

Safety of transesophageal echocardiography-guided electrical cardioversion in patients with atrial fibrillation and inadequate anticoagulation

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KEY WORDS

anticoagulation, electrical cardioversion, spontaneous echo contrast, thrombus, transesophageal echocardiography

ABSTRACT

INTRODUCTION Restoring sinus rhythm in patients with atrial fibrillation (AF)/atrial flutter (AFI) requires adequate oral anticoagulation prior to direct current cardioversion (DCC). Some patients eligible for DCC are not properly anticoagulated.

OBJECTIVES The aim of the study was to assess risk factors for thrombus and spontaneous echo contrast (SEC) in the left atrium (LA) as well as the safety profile of transesophageal echocardiography (TEE)-guided DCC in patients with inadequate anticoagulation.

PATIENTS AND METHODS From the cohort of 316 patients admitted for DCC, 139 patients (mean [SD] age, 63.4 [11.5] years) had inadequate anticoagulation; 91 patients were admitted urgently for acute coronary syndrome, heart failure (HF), or poor tolerance of arrhythmia. The mean (SD) CHA₂DS₂-VASc score was 3.0 (1.7).

RESULTS TEE revealed a left atrial appendage (LAA) thrombus in 16 patients (11.5%), and SEC in the LA in 63 patients (45.3%). In a univariate analysis, LAA thrombus was more common in patients after myocardial infarction (odds ratio [OR], 3.92; 95% CI, 1.34–11.48; $P = 0.009$), while SEC in the LA was more common in patients with HF (OR, 2.23; 95% CI, 1.1–4.53; $P = 0.02$) and left ventricular ejection fraction of less than 40% (OR, 3.65; 95% CI, 1.66–8.06; $P = 0.001$). In a multivariate model, the most powerful SEC-predicting factor was the LA size exceeding 45 mm (OR, 3.08; 95% CI, 1.3–7.29). DCC was performed in 105 patients. No complications of TEE or DCC were observed.

CONCLUSIONS AF/AFI inadequately treated with oral anticoagulation predisposes to thrombus formation and SEC in the LA. Once thrombus is excluded, DCC is a safe procedure. There were no predictors of LAA thrombus; therefore, TEE before DCC should be performed in all patients with AF/AFI in accordance with the guidelines.

INTRODUCTION Restoration of sinus rhythm in patients with atrial fibrillation (AF) or atrial flutter (AFI) requires proper anticoagulation prior to direct current cardioversion (DCC) due to the increased risk of thromboembolic complications, including stroke.^{1,2} The European Society of Cardiology guidelines concerning the preparation of patients with nonvalvular AF for DCC recommend

the use of new oral anticoagulants (NOACs; dabigatran, rivaroxaban, apixaban, and edoxaban), to be taken for 3 weeks prior to cardioversion, just as in the case of vitamin K antagonists (VKAs).

In clinical practice, a significant number of patients admitted to undergo DCC are not properly treated with oral anticoagulants (OACs).^{3,4} Scheduled patients have a nontherapeutic level of

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international normalized ratio (INR) when using VKA before hospitalization or they do not take 1 or more doses of NOACs. The second group consists of patients admitted urgently due to hemodynamic deterioration: with heart failure (HF), acute coronary syndrome (ACS), or poor tolerance of arrhythmia. In these cases, it is often difficult to determine the exact duration of arrhythmia as these patients do not use anticoagulation or the efficacy of the treatment is uncertain. This group of patients also has the highest risk of thrombus in the left atrial appendage (LAA).^{5,6} In such situations, when it is necessary to treat the patient with DCC, it is recommended to perform transesophageal echocardiography (TEE).⁷ It has been documented that a reduction in the duration of OAC treatment by performing TEE and, in the absence of contraindications, DCC on the same day may improve the clinical status and well-being of the patients, as well as reduce the duration of hospital stay and the number of complications.⁸⁻¹¹

There have been few studies assessing the value of TEE in patients with inadequate or irregular anticoagulation. Moreover, there are scarce data on patients admitted urgently due to hemodynamic deterioration resulting from poorly tolerated AF.^{12,13} DCC performed to achieve hemodynamic stability without prior TEE may lead to thromboembolic complications.

The aim of this study was to evaluate the risk factors for spontaneous echo contrast (SEC) in the left atrium (LA) and the presence of thrombus in the LAA on TEE in patients with AF or AFL. We included patients who were admitted to the hospital to undergo DCC and who had an inadequate anticoagulation prior to hospitalization. In addition, the safety of DCC in elective and urgently admitted patients was evaluated.

PATIENTS AND METHODS This was a retrospective study involving patients with persistent AF/AFL who underwent TEE prior to DCC. The inclusion criteria were the absence or inadequacy of anticoagulation in the 3 weeks prior to cardioversion (omission of 1 or more doses of NOACs or a documented INR of less than 2 during the 3 to 4 weeks preceding the scheduled DCC). The study included patients admitted for elective DCC as well as for urgent reasons such as poorly tolerated symptoms of arrhythmia (palpitations, fainting, weakness), ACS, or HF exacerbation. ACS was diagnosed on the basis of clinical evaluation, electrocardiography, and cardiac troponin levels. The diagnosis of HF exacerbation was based on previous medical history, clinical presentation, laboratory results (N-terminal pro-B-type natriuretic peptide levels), and transthoracic echocardiography (TTE). In all patients, the risk of thromboembolic complications was estimated with the CHA₂DS₂-VASc score on admission to the hospital.⁷ TEE was performed in the fasting state on the same day as DCC. In the case of a suspected or evident thrombus, DCC

was postponed for a minimum of 3 weeks. All patients gave their written informed consent to undergo both TEE and DCC under a short general anesthesia.

The study exclusion criteria were as follows: age <18 years, valvular heart disease, contraindications to undergo DCC (eg, LAA thrombus, stroke, pulmonary edema) or TEE (eg, esophageal disease), contraindications to anticoagulation, and the lack of the patient's informed consent.

Prior to DCC, every patient was administered unfractionated or low-molecular-weight heparin at therapeutic doses. Cardioversion was performed with biphasic defibrillator under a short general anesthesia (fentanyl/propofol).

The effectiveness of DCC was determined on the basis of sinus rhythm restoration immediately after cardioversion and on the day of hospital discharge. The safety of DCC was assessed on the basis of the following endpoints: stroke, transient ischemic attack (TIA), symptomatic systemic embolic event, and death. The study was positively assessed by the Bioethics Committee of the Poznan University of Medical Sciences, Poznań, Poland.

Echocardiographic examination TTE and TEE were performed using a Vivid 9 device (General Electric Healthcare, General Electric Healthcare, Horten, Norway). In TTE, we evaluated the basic dimensions of the left ventricle (LV, in diastole) and LA (in systole), aortic dimensions, blood flow through the valves, and LV ejection fraction (LVEF). A TEE multiplane transducer was used. The study evaluated the presence of a thrombus in the LAA and SEC in both LA and LAA. Blood clots were identified as a circular or irregular mass inside or in the lumen of the LA, not being a part of the endocardium or pectinate muscles. SEC was defined as a smoke-like echo with a characteristic motion during the cardiac cycle.¹⁴⁻¹⁶ The presence of a thrombus in the LA/LAA was a contraindication to DCC, while in the case of the SEC, the decision was made after consultation with other cardiologists.

Statistical analysis A statistical analysis was performed using STATISTICA ver. 12 (StatSoft Inc., 1984–2014, Tulsa, Oklahoma, United States). Qualitative variables were presented as percentage, and quantitative ones—as the arithmetic mean and standard deviation (SD) for normal distribution and median for nonnormal distribution. The Mann–Whitney test was used to compare the 2 groups in a nominal scale and an interval scale in the absence of normality. More than 2 groups were compared using the Kruskal–Wallis test with the post-hoc Dunn test. The χ^2 test of independence was used for the nominal scale. To evaluate the risk of LAA thrombus and SEC, the logistic regression model was used in a univariate analysis and a stepwise backward regression model in a multivariate analysis. To determine the relationship between the mode

TABLE 1 Clinical characteristics of the study group

Parameter	Value
Type of arrhythmia	
Atrial fibrillation	103 (74.1)
Atrial flutter	36 (25.9)
Duration of arrhythmia	
≤48 hours	9
>48 hours	97
>30 days	21
Indefinite	12
Concomitant disorders	
HF	50 (35.9)
NYHA class on admission, n = 50, mean (SD)	2.6 (0.7)
Hypertension	99 (71.2)
Type 2 diabetes	31 (22.3)
Previous stroke/TIA	19 (13.6)
Previous MI	33 (23.7)
Previous CABG/PCI	34 (24.4)
CKD	9 (6.4)
COPD	11 (7.9)
Echocardiographic data	
LA, mm, mean (SD)	44.7 (6.0)
LVEDd, mm, mean (SD)	54.2 (8.7)
LVEF, %, mean (SD)	43.9 (14.6)
LVEF <40%	40 (32.5)

Data are presented as number (percentage) of patients unless otherwise indicated.

Abbreviations: CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HF, heart failure; LA, left atrium; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; TIA, transient ischemic attack

TABLE 2 Reason for hospital admission and performing transesophageal echocardiography of the left atrium

Reason for admission	n	LAA thrombus	SEC
Elective admission	48	3 (6)	20 (42)
Poor tolerance of arrhythmia	57	6 (11)	24 (42)
ACS	13	4 (31)	8 (62)
HF	21	3 (14)	11 (52)

Data are presented as number (percentage) of patients.

Abbreviations: ACS, acute coronary syndrome; LAA, left atrial appendage; SEC, spontaneous echo contrast; others, see [TABLE 1](#)

of admission, duration of arrhythmia, a type of anticoagulant used, and the presence of thrombus in the LAA or the SEC, the χ^2 test was used. To evaluate the prediction of thrombi and SEC on the basis of the CHA₂DS₂-VASc score, the receiver operating characteristic curve (ROC) analysis was used. A P value of less than 0.05 was considered statistically significant.

RESULTS Between the years 2011 and 2013, 316 patients with AF or AFl scheduled to undergo

DCC were admitted to the Department of Cardiology at the Poznan University of Medical Sciences. A total of 139 patients (46 women and 93 men) met the inclusion criteria; the mean (SD) age was 63.4 (11.5) years. Forty-eight patients were admitted electively, and 91 patients—urgently. The reasons for performing urgent cardioversion were poor tolerance of arrhythmia (57 patients), ACS (13 patients), and exacerbation of HF (21 patients). On admission, 83 patients (60%) were taking VKAs, 15 patients (11%) were administered NOACs, and 41 patients (29%) did not take any OACs. Aspirin (75 mg/d) was administered in 45 patients (32%), and 20 patients (14%) were on dual antiplatelet therapy (aspirin and clopidogrel, both at a dose of 75 mg/d). Four patients were on triple antithrombotic treatment (VKA, aspirin, and clopidogrel).

TEE revealed an LAA thrombus in 16 patients (11.5%) and LA SEC in 63 patients (45.3%). In 15 patients (94%), the thrombus was accompanied by SEC. Six patients with LAA thrombus were on treatment with dual antithrombotic therapy (OAC plus a single antiplatelet: aspirin or clopidogrel) before admission. Triple antithrombotic therapy (OAC, aspirin, and clopidogrel) was administered in 1 patient; single VKA, in 3 patients; single aspirin, in 1 patient; single clopidogrel, in 1 patient; and dual antiplatelet treatment (aspirin and clopidogrel), in 2 patients. Only 1 patient was on NOAC (rivaroxaban) and 1 patient was not treated with any OAC or antiplatelet agent.

The mean (SD) CHA₂DS₂-VASc score was 3.0 (1.7); 83 patients (60%) had a CHA₂DS₂-VASc score exceeding 2. The clinical characteristics of the study group are shown in [TABLE 1](#).

Reasons for hospital admission and echocardiographic image of the left atrium

More than half of the patients admitted with ACS (62%) and HF (52%) had SEC, and 30% of the patients with ACS had LAA thrombus. The LAA thrombus was twice as common in patients admitted urgently (13 of 91 patients) as in patients admitted electively (3 of 48 patients) ([TABLE 2](#)). Among patients admitted within up to 48 hours since the onset of arrhythmia, LAA thrombus was observed in 2 patients (1%) and SEC—in 4 patients (3%).

Predictors of thrombus and spontaneous echo contrast on transesophageal echocardiography

A comparison of patients with LAA thrombus and SEC with those without any LA abnormalities on TEE is presented in [TABLES 3](#) and [4](#). Only a history of myocardial infarction was significantly more frequent in patients with an LAA thrombus compared with those without thrombus. HF, a higher New York Heart Association class reduced LVEF, and enlarged LA were significantly more common in patients with LA SEC and enlarged LA were significantly more common in patients with LA SEC compared with those without any LA abnormalities.

TABLE 3 Comparison of patients with left atrial appendage thrombus and without thrombus

Parameter	LAA thrombus (n = 16)	No thrombus (n = 123)	P value
Age, y, mean (SD)	68.6 (10.6)	62.7 (11.4)	0.1
CHA ₂ DS ₂ -VASc score, mean (SD)	3.8 (2.0)	2.9 (1.7)	0.08
HF, n (%)	8 (50)	42 (34.2)	0.2
NYHA class, n = 50, mean (SD)	2.9 (0.6)	2.5 (0.7)	0.2
Hypertension, n (%)	11 (68.8)	88 (71.5)	0.95
Type 2 diabetes, n (%)	5 (31.2)	26 (21.1)	0.6
Female sex, n (%)	4 (25.0)	41 (33.3)	0.5
Previous stroke/TIA, n (%)	3 (18.8)	16 (13.0)	0.8
Previous MI, n (%)	8 (50.0)	25 (20.3)	0.02
Previous CABG/PCI, n (%)	7 (43.8)	27 (22.0)	0.1
COPD, n (%)	1 (6.3)	10 (8.1)	0.8
CKD, n (%)	1 (6.3)	8 (6.5)	0.6
Echocardiographic data			
LA, mm, mean (SD)	46.1 (3.7)	44.5 (6.2)	0.3
LA >45 mm, n (%)	8 (57.1)	43 (37.4)	0.2
LVEDd, mm, mean (SD)	52.7 (8.7)	54.9 (8.7)	0.5
LVEF, %, mean (SD)	41.2 (13.8)	44.3 (14.7)	0.5
LVEF <40%, n (%)	6 (46.2)	34 (30.9)	0.4

Abbreviations: see TABLES 1 and 2

TABLE 4 Comparison of patients with and without spontaneous echo contrast in the left atrium

Parameter	SEC (n = 63)	No SEC (n = 76)	P value
Age, y, mean (SD)	63.3 (11.0)	63.5 (11.9)	0.7
CHA ₂ DS ₂ -VASc score, mean (SD)	3.1 (1.8)	2.8 (1.7)	0.5
HF, n (%)	29 (46.0)	21 (27.6)	0.02
NYHA class, n = 50, mean (SD)	2.8 (0.6)	2.3 (0.7)	0.02
Hypertension, n (%)	46 (73.0)	53 (69.7)	0.8
Type 2 diabetes, n (%)	17 (26.9)	14 (18.4)	0.3
Female sex, n (%)	16 (25.4)	29 (38.2)	0.1
Previous stroke/TIA, n (%)	10 (15.9)	9 (11.8)	0.7
Previous MI, n (%)	19 (30.2)	14 (18.4)	0.2
Previous CABG/PCI, n (%)	17 (27.0)	17 (22.4)	0.7
COPD, n (%)	6 (9.5)	5 (6.6)	0.8
CKD, n (%)	3 (4.8)	6 (7.9)	0.7
Echocardiographic data			
LA, mm, mean (SD)	47.3 (5.3)	42.8 (5.8)	0.001
LA >45 mm, n (%)	32 (58.2)	25.7 (37.3)	<0.001
LVEDd, mm, mean (SD)	56.1 (9.0)	53.6 (8.3)	0.07
LVEF, %, mean (SD)	38.8 (13.9)	48.1 (13.9)	0.003
LVEF <40%, n (%)	25 (49.0)	15 (20.8)	0.02

Abbreviations: see TABLES 1 and 2

In the univariate analysis, thrombus was 4-fold more common in patients with a history of myocardial infarction (OR, 3.92; 95% CI, 1.34–11.48; $P = 0.009$). SEC in the LA was diagnosed twice more often in patients with a history of HF (OR, 2.23; 95% CI, 1.1–4.53, $P = 0.02$) and over 3-fold more often in the case of LVEF lower than 40% (OR, 3.65; 95% CI, 1.6–8.06; $P = 0.001$). Furthermore, the LA diameter exceeding 45 mm was diagnosed 4-fold more often in patients with SEC (OR, 4.03; 95% CI, 1.91–8.51; $P < 0.001$). In the multivariate analysis, the best predictor of SEC in the LA was the LA diameter exceeding 45 mm (OR, 3.08; 95% CI, 1.3–7.29). Both the ejection fraction of less than 40% and a history of HF appeared to be nonsignificant predictors (OR, 1.86; 95% CI, 0.63–5.4 for LVEF <40% and OR, 0.54; 95% CI, 0.51–3.59 for HF).

The presence of the LAA thrombus was not associated with the mode of hospital admission (elective vs urgent; $P = 0.16$), duration of arrhythmia (≤ 48 hours, >48 hours, >30 days; $n = 127$; $P = 0.56$), or the type of anticoagulation (VKA, NOAC, no OAC; $P = 0.82$). There were no correlations between LA SEC and the mode of admission ($P = 0.65$), duration of arrhythmia ($P = 0.99$), or type of anticoagulation ($P = 0.57$).

CHA₂DS₂-VASc score and the presence of spontaneous echo contrast and left atrial appendage thrombus

There were no correlations between the CHA₂DS₂-VASc score and the presence of thrombus in the LAA ($P = 0.08$) or the CHA₂DS₂-VASc score and SEC in the LA ($P = 0.53$). LAA thrombus was diagnosed in patients with at least 1 thromboembolic risk factor (CHA₂DS₂-VASc ≥ 1), and LA SEC was found in 1 man with a CHA₂DS₂-VASc of 0 (FIGURE 1). Patients with a CHA₂DS₂-VASc of 1 and LAA thrombus were men admitted urgently due to poor tolerance of arrhythmia, with hypertension (the first patient) and congestive HF (the second patient). None of them was taking OACs according to the guidelines.

There was no correlation between the mode of admission (elective vs urgent; $P = 0.47$), the type of anticoagulants taken (VKA, NOAC, no OAC; $P = 0.56$), the duration of arrhythmia (≤ 48 h, >48 h, >30 days; $P = 0.351$), and the CHA₂DS₂-VASc score.

The CHA₂DS₂-VASc score proved to be a poor predictor of thrombus or SEC (FIGURE 2A and 2B). The ROC analysis showed an area under the ROC curve (AUC) of 0.63 (95% CI, 0.55–0.71; $P = 0.09$) for thrombus and an AUC of 0.53 (95% CI, 0.45–0.62; $P = 0.52$) for SEC.

DCC was performed in 105 patients (76%). It was not performed in 16 patients with LAA thrombus, 8 patients with SEC, 6 patients with sinus restoration directly before DCC, and 3 patients due to an ablation procedure. DCC was effective in 93 patients (89% of the performed cardioversions), but in 2 patients, the sinus rhythm was restored after the second DCC (performed <24 hours after the first one). Twelve patients were discharged home with AF/AFL. The mean

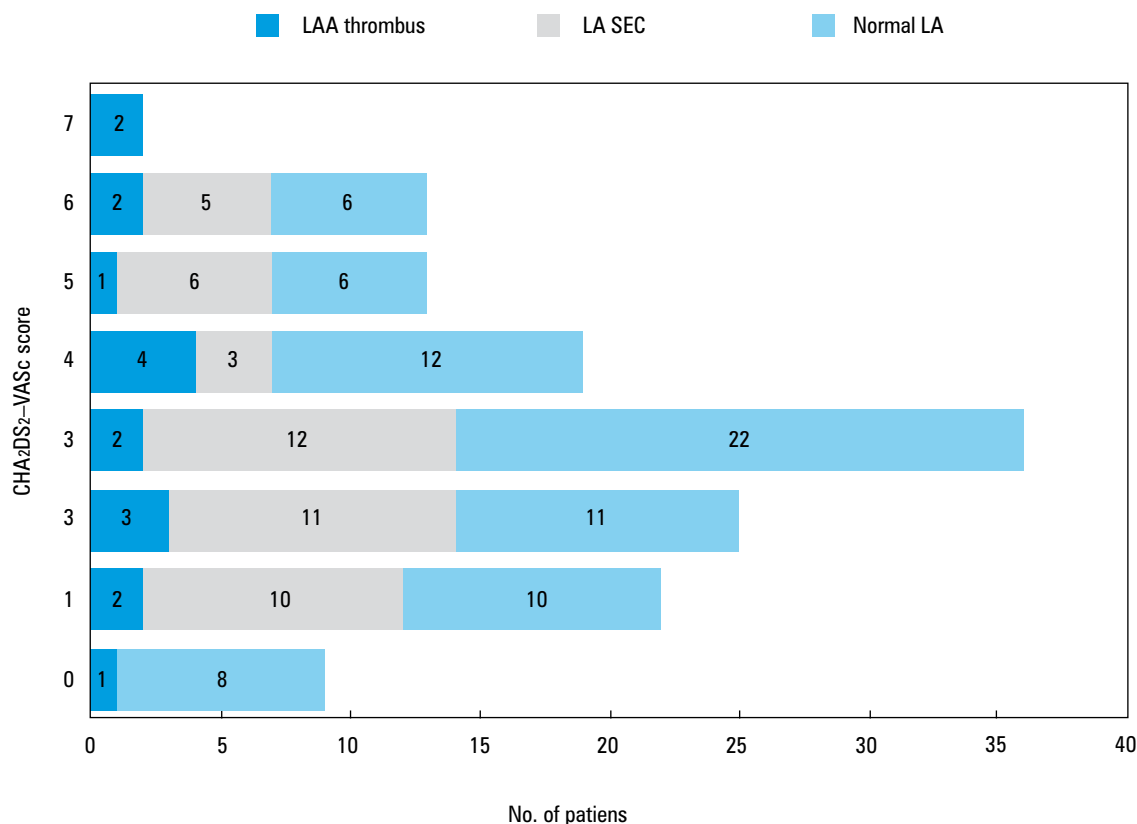


FIGURE 1 Patients with left atrial appendage (LAA) thrombus and spontaneous echo contrast (SEC) in the left atrium (LA) according to the CHA₂DS₂-VASc score

(SD) length of hospitalization was 5.6 (4.6) days (median, 4 days). No complications of TEE or DCC were reported.

DISCUSSION AF is associated with a 3.5- to 5-fold higher risk of stroke, 3-fold higher risk of congestive HF, and higher mortality.^{8,12} DCC is a recognized method for sinus rhythm restoration; however, it is associated with a risk for stroke.^{17,18} Thus, treatment with OACs is recommended prior to DCC.^{7,19} In clinical practice, it is difficult to achieve this goal within 3 weeks in a large group of patients treated with VKAs.²⁰ According to the ORBIT-AF study,²¹ only 59% of the INR results were within the therapeutic range. In the case of NOACs, the difficulty lies in the fact that there are no tests to assess the regularity of use; therefore, it requires good cooperation with the patient and the patient's compliance with the physicians recommendations. Based on the results of the RE-LY study,²² about one-fifth of the patients stopped taking dabigatran after 2 years, even though they had indications for follow-up treatment due to risk factors for stroke.

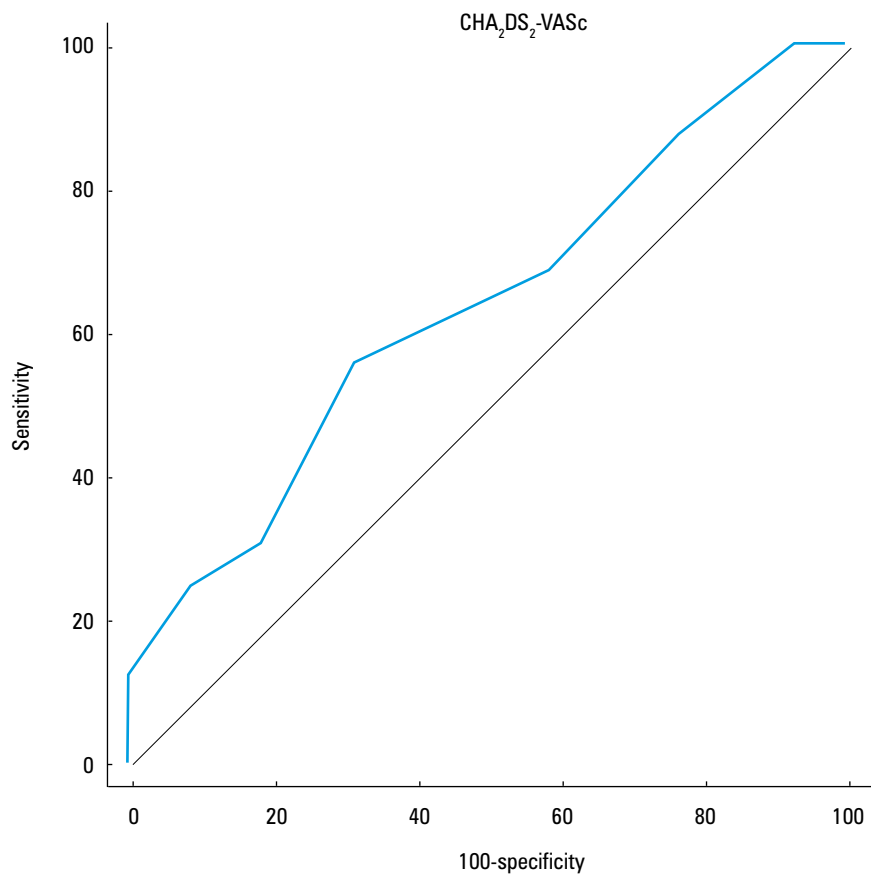
Prevalence of left atrial appendage thrombus and spontaneous echo contrast in the left atrium Echocardiographic indicators of thromboembolic risk factors (thrombus, impaired blood flow in the LA, LA SEC) are helpful in deciding about

DCC. The lack of these risk factors can reduce the time of anticoagulation prior to cardioversion.²⁰ In our study group, thrombus was reported in 11.5% of the patients, and simultaneous SEC was reported in 45.3% of the patients (in 15 of 16 patients with thrombus). Based on a meta-analysis of more than 20 000 patients who had underwent TEE prior to DCC, thrombus was found in approximately 10% of the patients with paroxysmal AF and approximately 15% of those with persistent or chronic arrhythmia.⁸ The prevalence of LAA thrombus, however, may vary considerably among populations.^{23,24} In the available literature, there are scarce data on TEE assessment of the LA in patients admitted urgently due to AF/AFL. In a study by Grewal et al,⁶ approximately 53% of the patients were hemodynamically unstable or presented symptoms of arrhythmia, and thrombus was diagnosed in 8.2% of the patients. Most studies included stable patients in whom no anticoagulation was used prior to TEE or the anticoagulation was inadequate.^{13,20,25-28}

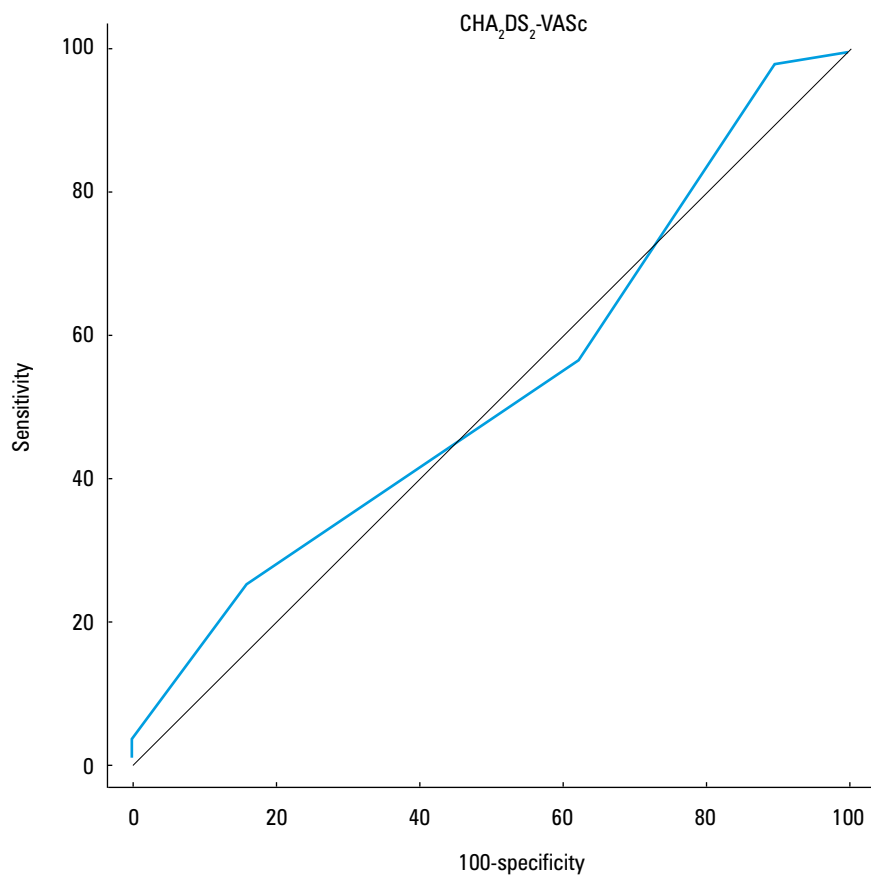
Cause of admission and the presence of thrombus in the left atrial appendage and spontaneous echo contrast in the left atrium In our study, 65% of the patients were urgently admitted to the hospital. The rate of LAA thrombus was 2-fold higher in these patients than in those admitted electively who underwent a TEE exam due to

FIGURE 2 Receiver operating characteristic curves in the evaluation of the risk of left atrial appendage thrombus (A) and spontaneous echo contrast in the left atrium (B) depending on the CHA₂DS₂-VASc score

A



B



inadequate anticoagulation (13% and 6%, respectively). Grewal et al⁶ reported that thrombus was more common in patients with poor tolerance of arrhythmia (14%) or with symptoms of HF or ACS (10.5%) compared with scheduled patients (7%).⁶ The presence of thrombus was also reported in 12% of hemodynamically stable patients in the ACUTE study.²⁰

Patients with arrhythmia lasting up to 48 hours Our results suggest that the duration of arrhythmia was not associated with an increased risk of LAA thrombus or SEC in the LA. However, TEE was performed in 9 patients with arrhythmia terminating within 48 hours. Two of these patients had thrombus in the LAA. In a study of Kleeman et al,²⁹ thrombus was found in 1.4% of the patients and SEC in 35% of hemodynamically stable patients with arrhythmia lasting no more than 48 hours. However, thrombus was found in only 4% of patients who had never been treated with OACs prior to admission (37% of the study group).²⁹ These results suggest that each patient should be treated individually, and despite a relatively short duration of arrhythmia (≤ 48 hours), the implemented procedures should depend on the clinical situation and the patient's condition.

Factors affecting the occurrence of thrombus in the left atrial appendage and spontaneous echo contrast in the left atrium In our study, patients with thrombus in the LAA more frequently suffered from diabetes, stroke, or TIA. These patients were older, had symptoms of HF, were in a higher NYHA class, and presented a higher CHA₂DS₂-VASc score. Interestingly, 7 of 16 patients with an LAA thrombus were on at least dual antithrombotic therapy (VKA plus aspirin or clopidogrel). It is probably due to the fact that 62% of the patients with LAA thrombus had myocardial infarction in the past. Moreover, they had lower LVEF and an enlarged LA on TTE. However, the only predictor of LAA thrombus was a history of myocardial infarction. The predictors of SEC included a previously diagnosed HF, LVEF of less than 40%, and an enlarged LA.

A reduced LVEF of less than 35% or less than 40% and an LA diameter enlarged to 45 mm or more were more frequently reported in patients with LAA thrombus and SEC.²⁹⁻³² Moderate or severe LV dysfunction is known to be an independent predictor of stroke¹⁰; moreover, HF and low LVEF are negative predictors of LA thrombus resolution in patients with nonvalvular AF.³³ Providencia et al²⁵ reported that the independent predictors of LAA thrombus in 180 patients were positive troponin levels and enlarged LA (indexed left atrial volume > 60.0 ml/m²).²⁵ In other studies, thrombus predictors included older age, female sex, hypertension, diabetes, chronic HF, and higher CHA₂DS₂ and CHA₂DS₂-VASc scores associated with these factors.^{8,34}

CHA₂DS₂-VASc score and the presence of thrombus in the left atrial appendage and spontaneous echo contrast in the left atrium The CHADS₂ and CHA₂DS₂-VASc scores are used to assess thromboembolic risk. An increased score is associated with more frequent detection of LAA thrombus and SEC in the LA as well as thromboembolic events.^{28,30,32} In our study, there was no relationship between the CHA₂DS₂-VASc score and the risk of thrombus or SEC. However, LAA thrombus and SEC in the LA were found in 2 patients with a CHA₂DS₂-VASc score of 7.

On the other hand, in patients with no thrombotic risk factors (CHA₂DS₂-VASc = 0; 9 patients) 1 patient was diagnosed with SEC. LAA thrombus was also found in 2 male patients (12.5% of all thrombi) with a CHA₂DS₂-VASc score of 1. Pawanat et al³⁰ analyzed mainly patients at low risk of stroke (80% of patients presented a CHA₂DS₂ of 1 or lower) admitted for AF ablation. SEC and thrombus in the LA were reported in 0.6% and 1.6% of the patients, respectively (of a total of 1058 patients). No thrombi in the LAA were found in patients with a CHA₂DS₂ score of 0.³⁰

In a study by Rader et al³¹ analyzing a group of patients admitted for DCC, thrombi in the LAA were found in 3% and SEC in 24% of the patients with a CHA₂DS₂ score of 0. In this study, in patients with a CHA₂DS₂ score of 2 or higher, thrombi were observed in 13% and SEC in at least 44% of the patients.³¹

In a multivariate analysis, Wysokiński et al³⁴ found that the CHADS₂ score was a predictor of thrombus in the LAA.³⁴ However, when analyzing individual components, only some parameters of this scale (HF, history of stroke/TIA, diabetes), as well as chronic AF, duration of arrhythmia, and the presence of SEC were found to be independent risk factors for thrombus. This model was characterized by high diagnostic power (AUC, 0.90). The above results confirm the validity of recommendations for DCC and a mandatory 3-week preparation period or the need to perform TEE before cardioversion. The current European Society of Cardiology guidelines clarify how to proceed with patients at a low risk of thromboembolic complications. Only the CHA₂DS₂-VASc score (not CHA₂DS₂) is recommended for assessing the risk of stroke in patients with nonvalvular AF. OAC is recommended for all men with a CHA₂DS₂-VASc score of 2 or higher and for all women with a score of 3 or higher. In the case of men with a CHA₂DS₂-VASc score of 1 or women with a CHA₂DS₂-VASc of 2, OAC should be considered depending on the individual characteristics of the patient and his or her preferences.⁷

Limitations Our study has a number of limitations. First, we did not use any specific tests to verify patient's compliance, test cognitive function, or monitor drug administration. It was a retrospective study and we did not have detailed data on the long-term history of the first and recurrent episodes of AF. We decided not to include these factors

into analysis. Secondly, in our patients, the TEE exams were performed by 2 experienced specialists. In doubtful cases, the third expert in the field was consulted. In fact, misinterpretation was possible. Due to the retrospective design of the study, we were not able to conduct inter- and intraobserver variability analysis as well as a 4-week follow-up of the patients. Moreover, patients who were not properly anticoagulated with NOACs (irrespective of the amount of missed medications) were classified as requiring TEE. We have no data on the number of missed drug doses.

Conclusions Persistent AF and AFL untreated or treated ineffectively with OACs predispose to thrombus formation in the LAA and SEC in the LA. In patients inadequately anticoagulated who require urgent DCC, the CHA₂DS₂-VASc score may be insufficient to determine the risk of thrombus. Thrombus occurs much more frequently in patients admitted urgently because of ACS or decompensated HF than in elective patients with inadequate anticoagulation before planned DCC. In patients admitted urgently, thrombus was observed despite the short duration of arrhythmia (≤ 48 hours). History of myocardial infarction is a predictor of thrombus in the LAA, and HF, decreased LVEF ($< 40\%$), and enlarged LA (> 45 mm) are predictors of SEC in the LA. TEE performed in this group of patients ensures the safety of cardioversion.

Contribution statement AB designed the study, collected the data, discussed the results, and coordinated funding for the study. JZ collected the data, performed statistical analysis, and wrote the manuscript. MM performed statistical analysis. KK, RSZ, and JK collected the data. RD and MM collected the data and discussed the results. AN, PK, and ASZ discussed the results. All authors contributed to the interpretation of the data, reviewed the manuscript, and approved the final version of the manuscript before submission.

REFERENCES

- 1 Fatkin D, Kuchar DL, Thorburn CW, et al. Transesophageal echocardiography before and during direct current cardioversion of atrial fibrillation: evidence for "atrial stunning" as a mechanism of thromboembolic complications. *J Am Coll Cardiol.* 1994; 23: 307-316.
- 2 Grimm RA, Stewart WJ, Black IW, et al. Should all patients undergo transesophageal echocardiography before electrical cardioversion of atrial fibrillation? *J Am Coll Cardiol.* 1994; 23: 533-541.
- 3 Bungard TJ, Ackman ML, Ho G, et al. Adequacy of anticoagulation in patients with atrial fibrillation coming to a hospital. *Pharmacotherapy.* 2000; 20: 1060-1065.
- 4 Choi EJ, Lee IH, Je NK. Inadequate stroke prevention in Korean atrial fibrillation patients in the post-warfarin era. *Int J Cardiol.* 2016; 220: 647-52.
- 5 Shen X, Li H, Rovang K, et al. Prevalence of intra-atrial thrombi in atrial fibrillation patients with subtherapeutic international normalized ratios while taking conventional anticoagulation. *Am J Cardiol.* 2002; 90: 660-662.
- 6 Grewal GK, Klosterman TB, Shrestha K, et al. Indications for TEE before cardioversion for atrial fibrillation: implications for appropriateness criteria. *JACC Cardiovasc Imaging.* 2012; 5: 641-648.
- 7 Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS: The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *Eur Heart J.* 2016; 37: 2893-2962.
- 8 Di Minno MN, Ambrosino P, Dello Russo A, et al. Prevalence of left atrial thrombus in patients with non-valvular atrial fibrillation. A systematic review and meta-analysis of the literature. *Thromb Haemost.* 2016; 115: 663-677.

- 9 Lip GY, Halperin JL. Improving stroke risk stratification in atrial fibrillation. *Am J Med.* 2010; 123: 484-488.
- 10 Atrial Fibrillation Investigators. Echocardiographic predictors of stroke in patients with atrial fibrillation: a prospective study of 1066 patients from 3 clinical trials. *Arch Intern Med.* 1998; 158: 1316-1320.
- 11 Wyse DG, Anter E, Callans DJ. Cardioversion of atrial fibrillation for maintenance of sinus rhythm: a road to nowhere. *Circulation.* 2009; 120: 1444-1452.
- 12 Camm AJ, Lip GY, De Caterina R, et al. ESC Committee for Practice Guidelines. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J.* 2012; 33: 2719-2747.
- 13 Takashima S, Nakagawa K, Hirai T, et al. Transesophageal echocardiographic findings are independent and relevant predictors of ischemic stroke in patients with nonvalvular atrial fibrillation. *J Clin Neurol.* 2012; 8: 170-176.
- 14 Fatkin D, Kelly RP, Feneley MP. Relations between left atrial appendage blood flow velocity, spontaneous echocardiographic contrast and thromboembolic risk in vivo. *J Am Coll Cardiol.* 1994; 23: 961-969.
- 15 Wazni OM, Tsao HM, Chen SA, et al. Cardiovascular imaging in the management of atrial fibrillation. *J Am Coll Cardiol.* 2006; 48: 2077-2084.
- 16 Aschenberg W, Schlüter M, Kremer P, et al. Transesophageal two-dimensional echocardiography for the detection of left atrial appendage thrombus. *J Am Coll Cardiol.* 1986; 7: 163-166.
- 17 Airaksinen KE, Grönberg T, Nuotio I, et al. Thromboembolic complications after cardioversion of acute atrial fibrillation: the FinCV (Finnish Cardio-Version) study. *J Am Coll Cardiol.* 2013; 62: 1187-1192.
- 18 Stein B, Halperin JL, Fuster V. Should patients with atrial fibrillation be anticoagulated prior to and chronically following cardioversion? *Cardiovasc Clin.* 1990; 21: 231-247.
- 19 Hansen ML, Jepsen RM, Olesen JB, et al. Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy. 2015; 17: 18-23.
- 20 Klein AL, Grimm RA, Murray RD, et al. Use of transesophageal echocardiography to guide cardioversion in patients with atrial fibrillation. *N Engl J Med.* 2001; 343: 1411-1420.
- 21 Pokorney SD, Simon DN, Thomas L, et al. Patients' time in therapeutic range on warfarin among US patients with atrial fibrillation: Results from ORBIT-AF registry. *Am Heart J.* 2015; 170: 141-148.
- 22 Connolly SJ, Wallentin L, Ezekowitz MD, et al. The Long-Term Multi-center Observational Study of Dabigatran Treatment in Patients With Atrial Fibrillation (RELY-ABLE) Study. *Circulation.* 2013; 128: 237-243.
- 23 Scherr D, Dalal D, Chilukuri K, et al. Incidence and predictors of left atrial thrombus prior to catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol.* 2009; 20: 379-384.
- 24 Bozdemir V, Kirmli O, Akdeniz B, et al. The association of beta-fibrinogen 455 G/A gene polymorphism with left atrial thrombus and severe spontaneous echo contrast in atrial fibrillation. *Anadolu Kardiyo Derg.* 2010; 10: 209-215.
- 25 Providência R, Faustino A, Paiva L, et al. Cardioversion safety in patients with nonvalvular atrial fibrillation: which patients can be spared transesophageal echocardiography? *Blood Coagul Fibrinolysis.* 2012; 23: 597-602.
- 26 Yarmohammadi H, Klosterman T, Grewal G, et al. Transesophageal echocardiography and cardioversion trends in patients with atrial fibrillation: a 10-year survey. *J Am Soc Echocardiogr.* 2012; 25: 962-968.
- 27 Corrado G, Beretta S, Sormani L, et al. Prevalence of atrial thrombi in patients with atrial fibrillation/flutter and subtherapeutic anticoagulation prior to cardioversion. *Eur J Echocardiogr.* 2004; 5: 257-261.
- 28 Sikorska A, Baran J, Pilichowska-Paszkiel E, et al. Risk of left atrial appendage thrombus in patients scheduled for ablation for atrial fibrillation: beyond the CHA₂DS₂-VASc score. *Pol Arch Med Wewn.* 2015; 125: 921-928.
- 29 Kleemann T, Becker T, Strauss M, et al. Prevalence of left atrial thrombus and dense spontaneous echo contrast in patients with short-term atrial fibrillation < 48 hours undergoing cardioversion: value of transesophageal echocardiography to guide cardioversion. *J Am Soc Echocardiogr.* 2009; 22: 1403-1408.
- 30 Puwanant S, Varr BC, Shrestha K, et al. Role of the CHADS₂ score in the evaluation of thromboembolic risk in patients with atrial fibrillation undergoing transesophageal echocardiography before pulmonary vein isolation. *J Am Coll Cardiol.* 2009; 54: 2032-2039.
- 31 Rader VJ, Khumri TM, Idupulapati M, et al. Clinical predictors of left atrial thrombus and spontaneous echocardiographic contrast in patients with atrial fibrillation. *J Am Soc Echocardiogr.* 2007; 20: 1181-1185.
- 32 Zhang E, Liu T, Li Z, et al. High CHA₂DS₂-VASc score predicts left atrial thrombus or spontaneous echo contrast detected by transesophageal echocardiography. *Int J Cardiol.* 2015; 184: 540-542.
- 33 Kowalczyk E, Kasprzak JD, Lipiec P. Heart failure as an independent predictor of thrombus persistence in nonvalvular atrial fibrillation: a transesophageal echocardiography-based study. *Pol Arch Med Wewn.* 2015; 125: 358-362.
- 34 Wysokinski WE, Ammash N, Sobande F, et al. Predicting left atrial thrombi in atrial fibrillation. *Am Heart J.* 2010; 159: 665-671.