexist in clinical practice. This was reflected in the present study by the fact that more than half of the unselected and consecutive patients referred for AFL ablation presented with a history of AF (87/149, 58%). Undoubtedly, the electrophysiological basis of the interrelation between AFL and AF needs further elucidation. The association generally reflects a similar arrhythmogenic substrate. One mechanism of AF occurrence is the electrical remodeling in the atrium induced by atrial flutter that predisposes to development of AF.[18-20] Another mechanism may be that AF is the primary arrhythmia that precedes the onset of AFL because formation of a functional line of block between the vena cava during AF leads to the development of cavotricuspid isthmus dependent AFL.[21] AF is then unmasked by elimination of the AFL substrate and continues to progress after AFL ablation.

Other theories include that AF development is part of the natural course of atrial flutter in these patients, as atrial flutter is occasionally observed to spontaneously disorganize into atrial fibrillation in the electrophysiology laboratory. The right atrial flutter circuit is postulated to play a critical role in the initiation and maintenance of atrial fibrillation in some patients.[22] These observations may explain the absence of recurrent atrial fibrillation in some patients with pre-ablation AF.

New-onset AF after AFL ablation

AF occurrence after RF ablation for AFL, either preexisting or de novo, is a phenomenon well documented in literature, with incidences ranging from 8%-82%.[1;3;15;23;24]. Though catheter ablation is an effective treatment for AFL and has become common, it is unclear if ablation is able to affect the risk for future AF development. Findings of a study by Halligan et al. all demonstrated that 56% of patients with AFL naturally developed new-onset AF after an average of 5 ± 6 years after the diagnosis of AFL in the absence of a preceding AFL ablation.[25;26] This rate is very similar to the 5-year cumulative incidence rate of new-onset

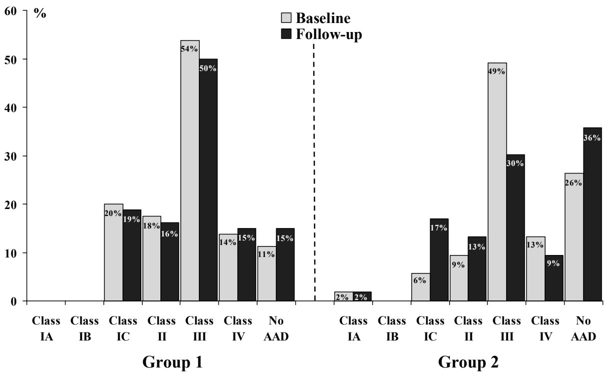


Figure 5. Antiarrhythmic drug use at baseline and at the end of follow-up.

AF found in the present study (57%, group 2). Ellis et al. reported a cumulative incidence of new-onset AF as high as 82% in patients with AFL after mean follow-up of 39 ± 11 months post-cavotricuspid isthmus ablation.[24] These results suggest that the long term (≥5 years) risk of developing AF is already high for patients with "lone" AFL, and may not be affected by AFL ablation.

AF recurrence after AFL ablation

Should ablation be then undertaken in patients with AFL who also have AF? The answer to that question at present seems to be yes as there is ample evidence that ablation of AFL in patients who have both AFL and AF is associated with reduced incidence of subsequent atrial fibrillation by approximately 50%.[1;2;16;27;28] It is suggested that, at least in a proportion of patients, reentry around a stable anatomical pathway such as the tricuspid annulus might serve as the underlying mechanism for maintaining AF.[7]

The present study found a high 5-year cumulative incidence of AF recurrence of 82% in the group with pre-existing paroxysmal AF (group 1). A recent observational study by Moubarak et al reported very similar results after AFL ablation, with an AF recurrence rate of 86% in patients with preexisting AF and a rate of new-onset AF of 62% after median follow-up of 7.8months in 135 patients who underwent successful isthmus-dependent AFL ablation.[26]

Is transisthmus ablation a definite cure for patients with AFL then, or can their follow up be characterized by the occurrence of other atrial arrhythmia, particularly in patients with a history of AF? Many studies have tried to answer these questions.[1;4] The high and mostly unchanged number of patients receiving AADs at the end of follow-up in this study highlights the importance of the arrhythmic burden independent of the relapse of AFL. Despite the relatively pessimistic results of the current study for this subgroup of patients, further data analysis (figure 4) demonstrated a particularly pronounced difference in the incidence rate of AF occurrence between groups 1 and 2 in the first 1.5 year post-ablation, after which cumulative first events of AF occurrence appeared to happen at a similar rate between the groups. In addition, a limited percentage of patients (19%) with preablation AF (group 1) still had no (documented) recurrence of AF after 5 years of follow-up. It is possible that cavotricuspid isthmus ablation to some extent had a positive effect on the clinical course of AF in these patients. However, at the same time it is also possible that AF recurrence rates were underestimated because of asymptomatic episodes that may not have been documented. Nevertheless, in the 40% of patients of group 1 who were still free of AF 1.5 years after successful AFL ablation, the risk of AF recurrence was comparable to the risk of developing new-onset AF in the group without a history of AF (group 2) (Figure 4). These patients probably benefited from the ablation of isthmus-dependent AFL in terms of AF recurrences.

Hypertension as additional treatment focus

Hypertension is frequently complicated by the development of AF though the mechanisms of this link are not completely understood. In a recent ovine study by Lau et al, investigators demonstrated that even short-duration hypertension (4-7weeks) may lead to significant atrial remodeling characterized by atrial enlargement/dysfunction, interstitial fibrosis, inflammation, slowed/heterogeneous conduction, increased ERP, and greater propensity for AF.[29] Multivariate analysis in the present study revealed that a high diastolic blood pressure (≥90mmHg) predisposed patients to twice the risk of AF occurrence after AFL ablation, independent of preexisting AF. Results shows that aggressive treatment of hypertension should be a prime focus of attention after successful AFL ablation, especially when considering the long-term risk of new-onset AF is >50% for patients with only AFL.

Limitations

Our study population was classified into 2 groups on the basis of documentation of AFL alone or in combination with AF. The exact incidence and burden of arrhythmia episodes, (i.e. asymptomatic episodes, or in- or decrease of AF burden post-ablation), is not known and may have affected our classification and the evaluation of clinical improvement regarding arrhythmia burden. Elimination of flutter may have resulted in symptomatic improvement and facilitated better pharmacological control of atrial arrhythmia. Thus, the results should not be interpreted as lack of utility of transisthmic ablation in patients with coexisting AF and AFL; rather they show that transisthmic ablation cannot completely cure AF in this subgroup of patients.

Although every procedure involved a right atrial isthmus ablation, the ablation protocol and the criteria for procedural success have changed over the study period in keeping with advances in our knowledge. A complete bidirectional isthmus block at the conclusion of a successful procedure was not obtained in all patients. This has obvious implications for analysis of arrhythmia recurrences.

Only 30% of the study population used no AAD at the end of follow-up. Thus, in these patients results should be interpreted as the consequence of the combination of RF ablation and AAD therapy rather than RF ablation alone.

CONCLUSION

Despite the efficacy of cavotricuspid isthmus RF ablation in the treatment of AFL, most patients cannot be considered completely cured, particularly with regard to AF occurrences. Patients with a preablation history of AF and high diastolic blood pressure were at significantly higher risk and should be monitored more closely and treated more aggressively for hypertension. However, preablation AF did not lead to an increased long-term (>1.5 year) risk after AFL ablation, and patients in this subgroup therefore may expect the same long-term risk of AF as patients without pre-existing AF.

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