Original paper

Left atrial appendage thrombus in patients referred to electrical cardioversion for typical atrial flutter

Skrzeplina uszka lewego przedsionka u pacjentów kierowanych do kardiowersji elektrycznej z powodu typowego trzepotania przedsionków

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Słowa kluczowe: antykoagulacja, trzepotanie przedsionków, kardiowersja, uszko lewego przedsionka, skrzeplina.

Abstract

Introduction: Patients with atrial flutter (AFL) are at risk of stroke; however, the stratification of stroke risk is difficult. It remains unknown whether left atrial appendage thrombus (LAAT) in AFL patients on chronic oral anticoagulation (OAC) contributes significantly to that risk.
Aim of the research: To assess the prevalence and predictors of LAAT, and its role in the prediction of mortality, stroke, and systemic thromboembolic events among consecutive AFL patients on OAC admitted for electrical cardioversion.
Material and methods: This was a prospective, single-centre cohort study. The participants underwent transoesophageal echocardiography before electrical cardioversion. A total of 69 patients were enrolled. The primary outcome was the presence of LAAT. All participants were followed up for 12 months to evaluate the incidence of systemic thromboembolic events, stroke, and death.
Results: Despite uninterrupted OAC, irrespective of the anticoagulant agent type, LAAT was present in 10.1% of patients referred for cardioversion due to typical AFL of > 48-hour duration. The significant predictor of LAAT was prior stroke/transient ischaemic attack/thromboembolic event (OR = 14.75; 95% CI: 2.17–108.33). No deaths, strokes, or systemic thromboembolic events occurred during the follow-up period.
Conclusions: The predictive role of LAAT in relation to mortality, stroke, and systemic thromboembolic events among patients with AFL and chronic oral anticoagulation remains unclear.

Streszczenie

Wprowadzenie: Pacjenci z trzepotaniem przedsionków (AFL) są zagrożeni udarem mózgu; jednak stratyfikacja ryzyka udaru mózgu jest trudnym zadaniem. Nie wiadomo, czy skrzeplina uszka lewego przedsionka (LAAT) u pacjentów z AFL w trakcie przewlekłej doustnej antykoagulacji (OAC) istotnie przyczynia się do tego ryzyka.
Cel pracy: Ocena częstości występowania i czynników predykcyjnych LAAT oraz predykcyjnej roli LAAT w odniesieniu do śmiertelności, udaru mózgu i ogólnoustrojowych incydentów zakrzepowo-zatorowych wśród kolejnych pacjentów z AFL w trakcie OAC przyjętych do kardiowersji elektrycznej.
Materiał i metody: Przeprowadzono prospektywne, jednoośrodkowe badanie kohortowe. Uczestnicy zostali poddani echokardiografii przezprzełykowej przed kardiowersją elektryczną. Do badania włączono 69 pacjentów. Pierwszorzędowym punktem końcowym była obecność LAAT. Wszyscy uczestnicy byli obserwowani przez 12 miesięcy w celu oceny występowania ogólnoustrojowych incydentów zakrzepowo-zatorowych, udaru mózgu i zgonu.
Wyniki: Pomimo nieprzerwanej doustnej antykoagulacji, niezależnie od rodzaju antykoagulantu, u pacjentów kierowanych do kardiowersji z powodu typowego AFL > 48 godzin stwierdzono wysoką częstość występowania LAAT (10,1%). Istotnym czynnikiem prognostycznym LAAT był przebyty udar mózgu lub napad przemijającego niedokrwienia mózgu, lub incydent zakrzepowo-zatorowy (OR = 14,75; 95% CI: 2,17–108,33). W okresie obserwacji nie wystąpiły zgony, udary mózgu ani ogólnoustrojowe incydenty zakrzepowo-zatorowe.
Wnioski: Predykcyjna rola LAAT w odniesieniu do śmiertelności, udaru mózgu i ogólnoustrojowych incydentów zakrzepowo-zatorowych wśród pacjentów z AFL i OAC jest niejasna.

Introduction

Typical atrial flutter (AFL) is a macro-reentry circuit involving the cavotricuspid isthmus. In a surface 12-lead electrocardiogram an inverted saw-tooth F-wave pattern with a rate of 250–330 beats per minute, no isoelectric line between deflections, and usually slower ventricular response are observed [1, 2]. The exact AFL epidemiology remains unknown. The overall incidence of AFL is estimated at 88/100,000 person-years in the US population annually [3]. AFL is associated with increased risk of heart failure (HF), stroke, systemic thromboembolism, and mortality [1, 4–8]. Stroke risk stratification in patients with AFL remains a complicated issue [1, 9–12]. Left atrial appendage thrombus (LAAT) is regarded as a risk factor for stroke in these patients; however, the actual LAAT-related health risk in patients with AFL on chronic anticoagulation remains unknown [13]. Moreover, the risk factors and prevalence of LAAT in patients with AFL on oral anticoagulation (OAC) (i.e. non-VKA oral anticoagulants (NOACs) and vitamin K antagonists (VKAs)) have not been fully established [13]. It seems that the actual LAAT-related health risk varies according to thrombus age, medical management, and procedures (i.e. cardioversion, conservative management) or left atrial appendage morphology [13]. Although the restoration of sinus rhythm in patients with AFL increases the stroke risk [11, 14–17], the stroke mechanism can be difficult to establish [13]. The proper anticoagulation reduces stroke risk following the sinus rhythm restoration [1, 13].

Aim of the research

The aim of this research was to evaluate the predictors and prevalence of LAAT and to assess the predictive role of LAAT in relation to mortality and the risk of stroke and systemic thromboembolic events among consecutive patients with typical AFL on oral anticoagulation referred to cardioversion.

Material and methods

Study group

Consecutive patients with typical AFL on OAC were admitted to the cardiology department for transoesophageal echocardiography (TEE)-guided direct current cardioversion (DCC). Of the 69 enrolled patients between April 2011 and March 2018, 26 (37.7%) underwent DCC. The inclusion criteria were age ≥ 18 years, arrhythmia duration > 48 h, symptomatic or poorly tolerated arrhythmia, and OAC for > 3 weeks. The exclusion criteria were as follows: systolic blood pressure < 90 mm Hg, bradycardia < 60/min, signs of exacerbation of HF, symptoms of peripheral hypoperfusion, history of electrical cardioversion, history of ablation, any prosthetic heart valve, moderate to severe mitral stenosis defined as mitral orifice area ≤ 1.5 cm^2 with mean pressure gradient ≥ 5 mm Hg, and history of intracardiac thrombus. All patients were followed up for 12 months from the day of the TEE. The evaluation of clinical events included systemic thromboembolic events, stroke, and death.

Anticoagulation therapy

All enrolled patients were on OAC therapy according to the current guidelines: VKA therapy with international normalized ratio (INR) ≥ 2.0, or uninterrupted NOAC for at least 3 weeks before study inclusion [18–21]. For patients on a VKA regimen, INR was tested every week for 3 weeks, with all the outcomes expected to be within the therapeutic range. For patients on dabigatran, treatment with 150 mg twice daily was required, but 110 mg twice daily was also allowed for those fulfilling the following criteria: age ≥ 80 years and/or concomitant use of verapamil and/or estimated glomerular filtration rate 30–49 ml/min/1.73 m^2 and/or a HAS-BLED score ≥ 3 [19]. In the case of rivaroxaban, treatment with 20 mg once daily was required; however, 15 mg once daily was also allowed in patients fulfilling the following criteria: estimated glomerular filtration rate 15–49 ml/min/1.73 m^2 and/or HAS-BLED score ≥ 3. In the case of apixaban, treatment with 5 mg twice daily was required, but 2.5 mg twice daily was also allowed in patients fulfilling at least 2 of the following criteria: age ≥ 80 years, body weight ≤ 60 kg, and serum creatinine level ≥ 1.5 mg/dl.

Echocardiographic examination

All examinations were performed by three independent certified echocardiographers using a Vivid E9 (GE Vingmed Ultrasound AS, Horten, Norway) ultrasound machine with a multiplanar transducer according to the approved protocol [22]. On TEE, the left atrial appendage was visualized in the mid-oesophageal view with an appropriate total gain and depth. The imaging plane of the TEE transducer was axially rotated from 0° to 180° to better visualize the contours of the endocardium. The thrombus was defined as a uniformly echo-dense intracavitary mass with defined margins distinct from the endocardium and seen throughout systole and diastole, observed in more than one imaging plane, and not related to the pectinate muscles [23, 24]. The left ventricular ejection fraction (LVEF) was calculated by the Simpson's biplane method using manual tracing on 2D apical 4- and 2-chamber views [25]. The anteroposterior diameter of the left atrium (LA) was assessed in end-systole in a plane perpendicular to the long axis of the ascending aorta in the parasternal long-axis view. All transthoracic echocardiogram and TEE examinations were recorded and stored and were available for re-evaluation if needed.

Ethics

The study protocol was approved by the local Ethics Committee (reg. no. 21/2010). All procedures performed in this study were in accordance with the ethical standards of the local Bioethics Committee and the Declaration of Helsinki. Written informed consent was obtained from all patients.

Statistical analysis

Quantitative data were presented as arithmetic mean and standard deviation or median and interquartile ranges, when appropriate. Numbers and percentages were used to describe qualitative data. Group comparisons were conducted using Fisher's exact test or the χ^2 test for qualitative variables. Due to a violation of the assumption of normality (normality of the distribution was checked with the Shapiro-Wilk test), the distributions of quantitative variables were compared using the Mann-Whitney U test (for 2 groups) or the Kruskal-Wallis test (for more than 2 groups). For the comparison of distributions of more than 2 groups, post-hoc tests were conducted to define differences in pairs when the global null hypothesis about identical compared distributions was rejected. Crude and adjusted odds ratios and 95% confidence intervals were calculated to determine the predictors of LAAT on TEE.

A multivariable logistic regression model was built using the variables from the age- (< 75 or ≥ 75 years) and sex-adjusted univariable analyses. Receiver operating characteristic (ROC) analysis was performed to assess whether quantitative variables had a statistically significant ability to distinguish between the group with LAAT and the group without LAAT. ROC analysis included calculation of the area under the curve. Quantitative predictors of LAAT on TEE received from the ROC analysis were transformed into qualitative variables with 2 categories and treated as dichotomous prior to further analyses using a previously defined cut-off point (optimal decision threshold). The optimal cut-off point was determined as the point maximizing Youden's index. For all tests, a p-value < 0.05 was considered significant (two-tailed). All statistical analyses were performed using the R software package version 3.6.2 (R: language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/).

Results

The baseline characteristics according to the anticoagulant agent administered are described in Table 1. LAA thrombi were detected in 7 (10.1%) patients. There was no difference in the prevalence of LAAT between different types of OAC (p = 0.1). Patients with LAAT more frequently had previous stroke/transient ischaemic attack/systemic thromboembolism (Table 2). In the dabigatran group, the dose was reduced in 7 (22.6%) patients without LAAT and in 2 (33.3%) patients with LAAT (p = 0.62). In the rivaroxaban group, the dose was reduced in 4 (20%) patients without LAAT and in 0 (0.0%) patients with LAAT. Statistical analysis demonstrated that the composite endpoint (prior stroke/transient ischaemic attack/thromboembolic event) was a significant predictor of thrombus formation in patients with AFL (OR = 14.75; 95% CI: 2.17–108.33, p = 0.005) (Table 3). ROC analysis demonstrated that the anteroposterior left atrial diameter was able to predict LAAT presence (Table 4). The optimal cut-off value based on the Youden index for this variable was ≥ 45 mm. However, that finding was not confirmed in the uni- and multivariable analyses (Table 5).

Effectiveness of electrical cardioversion

DCC was performed in 26 patients (without complications), and sinus rhythm was restored in 26 subjects. In 36 patients directly after TEE a catheter ablation without DCC was performed (without complications), and sinus rhythm was restored in 36 subjects.

Follow-up

Follow-up was completed for all participants. No deaths, strokes, or systemic thromboembolic events occurred during the 12 months following TEE. In the group who had undergone DCC, 8 had a subsequent catheter ablation for AFL during the follow-up period.

Discussion

Despite the uninterrupted OAC therapy according to the guidelines [18, 19, 21, 26, 27] in patients with typical AFL of > 48-hour duration referred for DCC, we were able to reveal an unexpectedly high (> 10%) LAAT prevalence irrespective of the anticoagulant agent type. A composite endpoint (prior stroke/transient ischaemic attack/thromboembolic event) was able to predict the LAAT presence. In accordance with European Society of Cardiology and American Heart Association recommendations [1, 28], the significant role of the AFL therapeutic management is stroke and thromboembolic events protection. However, there are no prospective randomized studies on the incidence of thromboembolic complications and the efficacy of anticoagulation in patients with AFL. The anticoagulant recommendations for AFL cardioversion are mainly based on the evidence from clinical trials on AF. The rules of DCC preparation for patients with persistent atrial fibrillation (AF) on VKAs have been developed following small, non-randomized trials [29, 30]. Dabigatran was added after a post-hoc analysis of the randomized RE-LY study [31]. Rivaroxaban was introduced after a post-hoc analysis of the randomized ROCKET-AF

Table 1. Baseline clinical characteristics according to the anticoagulant agent

Variable	VKA (*n* = 9)	Rivaroxaban (*n* = 20)	Dabigatran (*n* = 37)	Apixaban (*n* = 3)	*P*-value
Age [years], MV ± SD	68.4 ±16.6	68.9 ±10.9	66.0 ±10.8	72.7 ±15.0	0.48
Age range [years]	30.0–87.0	49.0–87.0	31.0–81.0	58.0–88.0	N/A
Female sex	4 (44.4%)	8 (40.0%)	14 (37.8%)	3 (100.0%)	0.94
BMI [kg/m^2], MV ± SD	29.1 ±3.2	28.9 ±3.3	30.1 ±4.9	32.1 ±6.7	0.61
SBP [mm Hg], MV ± SD	122.1 ±10.6	121.8 ±11.5	123.0 ±11.0	110.0 ±10.0	0.98
DBP [mm Hg], MV ± SD	73.7 ±5.8	78.1 ±5.1	78.7 ±7.8	73.3 ±11.5	0.1
HR [bpm], MV ± SD	103.0 ±20.1	114.6 ±29.2	108.4 ±27.6	130.0 ±10.0	0.48
COPD	1 (11.1%)	0 (0.0%)	2 (5.4%)	1 (33.3%)	0.24
AH	8 (88.9%)	17 (85.0%)	27 (73.0%)	2 (66.7%)	0.48
HF	2 (22.2%)	7 (35.0%)	12 (32.4%)	1 (33.3%)	0.87
MI	0 (0.0%)	1 (5.0%)	4 (10.8%)	2 (66.7%)	0.68
CABG	0 (0.0%)	0 (0.0%)	2 (5.4%)	0 (0.0%)	0.65
DM	2 (22.2%)	6 (30.0%)	11 (29.7%)	1 (33.3%)	> 0.99
Stroke/TIA/systemic thromboembolism	0 (0.0%)	1 (5.0%)	5 (13.5%)	0 (0.0%)	0.49
PPM	1 (11.1%)	2 (10.0%)	8 (21.6%)	0 (0.0%)	0.58
PFO	0 (0.0%)	4 (20.0%)	3 (8.1%)	0 (0.0%)	0.26
Current smoker	0 (0.0%)	4 (20.0%)	5 (13.5%)	0 (0.0%)	0.47
Former smoker	2 (22.2%)	3 (15.0%)	4 (10.8%)	1 (33.3%)	0.61
Non-smoker	7 (77.8%)	13 (65.0%)	28 (75.7%)	2 (66.7%)	0.68
eGFR [ml/min/1.73 m^2], MV ± SD	59.5 ±10.7	61.5 ±16.0	65.8 ±15.9	48.0 ±29.7	0.33
LA diameter [mm], MV ± SD	42.6 ±4.7	43.6 ±6.1	45.1 ±4.7	41.0 ±5.0	0.25
LVEF (%), MV ± SD	51.1 ±8.6	53.0 ±11.4	50.7 ±11.9	47.3 ±26.4	0.74
CHA2DS2-VASc score, MV ± SD	3.0 ±1.9	3.1 ±1.7	3.1 ±1.7	4.0 ±2.6	0.94
β-Blocker	8 (88.9%)	15 (75.0%)	32 (86.5%)	3 (100.0%)	0.52
ACE inhibitor/ARB	8 (88.9%)	14 (70.0%)	21 (56.8%)	1 (33.3%)	0.16
Statin	5 (55.6%)	13 (65.0%)	21 (56.8%)	2 (66.7%)	0.78
LAAT	0 (0.0%)	0 (0.0%)	6 (16.2%)	1 (33.3%)	0.1

MV ± SD – mean value ± standard deviation, ACE – angiotensin converting enzyme, AH – arterial hypertension, ARB – angiotensin II receptor blocker, BMI – body mass index, CABG – coronary artery bypass grafting, CHA_2DS_2-VASc – scale for stroke and thromboembolic risk assessment in patients with atrial fibrillation, COPD – chronic obstructive pulmonary disease, DM – diabetes mellitus, eGFR – estimated glomerular filtration rate, HF – heart failure, HR – heart rate, LA – left atrium, LAAT – left atrial appendage thrombus, LVEF – left ventricular ejection fraction, MI – myocardial infraction, PFO – patent foramen ovale, PPM – permanent pacemaker, S/DBP – systolic/diastolic systemic blood pressure, TIA – transient ischaemic attack

study and the outcomes of the X-VeRT study, which compared its effectiveness with that of VKAs [32, 33]. Apixaban was approved after a post-hoc analysis of the randomized ARISTOTLE study and the outcomes of the EMANATE study, which compared its effectiveness with VKAs [34, 35].

Despite the high rate of the presence of LAAT in the current study, we did not note long-term clinical consequences of LAAT in relation to strokes, systemic thromboembolic events, and deaths in our study population during the 12-month follow-up. We speculate that the presence of LAAT in AFL patients on chronic

Table 2. Clinical characteristics of patients with and without left atrial appendage thrombus

Variable	AFL without LAAT (*n* = 62)	AFL with LAAT (*n* = 7)	*P*-value
Age [years], MV ± SD	67.2 ±11.8	69.1 ±11.9	0.93
Age < 65 years	23 (37.1%)	3 (42.9%)	0.69
Age 65–74 years	20 (32.3%)	1 (14.3%)	
Age ≥ 75 years	19 (30.6%)	3 (42.9%)	
Age ≥ 75 years	19 (30.6%)	3 (42.9%)	0.67
Female gender	26 (41.9%)	3 (42.9%)	> 0.99
BMI [kg/m^2], MV ± SD	29.4 ±3.9	32.8 ±7.0	0.32
SBP [mm Hg], MV ± SD	121.7 ±11.3	124.7 ±9.9	0.53
DBP [mm Hg], MV ± SD	77.5 ±7.2	78.6 ±6.9	0.77
HR [bpm], MV ± SD	110.2 ±27.0	112.1 ±27.9	0.94
COPD	4 (6.5%)	0 (0.0%)	> 0.99
AH	49 (79.0%)	5 (71.4%)	0.64
HF	19 (30.6%)	3 (42.9%)	0.67
MI	6 (9.7%)	1 (14.3%)	0.54
CABG	2 (3.2%)	0 (0.0%)	> 0.99
DM	19 (30.6%)	1 (14.3%)	0.66
Stroke/TIA/systemic thromboembolism	3 (4.8%)	3 (42.9%)	0.01
eGFR [ml/min/1.73 m^2], MV ± SD	63.6 ±15.6	56.9 ±20.9	0.31
PFO	6 (9.7%)	1 (14.3%)	0.54
ASD type 2	1 (1.6%)	0 (0.0%)	> 0.99
PPM	9 (14.5%)	2 (28.6%)	0.31
Current smoker	9 (14.5%)	0 (0.0%)	0.58
Former smoker	8 (12.9%)	2 (28.6%)	0.27
Non-smoker	45 (72.6%)	5 (71.4%)	> 0.99
Gastrointestinal bleeding	0 (0.0%)	1 (14.3%)	0.1
LA diameter [mm], MV ± SD	43.9 ±5.3	46.7 ±2.6	0.1
LA diameter > 40 mm	44 (71.0%)	7 (100.0%)	0.18
LVEF (%), MV ± SD	52.0 ±11.1	45.4 ±17.5	0.39
LVEF ≥ 50%	42 (67.7%)	4 (57.1%)	0.5
LVEF 40–49%	12 (19.4%)	1 (14.3%)	
LVEF < 40%	8 (12.9%)	2 (28.6%)	
LVEF < 40%	8 (12.9%)	2 (28.6%)	0.27
CHA2DS2-VASc score, MV ± SD	3.0 ±1.6	3.7 ±2.6	0.38
CHA2DS2-VASc score 0	5 (8.1%)	1 (14.3%)	0.43
CHA2DS2-VASc score 1	7 (11.3%)	1 (14.3%)	
CHA2DS2-VASc score ≥ 2	50 (80.6%)	5 (71.4%)	
CHA2DS2-VASc score ≥ 2	50 (80.6%)	5 (71.4%)	0.62
ACE inhibitor/ARB	42 (67.7%)	2 (28.6%)	0.09
Statin treatment	36 (58.1%)	5 (71.4%)	0.69
VKA	9 (14.5%)	0 (0.0%)	0.28
Rivaroxaban	20 (32.3%)	0 (0.0%)	0.07
Dabigatran	31 (50.0%)	6 (85.7%)	0.07
Apixaban	2 (3.2%)	1 (14.3%)	0.17

MV ± SD – mean value ± standard deviation, ACE – angiotensin converting enzyme, AFL – atrial flutter, AH – arterial hypertension, ARB – angiotensin II receptor blocker, ASD – atrial septal defect, BMI – body mass index, CABG – coronary artery bypass grafting, CHA2DS2-VASc – scale for stroke and thromboembolic risk assessment in patients with atrial fibrillation, COPD – chronic obstructive pulmonary disease, DM – diabetes mellitus, eGFR – estimated glomerular filtration rate, HF – heart failure, HR – heart rate, LA – left atrium, LAAT – left atrial appendage thrombus, LVEF – left ventricular ejection fraction, MI – myocardial infraction, PFO – patent foramen ovale, PPM – permanent pacemaker, S/DBP – systolic/diastolic systemic blood pressure, TIA – transient ischaemic attack.

Table 3. Univariate logistic regression analysis for prediction of LAAT in patients with AFL on chronic anticoagulation

Variable	Crude OR	*P*-value
Age [years]	1.02 (0.95–1.1)	0.68
Age ≥ 65 years	0.79 (0.16–4.28)	0.77
Age ≥ 75 years	1.7 (0.31–8.44)	0.51
Female gender	1.04 (0.19–5.1)	0.96
BMI [kg/m^2]	1.18 (1–1.41)	0.06
BMI ≥ 30 kg/m^2	2.26 (0.46–12.34)	0.31
SBP [mm Hg]	1.03 (0.96–1.1)	0.49
DBP [mm Hg]	1.02 (0.91–1.15)	0.71
HR [bpm]	1 (0.97–1.03)	0.86
AH	0.66 (0.13–5)	0.64
HF	1.7 (0.13–5)	0.51
MI	1.56 (0.08–11.53)	0.7
DM	0.38 (0.02–2.42)	0.38
Stroke/TIA/systemic thromboembolism	14.75 (2.17–108.33)	0.005
eGFR [ml/min/1.73 m^2]	0.97 (0.92–1.02)	0.3
PFO	1.56 (0.08–11.53)	0.7
PPM	2.36 (0.31–12.95)	0.35
Former smoker	2.7 (0.35–15.13)	0.28
Non-smoker	0.94 (0.18–7.03)	0.95
LA diameter [mm]	1.11 (0.96–1.31)	0.18
LVEF (%)	0.96 (0.9–1.02)	0.18
LVEF < 50%	1.57 (0.29–7.81)	0.57
LVEF < 40%	2.7 (0.35–15.13)	0.28
CHA2DS2-VASc score [point]	1.27 (0.8–2.13)	0.33
CHA2DS2-VASc score ≥ 2	0.6 (0.11–4.54)	0.57
ACE inhibitor/ARB	0.19 (0.03–0.97)	0.06
Statin treatment	1.81 (0.36–13.29)	0.5

ACE – angiotensin converting enzyme, AFL – atrial flutter, AH – arterial hypertension, ARB – angiotensin II receptor blocker, BMI – body mass index, CHA2DS2-VASc – scale for stroke and thromboembolic risk assessment in patients with atrial fibrillation, DM – diabetes mellitus, eGFR – estimated glomerular filtration rate, HF – heart failure, HR – heart rate, LA – left atrium, LAAT – left atrial appendage thrombus, LVEF – left ventricular ejection fraction, MI – myocardial infraction, PFO – patent foramen ovale, PPM – permanent pacemaker, S/DBP – systolic/diastolic systemic blood pressure, TIA – transient ischaemic attack.

Table 4. Receiver operating characteristic (ROC) curve analysis for prediction of thrombus occurrence

Variable	AUC	95%CI (for AUC)	Ability to predict thrombus
Age	0.51	0.24–0.78	No
BMI	0.61	0.31–0.92	No
SBP	0.57	0.35–0.79	No
DBP	0.53	0.29–0.77	No
HR	0.51	0.27–0.75	No
eGFR	0.62	0.35–0.88	No
LA diameter	0.69	0.54–0.83	Yes
LVEF	0.6	0.35–0.84	No
CHA2DS2-VASc	0.6	0.3–0.89	No

AFL – atrial flutter, AUC – the area under the ROC curve, BMI – body mass index, CHA2DS2-VASc – scale for stroke and thromboembolic risk assessment in patients with atrial fibrillation, eGFR – estimated glomerular filtration rate, HR – heart rate, LA – left atrium, LVEF – left ventricular ejection fraction, S/DBP – systolic/diastolic systemic blood pressure.

OAC might not serve as a real indicator of the inadequacy of oral anticoagulant therapy.

To the best of our knowledge, this is the first report on the prevalence of LAAT, its predictive factors, and the possible risk of stroke, thromboembolic events, and death associated with this pathology in patients referred for DCC on chronic anticoagulation.

Our study has several limitations. First, the sample size was small. Even though all consecutive patients were included, the referral for DCC is rare in this group due to the increasing ablation rates. In addition, the sample size was limited by the detection of LAAT. Second, we did not examine patients on edoxaban. Third, we used the Modification of Diet in Renal Disease formula to estimate the glomerular filtration rate, which was designed for individuals with a body surface area of 1.73 m^2, and we did not calculate the body surface area; therefore, misdosing of dabigatran and rivaroxaban may have occurred. Fourth, we did not examine the total duration of OAC intake prior to study inclusion. Fifth, we did not examine the total duration of arrhythmia prior to study inclusion. Sixth, we did not calculate the LA area and volume. Seventh, we did not examine the association between the morphology of the left atrial appendage and the emptying velocities of the left atrial appendage and LAAT. Finally, a 12-month follow-up period might be too short to reveal thromboembolic complications.

Table 5. Univariate and multivariate logistic regression analysis for prediction of LAAT in patients with AFL on chronic anticoagulation

Variable	Crude OR	*P*-value	Sex- and age- adjusted OR	*P*-value
LA diameter ≥ 45 mm	7.29 (1.15–141.94)	0.07	7.09 (1.1–139.36)	0.08

AFL – atrial flutter, LA – left atrium, LAAT – left atrial appendage thrombus.

Conclusions

In patients on OAC an unexpectedly high prevalence of LAAT was observed. History of stroke/transient ischaemic attack/thromboembolic event could be used to predict the LAAT presence. No deaths, strokes, or systemic thromboembolic events occurred during the follow-up period.

Conflict of interest

The authors declare no conflict of interest.

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