



ORIGINAL ARTICLE

DOI: 10.5603/CJ.a2021.0010 Copyright © 2021 Via Medica ISSN 1897-5593 eISSN 1898-018X

Elective cardioversion of atrial fibrillation is safe without transesophageal echocardiography in patients treated with non-vitamin K antagonist oral anticoagulants: Multicenter experience

Iwona Gorczyca^{1, 2}, Beata Uziębło-Życzkowska³, Anna Szpotowicz⁴, Magdalena Chrapek⁵, Paweł Krzesiński³, Bernadetta Bielecka¹, Agnieszka Woronowicz-Chróściel¹, Paweł Wałek¹, Małgorzata Krzciuk⁴, Beata Wożakowska-Kapłon^{1, 2}

¹1st Clinic of Cardiology and Electrotherapy, Swietokrzyskie Cardiology Center, Kielce, Poland
²Collegium Medicum, The Jan Kochanowski University, Kielce, Poland
³Department of Cardiology and Internal Diseases, Military Institute of Medicine, Warsaw, Poland
⁴Department of Cardiology, District Hospital, Ostrowiec Swietokrzyski, Poland
⁵Faculty of Natural Sciences, The Jan Kochanowski University, Kielce, Poland

Abstract

Background: Current guidelines recommend electrical cardioversion (ECV) in patients with atrial fibrillation (AF) after at least 3 weeks of adequate non-vitamin K antagonist oral anticoagulant (NOAC) treatment without prior transesophageal echocardiography (TEE). However, in clinical practice in some centres, TEE is performed before ECV in patients with AF. The aim of the study was to evaluate prevalence of thromboembolic and hemorrhagic complications in patients with AF treated with NOACs and undergoing ECV without prior TEE.

Methods: This observational, multicentre study included consecutive patients with AF treated with NOACs who were admitted for ECV without prior TEE. Thromboembolic events and major bleeding complications were investigated during a 30-day follow-up.

Results: In the study group there were 611 patients, mean age was 66.3 ± 9.2 years, 40% were women. 52 (8.5%) patients had a low thromboembolic risk, 148 (24.2%) patients had an intermediate thromboembolic risk and 411 (67.2%) patients had a high thromboembolic risk. In the study group 253 (41.4%) patients were treated with rivaroxaban, 252 (41.2%) patients were treated with abigatran and 106 (17.3%) patients were treated with apixaban. Reduced doses of NOACs were administered to 113 (18.9%) patients. In the entire study group, there were no thromboembolic events or major bleeding complications during the in-hospital stay and the 30-day follow-up.

Conclusions: In this "real-world" study of AF patients treated with NOACs, it was proved that ECV is safe without a preceding TEE, regardless of the risk of thromboembolic complications and of the type of NOAC used. (Cardiol J)

Key words: atrial fibrillation, electrical cardioversion, non-vitamin K antagonist oral anticoagulant, thrombus, transesophageal echocardiography

Address for correspondence: Beata Uziębło-Życzkowska, MD, PhD, Department of Cardiology and Internal Diseases, Military Institute of Medicine, ul. Szaserów 128, 04–141 Warszawa 44, Poland, tel: +48 608442670, e-mail: buzieblo-zyczkowska@wim.mil.pl

Received: 1.09.2020 Accepted: 17.01.2021 Early publication date: 5.02.2021

This article is available in open access under Creative Common Attribution-Non-Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) license, allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.

Introduction

Electrical cardioversion (ECV) is an integral part of the management of patients with atrial fibrillation (AF) who require a rhythm control strategy [1]. This procedure is available and s to perform, however, it requires an appropriate qualification of patients and their proper preparation. Although ECV is considered safe in general, it is associated with an increased risk of thromboembolic events. The risk of peri-cardioversion thromboembolic event is between 1.1% and 2% in patients not or insufficiently anticoagulated and between 0.28% and 0.8% in patients sufficiently anticoagulated [2–4]. According to the current AF guidelines, adequate oral anticoagulation is recommended for at least 3 weeks before and for a minimum of 4 weeks after ECV in patients with AF > 48 hours or of unknown duration regardless of their stroke risk profiles. Both the European and the American Society of Cardiology state that transesophageal echocardiography (TEE) is not necessary in AF patients treated regularly with non-vitamin K antagonist oral anticoagulant (NOAC) for least 3 weeks before cardioversion, but it is an alternative to pre-procedural anticoagulation [1, 5]. Secondary analyses from the landmark NOAC trials, as well as prospective randomized trials evaluating NOACs for cardioversion, have found NOACs safe in patients with AF undergoing cardioversion [6–12]. There are limited data on post cardioversion outcomes of patients treated with NOACs (especially in the group without TEE before ECV) in clinical practice outside clinical trials. The aim of the study was to evaluate prevalence of thromboembolic and hemorrhagic complications in patients with AF treated with NOACs and undergoing ECV without prior TEE.

Methods

Study design and participants

This multicenter, observational study included patients with AF from three cardiology centers — an academic one, a military hospital and a regional hospital. The data were collected from January 2013 to December 2019. All consecutive adult patients with non-valvular AF treated with NOACs who underwent ECV were enrolled in the study. Exclusion criteria were TEE prior to ECV or moderate or severe mitral valve stenosis.

In the presented study based on the results of the hospital registry, patients with AF treated with NOACs before ECV were evaluated. During the study period, 1321 patients with AF treated with

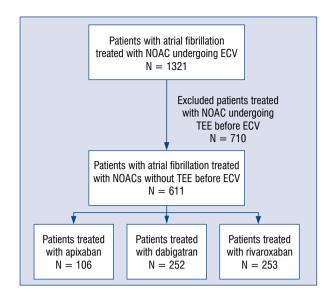


Figure 1. Flow chart of the study; ECV — electrical cardioversion, NOAC — non-vitamin K antagonist oral anticoagulant, TEE — transesophageal echocardiography.

NOACs before ECV were included. After applying the exclusion criteria described above, a total of 611 patients were included in the study (Fig. 1).

The study was approved by the ethics committees of each institution. The Bioethical Commission waived the requirement of obtaining patients' informed consent.

Assessment data

Investigators collected retrospectively baseline characteristics regarding demographics, medical history, type of AF, diagnostic test results and pharmacotherapy.

Thromboembolic risk was defined according to CHA₂DS₂-VASc (Congestive Heart Failure, Hypertension, Age ≥ 75 years, Diabetes Mellitus, Stroke/Transient Ischemic Attack, Vascular Disease, Age 65–74 years, Sex Category) score.

Vascular disease was defined as angiographically significant coronary artery disease, previous myocardial infarction, peripheral arterial disease or aortic plaque.

According to CHA_2DS_2 -VASc score, low thromboembolic risk patients were classed as having a score of 0 (1 in women), intermediate thromboembolic risk patients as having a score of 1 (2 in women), and high thromboembolic risk patients as having score \geq 2 (\geq 3 in women).

Patients were divided into three groups according to the AF type (paroxysmal, persistent, and permanent AF) based on a careful and thorough

analysis of all available medical documentation. AF was defined as permanent in patients whose ECVs were ineffective and another ECVs were not planned.

The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease Study equation.

Management of anticoagulation therapy

All patients received NOACs (apixaban, dabigatran, or rivaroxaban) for at least 3 weeks before ECV and all of them declared regular NOAC use.

Echocardiographic evaluation

In all the centers, transthoracic echocardiography examinations were conducted prior to the scheduled ECV in most patients. All exams were performed by certified echocardiographers (second-degree accreditation in echocardiography of the Section of Echocardiography of the Polish Cardiac Society [PCS]), using the General Electric Vivid 7 or E95 Ultrasound System (General Electric, Milwaukee, Wisconsin), the EPIQ 7 Ultrasound Machine (Philips Medical Systems, Andover, Massachusetts, USA), or the iE33 Ultrasound Machine (Philips Medical Systems, Andover, Massachusetts, USA). The analysis included the left atrial anteroposterior diameter, the left ventricular end-diastolic diameter, the left ventricular end-systolic diameter and the left ventricular ejection fraction (LVEF).

Study endpoints

The information about major bleeding and such thromboembolic events as stroke, transient ischemic attack, and systemic embolism was collected at the hospital stay and during the 30-day follow-up. The data connected with endpoint occurrence were obtained during phone visits.

Stroke was defined as a sudden onset of a new, focal neurological deficit in a location consistent with the territory of a major cerebral artery, confirmed by imaging techniques, with symptoms that persisted for at least 24 hours.

Transient ischemic attack (TIA) was classified as a brief episode of a focal neurological deficit with symptoms lasting < 24 hours.

Systemic embolism was defined as an ischemic episode with an acute vascular occlusion of the artery of an extremity or organ documented by imaging or surgery.

Major bleeding events were defined according to the criteria identified by The International Society of Thrombosis and Hemostasis which

included fatal bleeding, symptomatic bleeding in the critical area or organ (such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome), and any bleeding causing a decrease in the haemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or packed red blood cells [13].

Statistical analysis

Continuous data were described by means, standard deviations, medians and interquartile range (IQR). Categorical data were summarized by frequencies and percentages. Group comparisons were performed using the χ^2 or the Fisher exact test for categorical variables, one-way analysis of variance for normally distributed variables or the Kruskal-Wallis test for continuous, non-normally distributed variables (normality of distribution was checked with the Shapiro-Wilk test).

A two-tailed p-value < 0.05 was considered statistically significant. All statistical analyses were performed using the R software package version 3.6.2

Results

Patient characteristics

A total of 611 patients were included, with a mean age of 66.3 ± 9.2 years, 40% were women.

In the study group 508 (83.1%) patients had hypertension, 126 (20.6%) diabetes mellitus, 168 (27.5%) heart failure and 172 (28.2%) vascular disease. Hypertension, impaired renal function and vascular disorders were the most common concomitant diseases in the study group. Previous stroke/TIA/peripheral thromboembolism were noted in 82 (13.4%) patients. Mean CHA_2DS_2VASc score was 2.7 ± 1.6 . Baseline characteristics of the study population are summarized in Table 1.

In the study group 253 (41.4%) patients were treated with rivaroxaban, 252 (41.2%) patients were treated with dabigatran and 106 (17.4%) patients were treated with apixaban. The reduced dose of NOACs was administered to 113 (18.9%) patients.

Comparison between clinical characteristics of patients according to the thromboembolism risk

In the study group, 52 (8.5%) patients had a low thromboembolic risk, 148 (24.2%) patients had an intermediate thromboembolic risk and 411

Table 1. Baseline characteristics of the study group.

Variable	All patients (n = 611)
Demographic data	
Age [years]	
Mean ± SD	66.3 ± 9.2
Median (IQR)	66.0 (59.0-73.0)
< 65	275 (45%)
65–74	203 (33.2%)
≥ 75	133 (21.8%)
Female	245 (40.1%)
Clinical history	
Heart failure	168 (27.5%)
Hypertension	508 (83.1%)
Diabetes mellitus	126 (20.6%)
Stroke, TIA, peripheral thromboembolic	82 (13.4%)
Vascular disease	172 (28.2%)
Bleeding	18 (2.9%)
eGFR < 60 mL/min/1.73 m ²	218 (35.6%)
Type of AF	
Paroxysmal	96 (15.7%)
Persistent	508 (83.1%)
Permanent	7 (1.2%)
Thromboembolic risk	
CHA ₂ DS ₂ -VASc score	
Mean ± SD	2.7 ± 1.6
Median (IQR)	3 (2–4)
CHA_2DS_2 -VASc = 0 (1 in female)	52 (8.5%)
CHA_2DS_2 -VASc = 1 (2 in female)	148 (24.2%)
CHA_2DS_2 -VASc ≥ 2 (≥ 3 in female)	411 (67.3%)
CHA_2DS_2 -VASc ≥ 3 (≥ 4 in female)	320 (52.4%)
CHA_2DS_2 -VASc \geq 4 (\geq 5 in female)	188 (30.8%)
CHA_2DS_2 -VASc ≥ 5 (≥ 6 in female)	88 (14.4%)
Echocardiography data	
LVEF [%]	N = 531
Mean ± SD	53.5 ± 8.0
Median (IQR)	55.0 (50.0–60.0)
LAd [mm]	N = 530
Mean ± SD	40.3 ± 8.1
Median (IQR) LVDd [mm]	42.0 (36.0–45.0) N = 532
Mean ± SD	10 = 532 51.9 ± 6.0
Median (IQR)	52.0 (48.0 - 56.0)
LVSd [mm]	N = 401
Mean ± SD	35.3 ± 6.1
Median (IQR)	34.0 (31.0–38.0)

AF — atrial fibrillation; eGFR — estimated glomerular filtration rate; IQR — interquartile range; LAd — left atrial anteroposterior diameter; LVDd — left ventricular end-diastolic diameter; LVEF — left ventricular ejection fraction; LVSd — left ventricular end-systolic diameter; NOAC — non-vitamin K antagonist oral anticoagulant; SD — standard deviation; TIA — transient ischemic attack

(67.3%) patients had a high thromboembolic risk. Patients in the groups of low, intermediate and high risks of thromboembolic complications did not differ in terms of particular AF type prevalence. Impaired renal function most often occurred in patients with a high risk of thromboembolic complications. Apixaban, dabigatran and rivaroxaban were used with a similar incidence in particular stroke risk groups of patients. Reduced NOAC doses were most frequently used in patients with a high risk of thromboembolic complications compared with patients of intermediate and low risks of thromboembolic complications (Table 1).

Comparison between clinical characteristics of patients treated with individual NOACs

Patients treated with particular NOACs presented similar age, sex and cardiovascular risk factors. There were no significant differences in CHA_2DS_2 -VASc score. Patients on apixaban compared with patients on dabigatran or rivaroxaban had more often impaired renal function defined as eGFR < 60 mL/min/1.73 m² and more often persistent type of AF. The reduced dose of NOAC was used in 30 (28.3%) apixaban patients, 52 (20.6%) dabigatran patients, and 31 (12.3%) rivaroxaban patients (p = 0.0009). Table 2 shows characteristic details in patients treated with apixaban, dabigatran and rivaroxaban.

Study endpoints

In the entire study group, there were no thromboembolic events or major bleeding complications during the in-hospital stay or the 30-day follow-up.

Discussion

The main finding of the present study was that in AF patients treated with NOACs, there were no thromboembolic events after ECV without prior TEE. The main clinical implication is that these findings show that the ECV in AF patients treated with NOACs can be safely performed without TEE in the routine clinical practice.

Electrical cardioversion is a commonly performed procedure in patients with AF with nearly 1 in 5 patients in ORBIT-AF II registry having an ECV during the study period [14]. In accordance with the international AF guidelines, TEE is a preprocedural examination recommended as an alternative to the adequate oral anticoagulation [1, 5].

Transesophageal echocardiography is a semiinvasive procedure generally safer when conducted

Table 2. Clinical characteristics across CHA₂DS₂-VASc groups treated with non-vitamin K oral anticoagulants.

	All patients N = 611	CHA ₂ DS ₂ -VASC = 0 (1 in female) N = 52	CHA ₂ DS ₂ -VASC = 1 (2 in female) N = 148	CHA₂DS₂-VASC ≥ 2 (≥ 3 in female) N = 411	Р
Clinical history					
Age [years]					
Mean ± SD	66.3 ± 9.2	53.5 ± 4.2	58.1 ± 7.2	70.3 ± 2.8	< 0.0001
Median (IQR)	66.0 (59.0–73.0)	56.0 (49.8–61.0)	59.0 (55.0–62.0)	71.0 (65.5–76.0)	
Bleeding	18 (2.9)	0 (0)	1 (0.7)	17 (4.1)	0.0535*
eGFR < 60 mL/min/1.73 m ²	218 (35.6)	9 (17.3)	28 (18.9)	181 (44)	< 0.0001
Type of AF					0.7761
Paroxysmal	96 (15.7%)	6 (11.5%)	21 (14.2%)	69 (16.8%)	
Persistent	508 (83.1%)	46 (88.5%)	126 (85.1%)	336 (81.8%)	
Permanent	7 (1.1%)	0 (0%)	1 (0.7%)	6 (1.5%)	
Echocardiography data					
LVEF [%]	N = 531	N = 46	N = 126	N = 359	0.0015
Mean ± SD	53.5 ± 8.0	54.7 ± 7.9	55.5 ± 7.7	52.7 ± 8.0	
Median (IQR)	55.0 (50.0–60.0)	55.0 (53.0-60.0)	57.5 (52.2–60.0)	55.0 (48.0–60.0)	
LAd [mm]	N = 530	N = 46	N = 126	N = 358	0.6731
Mean ± SD	40.3 ± 8.1	40.7 ± 7.9	40.4 ± 8.4	40.2 ± 8.1	
Median (IQR)	42.0 (36.0–45.0)	42.5 (35.2–45.0)	42.0 (36.0–46.0)	41.0 (35.0–45.0)	
LVDd [mm]	N = 532	N = 46	N = 127	N = 359	0.0019
Mean ± SD	51.9 ± 6.0	50.0 ± 4.4	51.2 ± 6.1	52.4 ± 6.1	
Median (IQR)	52.0 (48.0–56.0)	50.0 (47.0-52.8)	52.0 (49.0–55.0)	53.0 (48.0–56.0)	
LVSd [mm]	N = 401	N = 38	N = 97	N = 266	0.2749
Mean ± SD	35.3 ± 6.1	33.6 ± 3.6	35.4 ± 6.0	35.5 ± 6.4	
Median (IQR)	34.0 (31.0–38.0)	34.0 (31.0–35.0)	35.0 (31.0–37.0)	34.0 (31.0–39.0)	
Anticoagulation therapy					0.8682
Apixaban	106 (17.3%)	9 (17.3%)	23 (15.5%)	74 (18%)	
Dabigatran	252 (41.2%)	17 (32.7%)	67 (45.3%)	168 (40.9%)	
Rivaroxaban	253 (41.3%)	26 (50%)	58 (39.2%)	169 (41.1%)	
Reduced dose of NOAC	113 (18.5%)	2 (3.8%)	9 (6.1%)	102 (24.8%)	< 0.0001

^{*}CHA2DS2-VASC = 0 excluded. Abbreviations — see Table 1

by an experienced physician. Nevertheless, it is time-consuming, carries patient discomfort, not readily available at all times and it is associated, although rarely, with potentially life-threatening complications [15].

Thromboemboli after ECV are considered due to embolization of already existing thrombi present in the atrium (especially in the left atrial appendage) at the time of ECV or due to the formation and subsequent embolization of de novo thrombi while the atrial function is still depressed in the first weeks after ECV [16, 17]. Therefore, performing TEE before EVC and ruling out thrombus in the

left atrium does not guarantee that emboli will not be formed after ECV.

The proportion of patients treated with NOACs, undergoing TEE prior to EVC is diversified in individual centers but high utilization of TEE before ECV these patients are still under observation to date, and may reflect a high accessibility to this imaging test but it is also a conservative approach to the safety of the procedure. TEE before ECV was performed in 41% of patients treated with rivaroxaban in X-VeRT study [18]. A post-hoc analysis of large studies has shown that 25% of patients treated with dabigatran (RE-LY) and 32% of

Table 3. Comparison of patients treated with apixaban, dabigatran and rivaroxaban in the study group.

	Apixaban group (n = 106)	Dabigatran group (n = 252)	Rivaroxaban group (n = 253)	Р
Demographic data				
Age [years]				0.9531
Mean ± SD	66.0 ± 10.0	66.2 ± 10.3	65.6 ± 10.4	
Median (IQR)	67.0 (59.0–73.0)	65.5 (59.0–74.0)	67.0 (60.0–73.0)	
Age < 65 years	48 (45.3%)	117 (30%)	110 (43.5%)	0.3707
Age 65–74 years	32 (30.2%)	76 (30%)	95 (37.5%)	
Age ≥ 75 years	26 (24.5%)	59 (23.3%)	48 (19%)	
Female	44 (41.5%)	97 (38.5%)	104 (41.1%)	0.7923
Clinical history				
Heart failure	26 (24.5%)	80 (31.6%)	62 (24.5%)	0.1433
Hypertension	84 (79.2%)	215 (85%)	209 (82.6%)	0.3587
Diabetes mellitus	26 (24.5%)	44 (17.4%)	56 (22.1%)	0.2369
Stroke, TIA, peripheral thromboembolic	13 (12.3%)	35 (13.8%)	34 (13.4%)	0.9187
Vascular disease	19 (17.9%)	68 (26.9%)	85 (33.6%)	0.0093
Bleeding	7 (6.6%)	5 (2%)	6 (2.4%)	0.0751
eGFR < 60 mL/min/1.73 m ²	45 (42.5%)	99 (39.1%)	74 (29.2%)	0.0174
Type of AF				
Paroxysmal	6 (5.7%)	45 (17.8%)	45 (17.8%)	0.0104
Persistent	99 (91.5%)	205 (81%)	204 (81%)	
Permanent	1 (1.5%)	2 (0.8%)	4 (1.6%)	
Thromboembolic risk				
CHA ₂ DS ₂ -VASc score				0.9772
Mean ± SD	2.7 ± 1.6	2.8 ± 1.7	2.7 ± 1.6	
Median (IQR)	2.0 (2.0–3.8)	3.0 (1.0–4.0)	3.0 (2.0–4.0)	
CHA_2DS_2 - $VASc = 0$	9 (8.5%)	17 (6.7%)	26 (10.3%)	0.5562
(1 in female)				
CHA_2DS_2 -VASc = 1	23 (21.7%)	67 (26.5%)	58 (22.9%)	
(2 in female)				
CHA_2DS_2 - $VASc \ge 2$	74 (69.8%)	168 (66.4%)	169 (66.8%)	
(≥ 3 in female)				
Echocardiography data				
LVEF [%]	N = 99	N = 214	N = 218	0.3456
Mean ± SD	54.6 ± 7.0	53.4 ± 7.9	53.1 ± 8.5	
Median (IQR)	56.0 (52.0–60.0)	55.0 (48.0–60.0)	55.0 (50.0–60.0)	
LAd [mm]	N = 96	N = 214	N = 220	0.0042
Mean ± SD	42.6 ± 8.3	39.5 ± 8.4	40.1 ± 7.7	
Median (IQR)	43.8 (39.8–48.0)	41.0 (35.0–45.0)	41.0 (35.0–45.0)	
LVDd [mm]	N = 98	N = 215	N = 219	0.6350
Mean ± SD	52.0 ± 4.5	52.1 ± 6.6	51.7 ± 6.0	
Median (IQR)	52.0 (48.2–55.0)	53.0 (48.5–56.0)	52.0 (48.0–55.0)	
LVSd [mm]	N = 94	N = 163	N = 144	0.4298
Mean ± SD	35.2 ± 4.4	35.5 ± 7.2	35.0 ± 5.9	
Median (IQR)	35.0 (32.0–37.0)	34.0 (31.0–38.0)	34.0 (31.0–38.0)	
Anticoagulation therapy				
Reduced dose of NOAC	30 (28.3%)	52 (20.6%)	31 (12.3%)	0.0009

Abbreviations — see Table 1

patients treated with apixaban (ARISTOTLE) had TEE performed before ECV [19, 20]. The European Heart Rhythm Association (EHRA) conducted a survey in 54 centers to examine contemporary clinical practice regarding pre-procedural diagnostic work-up in AF patients. Only 12% of centres routinely performed TEE prior to the left atrial procedures, regardless of the type or duration of AF [21].

There is growing evidence that NOACs can safely be used for stroke prevention in AF patients undergoing ECV. In the presented study no thromboembolic events or major bleeding complications were noted during the first month after ECV. There are limited data on outcomes of patients treated with NOACs undergoing ECV without prior TEE. Many studies show prognosis in AF patients post ECV but part of them had TEE performed before ECV. Geurink et al. [14] showed that TEE was performed in 24% of NOAC treated patients and the incidence of stroke/TIA was low and was the same for patients with and without TEE. Frederiksen et al. [22] showed that in the group of patients treated with NOACs and undergoing ECV one of the patients had a thromboembolic complication within a 60-day observation.

In the presented study most of the patients had a high thromboembolic risk. Results of some studies suggest that in patients with a high risk of thromboembolic complications, the risk of left atrial appendage thrombus (LAAT) is high and in these patients TEE should be performed before cardioversion. In the group of 1148 patients treated with NOACs, CHA₂DS₂-VASc score \geq 2 was an independent predictor of LAAT [23]. Barysiene et al. [24] showed that the risk of LAAT increases significantly in patients with CHA₂DS₂-VASc score \geq 5 points.

Although in the presented study most patients were of high risk of thromboembolic complications, we did not observe a high proportion of patients with significantly reduced LVEF or patients with notably extended left atrium. Extension of left atrium and reduced LVEF are acknowledged factors increasing the prevalence of LAAT. Therefore, the study group of patients who did not have TEE before ECV did not include patients with significant enlargement of left atrium or with reduced LVEF. Arguably, this fact influences the results of the study.

In the present study, what attracted attention was the high proportion of patients after past thromboembolic complications (13%). In the study of Friedriksen et al. [22] the proportion of patients

treated with NOACs undergoing ECV after a past thromboembolic complication was 9.8% and in the study of Geurink et al. [14] — 6.8%. By extension, in the present study, the group of patients undergoing ECV without prior TEE was significantly burdened with concomitant diseases, which is also confirmed by a higher than in patients from cited examinations mean CHA₂DS₂-VASc score.

In the current examination, the lowest proportion was constituted by patients treated with apixaban. Dabigatran was the first, rivaroxaban the second, and apixaban the third NOAC available in Poland, and all of them were available during the whole study period, thus probably apixaban patients were not a numerous group in the present study. Patients treated with individual NOACs did not differ in terms of thromboembolic complication risk, whereas apixaban patients were observed to have more frequent impaired renal function. Meta-analysis including 15 studies showed that the incidence of LAAT among different types of NOACs is similar [25].

The data from the present study remains in line with observational studies of other authors and are reassuring regarding the safety of NOACs for ECV in the routine clinical practice in patients without previous TEE as in the NOAC cardioversion clinical trials. However, significant discrepancies can still be observed in pre cardioversion procedures in individual centers.

Strength and limitations

The current study has some strengths. First, the multicenter nature of this study can be representative of the reality of the studied subgroup of patients in our region. What is more, the data were collected in three centers of different referential levels and in various regions of the country, which significantly influences the representative picture of the researched group of patients.

On the other hand, the presented study has some limitations. The first one is the small size of the study group (especially of apixaban treated patients). Secondly, a limitation of study lies primarily in its partly retrospective nature. A retrospective analysis does not allow one to characterize the study cohort as precisely as with a prospective trial. This obviously limits the completeness of available data. In this case, there was no information about the reason for the reduced NOAC dose. Due to the unknown duration of AF it was not possible to differentiate between persistent and long-lasting persistent AF. Also, transthoracic echocardiography was not performed in every patient in a real-life

setting and comprehensive data could not be collected. In the examination of left atrium, left atrial volume index is a referential measurement. In the presented study, only left atrial anteroposterior diameter was available. Lastly, due to a lack of outcomes, the power of the study does not allow for a reasonable estimation of differences between the patients in particular thromboembolic risk groups and between particular NOAC groups.

Conclusions

In this "real-world" study of AF patients treated with NOACs it was proved that ECV is safe without a preceding TEE regardless of the risk of thromboembolic complications and the treatment used.

Acknowledgements

Project financed under the program of the Minister of Science and Higher Education called "Regional Initiative of Excellence" in the years 2019–2022, project no. 024/RID/2018/19, amount of financing 11 999 000,00 PLN.

Conflict of interest: Iwona Gorczyca — paid lectures for Bayer, Boehringer Ingelheim, Beata Uziębło-Życzkowska — none; Anna Szpotowicz — none; Magdalena Chrapek — none; Paweł Krzesiński — none; Bernadetta Bielecka — none; Agnieszka Woronowicz-Chróściel — none; Paweł Wałek — none; Małgorzata Krzciuk — none; Beata Wożakowska-Kapłon — paid lectures for Bayer, Boehringer Ingelheim, Pfizer.

References

- Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016; 18(11): 1609–1678, doi: 10.1093/ europace/euw295, indexed in Pubmed: 27567465.
- Moreyra E, Finkelhor RS, Cebul RD. Limitations of transesophageal echocardiography in the risk assessment of patients before nonanticoagulated cardioversion from atrial fibrillation and flutter: an analysis of pooled trials. Am Heart J. 1995; 129(1):71–75, doi:10.1016/0002-8703(95)90045-4, indexed in Pubmed: 7817928.
- 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. Europace. 2015; 17(1): 18–23, doi: 10.1093/europace/euu189, indexed in Pubmed: 25231909.
- Gallagher MM, Hennessy BJ, Edvardsson N, et al. Embolic complications of direct current cardioversion of atrial arrhythmias: association with low intensity of anticoagulation at the time of cardioversion. J Am Coll Cardiol. 2002; 40(5): 926–933,

- doi: 10.1016/s0735-1097(02)02052-1, indexed in Pubmed: 12225717.
- Apostolakis S, Haeusler KG, Oeff M, et al. Low stroke risk after elective cardioversion of atrial fibrillation: an analysis of the Flec-SL trial. Int J Cardiol. 2013; 168(4): 3977–3981, doi: 10.1016/j.ijcard.2013.06.090, indexed in Pubmed: 23871349.
- Cappato R, Ezekowitz M, Klein A, et al. Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation. Eur Heart J. 2014; 35(47): 3346–3355, doi: 10.1093/eurhearti/ehu367.
- Ezekowitz MD, Pollack CV, Halperin JL, et al. Apixaban compared to heparin/vitamin K antagonist in patients with atrial fibrillation scheduled for cardioversion: the EMANATE trial. Eur Heart J. 2018; 39(32): 2959–2971, doi: 10.1093/eurheartj/ ehy148, indexed in Pubmed: 29659797.
- Goette A, Merino JL, Ezekowitz MD, et al. Edoxaban versus enoxaparin-warfarin in patients undergoing cardioversion of atrial fibrillation (ENSURE-AF): a randomised, open-label, phase 3b trial. Lancet. 2016; 388(10055): 1995–2003, doi: 10.1016/ S0140-6736(16)31474-X, indexed in Pubmed: 27590218.
- Nagarakanti R, Ezekowitz MD, Oldgren J, et al. Dabigatran versus warfarin in patients with atrial fibrillation: an analysis of patients undergoing cardioversion. Circulation. 2011; 123(2): 131–136, doi: 10.1161/CIRCULATIONAHA.110.977546, indexed in Pubmed: 21200007.
- Flaker G, Lopes RD, Al-Khatib SM, et al. Efficacy and safety
 of apixaban in patients after cardioversion for atrial fibrillation:
 insights from the ARISTOTLE Trial (Apixaban for Reduction in
 Stroke and Other Thromboembolic Events in Atrial Fibrillation).
 J Am Coll Cardiol. 2014; 63(11): 1082–1087, doi: 10.1016/j.
 jacc.2013.09.062, indexed in Pubmed: 24211508.
- Pallisgaard JL, Lindhardt TBo, Hansen ML, et al. Cardioversion and risk of adverse events with dabigatran versus warfarin: a nationwide cohort study. PLoS One. 2015; 10(10): e0141377, doi: 10.1371/journal.pone.0141377, indexed in Pubmed: 26513589.
- Itäinen S, Lehto M, Vasankari T, et al. Non-vitamin K antagonist oral anticoagulants in atrial fibrillation patients undergoing elective cardioversion. Europace. 2018; 20(4): 565–568, doi: 10.1093/europace/eux116, indexed in Pubmed: 29016758.
- Schulman S, Kearon C. Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis.
 Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients.
 J Thromb Haemost. 2005; 3(4): 692–694, doi: 10.1111/j.1538-7836.2005.01204.x, indexed in Pubmed: 15842354.
- Geurink K, Holmes D, Ezekowitz MD, et al. Patterns of oral anticoagulation use with cardioversion in clinical practice. Heart. 2020 [Epub ahead of print], doi: 10.1136/heartjnl-2019-316315, indexed in Pubmed: 32591363.
- Hilberath JN, Oakes DA, Shernan SK, et al. Safety of transesophageal echocardiography. J Am Soc Echocardiogr. 2010; 23(11): 1115–27; quiz 1220, doi: 10.1016/j.echo.2010.08.013, indexed in Pubmed: 20864313.
- Ito T, Suwa M, Otake Y, et al. Assessment of left atrial appendage function after cardioversion of atrial fibrillation: relation to left atrial mechanical function. Am Heart J. 1998; 135(6 Pt 1): 1020–1026, doi: 10.1016/s0002-8703(98)70067-5, indexed in Pubmed: 9630106.
- 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(2): 307-316, doi: 10.1016/0735-1097(94)90412-x, indexed in Pubmed: 8294679.
- Cappato R, Ezekowitz M, Klein A, et al. Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation. Eur Heart J. 2014; 35(47): 3346–3355, doi: 10.1093/eurheartj/ehu367.
- Nagarakanti R, Ezekowitz MD, Oldgren J, et al. Dabigatran versus warfarin in patients with atrial fibrillation: an analysis of patients undergoing cardioversion. Circulation. 2011;123(2):131–136, doi: 10.1161/CIRCULATIONAHA.110.977546, indexed in Pubmed: 21200007.
- Flaker G, Lopes RD, Al-Khatib SM, et al. Efficacy and safety
 of apixaban in patients after cardioversion for atrial fibrillation:
 insights from the ARISTOTLE Trial (Apixaban for Reduction in
 Stroke and Other Thromboembolic Events in Atrial Fibrillation).
 J Am Coll Cardiol. 2014; 63(11): 1082–1087, doi: 10.1016/j.
 iacc.2013.09.062. indexed in Pubmed: 24211508.
- Farkowski MM, Jubele K, Marín F, et al. Diagnosis and management of left atrial appendage thrombus in patients with atrial fibrillation undergoing cardioversion or percutaneous left atrial procedures: results of the European Heart Rhythm Association survey. Europace. 2020; 22(1): 162–169, doi: 10.1093/europace/euz257, indexed in Pubmed: 31501852.

- Frederiksen AS, Albertsen AE, Christesen AM, et al. Cardioversion of atrial fibrillation in a real-world setting: non-vitamin K antagonist oral anticoagulants ensure a fast and safe strategy compared to warfarin. Europace. 2018; 20(7): 1078–1085, doi: 10.1093/europace/eux188, indexed in Pubmed: 28655151.
- Gorczyca I, Michalska A, Chrapek M, et al. Thrombus in the left atrial appendage in patients with atrial fibrillation treated with non-vitamin K antagonist oral anticoagulants in clinical practice-A multicenter registry. J Cardiovasc Electrophysiol. 2020; 31(8): 2005–2012, doi: 10.1111/jce.14589, indexed in Pubmed: 32458520.
- Barysienė J, Žebrauskaitė A, Petrikonytė D, et al. Findings of transoesophageal echocardiogram in appropriately anticoagulated patients with persistent atrial fibrillation prior to planned cardioversion. BMC Cardiovasc Disord. 2017; 17(1): 67, doi: 10.1186/s12872-017-0503-8, indexed in Pubmed: 28228120.
- 25. Yang J, Zhang X, Wang XY, et al. Comparison of transesophageal echocardiography findings after different anticoagulation strategies in patients with atrial fibrillation: a systematic review and meta-analysis. BMC Cardiovasc Disord. 2019; 19(1): 261, doi: 10.1186/s12872-019-1209-x, indexed in Pubmed: 31771529.