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Is transesophageal echocardiography necessary before electrical cardioversion in patients treated with non-vitamin K antagonist oral anticoagulants? Current evidence and practical approach

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Abstract

According to current guidelines, non-vitamin K antagonist oral anticoagulants (NOACs) should be used at least 3 weeks before planned electrical cardioversion. In accordance with international atrial fibrillation (AF) guidelines, transesophageal echocardiography (TEE) is a pre-procedural examination recommended as an alternative to adequate oral anticoagulation. The strategy related to qualifying patients treated with NOACs for pre-procedural TEE differs in individual centers. Therefore, it is necessary to create an algorithm that will standardize estimation of left atrial appendage thrombus (LAAT) prevalence risk and thereby qualify NOAC-treated patients to TEE in the most effective way. We assessed the available studies on LAAT predictors. Risk factors for LAAT formation are not necessarily the same as the risk factors for thromboembolic events in patients with AF. The main risk factor for LAAT are as follows: previous intracardiac thrombus, irregular use of NOAC, inappropriate dose reduction of NOAC, previous stroke, CHA_2DS_2-VASc score ≥ 3 points, glomerular filtration rate < 60 mL/min/1.73 m^2, reduced left ventricular ejection fraction, or left atrial enlargement. Based on available evidence, we proposed algorithm guarantees more systematic approach to performing TEE in patients undergoing electrical cardioversion. (Cardiol J 2023; 30, 4: 646–653)

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

Introduction

Electrical cardioversion (ECV) is a procedure commonly used in atrial fibrillation (AF) patients for whom a strategy of restoring sinus rhythm was adopted. The EAST (Early treatment of Atrial fibrillation for Stroke prevention Trial) study found that early rhythm-control therapy was associated with lower risk of cardiovascular outcomes than usual care among patients with early AF and cardiovascular diseases [1]. ECV is a safe practice provided a patient is appropriately prepared and procedures minimizing risk of thromboembolic complications are introduced. In patients with AF undergoing ECV, secondary analyses from the landmark non-vitamin K antagonist oral anticoagulant (NOAC)

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trials, as well as prospective randomized trials, showed that NOACs are of similar efficacy and safety to warfarin [2–6].

Thromboembolic risk in the peri-cardioversion period

Occurrence mechanisms of thromboembolic complications in patients after ECV can be different. Thromboemboli after ECV are thought to be caused by embolization of already existing thrombi present in the left atrial appendage (LAA) at the time of ECV. In the first weeks after ECV atrial function is depressed, impairing the left atrium's ability to empty sufficiently.

This impairment could lead to formation of thrombi even if their presence had not been diagnosed before ECV [7, 8]. Therefore, performing transesophageal echocardiography (TEE) before ECV and excluding thrombus in the left atrium does not guarantee that after ECV emboli will not be formed. In the analysis of the data from 32 studies and a total number of 4621 patients, 92 patients had a thromboembolic event after ECV. Thromboembolic complications appeared from 1 to 18 days after ECV. It was shown that the vast majority of events occurred within 72 hours of ECV, 82% of thromboembolic complications appeared in 3 days, 96% in 1 week, and 98% within 10 days of ECV [9].

The results of studies to date confirm that the proportion of thromboembolic complications after ECV in patients effectively treated with anticoagulant drugs is not high. Among 1613 AF patients treated with NOACs or vitamin K antagonists (VKAs) and undergoing ECV there were no differences in the incidence of stroke or transient ischemic attack (TIA) within the first year after ECV [10]. The results of the study by Frederiksen et al. [11] involving a group of 2150 patients undergoing ECV were consistent with the results of the previous study. Thromboembolic complications were not observed in any of the patients during the 30-day follow-up period of this study, which included 668 patients treated with NOACs before ECV [12]. Also, Barysiene et al. [13] did not acknowledge thromboembolic events in the 30-day follow-up period for a group of 432 patients receiving pertinent anticoagulant therapy prior to ECV. A meta-analysis of four randomized controlled trials comparing NOAC therapy with VKA, including 4517 cardioversions, showed that the thromboembolic complication rate was 0.4% in patients treated with NOACs and 0.6% in patients treated with VKAs [14]. Another meta-analysis involving seven trials and 7588 patients undergoing ECV showed that NOACs, as compared to warfarin, resulted in similar risks of ischemic stroke (0.19% vs. 0.53%) after ECV [15].

Prevalence of thrombi in the LAA and their risk factors

In AF patients, thromboembolic material localized in the left atrium is most frequently observed in the LAA. The prevalence of LAA thrombus (LAAT) in patients undergoing anticoagulant therapy was assessed in numerous studies (Table 1) [16–30].

Risk factors for LAAT formation are not clearly defined and are not necessarily the same as the risk factors for thromboembolic events in patients with AF. The main pathophysiological theory of atrial thrombogenesis in AF relates to endocardial remodeling [31]. Oxidative stress and inflammation in fibrillating atrial tissue are the main factors influencing up-regulation of thrombogenic proteins at the endocardial surface.

The precursor of LAAT is a spontaneous echo contrast (SEC) described as discrete reflections that are visible in blood inside cardiac cavities, chambers, or vessels. Smoke-like SEC is defined as swirling, amorphous, light gray haze [32]. Its acoustic density and configuration alter within several cardiac cycles. It is possible to notice it in veins, great vessels, and in left and right heart chambers. Smoke-like SEC shows a strong connection to thromboembolic events and stroke [33] and its probable cause is blood stasis [34]. Non-smoke SEC looks like a 'snowstorm' or like discrete dispersed reflections in normal conditions. Respiratory maneuvers can enhance such SEC in the left atrium. Its intensity can be mild to moderate and conditioned by transient stasis, especially in the pulmonary circulation. LAA sludge signalizes a dynamic, viscid, layered echo dense finding without a discrete mass. Its density seems higher than that of SEC and lower than that of a thrombus. Thus, it is believed to be a stage between SEC and thrombus formation [35].

Concomitant diseases such as arterial hypertension, diabetes mellitus, heart failure, and advanced age appear to have an important impact on endocardial remodeling.

In most studies LAAT prevalence was higher in patients with the higher CHA_2DS_2-VASC score. However, it was proven that LAAT appeared in patients without risk factors included in the CHA_2DS_2-VASC score. Therefore, it is necessary to search for LAAT risk factors that are different

Table 1. The prevalence and risk factors of a left atrial appendage thrombus in the selected studies.

Reference, year	No. of patients	Age	Male, %	LAAT, %	Independent factors predisposing to LAAT
Puwanant [16], 2009	1058	57 (11)	80	0.6	LV function Congestive heart failure
Gunawardene [17], 2017	1658	63 (11)	65.7	0.78	CHA_2DS_2-VASC ≥ 4 LVEF < 30% Hypertrophic cardiomyopathy Non-paroxysmal AF
Scherr [18], 2009	732	57 (11)	77	1.6	$CHADS_2$ ≥ 2 LA diameter ≥ 45 mm
McCready [19], 2010	635	59 (12)	67	1.9	Cardiomyopathy Hypertension Age > 75
Dorenkamp [20], 2013	329	62 (10)	65	2.1	CHA_2DS_2-VASC ≥ 4 $CHADS_2$ ≥ 3 Diabetes mellitus
Wu [21], 2018	608	65 (58–71)	72	2.8	Congestive heart failure Moderate/severe LA enlargement
Yamashita [22], 2010	446	59 (11)	70	2.9	Persistent AF Structural heart disease Advanced age
Huang [23], 2017	2695	58 (12)	67.7	3	Stroke/TIA Non-paroxysmal AF LV dysfunction LA enlargement Cardiomyopathy
Frenkel [24], 2016	388	65 (58–71)	74	3.6	Heart failure Persistent AF
Han [25], 2020	1102	60.6 (5.8)	67.5	4.36	Hypertension Stroke/TIA/systemic embolism LVEF < 50% LA enlargement GFR < 60 mL/min/1.73 m^2
Gorczyca [26], 2020	1148	62.1	61.9	4.4	CHA_2DS_2-VASc ≥ 2 Non-paroxysmal AF GFR < 60 mL/min/1.73 m^2
Harada [27], 2018	407	63 (12)	71	4.4	Persistent AF Inappropriate dose reduction of NOACs
Huang [28], 2018	2173	57.8 (11.8)	67.1	4.9	Non-paroxysmal LVEF ≤ 55% LA enlargement
Kapłon-Cieślicka [29], 2019	1033	60 (53–66)	66	5.71	CHA_2DS_2-VASC score GFR < 56 mL/min/1.73 m^2 Non-paroxysmal AF
Merino [30], 2019	1183	–	–	8.2	Heart failure Age

AF — atrial fibrillation; GFR — glomerular filtration rate; LA — left atrial; LAAT — left atrial appendage thrombus; LV — left ventricle; LVEF — left ventricular ejection fraction; NOACs — non-vitamin K antagonist oral anticoagulants; TIA — transient ischemic attack

Table 2. The proposal of a left atrial appendage thrombus risk stratification model: the CHA_2DS_2-VASc--RAF score and the left atrial appendage thrombus/spontaneous echo contrast score (LAAT/SEC).

Risk factors	Scales	
	CHA_2DS_2-VASc-RAF [28]	LAAT/SEC score [29]
Congestive heart failure	1	–
Hypertension	1	–
Diabetes mellitus	1	–
Vascular disease	1	–
Age 65–74 years	1	–
Stroke/TIA/systemic embolism	2	–
Age ≥ 75 years	2	–
Female sex	1	–
GFR < 56 mL/min/1.73 m^2	2	–
Persistent AF	4	1
Permanent AF	10	1
LVEF < 55%	–	2
LA enlargement (> 38 mm for women, > 40 mm for men)	–	3
Risk categories		
Low	0–4 points in men 1–5 points in women	0–1 point
Intermediate	–	2–3 points
High	≥ 5 points in men ≥ 6 points in women	4–6 points

AF — atrial fibrillation; GFR — glomerular filtration rate; LA — left atrial; LVEF — left ventricular ejection fraction; TIA — transient ischemic attack

from the classic thromboembolic ones. A study of 1033 patients revealed renal function and AF type as strong and independent predictors of LAAT. This same study suggested the CHA_2DS_2-VASC score be extended and that it might be considered an effective tool for LAAT prevalence assessment (Table 2) [29]. Further studies showed that the CHA_2DS_2--VASc-RAF score was a better LAAT prevalence predictor than the CHA_2DS_2-VASc score in patients treated with NOACs [36]. Therefore, using the CHA_2DS_2-VASc-RAF score or taking into account all additional factors included in it (renal function, AF type) in the assessment of LAAT prevalence risk may be helpful in making decisions on TEE performance. Huang et al. [23] proposed a new scoring system established as the LAAT/SEC predictive score, in which the following parameters were included: non-paroxysmal AF, left ventricular ejection fraction (LVEF) < 55%, and left atrial enlargement (Table 2).

TEE-guided cardioversion

According to current guidelines issued by the European Society of Cardiology (ESC), early cardioversion can be done without TEE in patients with AF duration < 48 hours. Suitable oral anticoagulation is recommended for at least 3 weeks before ECV in patients with AF > 48 hours or of unknown duration [37]. This recommendation is the same for all patients, independent of stroke risk, according to the CHA_2DS_2-VASC score. This 3-week period of adequate anticoagulant treatment is necessary, based on the time presumably needed for endothelialization or resolution of possible LAAT. To shorten this time, experts recommended TEE to exclude LAAT as an alternative to a 3-week anticoagulation period when early cardioversion is planned [37]. Recommendations from the ESC and the American Society of Cardiology for the aforementioned issue are consistent [37, 38] with previous ESC guidelines [39].

TEE before ECV in clinical practice

In clinical practice, procedures related to performing TEE in patients using NOACs and undergoing planned ECV are different at individual centers. In the case of patients treated with VKAs, the international normalized ratio value from 3 weeks before ECV proves that anticoagulant

treatment is adequate. Thus far, none of the coagulation parameters were considered to be indicators confirming regular use of NOACs. Therefore, in the absence of laboratory confirmation of regular NOAC use, patients undergo TEE prior to ECV.

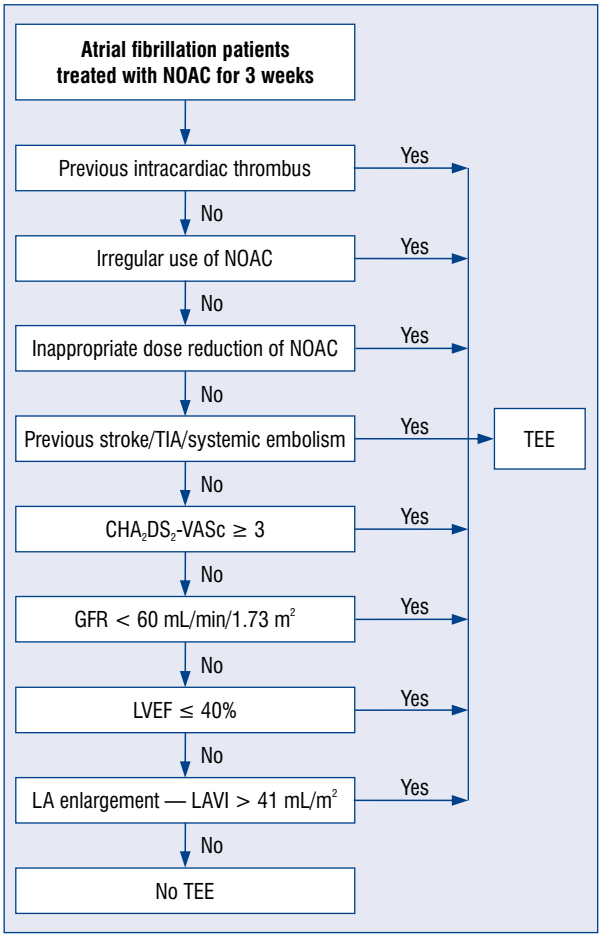
Results of the European Heart Rhythm Association survey from 2019 included 54 centers and found that most would also perform TEE in patients with AF lasting ≥ 48 hours in case of no or incomplete information (80% and 78%, respectively) about adequate anticoagulation. Only 12% of the centers would routinely perform TEE before any left atrial procedure, regardless of the thromboembolic risk [40]. The results of the same survey from 2013 are not consistent with the above-mentioned practice. In 56.5% of centers where patients were not on adequate anticoagulation therapy, TEE was performed. An additional 4.6% of the centers recommended TEE routinely for all patients [41]. In the study including 668 AF patients treated with NOACs before ECV, TEE was performed in 54% of patients [12]. Data from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II showed that 25% of patients had pre-cardioversion TEE [10].

When TEE should be made before ECV: Practical decision algorithm

Data referring to the frequency of TEE procedures in patients with AF treated with NOACs are not consistent and show diverse strategies among individual centers performing ECV.

Current ESC guidelines lack the possibility of standardizing how NOAC action is monitored, indicating the need to search for new patterns that can be used to determine which AF patients would be served with TEE prior to ECV. The data indicates that performing pre-cardioversion TEE in all patients treated with NOACs is not optimal, nor is exempting them all from TEE before ECV.

There is a great deal of evidence indicating that, according to the CHA_2DS_2-VASc score, high risk of thromboembolic complications in patients treated with NOACs is a predictor of LAAT. In the study of Gorczyca et al. [26] the LAAT predicting factor was a CHA_2DS_2-VASc score ≥ 2 points, and in the study of Gunawardene et al. [17] CHA_2DS_2-VASc score ≥ 4 points was predictive. However, using this score alone for patient assessment may not be the most thorough approach possible, given that other conditions also present the same results. In some situations, it is necessary to diagnose LAAT risk based on a patient's detailed clinical characteristics and not the result of a particular score.



Central illustration. The algorithm proposed for assessing indications for transesophageal echocardiography (TEE) before planned electrical cardioversion in patients treated with non-vitamin K oral anticoagulants (NOACs); GFR — glomerular filtration rate; LA — left atrial; LAVI — left atrial volume index; LVEF — left ventricular ejection fraction; TIA — transient ischemic attack.

For the systematic approach to performing TEE before ECV we propose a decision-making algorithm, presented in Central illustration. We have merged widely accessible clinical features, identified in the above-discussed studies as the risk factors of LAAT, in a simple screening path. In patients with AF using NOACs before planned ECV, pre-procedural TEE should be performed in those who had LAAT in the past, regardless of treatment strategy, and also in those with any suspicion of unsystematic NOAC use. In the remaining patients, the necessity for TEE should be decided upon after considering individual thromboembolic risk. According to the presented algorithm, TEE should be performed in patients with any strong LAAT risk factor such as: previous intracardiac

thrombus, irregular use of NOAC, inappropriate dose reduction of NOAC, previous stroke/TIA/systemic embolism, CHA_2DS_2-VASc score ≥ 3 points, glomerular filtration rate < 60 mL/min/1.73 m^2, reduced LVEF, or moderate or severe left atrial enlargement (Central illustration).

TEE: Limitations of the methods

Transesophageal echocardiography is a minimally invasive procedure that is usually safer when conducted by an experienced physician. However, it is time consuming, carries patient discomfort, is not readily available in all centers, and sometimes it is associated with potential life-threatening complications. Although TEE is regarded as the gold standard to exclude a thrombus in the LAA before scheduled ablation or AF cardioversion, the accuracy of this technique is far from 100%. In patients who present contraindication to TEE or do not agree to have this examination, computed tomography or magnetic resonance imaging can be considered reasonable alternatives to TEE in the identification of LAAT. Multidetector computed tomography provides three-dimensional volumetric data of the entire heart, including the LAA. It is of high spatial and temporal resolution, which allows the identification of LAAT and spontaneous contrast formation similar to the SEC observed by TEE. Cardiac magnetic resonance with its high temporal resolution shows the LAA size and function and can detect LAAT in AF patients. A recently conducted systematic review and meta-analysis of 4 cardiac magnetic resonance and 22 multidetector computed tomography studies juxtaposed TEE with the diagnostic performance of listed methods for LAAT identification. Sensitivity and specificity of multidetector computed tomography were, respectively, 0.99 and 0.94 compared to TEE, with notably increased specificity of the delayed imaging protocols. Cardiac magnetic resonance, in comparison to TEE, demonstrated sensitivity and specificity of 0.80 and 0.98, respectively [42]. It seems that in clinical practice the main limitation of TEE is lack of common TEE accessibility in all centers performing ECV.

Summary

Due to the high risk of LAAT and lack of standardized laboratory tests confirming the efficacy of NOAC, it seems necessary to define guidelines for performing TEE prior to ECV. It appears that risk factors of thromboembolic complications and LAAT are not the same. In patients with low thromboembolic risk, it is especially important to consider additional factors that increase the risk of LAAT prevalence. The proposed algorithm guarantees a more systematic approach to performing TEE in patients undergoing ECV.

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References

1. Kirchhof P, Camm AJ, Goette A, et al. Early rhythm-control therapy in patients with atrial fibrillation. N Engl J Med. 2020; 383(14): 1305–1316, doi: 10.1056/NEJMoa2019422, indexed in Pubmed: 32865375.
2. 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.
3. 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.
4. 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.
5. Telles-Garcia N, Dahal K, Kocherla C, et al. Non-vitamin K antagonists oral anticoagulants are as safe and effective as warfarin for cardioversion of atrial fibrillation: A systematic review and meta-analysis. Int J Cardiol. 2018; 268: 143–148, doi: 10.1016/j.ijcard.2018.04.034, indexed in Pubmed: 30041779.
6. Kotecha D, Pollack CV, De Caterina R, et al. Direct oral anticoagulants halve thromboembolic events after cardioversion of AF compared with warfarin. J Am Coll Cardiol. 2018; 72(16): 1984–1986, doi: 10.1016/j.jacc.2018.07.083, indexed in Pubmed: 30309478.
7. 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.
8. 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.
9. Berger M, Schweitzer P. Timing of thromboembolic events after electrical cardioversion of atrial fibrillation or flutter: a retrospective analysis. Am J Cardiol. 1998; 82(12): 1545–7, A8, doi: 10.1016/s0002-9149(98)00704-8, indexed in Pubmed: 9874066.

10. Geurink K, Holmes D, Ezekowitz MD, et al. Patterns of oral anticoagulation use with cardioversion in clinical practice. Heart. 2021; 107(8): 642–649, doi: 10.1136/heartjnl-2019-316315, indexed in Pubmed: 32591363.
11. 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.
12. Uziębło-Życzkowska B, Kiliszek M, Gorczyca I, et al. Factors determining elective cardioversion preceded by transesophageal echocardiography: experiences of 2 cardiology centers. Pol Arch Intern Med. 2020; 130(10): 837–843, doi: 10.20452/pamw.15546, indexed in Pubmed: 32785205.
13. 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.
14. Dentali F, Botto GL, Gianni M, et al. Efficacy and safety of direct oral anticoagulants in patients undergoing cardioversion for atrial fibrillation: A systematic review and meta-analysis of the literature. Int J Cardiol. 2015; 185: 72–77, doi: 10.1016/j.ijcard.2015.03.096, indexed in Pubmed: 25791094.
15. Telles-Garcia N, Dahal K, Kocherla C, et al. Non-vitamin K antagonists oral anticoagulants are as safe and effective as warfarin for cardioversion of atrial fibrillation: A systematic review and meta-analysis. Int J Cardiol. 2018; 268: 143–148, doi: 10.1016/j.ijcard.2018.04.034, indexed in Pubmed: 30041779.
16. 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(22): 2032–2039, doi: 10.1016/j.jacc.2009.07.037, indexed in Pubmed: 19926009.
17. Gunawardene MA, Dickow J, Schaeffer BN, et al. Risk stratification of patients with left atrial appendage thrombus prior to catheter ablation of atrial fibrillation: An approach towards an individualized use of transesophageal echocardiography. J Cardiovasc Electrophysiol. 2017; 28(10): 1127–1136, doi: 10.1111/jce.13279, indexed in Pubmed: 28635023.
18. 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(4): 379–384, doi: 10.1111/j.1540-8167.2008.01336.x.
19. McCready JW, Nunn L, Lambiase PD, et al. Incidence of left atrial thrombus prior to atrial fibrillation ablation: is pre-procedural transoesophageal echocardiography mandatory? Europace. 2010; 12(7): 927–932, doi: 10.1093/europace/euq074, indexed in Pubmed: 20304842.
20. Dorenkamp M, Sohns C, Vollmann D, et al. Detection of left atrial thrombus during routine diagnostic work-up prior to pulmonary vein isolation for atrial fibrillation: role of transesophageal echocardiography and multidetector computed tomography. Int J Cardiol. 2013; 163(1): 26–33, doi: 10.1016/j.ijcard.2011.06.124, indexed in Pubmed: 21764466.
21. Wu M, Gabriels J, Khan M, et al. Left atrial thrombus and dense spontaneous echocardiographic contrast in patients on continuous direct oral anticoagulant therapy undergoing catheter ablation of atrial fibrillation: Comparison of dabigatran, rivaroxaban, and apixaban. Heart Rhythm. 2018; 15(4): 496–502, doi: 10.1016/j.hrthm.2017.12.005, indexed in Pubmed: 29605015.
22. Yamashita E, Takamatsu H, Tada H, et al. Transesophageal echocardiography for thrombus screening prior to left atrial catheter ablation. Circ J. 2010; 74(6): 1081–1086, doi: 10.1253/circj.cj-09-1002, indexed in Pubmed: 20453390.
23. Huang J, Wu SL, Xue YM, et al. Association of CHADS and CHADS-VASc Scores with Left Atrial Thrombus with Nonvalvular Atrial Fibrillation: A Single Center Based Retrospective Study in a Cohort of 2695 Chinese Subjects. Biomed Res Int. 2017; 2017: 6839589, doi: 10.1155/2017/6839589, indexed in Pubmed: 28373985.
24. Frenkel D, D'Amato SA, Al-Kazaz M, et al. Prevalence of left atrial thrombus detection by transesophageal echocardiography: a comparison of continuous non-vitamin K antagonist oral anticoagulant versus warfarin therapy in patients undergoing catheter ablation for atrial fibrillation. JACC Clin Electrophysiol. 2016; 2(3): 295–303, doi: 10.1016/j.jacep.2016.01.004, indexed in Pubmed: 29766887.
25. Han D, Chu Y, Wu Y, et al. Determinants of left atrial thrombus or spontaneous echo contrast in nonvalvular atrial fibrillation. Thromb Res. 2020; 195: 233–237, doi: 10.1016/j.thromres.2020.07.055, indexed in Pubmed: 32799130.
26. 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.
27. Harada M, Koshikawa M, Motoike Y, et al. Left atrial appendage thrombus prior to atrial fibrillation ablation in the era of direct oral anticoagulants. Circ J. 2018; 82(11): 2715–2721, doi: 10.1253/circj.CJ-18-0398, indexed in Pubmed: 30101809.
28. Huang J, Liao HT, Fei HW, et al. Association of thromboembolic risk score with left atrial thrombus and spontaneous echocardiographic contrast in non-anticoagulated nonvalvular atrial fibrillation patients. Cardiology. 2018; 140(2): 87–95, doi: 10.1159/000489390, indexed in Pubmed: 29920487.
29. Kapłon-Cieślicka A, Budnik M, Gawałko M, et al. Atrial fibrillation type and renal dysfunction as important predictors of left atrial thrombus. Heart. 2019; 105(17): 1310–1315, doi: 10.1136/heartjnl-2018-314492, indexed in Pubmed: 31040170.
30. Merino JL, Lip GYH, Heidbuchel H, et al. Determinants of left atrium thrombi in scheduled cardioversion: an ENSURE-AF study analysis. Europace. 2019; 21(11): 1633–1638, doi: 10.1093/europace/euz213, indexed in Pubmed: 31436835.
31. Bukowska A, Hammwöhner M, Corradi D, et al. Atrial thrombogenesis in atrial fibrillation: Results from atrial fibrillation models and AF-patients. Herzschr Elektrophys. 2018; 29(1): 76–83, doi: 10.1007/s00399-017-0543-x, indexed in Pubmed: 29234866.
32. Merino A, Hauptman P, Badimon L, et al. Echocardiographic "smoke" is produced by an interaction of erythrocytes and plasma proteins modulated by shear forces. J Am Coll Cardiol. 1992; 20(7): 1661–1668, doi: 10.1016/0735-1097(92)90463-w, indexed in Pubmed: 1452941.
33. Chimowitz MI, De Ge, Poole RM, et al. Left atrial spontaneous echo contrast is highly associated with previous stroke in patients with atrial fibrillation or mitral stenosis. Stroke. 1994; 25: 1295–1305.
34. Black IW, Hopkins AP, Lee LC, et al. Left atrial spontaneous echo contrast: a clinical and echocardiographic analysis. J Am Coll Car-

diol. 1991; 18(2): 398–404, doi: 10.1016/0735-1097(91)90592-w, indexed in Pubmed: 1856407.

35. Lowe BS, Kusunose K, Motoki H, et al. Prognostic significance of left atrial appendage "sludge" in patients with atrial fibrillation: a new transesophageal echocardiographic thromboembolic risk factor. J Am Soc Echocardiogr. 2014; 27(11): 1176–1183, doi: 10.1016/j.echo.2014.08.016, indexed in Pubmed: 25262162.
36. Michalska A, Gorczyca I, Chrapek M, et al. Does the CHA2DS2--VASc scale sufficiently predict the risk of left atrial appendage thrombus in patients with diagnosed atrial fibrillation treated with non-vitamin K oral anticoagulants? Medicine (Baltimore). 2020; 99(25): e20570, doi: 10.1097/MD.0000000000020570, indexed in Pubmed: 32569181.
37. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021; 42(5): 373–498, doi: 10.1093/eurheartj/ehaa612, indexed in Pubmed: 32860505.
38. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019; 74(1): 104–132, doi: 10.1016/j.jacc.2019.01.011_, indexed in Pubmed: 30703431.
39. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016; 37(38): 2893–2962, doi: 10.1093/eurheartj/ehw210, indexed in Pubmed: 27567408.
40. 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.
41. Hernández-Madrid A, Svendsen JH, Lip GYH, et al. Cardioversion for atrial fibrillation in current European practice: results of the European Heart Rhythm Association survey. Europace. 2013; 15(6): 915–918, doi: 10.1093/europace/eut143, indexed in Pubmed: 23709570.
42. Vira T, Pechlivanoglou P, Connelly K, et al. Cardiac computed tomography and magnetic resonance imaging vs. transoesophageal echocardiography for diagnosing left atrial appendage thrombi. Europace. 2019; 21(1): e1–e10, doi: 10.1093/europace/euy142, indexed in Pubmed: 29961869.