

# Prevalence of Left Atrial Chamber and Appendage Thrombi in Patients With Atrial Flutter and Its Clinical Significance

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<b>OBJECTIVES</b>	The study was done to assess the prevalence of left atrial (LA) chamber and appendage thrombi in patients with atrial flutter (AFL) scheduled for electrophysiologic study (EPS), to evaluate the prevalence of thromboembolic complications after transesophageal echocardiographic (TEE)-guided restoration of sinus rhythm and to evaluate clinical risk factors for a thrombogenic milieu.
<b>BACKGROUND</b>	Recent studies showed controversial results on the prevalence of atrial thrombi and the risk of thromboembolism after restoring sinus rhythm in patients with AFL.
<b>METHODS</b>	Between 1995 and 1999, patients with AFL who were scheduled for EPS were included in the study. After transesophageal assessment of the left atrial appendage and exclusion of thrombi, an effective anticoagulation was initiated and patients underwent EPS within 24 h.
<b>RESULTS</b>	We performed 202 EPSs (radiofrequency catheter ablation, n = 122; overdrive stimulation, n = 64; electrical cardioversion, n = 16) in 139 consecutive patients with AFL. Fifteen patients with a thrombogenic milieu were identified. All of them had paroxysmal atrial fibrillation (AF). Transesophageal echocardiography revealed LA thrombi in two cases (1%). After EPS no thromboembolic complications were observed. Diabetes mellitus, arterial hypertension and a decreased left ventricular ejection fraction were found to be independent risk factors associated with a thrombogenic milieu.
<b>CONCLUSIONS</b>	The findings of a low prevalence of LA appendage thrombi (1%) in patients with AFL and a close correlation between a history of previous embolism and paroxysmal AF support the current guidelines that patients with pure AFL do not require anticoagulation therapy, whereas patients with AFL and paroxysmal AF should receive anticoagulation therapy. In addition, the presence of clinical risk factors should alert the physician to an increased likelihood for a thrombogenic milieu. (J Am Coll Cardiol 2001;38:778-84) © 2001 by the American College of Cardiology

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Routine anticoagulation therapy is not recommended in patients with atrial flutter (AFL) undergoing cardioversion (1). Nevertheless, more recent studies have shown that AFL may be associated with atrial thrombi and thromboembolism and that thromboembolic events may occur after cardioversion of AFL (2-5). Therefore, the current guidelines state that anticoagulation therapy should be considered prior to cardioversion of AFL (1). Radiofrequency catheter

ablation of AFL may allow restoration of sinus rhythm and is now considered as a curative therapy of chronic AFL (6-8). However, restoring sinus rhythm by radiofrequency catheter ablation may cause atrial stunning, with a thrombogenic milieu as defined as the induction of spontaneous

echo contrast and depressed mechanical left atrial (LA) appendage function (9). This thrombogenic milieu may lead to atrial thrombus formation (10). Therefore, prophylactic anticoagulation therapy prior to radiofrequency catheter ablation of AFL has been suggested (9,10). The aims of this study were: 1) to determine the prevalence of atrial thrombi in patients with AFL scheduled for electrophysiologic study (EPS); 2) to analyze the value of transesophageal echocardiographic (TEE)-guided restoration of sinus rhythm in patients with AFL; and 3) to correlate clinical and transthoracic echocardiographic (TTE) parameters with the presence of a thrombogenic milieu in patients with AFL.

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ablation of AFL may allow restoration of sinus rhythm and is now considered as a curative therapy of chronic AFL (6-8). However, restoring sinus rhythm by radiofrequency catheter ablation may cause atrial stunning, with a thrombogenic milieu as defined as the induction of spontaneous

## METHODS

**Study patients.** Between 1995 and 1999 all patients >18 years of age with AFL of  $\geq 2$  days' duration who underwent EPS were included in the study. Inclusion criteria were a history of AFL and an electrocardiographic documentation of AFL. Exclusion criteria were a recent myocardial infarc-

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Manuscript received October 5, 2000; revised manuscript received March 19, 2001, accepted June 8, 2001.

#### Abbreviations and Acronyms

AfI	=	atrial flutter
AF	=	atrial fibrillation
DC	=	direct current
ECG	=	electrocardiogram
EPS	=	electrophysiologic study
INR	=	International Normalized Ratio
IV	=	intravenous
LA	=	left atrium/atrial
LVEF	=	left ventricular ejection fraction
TEE	=	transesophageal echocardiography/ echocardiographic
TTE	=	transthoracic echocardiography/echocardiographic

tion and/or cardiothoracic surgery (<30 days) and the inability to give written informed consent. Written informed consent was obtained from all patients, and the study was approved by the Institutional Review Board of the University of Bonn.

**Study protocol.** All patients were examined clinically, and both the cardiovascular risk factors (arterial hypertension, smoking, diabetes mellitus, dyslipoproteinemia and positive family history) and a history of previous embolism were assessed. A 12-lead surface electrocardiogram (ECG) was obtained. To assess LA appendage function and the prevalence of echocardiographic markers of thromboembolic risk, both TTE and TEE were performed <24 h before EPS. All patients were followed for four weeks after the electrophysiological procedure for thromboembolic complications.

**Echocardiographic studies.** All studies were conducted with commercially available equipment (Vingmed 800c, System V, GE). For TTE, a 3.4-MHz electronic transducer was used. The M-mode LA dimension and left ventricular ejection fraction (LVEF) were measured according to recommendations of the American Society of Echocardiography (11).

The TEE procedure was performed with either a 5-MHz or a 6.7-MHz multiplane electronic or multiplane mechanical transducer as previously reported by our study group (12,13). Cine loops of the LA and the LA appendage were stored. The sample volume of the pulsed Doppler was placed 1 cm into the orifice of the LA appendage, and the profile of the velocities recorded.

**Echocardiographic data analysis.** Echocardiographic evaluations were performed by two independent observers examining the digitized images after the original examination. The images were displayed in random order without clinical information about the patient and were analyzed by means of the evaluation software provided by the manufacturer (Echopac, GE). Interobserver differences were resolved by a third observer.

The cine loops of the LA and LA appendage were examined for thrombi and spontaneous echo contrast. A thrombus was defined as an echodense intracavitary mass

distinct from the underlying endocardium and not caused by pectinate muscles (14). The degree of spontaneous echo contrast was categorized as being either absent (0), mild (1+), mild-to-moderate (2+), moderate (3+) or severe (4+), on the basis of the system described by Fatkin et al. (15). The LA appendage area and peak emptying velocities were measured as previously reported (12).

**EPS.** Typical AfI was defined by its characteristic 12-lead surface ECG. This was confirmed at EPS on the basis of established criteria in those patients who underwent invasive EPS (8).

**RADIOFREQUENCY CATHETER ABLATION OF AFL.** Radiofrequency catheter ablation was performed on patients with typical AfI in a standard manner, including multipolar catheters in the His bundle region, coronary sinus and tricuspid annulus (6,8). Typical AfI with clockwise and counterclockwise activation of the right atrium was diagnosed by demonstrating involvement of the cava-tricuspid isthmus as an essential part of the macroreentrant circuit.

**OVERDRIVE STIMULATION.** A Josephson quadripolar catheter (EPT Boston Scientific, San Jose, California) was placed in the high right atrium, and AfI was treated by high rate burst pacing starting at 30 ms below tachycardia cycle length.

**EXTERNAL ELECTRICAL CARDIOVERSION.** For external electrical cardioversion, fasting patients received intravenous (IV) sedation with propofol (1 to 3 mg/kg body weight). A Physio-Control (Lifepak) direct current (DC) cardioverter was used in all patients. Incremental DC electrical shocks were delivered at 200, 300 and 360 J using cutaneous patch electrodes placed on the chest in the anteroposterior position.

**Anticoagulation.** Patients without effective anticoagulation received IV weight-adjusted heparin (17 U/kg/h)  $\leq$ 24 h prior to the EPS. An activated partial thromboplastin time ratio of 1.5 to 2.5 times of the control value was achieved by adjusting the dosage. Two hours before the invasive procedure, heparin was discontinued to minimize bleeding complications and to allow safe puncture of the femoral or subclavian vein. After the procedure all sheaths were removed. Intravenous heparin was reintroduced 4 h later as a bolus of 5,000 U and readjusted to the level before the procedure. Heparin was continued for 24 h after the procedure. Anticoagulation therapy with heparin was not interrupted in patients undergoing DC cardioversion.

In patients who received coumarin, anticoagulation with coumarin was discontinued prior to the EPS. Therapy with heparin was started at weight-adjusted dosage, and the EPS was performed as mentioned above when the International Normalized Ratio (INR) was <1.5. After the procedure, coumarin therapy was reintroduced and heparin was continued until the INR was  $\geq$ 2.

**Statistical analysis.** Data are reported as the mean  $\pm$  SD. Continuous variables between groups were compared by a *t*

**Table 1.** Patient Characteristics

	Total	Typical Atrial Flutter	Atypical Atrial Flutter	p Value
Number	139	114	25	
Age	60 ± 12	61 ± 12	57 ± 12	0.18
Male gender	121 (87%)	98 (86%)	23 (92%)	0.42
Clinical risk factors				
Arterial hypertension	53 (38%)	42 (37%)	11 (44%)	0.50
Smoking	48 (35%)	38 (33%)	10 (40%)	0.53
Dyslipoproteinemia	71 (51%)	60 (53%)	11 (44%)	0.43
Diabetes mellitus	30 (22%)	25 (22%)	5 (20%)	0.83
Positive family history	20 (14%)	17 (15%)	3 (12%)	0.71
Previous embolism	7 (5%)	6 (5%)	1 (4%)	0.79
Underlying heart disease				
Coronary artery disease	41 (29%)	36 (32%)	5 (20%)	0.25
Congenital heart disease	3 (2%)	3 (2.6%)	0	0.41
Valvular heart disease	11 (8%)	10 (9%)	1 (4%)	0.42
Cardiomyopathy	8 (6%)	7 (6.1%)	1 (4%)	0.68
Other	4 (3%)	3 (3%)	1 (4%)	0.71
None	45 (32%)	35 (31%)	10 (40%)	0.37
Duration of atrial flutter (<3 months)	36 (26%)	31 (27%)	5 (20%)	0.46

Age is expressed as mean ± SD. Remaining data are given as number (%) of patients.

test for unpaired observations. Nominal data were compared by the chi-square test and/or the Fisher exact test. Categorical data (degree of spontaneous echo contrast) were compared by the Wilcoxon signed rank test for matched pairs. In all cases, a p value <0.05 was considered statistically significant. In addition, 95% confidence intervals (95% CI) are given. Logistic regression analysis was performed to evaluate the relationship between the presence of thrombogenic milieu defined as existence of spontaneous echo contrast graded ≥3+ and/or thrombus and clinical (presence of one risk factor of embolism defined as the presence of paroxysmal atrial fibrillation [AF], diabetes mellitus, arterial hypertension and previous embolism) and TTE markers of thromboembolism (LA diameter >4 cm and LVEF <40%).

## RESULTS

**Patients.** A total of 139 patients were included in the study. Forty patients had two or more repeated EPSs during the follow-up period. Thus, the number of EPS and echocardiographic studies totaled 202. Patient data are provided in Table 1. A total of 114 patients had typical AFl; 25 patients had atypical AFl; 69 patients had ≥1 episodes of documented paroxysmal AF; and 38 patients (55%) with paroxysmal AF received anticoagulation therapy with coumarin. An additional 11 patients with pure AFl had anticoagulation therapy for other reasons. Seven patients (5%) had a history of previous embolism. Six of those patients presented with typical AFl. All patients with history of previous embolism had a history of paroxysmal AF.

**Echocardiography.** Measurements are given in Table 2. The flow velocity profile over the LA appendage showed a

regular sawtooth pattern corresponding to the flutter waves of the ECG.

**Prevalence of spontaneous echo contrast and thrombi.** Spontaneous echo contrast was found in 56 cases (28%) of 202 TEE studies: 24 patients had grade 1+ (12%), 17 had grade 2+ (8%), 10 had grade 3+ (5%) and 5 had grade 4+ (2%). Out of 202 TEE studies, 2 (1%) thrombi were found. The thrombi measured 0.8 cm × 0.6 cm and 0.6 cm × 0.4 cm and were located in the tip of the LA appendage. The two patients with thrombi had congestive heart failure with a LVEF of 0.30 (Patient 1, Table 3) and 0.46 (Patient 8, Table 3), respectively. Both patients had paroxysmal AF. An attempt to restore sinus rhythm was not performed in the latter patients. Both patients were treated with phenprocoumon. During the follow-up, one patient developed persistent AF. In both cases the thrombi disappeared on repeated TEE examination. Neither of those patients had clinical signs of thromboembolism.

**Comparison of patients with typical and atypical AFl.** Patients with atypical and typical AFl did not differ in LA diameter (4.3 ± 0.64 vs. 4.4 ± 0.64; p = 0.68; 95% CI -0.3 to 0.2; LVEF (54.3 ± 10.6; p = 0.24; 95% CI -1.7 to

**Table 2.** Comparison of Patients With Pure AFl and Patients With Paroxysmal AF

	Paroxysmal AF	Pure AFl	p Value	95% CI
Number	69	70		
LA diameter	4.4 ± 0.6	4.3 ± 0.6	0.49	-0.12-0.24
LVEF	52 ± 10	52 ± 13	0.70	-0.13-2.6
LAA max	4.5 ± 1.6	3.9 ± 1.3	0.016	0.13-1.2
LAAv	0.52 ± 0.25	0.55 ± 0.2	0.45	-0.1-0.05
SEC	0.83 ± 1.2	0.5 ± 0.9	0.06	-0.02-0.68

AF = atrial fibrillation; AFl = atrial flutter; CI = confidence interval; LA = left atrial; LAA max = maximal left atrial appendage area; LAAv = peak emptying velocities of the left atrial appendage; LVEF = left ventricular ejection fraction; SEC = spontaneous echo contrast.

**Table 3.** Individual Clinical and Echocardiographic Parameters of Patients With a Thrombogenic Milieu

Patient No.	Age (yrs)	Clinical Parameters			Echocardiographic Parameters					
		Diabetes Mellitus	Arterial Hypertension	Previous Embolism	Paroxysmal AF	LAD (cm)	LVEF (%)	LAAv (m/s)	SEC	Thrombus
1	67	Yes	No	No	Yes	5.6	30	0.15	3	Yes
2	67	Yes	Yes	No	No	6.2	24	0.40	3	No
3	73	Yes	Yes	No	Yes	4.3	50	0.50	3	No
4	73	Yes	Yes	No	Yes	4.3	50	0.35	3	No
5	67	Yes	Yes	No	No	6.5	24	0.20	3	No
6	68	No	Yes	No	Yes	4.2	50	0.28	4	No
7	60	Yes	Yes	No	No	5.5	34	0.24	3	No
8	58	No	Yes	No	Yes	5.0	46	0.23	4	Yes
9	67	Yes	No	No	Yes	5.5	30	0.12	3	No
10	77	Yes	Yes	No	No	4.1	44	0.71	3	No
11	68	No	No	No	Yes	4.7	55	0.20	3	No
12	63	No	Yes	No	Yes	5.6	40	0.15	4	No
13	78	No	Yes	Yes	Yes	5.2	41	0.22	4	No
14	53	Yes	Yes	No	Yes	5.3	33	0.18	4	No
15	52	No	Yes	No	Yes	4.8	37	0.58	3	No

See Table 2 for abbreviations.

6.8); maximal area of the LA appendage ( $4.4 \pm 1.6$  vs.  $4.2 \pm 1.5$ ;  $p = 0.57$ ; 95% CI  $-0.48$  to  $0.86$ ); peak emptying velocities of the LA appendage ( $0.51 \pm 0.26$  vs.  $0.54 \pm 0.22$ ;  $p = 0.57$ ; 95% CI  $-0.12$  to  $0.07$ ); and the degree of spontaneous echo contrast ( $0.68 \pm 1.1$  vs.  $0.69 \pm 1.1$ ;  $p = 0.95$ ; 95% CI  $-0.47$  to  $0.44$ ).

**Comparison of patients with pure AF and patients with paroxysmal AF.** Patient data are given in Table 2. Patients with pure AF and patients with paroxysmal AF did not differ significantly in LA diameter (95% CI  $-0.12$  to  $0.24$ ), LVEF (95% CI  $-0.13$  to  $0.05$ ) and the degree of spontaneous echo contrast appendage (95% CI  $-0.1$  to  $0.05$ ) and the degree of spontaneous echo contrast (95% CI  $-0.02$  to  $0.68$ ). However, the maximal LA appendage area (95% CI  $0.13$  to  $1.2$ ) was significantly larger in patients with paroxysmal AF. Patients with paroxysmal AF more often had a history of previous embolism than did patients with pure AF ( $p = 0.01$ ).

**Electrophysiologic treatment.** The EPS consisted of 122 radiofrequency catheter ablations, 64 overdrive stimulation procedures and 16 electrical cardioversions. Sinus rhythm was restored in 160 cases (79%). Radiofrequency catheter ablation was successful in 106 cases (87%), overdrive stimulation in 42 cases (66%) and cardioversion resulted in the restoration of sinus rhythm in 12 cases (75%). Thromboembolism was not observed during the follow-up period.

**Relationship between clinical and TTE markers of thromboembolic risk and transesophageal parameters of a thrombogenic milieu.** A thrombogenic milieu—as defined as either the presence of thrombus or dense spontaneous echo contrast—was found in 15 of 202 studies (7%). Table 3 gives the individual values of those patients. Previous embolism ( $p = 0.75$ ), paroxysmal AF ( $p = 0.1$ ) and a LA diameter  $>40$  mm ( $p = 0.98$ ) were not significantly correlated to a thrombogenic milieu. However, patients without thrombogenic milieu may also present with considerably enlarged LA. The sensitivity of an enlarged

LA diameter for the presence of a thrombogenic milieu was 100%, whereas the specificity was only 36%.

A decreased ejection fraction  $<40\%$  ( $p = < 0.0002$ , relative risk = 8.4, 95% CI 2.7 to 26.2), the presence of diabetes mellitus ( $p = 0.0004$ , relative risk = 7.4, 95% CI 2.4 to 22.8) and a history of arterial hypertension ( $p = 0.002$ , relative risk = 8.1, 95% CI 2.2 to 30.2) were significantly correlated with the presence of a thrombogenic milieu. Logistic regression analysis revealed that all parameters were independent risk factors.

All 15 patients with a thrombogenic milieu had at least one clinical risk factor. Four patients (27%) had three clinical risk factors, ten (66%) had two clinical risk factors and one patient (7%) had only one clinical risk factor. In addition, 7 out of the 15 patients (47%) had a LVEF  $<40\%$ .

## DISCUSSION

The primary findings of our study are: 1) that LA thrombi are uncommon in patients with AF scheduled for EPS; 2) that TEE-guided restoration of sinus rhythm in conjunction with short-term periprocedural anticoagulation is safe in patients with AF; and 3) that the presence of diabetes mellitus, arterial hypertension and a LVEF  $<40\%$  were independent parameters for predicting the presence of a thrombogenic milieu in patients with AF.

**LA appendage morphology and function in patients with AF.** Use of TEE may allow detection of a thrombogenic milieu (15,16). Reduced peak emptying velocities of the LA appendage and the presence of dense spontaneous echo contrast have been correlated with an increased thromboembolic risk in patients with AF (15,17). However, there are only few studies correlating those parameters with the thromboembolic risk in patients with AF (3,18). In accordance with previous reports, our study found that patients with AF have a regular flow velocity profile over the LA appendage (19,20). Spontaneous echo contrast was found in

56 cases of 202 echocardiographic studies (28%). However, only 15 (7%) of the latter patients had dense spontaneous echo contrast, whereas the remaining patients (n = 41) had only mild or moderate spontaneous echo contrast.

Another important result of our study is that we found only 2 thrombi out of 202 echocardiographic studies (1%). This finding of a low prevalence of thrombi in patients with AFl accords with four other studies that did not find thrombi in patients with AFl (5,9,10,18). Nevertheless, more recent echocardiographic studies found a higher prevalence of LA thrombi and spontaneous echo contrast in patients with AFl. Thus, there is conflicting evidence of the prevalence of LA thrombi and spontaneous echo contrast in patients with AFl. One study found 5 thrombi in 47 patients and spontaneous echo contrast in 32% of the patients (3). However, 26 % of those patients had heart failure, and an abnormal left ventricular function was present in 53%, whereas in our study only 11% of the patients had a LVEF <40%. Furthermore, 10% of the patients of the previous study had a prior cerebrovascular accident. Thus, the patients in the study by Irani et al. (3) had an increased risk of atrial thrombi irrespective of the underlying arrhythmia. Another study found 2 thrombi in 30 patients and spontaneous echo contrast in 25% of the patients (21). It is interesting that the latter study did not find a difference in LVEF between patients with and without spontaneous echo contrast. However, the patient number was limited. Another possible explanation for the lower prevalence of thrombi in our patient cohort might be that 55% of patients with AFl and paroxysmal AF were anticoagulated. Nevertheless, the low prevalence of thrombi and spontaneous echo contrast in our study supports the results of earlier reports demonstrating a low prevalence of thromboembolic complications in patients with AFl (22-26).

**Comparison of patients with pure AFl and patients with paroxysmal AF.** Patients with pure AFl are regarded to have a lower thromboembolic risk than are patients with AFl and paroxysmal AF. Thus, the current guidelines for anticoagulation therapy recommend anticoagulation therapy in patients with AFl and paroxysmal AF. The results of our study show that patients with pure AFl and patients with AFl and paroxysmal AF did not differ significantly in LA diameter, LVEF, peak emptying velocities of the LA appendage, maximal area of the LA appendage and the degree of spontaneous echo contrast. Thus, the echocardiographic markers of thromboembolic risk did not differ for patients with pure AFl and those with paroxysmal AF. This result seems to contradict the finding of previous studies showing that AF is often correlated with a thrombogenic milieu. However, it has to be recognized that our TEE studies were not conducted during episodes of AF. It is possible that the conversion of AFl to AF may induce or worsen a thrombogenic milieu. Nevertheless, all seven patients with a history of previous embolism had paroxysmal AF. Furthermore, 11 of 15 (73%) patients with a throm-

bogenic milieu had paroxysmal AF, and both patients with thrombi had paroxysmal AF. A possible explanation for the relatively low prevalence of thrombi in patients with paroxysmal AF may be that most of the patients with paroxysmal AF were anticoagulated.

**Comparison of patients with atypical and typical AFl.** The findings of our study show that patients with typical and atypical AFl did not differ in LA diameter, LVEF, peak emptying velocities of the LA appendage, maximal area of the LA appendage and the degree of spontaneous echo contrast, indicating that the echocardiographic markers of thromboembolic risk were not different between the two groups. Thus, the type of AFl does not seem to influence the thromboembolic risk in patients with AFl.

**Thromboembolism after TEE-guided electrophysiologic restoration of sinus rhythm in patients with AFl.** Transesophageal echocardiography has a high accuracy for identifying atrial thrombi (27). Furthermore, a TEE-guided approach of cardioversion of AF in concert with periprocedural therapeutic anticoagulation has been shown to have a similar safety profile to that of conventional therapy (28,29). However, the value of TEE prior to electrophysiologic treatment in patients with AFl has not yet been investigated. The results of our study show that after TEE exclusion of LA thrombi and short-term periprocedural anticoagulation with heparin, no thromboembolic complications were observed after restoration of sinus rhythm. This finding agrees with an earlier study that demonstrated a low thromboembolic risk after restoration of sinus rhythm even without anticoagulation therapy (22). However, the findings of the latter study and our results are in contrast with more recent studies reporting a higher prevalence of thromboembolic complications after restoration of sinus rhythm (2,4,5). Nevertheless, those studies included only a small number of selected patients. Furthermore, most patients in those studies did not receive periprocedural anticoagulation therapy.

Recent studies showed that radiofrequency catheter ablation of AFl may be associated with a postprocedural atrial stunning (9,10). One study could also demonstrate that the postprocedural atrial stunning was associated with the generation of a new atrial thrombus after successful radiofrequency catheter ablation therapy for AFl (9). Consequently, it was suggested to anticoagulate patients with chronic AFl undergoing radiofrequency catheter ablation. The results of our study demonstrate that radiofrequency catheter ablation may be performed safely in patients in whom thrombi were excluded by TEE and who received periprocedural anticoagulation therapy.

**Relationship between clinical and echocardiographic thromboembolic risk factors and a thrombogenic milieu.** Previous studies have shown that the presence of a thrombogenic milieu is associated with an increased thromboembolic risk in patients with AF (16,30). In addition, large multicenter studies have shown that clinical and TTE parameters may allow estimation of the thromboembolic

risk in patients with AF (31–33). The most important risk factors are a history of previous embolism, a history of arterial hypertension, diabetes mellitus, an enlarged LA and decreased LVEF. The results of our study show that a history of previous embolism and an enlarged LA were not associated with a thrombogenic milieu in the LA in patients with AFL. The finding of our study that an enlarged LA was not specific for a thrombogenic milieu accords with more recent results showing that an enlarged LA is not indicative of an increased thromboembolic risk in patients with AF (34). An interesting result of our study was that the presence of diabetes mellitus, a history of arterial hypertension and a decreased LVEF was significantly associated with the presence of a thrombogenic milieu. The finding of an increased risk of a thrombogenic milieu in patients with decreased LVEF is in agreement with the finding of a previous study showing that patients with a LVEF <40% have a higher prevalence of atrial thrombi (35). In our study, all patients with a thrombogenic milieu had at least one clinical risk factor. In addition, 47% of the patients had a LVEF <40%. Because the presence of clinical risk factors and/or a decreased LVEF is closely associated with a thrombogenic milieu, those patients should receive a TEE examination to exclude atrial thrombi before restoration of sinus rhythm.

**Clinical implications.** The finding of our study that the prevalence of LA thrombi is low in patients with AFL scheduled for EPS supports the current guidelines that patients with pure AFL should not automatically receive anticoagulation therapy. The result of our study that those patients with paroxysmal AF had significantly more often a history of previous embolism than did those patients with pure AFL underlines the importance of anticoagulation therapy in patients with AFL and paroxysmal AF. Patients with paroxysmal AF should be considered to receive long-term anticoagulation therapy.

The results of our study demonstrate that TEE-guided restoration of sinus rhythm in conjunction with short-term periprocedural anticoagulation with heparin in patients with AFL is safe. Therefore, this procedure may be suggested to prevent thromboembolic complications after electrophysiologic treatment of AFL.

The finding that the presence of diabetes mellitus, arterial hypertension and a decreased LVEF (<40%) is associated with a thromboembolic milieu allows clinical and TTE risk stratification of patients with AFL and should alert the physician of an increased likelihood of atrial thrombi.

**Study limitations.** This study was a large prospective observational study of patients with AFL scheduled for EPS. However, patients were not randomized to receive anticoagulation therapy prior to restoring sinus rhythm. Thus, the impact of the periprocedural anticoagulation therapy may not be ultimately defined.

Finally, because the number of patients with a history of embolism was small, the statistical power to detect a correlation between previous embolism and a thrombogenic milieu is limited.

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