



Atrial flutter and embolic risk: The relationship between atrial flutter cycle length and left atrial appendage function

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ARTICLE INFO

Keywords:

Atrial flutter
Flutter cycle length
Left appendage emptying velocity
Thromboembolic risk
Transoesophageal echocardiography
Left atrial appendage

ABSTRACT

Background: The potential for thromboembolism in atrial flutter (AFL) is different from atrial fibrillation. AFL cycle length (AFL-CL) may be related to reduced left atrial appendage (LAA) function. Very rapid AFL-CL can lead to mechanical and electrophysiological disorders that contribute to lower LAA emptying velocity (LAEV). The aim of this study is to relate atrial flutter cycle length with LAEV and its role in thrombogenesis.

Methods: Cross-sectional study of patients with atrial flutter AFL who underwent transoesophageal echocardiography (TEE) before catheter ablation or electric cardioversion. AFL-CL in milliseconds was measured with a 12-lead EKG or in intracardiac records.

Results: We included 123 patients. There was correlation between AFL-CL and LAEV ($r = 0.34$; $p = 0.003$) in typical AFL. Cycle length, LA size and atypical flutter were predictors of low LAEV on multivariate analysis. An index multiplying atrial rate (bpm) during the arrhythmia versus left atrial size (mm) $>11,728$ was associated with spontaneous echogenic contrast and/or left atrial thrombus on TEE (C-statistic = 0.71; CI95%0.60–0.81).

Conclusions: There was a significant relationship between the AFL-CL and LAEV. The LAEV was affected by the LA size, the type of atrial flutter and the AFL-CL. A new index, relating the atrial rate with the left atrial size, was able to identify a higher occurrence of spontaneous echogenic contrast and/or left atrial thrombus.

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Introduction

The thromboembolic risk in typical atrial flutter (AFL) is considered low by some authors, with studies showing 1.6% prevalence of left intra-atrial thrombi in unselected patients [1,2]. The thromboembolic risk associated exclusively with AFL by itself is difficult to assess, since AFL and AF generally coexist and may also share similar pathophysiological mechanisms [3–6]. Patients treated with AFL ablation may develop AF during a 5-year follow-up in up to 82% of cases [7,8].

In a recently published study, Cresti and colleagues showed that at 17-year follow-up of patients with AF and AFL, the presence of intra-atrial thrombi during transoesophageal echocardiography (TEE) before cardioversion is not uncommon and does not differ significantly from patients with AF [9]. The use of methods with a higher-quality image

for the left atrium (LA) and left atrial appendage (LAA) has led to the identification of thrombi and spontaneous echogenic contrast more frequently [10].

Anticoagulant therapy is recommended to minimize embolic events, based on current guidelines [3,11–13]. These recommendations, however, are based on studies and scores, such as CHADS₂ and CHA₂DS₂-VASc, in which the population had AFL, AF or both [14,15]. Until now, there have been no guidelines or specific scores to guide the prescription of anticoagulants in patients with only AFL [16].

The main structure related to cardioembolic events is the LAA [15]. LAA dysfunction has been associated with spontaneous echogenic contrast, thrombus formation and thromboembolism [17]. There is an inverse correlation between LAA function, assessed by its emptying velocity on the TEE, and thromboembolic phenomena [1,18–21].

In this context, the measure of the atrial flutter cycle length (AFL CL), easily measured on the electrocardiogram (EKG) as the interval between F waves, could act as a potential thromboembolic risk marker. It is assumed that faster cycles are associated with greater mechanical

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and electrophysiological disorganization, leading to a smaller LAA contraction and reduction of its emptying rate and generating a greater thrombus formation. Until today, only a few studies have evaluated AFL CL as a thromboembolic risk predictor, but there was no significant relationship [22].

The aim of this study was to evaluate the correlation between the AFL CL and the left atrial appendage emptying velocity (LAEV). We also analyzed the relation of slower empty velocities with electrocardiographic and echocardiographic parameters to identify markers for thromboembolic risk in patients with AFL.

Material and methods

Study population and design

Cross-sectional study of patients undergoing transoesophageal echocardiography in the *Rio Grande do Sul Heart Institute* during the period January 2011 to December 2015.

We included all patients who were in AFL rhythm during TEE and had electrocardiographic recording or electrophysiological study of this arrhythmia in medical records.

We excluded those with other rhythms (sinus or other arrhythmias) on the EKG done at the time of the TEE and those who had no description of LAEV on the final echocardiographic report.

Logistics

For patient screening and selection, each TEE report was reviewed individually, seeking patients who were in AFL during the examination. After this first phase of selection, we searched medical records, clinical data and EKGs or tracings recorded during the electrophysiological or ablation procedures.

Electrocardiogram/electrophysiological study

The EKGs and electrophysiological study registries were obtained from each medical record. They were scanned for the precise evaluation of AFL CL, heart rate, atrial rate and AFL type. We selected the electrocardiograms performed on the same day of the transoesophageal echocardiogram or the ablation procedure, with a maximum time of up to 24 h. All tracings were reviewed by the researchers to confirm whether the rhythm was atrial flutter. The analysis was conducted by the study authors blinded to the result of the TEE.

The electrocardiograms were performed using the 12-lead system with 25 mm/s, being scanned for analysis of variables.

The AFL cycle length was evaluated by measuring the interval between F waves in milliseconds (ms). The atrial rate was also assessed through the interval between the F waves but in beats per minute (bpm).

AFL was defined as a macroreentrant atrial arrhythmia characterized by a regular rhythm, constant F-wave morphology and atrial rate >250 bpm. It was considered **typical** atrial flutter when the electrocardiogram had negative F waves in leads II, III and aVF and positive in V1. **Atypical** atrial flutter was classified as the presence of F waves with polarity that did not fit typical flutter (F waves with concordant polarity between V1 and the inferior leads) [3].

Trans-oesophageal echocardiography

All TEE reports were reviewed by the authors and data for left ventricular ejection fraction (LVEF), left atrial (LA) size, right atrial (RA) size, left atrial appendage emptying velocity (LAEV) and the presence of thrombus or spontaneous echocardiographic contrast (SEC) were collected.

Trained medical echo-cardiographers performed the TEEs using the following ultrasound machines: Vivid I, Vivid S6 Vivid E9 (GE Vingmed

Ultrasound; Horten, Norway) and iE33 (Philips; Bothell, USA). The LAEV was measured with a pulsed Doppler with the sample volume positioned in the proximal third of the appendix, and the flow velocity was recorded at end-diastole (average of three cycles) [23,24].

Based on a previous study, we considered normal emptying velocities greater than or equal to 55 cm/s, and reduced those below 55 cm/s, according to the study conducted by Handke et al., which examined 500 patients with stroke or TIA who underwent TEE and determined the value of 55 cm/s as a cut-off point for the occurrence of spontaneous echogenic contrast and/or intra-atrial thrombus [25].

Spontaneous echocardiographic contrast was defined by the echo density with similar appearance to *smoke*, located inside the LA or LAA, present after gain adjustment. All SEC graduations were considered [18,24].

A thrombus was considered a well-defined intracardiac mass with uniform echodensity adhered to the LA or LAA endocardial and the pectinate muscles and present in more than one echocardiographic projection [18,22].

Clinical data

We also collected, through medical records, clinical data including the CHA₂DS₂VASc score (*congestive heart failure, hypertension, age, diabetes, stroke, vascular disease, and female gender*): sex, age, history of hypertension, diabetes, congestive heart failure, peripheral arterial disease and stroke or transient ischaemic attack. These diagnoses were defined according to a prior publication [15].

Anticoagulation data prior to the TEE exam were recorded. We considered anticoagulated patients who were receiving the following medications at least 24 h before the echocardiographic evaluation: vitamin K-dependent anticoagulant (warfarin and phenprocoumon), anticoagulants not dependent on vitamin K (dabigatran, rivaroxaban and apixaban), low-molecular-weight heparin in full dose or unfractionated heparin in continuous intravenous infusion.

Data on the use of antiarrhythmic drugs prior to TEE exam were also collected, including all classes of antiarrhythmic drugs.

Statistical analysis

The collected data were stored in Excel spreadsheets and analyzed using the software SPSS version 23.0 and MedCalc version 8.2.

Continuous variables were expressed as the mean and standard deviation or median and interquartile range. Categorical variables were presented as absolute and percentage numbers.

Bivariate comparisons were made with a chi-squared test or two-tailed *t*-test as appropriate.

For correlation analysis between the AFL CL and the LAEV, Spearman's coefficient (*r_s*) was used. The data were transformed to rankings to analyze the differences between the obtained values and the standard error.

We performed a multivariate logistic regression analysis to identify predictors of LAEV, using a conditional Backward method, excluding factors in which *p* > 0.20.

We considered a *p* value < 0.05 statistically significant.

For the calculation of sample size, we aimed a moderate correlation (Spearman's coefficient of 0.63) between the AFL cycle measured in milliseconds and LAEV in cm/s. Considering an alpha error of 5% and beta error of 80%, 47 echocardiographic analyses would be necessary.

The cut-off value for LAEV of 55 cm/s was also accessed by the area under the ROC curve by the *c*-statistic to confirm if the historical data gathered in atrial fibrillation patients could also be used in our AFL population.

The index, consisting of the atrial heart rate during AFL multiplied by the LA size in (mm), was assessed as to its discrimination ability relative to identification of LAA thrombus or LA smoke based on the area under the ROC curve by the *c*-statistic.

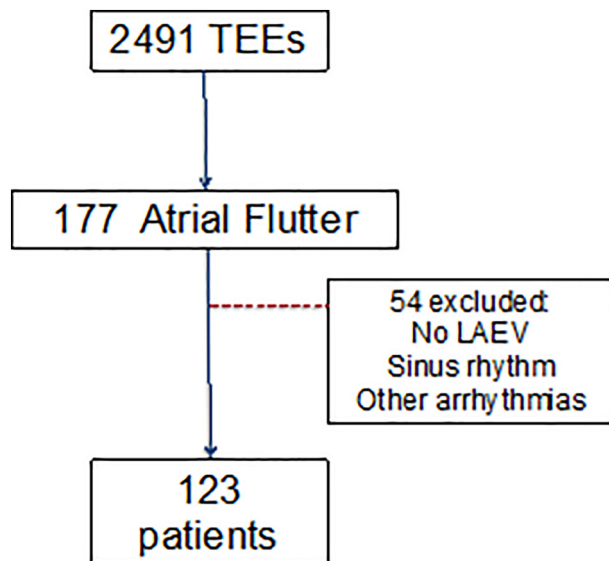


Fig. 1. Patient selection.

The study was approved by the local Ethics and Research Committee under the UP protocol 5245/16.

Results

During the period from January 01, 2011, to December 31, 2015, 2491 TEEs were performed at our Institution, and 177 patients were identified as having an AFL rhythm during the examination. We excluded 54 patients due to lack of description of the LAEV on the echocardiographic report or electrocardiographic recording of AFL. The remaining 123 patients with AFL during TEE were included in the study (Fig. 1).

Male patients were more prevalent (77.2%). The mean age of all patients was 64 years. The CHA₂DS₂-VASc score ranged from 0 to 8 points,

averaging 2.37 points. Seventy-eight percent of the patients were using anticoagulant therapy prior to the TEE. Twenty-eight patients (23%) had previous AF history. Table 1 shows the clinical, echocardiographic and electrocardiographic characteristics of patients with AFL stratified by the arrhythmia type.

In relation to the echocardiographic characteristics, the LA size, measured linearly on the parasternal long axis at the end of systole, ranged from 23 to 62 mm, with an average of 46 mm. The mean LVEF was 55%. The LAEV ranged from 13 to 95 cm/s, with an average of 45 cm/s. Fifty-two (40.9%) patients had left atrial SEC, and 6.3% had a thrombi detected on the LAA. The c-statistic for the LAEV was 0.758 (Standard error = 0.046; 95% Confidence interval = 0.666 to 0.836) for the identification or SEC or LAA thrombus. Because we aimed for a higher sensitivity, the cut-off 55 cm/s gave us the following results: sensitivity 92.3% (79.1–98.3) and a specificity of 29.9% (19.3–42.3). Based on this analysis, we decided to keep the cut-off 55 cm/s, as a reference for our AFL patients, as it was also used, on atrial fibrillation cases, in the SPAF-III trial [19]. We were not able to find any relation between right atrial sizes and AFL cycle lengths or the presence of LAA thrombus or smoke.

Table 2 describes the use of stratified anticoagulants by type of drug and its relation with the formation of intra-atrial thrombi.

Ninety patients (73.2%) were classified as having typical AFL, and 33 (26.8%) as atypical AFL on the basis of the electrocardiogram or electrophysiological study/ablation records. The atypical AFL patients had lower LVEF (46.83% vs. 56.85%; $p = 0.010$) and LAEV (34.59 cm/s vs. 48.36 cm/s; $p = 0.001$) than typical atrial flutter. There was no difference in relation to other variables.

There was a significant and directly proportional relationship between the AFL CL and the LAEV ($r = 0.32$; $p = 0.002$). The same was found for typical flutter ($r = 0.34$; $p = 0.003$) (Fig. 2) but was not found in the atypical group ($r = 0.16$; $p = 0.462$).

History of previous AF was similar between both AFL types. There was also no relation between previous AF and AFL CL or LAEV.

Regarding the use of antiarrhythmic drugs, amiodarone was the only one used in our patient population. There was no statistically significant difference between the prevalence of drug use when groups were stratified by AFL type.

Table 1
Clinical, echocardiographic and electrocardiographic characteristics of patients stratified by atrial flutter type.

	Total	Typical AFL $n = 90$ (%)	Atypical AFL $n = 33$ (%)	P
Age	64.15 ± 13.6	65.1	63.2	0.47
Men	98 (77.2%)	72 (80.9%)	21 (65.5%)	0.14
Echocardiographic Characteristics				
LA size (mm)	46.5 ± 5.2	47.0	46.0	0.40
LV ejection fraction (%)	55.1 ± 15.5	56.8	46.8	0.01*
Left appendage emptying velocity (cm/s)	45.2 ± 17.8	48.3	34.5	0.001*
Spontaneous echogenic contrast	52 (40.9%)	37 (41.1%)	15 (45.5%)	0.66
LA thrombi	8 (6.3%)	4 (4.5%)	4 (12.5%)	0.20
Electrocardiographic Characteristics				
AFL cycle (ms)	239.6 ± 52.5	242.2	234.3	0.17
Heart rate (bpm)	96.0 ± 30.4	92	101	0.17
Clinical Characteristics				
Previous AF	28 (23%)	20 (22.7%)	8 (25.8%)	0.80
CHA ₂ DS ₂ -VASc	2.3 ± 1.5	2.2	2.7	0.16
Anticoagulant use	99 (78%)	71 (79.8%)	22 (71%)	0.44
Antiarrhythmic Drugs	36 (29.3%)	25 (27.7%)	11 (33.3%)	0.71
Hypertension	76 (59.8%)	51 (56.6%)	23 (69.6%)	0.21
Diabetes	27 (21.3%)	18 (20%)	8 (24%)	0.62
Heart failure	36 (28.3%)	24 (26.6%)	11 (33.3%)	0.50
Thromboembolic event	12 (9.4%)	8 (8.8%)	4 (12.1%)	0.73
Vascular disease	27 (21.3%)	19 (21.3%)	8 (24.2%)	0.80
Heart transplant	1 (0.8%)	0 (0%)	1 (3.03%)	0.56
Previous heart surgery	16 (13.0%)	6 (6.6%)	10 (30.3%)	0.01
Pacemaker	3 (2.4%)	1 (1.1%)	2 (6.0%)	0.36
Valvular heart disease	5 (4.0%)	3 (3.3%)	2 (6.0%)	0.87
Acyanotic congenital heart disease	17 (13.8%)	12 (13.3%)	5 (15.1%)	0.96

AFL: atrial flutter; LAEV: left atrial appendage velocity; LV: left ventricle; LA: left atrium; AF: atrial fibrillation; CHA₂DS₂-VASc: congestive heart failure, hypertension, age, diabetes, stroke, vascular disease, female gender.

Table 2

Anticoagulant in use during TEE according to the type of drug and its relation with left intra-atrial thrombus.

Anticoagulant in use during TEE	LA thrombus present N = 8 (6,5%)	LA thrombus absent N = 115 (93,5%)	Total N = 123
Apixaban	0	7	7 (5,7%)
Dabigatran	0	4	4 (3,3%)
Low-molecular-weight heparin	2	34	36 (29,3%)
Unfractionated heparin	0	13	13 (10,6%)
None	2	22	24 (19,5%)
Phenprocoumon	1	4	5 (4,1%)
Rivaroxaban	1	11	12 (9,8%)
Warfarin	2	20	22 (17,9%)

TEE: transoesophageal echocardiography; LA: left atrium.

When we grouped the patients with normal or reduced LAEV, establishing a 55 cm/s cut-off, the patients with LAEV <55 cm/s had shorter AFL cycles, and patients with preserved LAEV had longer cycles. (Fig. 3).

The atrial flutter type was related significantly with LAEV ($p = 0.003$). The atypical type was associated with lower velocities. (Fig. 4). Patients were censored for the regression if they were only categorized as reduced LAEV.

It was not possible to demonstrate a significant relationship between the duration of the flutter cycle and intra-atrial spontaneous echogenic contrast and/or thrombus.

The presence of intra-atrial spontaneous echogenic contrast and/or thrombus was associated with AFL-CL averaging 236.8 ± 50.9 ms, while patients without this finding had an average cycle length of 241.6 ± 53.8 ms, with no difference between the groups ($p = 0.613$).

Multivariate logistic regression analysis was used to identify predictors of reduced LAEV (<55 cm/s). We included in the model the variables AFL-CL, LA size and AFL type. The three variables were able to predict reductions in LAEV (Table 3).

Atrial rate, LA size and LA thrombus or spontaneous contrast

We created a new index, consisting of the multiplication of the atrial heart rate during AFL, in beats per minute, by the LA size in millimeters. This variable showed a statistically significant correlation with the presence of thrombus or spontaneous echogenic contrast, when considering the typical AFL ($p = 0,01$) (Fig. 5).

For this analysis we considered 78 patients with typical AFL. In the other 12, we did not have the absolute value of left atrial size in millimeters, so they were excluded.

This index, when analyzed on a receiver operating characteristic (ROC) curve, had an area under the curve of 0.71 (95%CI: 0.60–0.81), with good ability to identify patients at higher risk of developing

spontaneous echogenic contrast and/or left atrial thrombus when its resulted in a score higher than 11,728 with a sensitivity of 84.21% (95%CI: 60.4–96.6) and specificity 57.63% (95%CI: 44.1–70.4). The positive likelihood ratio was 1.99 (95%CI: 1.4–2.8) and the negative one was 0.27 (95%CI: 0.09–0.8) for the value of 11,728 in our index (Fig. 6).

Discussion

This study assessed the relationship between AFL-CL and the LAEV. We found a significant relationship whereby longer CLs were associated with higher LAEVs. This finding raises the hypothesis that the AFL-CL, easily measured on the electrocardiogram, could be used to identify patients with a reduced LAEV who were therefore at higher risk of thromboembolic events. Although the correlation between AFL-CL and LAEV was moderate it was statistically significant. Previous studies in patients with atrial fibrillation (AF) in mitral stenosis and non-valvular AF have also demonstrated that certain features of the tachyarrhythmia were related to SEC and LA thrombus [19–21]

There is little evidence regarding thromboembolic risk factors in AFL patients. In current clinical practice, the risk estimation is carried out using scores of CHADS₂ and CHA₂DS₂-VASc, which included mostly patients with AF. Wood et al. assessed embolic risk factors in a cohort of 86 AFL patients referred for catheter ablation. The flutter cycle length was included in a multiple regression model to assess predictors. However, this study could not identify any clearly significant predictor [22].

In a cohort of 191 unselected patients referred for AFL treatment, Seidl et al. assessed embolic risk indicators. After multivariate analysis, only hypertension history was an independent risk predictor, with an odds ratio of 6.5 [26].

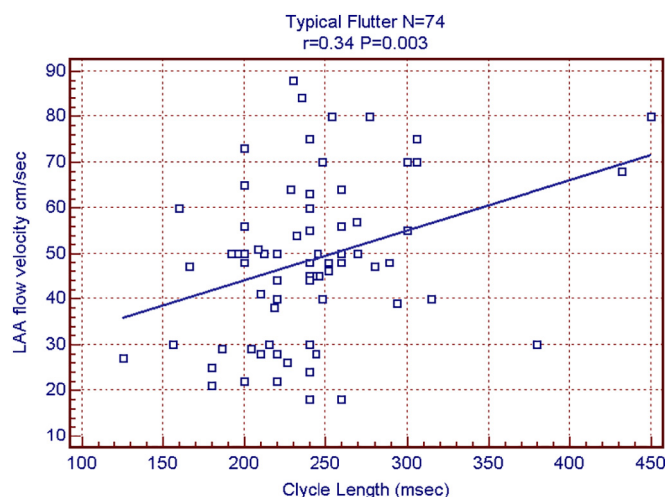


Fig. 2. Correlation between atrial flutter cycle (ms) and left appendage velocity in patients with typical atrial flutter.

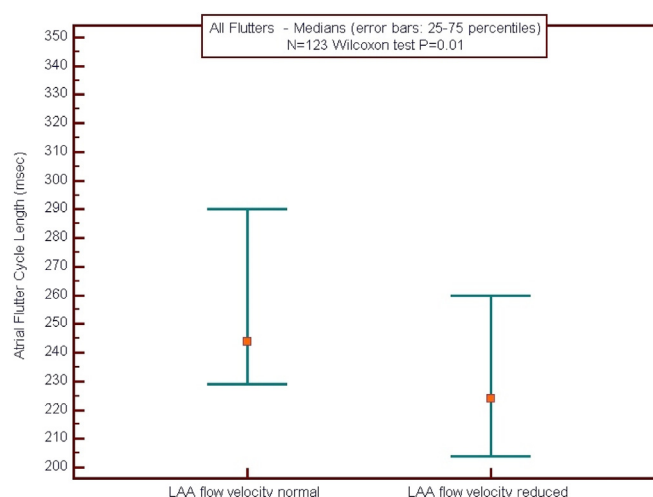


Fig. 3. Relationship between flutter cycle (ms) and left appendage emptying velocity. Missing values (N = 11) were replaced by the method of linear interpolation.

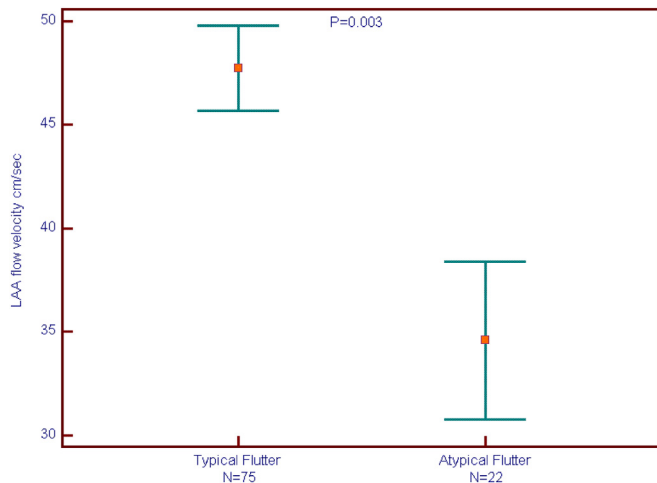


Fig. 4. Left appendage emptying velocity and flutter type. Patients were censored for the regression if they were only categorized as reduced LAEV.

Parikh and colleagues evaluated the CHA₂DS₂-VASc score as an intra-atrial thrombus or SEC predictor in 455 patients with AFL. This score had a sensitivity of 88.7 but a low specificity of 28.9% [16].

In our study, it was also possible to develop a new variable, combining the atrial rate measured on the electrocardiogram with the left atrium size evaluated on echocardiography. This variable correlated significantly with left intra-atrial spontaneous echogenic contrast and/or thrombus in patients with typical AFL. This index performed well when analyzed on a ROC curve, with a high area under the curve (0.71), having the potential to be a simple and practical tool for identifying patients at increased risk of thromboembolic events.

We already know the implication of the LA size in the development of supraventricular arrhythmias, such as AF. The increase in this cavity is a good predictor but is inaccurate in women for thrombus formation and thromboembolic events as previous studies showed. In this study, the LA dimension was also measured on the parasternal long axis, at the end of systole [27]. Our study found a statistically significant correlation between the presence of atrial thrombus or SEC and atrial rate plus LA size. This finding could improve the accuracy of risk assessment of embolic episodes through LA measures. Furthermore, in our multivariate analysis, LA size was also able to predict reduced LAEV.

Gaibazzi et al. evaluated in 106 patients a risk score called Atrial Flutter Atrial Thrombus (AFLAT) for prediction of an intra-atrial thrombus before AFL cardioversion. This score also included increasing the LA size to >45 mm in addition to the following variables: previous AF, mitral stenosis, stroke/TIA, LVEF <35%, coronary artery disease, hypertension, diabetes mellitus and severe mitral regurgitation. A score lower than or equal to 2 was able to identify a population of very low risk for left atrial thrombosis, suggesting that TEE may be not necessary before cardioversion [28].

The influence of AFL type on the risk of embolic events has also rarely been studied. Through the presented data, we observed that patients with atypical AFL have lower LVEF and LAEV, as they are associated with shorter CL. In the logistic regression model, atypical flutter was

Table 3
Predictors of reduced LAEV (≤ 55 cm/s) in multivariate analysis.

Variable	Odds ratio	p	CI 95%
Flutter cycle length (ms)	0.98	0.011	0.97–0.99
LA size (mm)	1.12	0.028	1.01–1.25
Atypical atrial flutter	13.14	0.023	1.41–122.10

Multivariate logistic regression analysis to identify predictors of reduced LAEV, using a conditional Backward method, excluding factors with $p > 0.20$. The variables flutter cycle length, LA size and atypical atrial flutter were included in the model. CI: confidence interval; LA: left atrium.

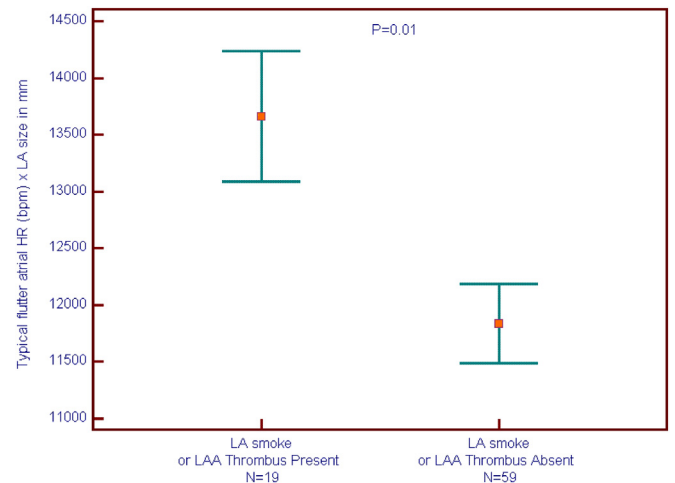


Fig. 5. Relationship between atrial rate (bpm) X left atrial size (mm) with the presence or absence of thrombus or spontaneous echogenic contrast in typical atrial flutter.

also shown to be a predictor of low LAEV, with an odds ratio of 13. These findings suggest that atypical AFL may represent a greater risk subgroup. Likewise, it can be inferred that atypical flutter shares similar features with atrial fibrillation, which may have a higher risk profile.

Demir et al. had already tested the influence of AFL type on thromboembolic risk. They evaluated 37 patients with typical AFL and 13 with atypical AFL and did not find any difference in relation to SEC and LAEV, but laboratory clotting tests (fibrinogen, D-dimer and thrombin-antithrombin 3) were higher in atypical AFL compared to typical AFL. The authors concluded that patients with atypical AFL had an activated coagulation system and therefore anticoagulation should be considered in this context [29].

In our analysis, there was no difference in thrombosis and or spontaneous echogenic contrast between AFL types. More recently, in the study of Cresti et al., the prevalence of atrial thrombosis was also similar between the flutter types.

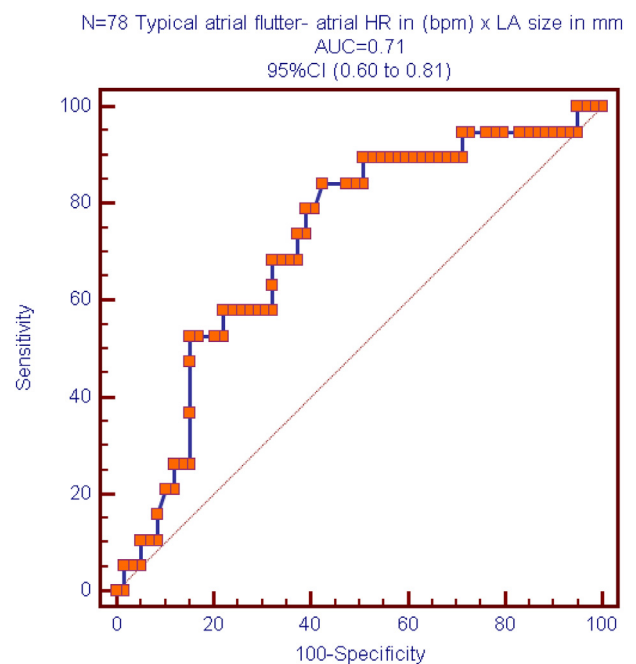


Fig. 6. ROC Curve - a score higher than 11,728 have sensitivity of 84.21% (95%CI: 60.4–96.6) and specificity 57.63% (95%CI: 44.1–70.4). The positive likelihood ratio is 1.99 (95%CI: 1.4–2.8) and the negative one is 0.27 (95%CI: 0.09–0.8) for this cutoff value.

Finally, as previously demonstrated in the literature, LAEV was related significantly with intra-atrial spontaneous echogenic contrast.

Study limitations

This was a retrospective study with data collected from medical records. Many patients undergoing TEE who had AFL rhythm had no description of LAEV on the echocardiographic report. Although atypical AFL was associated with lower LVEF and LAEV and was shown to predict LAEV reductions in the multivariate analysis, the study was not able to detect differences in spontaneous echogenic contrast and/or left intra-atrial thrombus between the different types of AFL. Also, we were not able to find a linear correlation between AFL cycle length and LAEV in patients with atypical flutter. This may have happened due to the fact that atypical AFL encompass a heterogeneous group of substrates and circuits for the arrhythmia maintenance. We did not have the precise information on the duration of the AFL before the TEE examination; nor the full data of prothrombin time in the four weeks before the TEE. But there was a low prevalence of thrombus in our patient population, possibly related to the high percentage (78%) of anticoagulant use in the sample, so we could not correlate the AFL cycle length with left atrial thrombosis. We did not evaluate thromboembolic events, and it was not possible to relate the cycle to clinic variables, such as stroke and transient ischaemic attack. Therefore, we could not establish the relationship between AFL CL and clinical events.

Conclusions

There is statistically significant relationship between the atrial flutter cycle length, measured by electrocardiogram and measurement of the left atrial appendage emptying velocity. This study also allowed, using the multivariate analysis, to identify the predictors of LAEV reduction: flutter cycle length, left atrial size and atypical flutter. The LA size, when analyzed in conjunction with atrial rate, is related to spontaneous echogenic contrast and thrombus. Thus raises the possibility of new markers for thromboembolic risk in patients with atrial flutter.

Conflict of interest

None.

Acknowledgment

The author would like to thank the Graduate Program in Health Sciences for providing all infrastructures necessary for the research. The authors also thank the Electrophysiology and Echocardiography Departments for data provision and support.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- [1] Corrado G, Sgalambro A, Mantero A, Gentile F, Gasparini M, Bufalino R, et al. Thromboembolic risk in atrial flutter. The FLASIEC (Flutter Atriale Società Italiana di Ecografia Cardiovascolare) multicentre study. *Eur Heart J* 2001;22:1042–51.
- [2] Vadmann H, Nielsen PB, Hjortshøj SP, Riahi S, Rasmussen LH, Lip GY, et al. Atrial flutter and thromboembolic risk: a systematic review. *Heart* 2015;101:1446–55.
- [3] Page RL, Joglar JA, Caldwell MA, Calkins H, Conti JB, Deal BJ, et al. ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia. *J Am Coll Cardiol* 2015;67:e27–115.
- [4] Waldo AL. The interrelationship between atrial fibrillation and atrial flutter. *Prog Cardiovasc Dis* 2005;48:41–56.
- [5] Tunick PA, McElhinney L, Mitchell T, Kronzon I. The alternation between atrial flutter and atrial fibrillation. *Chest* 1992;10:34–6.
- [6] Delise P, Sitta N, Corò L, Marras E, Sciarra L, Bocchino M, et al. Common atrial flutter and atrial fibrillation are not always two stages of the same disease. A long-term follow-up study in patients with atrial flutter treated with cavo-tricuspid isthmus ablation. *J Cardiovasc Med* 2006;7:800–5.
- [7] Ellis K, Wazni O, Marrouche N, Martin D, Gillinov M, McCarthy P, et al. Incidence of atrial fibrillation post-cavotricuspid isthmus ablation in patients with typical atrial flutter: left-atrial size as an independent predictor of atrial fibrillation recurrence. *J Cardiovasc Electrophysiol* 2007;18(8):799–802.
- [8] Jozá J, Filion KB, Eberg M, Proietti R, Nascimento T, Bernier M, et al. Prognostic value of atrial fibrillation inducibility after right atrial flutter ablation. *Heart Rhythm. Elsevier*; 2014. p. 1870–6.
- [9] Cresti A, García-Fernández MA, De Sensi F, Miracapillo G, Picchi A, Scalese M, et al. Prevalence of auricular thrombosis before atrial flutter cardioversion: a 17-year transoesophageal echocardiographic study. *Europace* 2015;18:450–6.
- [10] Weiss R, Marcovitz P, Knight BP, Bahu M, Souza JJ, Zivin A, et al. Acute changes in spontaneous echo contrast and atrial function after cardioversion of persistent atrial flutter. *Am J Cardiol* 2016;82:1052–5.
- [11] Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. Focused update of the ESC guidelines for the management of atrial fibrillation. *Eur Heart J* 2012;33:2719–47.
- [12] January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland Jr JC, et al. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary. *J Am Coll Cardiol* 2014;21:2246–80.
- [13] Magalhães LP, Figueiredo MJO, Cintra FD, Saad EB, Kuniyoshi RR, Teixeira RA, et al. OF II Diretrizes Brasileiras de Fibrilação Atrial. *Arq Bras Cardiol* 2016;106:1–22.
- [14] Gage BF, van Walraven C, Pearce L, Hart RG, Koudstaal PJ, Boode BS, et al. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation* 2004;110:2287–92.
- [15] Lip GY, Nieuwlaar R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010;137:263–72.
- [16] Parikh MG, Aziz Z, Krishnan K, Madias C, Trohman RG. Usefulness of transesophageal echocardiography to confirm clinical utility of CHA2DS2-VASc and CHADS2 scores in atrial flutter. *Am J Cardiol* 2012;109:550–5.
- [17] Agmon Y, Khandheria BK, Gentile F, Seward JB. Echocardiographic assessment of the left atrial appendage. *J Am Coll Cardiol* 1999;34:12–20.
- [18] Beigel R, Wunderlich NC, Ho SY, Arsanjani R, Siegel RJ. The left atrial appendage: anatomy, function and noninvasive evaluation. *JACC Cardiovasc Imaging* 2014;7:1251–65.
- [19] Goldman ME, Pearce LA, Hart RG, Zabalgoitia M, Asinger RW, Safford R, et al. Pathophysiologic correlates of thromboembolism in nonvalvular atrial fibrillation: I. Reduced flow velocity in the left atrial appendage (The Stroke Prevention in Atrial Fibrillation [SPAF-III] Study). *J Am Soc Echocardiogr* 1999;12:1080–5.
- [20] Asinger RW, Koehler J, Pearce LA, Zabalgoitia M, Blackshear JL, Fenster PE, et al. Pathophysiologic correlates of thromboembolism in nonvalvular atrial fibrillation: II. Dense spontaneous echocardiography contrast (The Stroke Prevention In Atrial Fibrillation [SPAF-III] Study). *J Am Soc Echocardiogr* 1999;12:1088–96.
- [21] Goswami KC, Yadav R, Rao MB, Bahl VK, Talwar KK, Manchanda SC. Predictors of left atrial spontaneous echo contrast and thrombi in patients with mitral stenosis and atrial fibrillation. *Am J Cardiol* 2000;86:529–34.
- [22] Wood KA, Eisenberg SJ, Kalman JM, Drew BJ, Saxon LA, Lee RJ, et al. Risk of thromboembolism in chronic atrial flutter. *Am J Cardiol* 1997;79:1043–7.
- [23] Saric M, Armour AC, Amout SM, Chaudhry FA, Grimm RA, Kronzon I, et al. Guidelines for the use of echocardiography in the evaluation of a cardiac source of embolism. *JASE* 2016;29:1–42.
- [24] Bansal M, Kasliwal RR. Echocardiography for left atrial appendage structure and function. *Indian Heart J* 2012;64:469–75.
- [25] Handke M, Harloff A, Hetzel A, Olschewski M, Bode C, Geibel A. Left atrial appendage flow velocity as a quantitative surrogate parameter for thromboembolic risk: determinants and relationship to spontaneous echocontrast and thrombus formation - a transesophageal echocardiographic study in 500 patients with cerebral ischemia. *J Am Soc Echocardiogr* 2005;18:1366–72.
- [26] Seidl K, Hauer B, Schwick NG, Zellner D, Zahn R, Senges J. Risk of thromboembolic events in patients with atrial flutter. *Am J Cardiol* 1998;82:580–3.
- [27] Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. *Circulation* 1995;92:835–41.
- [28] Gaibazzi N, Piepoli M. TEE screening in atrial flutter: a single-centre experience with retrospective validation of a new risk score for the presence of atrial thrombi. *Int J Cardiol* 2008;129:149–51.
- [29] Demir AD, Soyul M, Ozdemir O, Topaloğlu S, Aras D, Şaşmaz A, et al. Do different atrial flutter types carry the same thromboembolic risk? *Angiology* 2005;56:593–9.