Can transesophageal echocardiography be safely omitted in patients scheduled for elective ablation of atrial arrhythmias? Data based on the LATTEE registry

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ABSTRACT

Background: According to the present guidelines, transesophageal echocardiography (TEE) before scheduled catheter ablation (CA) for atrial arrhythmias (atrial fibrillation [AF] or atrial flutter [AFL]) is not deemed obligatory for optimally anticoagulated patients. However, daily clinical practice significantly differs from the recommendations.

Aims: We aimed to identify transthoracic echocardiographic parameters that could be useful in identifying patients without left atrial thrombus (LAT), which makes it possible to avoid unnecessary TEE before scheduled CA.

Methods: This is a sub-analysis of a multicenter, prospective, observational study — the LATTEE registry. A total of 1346 patients referred for TEE before scheduled CA of AF/AFL were included.

WHAT'S NEW?

In this study, we aimed to address the incongruity between guidelines and clinical practices regarding the necessity of performing transesophageal echocardiography (TEE) before scheduled catheter ablation (CA) for atrial arrhythmias. Although guidelines do not mandate TEE for optimally anticoagulated patients, in many centers, such examinations are performed and may be potentially overused. After analyzing the LATTEE registry with 1346 patients scheduled for CA due to atrial fibrillation or atrial flutter, we propose an innovative approach. By focusing on specific transthoracic echocardiographic parameters and indices, we can accurately identify individuals without left atrial thrombus with 100% sensitivity and negative predictive value. This facilitates a more personalized approach, allowing for omitting unnecessary TEE in 35% of cases. It sets the stage for an enhanced pre-ablation assessment, promoting efficiency and advancing standards in cardiac care.

Results: LAT was present in 44 patients (3.3%) and absent in the remaining 1302, who were younger, more likely to have paroxysmal AF, and displayed sinus rhythm during TEE. Additionally, they exhibited a lower incidence of heart failure, diabetes, systemic connective tissue disease, and chronic obstructive pulmonary disease. Furthermore, they had a lower CHA_2DS_2-VASc score and a higher prevalence of direct oral anticoagulants. Echocardiographic parameters, including left ventricular ejection fraction (LVEF) >65%, left atrial diameter (LAD) <40 mm, left atrial area (LAA) <20 cm^2, left atrial volume (LAV) <113 ml, and left atrial volume index (LAVI) <51 ml/m^2, demonstrated 100% sensitivity and 100% negative predictive value for the absence of LAT and were met by 417 patients. Additional echocardiographic indices: LVEF/LAD ≥1.4, LVEF/LAVI ≥1.6, and LVEF/LAA ≥2.7 identified 57 additional patients, bringing the total of predicted LAT-free patients to 474 (35%).

Conclusions: Simple echocardiographic parameters could help identify individuals for whom TEE could be safely omitted before elective CA due to atrial arrhythmias.

Key words: atrial arrhythmias, atrial fibrillation, catheter ablation, echocardiography, left atrial thrombus

INTRODUCTION

Atrial fibrillation and flutter (AF/AFL) are the most common sustained cardiac arrhythmias in adults, posing a significant risk of thromboembolic complications that contribute to substantial morbidity and mortality [1, 2]. Catheter ablation (CA) is an effective treatment option for a range of atrial arrhythmias [3].

A thrombus in the left atrium (LAT) is regarded as a contraindication for ablation procedures of left atrial arrhythmias (AF, atypical AFL, and focal atrial tachycardia) and for CA in cases of persistent typical atrial flutter. Consequently, current guidelines from the European Society of Cardiology advocate the routine application of oral anticoagulation (Class I, Level C) or, in cases of inadequate or absent anticoagulation, recommend performing transesophageal echocardiography (TEE) (Class IIa, Level C) to assess the presence of LAT before undertaking CA procedures [1]. On the other hand, the 2019 American Heart Association Guidelines state that it is reasonable to conduct a TEE before AF CA for patients who are in AF before the procedure [4]. The population of AF patients exhibits significant heterogeneity, and the available literature on LAT occurrence in patients treated with anticoagulants before AF/AFL CA may present conflicting findings [5–9]. For instance, some studies may indicate a non-negligible, 3%–5% risk of LAT presence [5–7], while others may suggest that the risk is extremely low and may not warrant routine TEE before the procedure [8, 9].

Given these discrepancies, it seems reasonable to conduct further studies in this area, and in particular, from a clinical point of view, it is important to search for parameters that would identify LAT-free patients, allowing for the safe omission of routine TEE before AF/AFL CA. In this light, some echocardiographic parameters could be of great interest. The existing body of literature encompasses a wealth of data concentrating on efforts to identify patients with or without LAT [7, 10–14]. Recently, the authors demonstrated the utility of some new echocardiographic indices, including left ventricular ejection fraction (LVEF) and left atrial (LA) parameters (diameter, area, and indexed volume), in predicting the presence of LAT. The study showed that LVEF/left atrial volume index (LAVI) ≤1.1 (OR, 6.77; 95% CI, 4.25–10.8; P <0.001), LVEF/left atrial area (LAA) ≤1.7 (OR, 5.64; 95% CI, 4.02–7.9; P <0.001), and LVEF/LAD ≤1.1 (OR, 5.64; 95% CI, 4.03–7.9;

P <0.001) indexes better predict the occurrence of LAT than the classic echocardiographic parameter. Moreover, LVEF/LAVI and LVEF/LAA ratios sustained their statistical significance in multivariate analysis [15].

Based on the aforementioned data, the primary aim of this study was to identify two distinct groups: LAT-negative (LAT–, without thrombus) and LAT-positive (LAT+, with thrombus), and establish cut-off values for echocardiographic parameters with 100% sensitivity and 100% negative predictive value (NPV) for the absence of LAT before scheduled AF/AFL CA procedures.

MATERIAL AND METHODS

Study population

The prospective, observational real-world Left Atrial Thrombus on Transesophageal Echocardiography (LATTEE) registry (ClinicalTrials.gov identifier: NCT03591627) enrolled 3109 consecutive patients with AF/AFL admitted to 13 cardiology departments between November 2018 and May 2020, in whom TEE was performed before direct current cardioversion or CA. The study rationale and detailed design have been previously published [15, 16]. The study was conducted under clinical practice guidelines and adhered to the principles of the Declaration of Helsinki. The Medical University of Warsaw Ethics Committee approved the study (AKBE/113/2018) and waived the requirement to obtain informed consent from the patients.

This present sub-analysis was conducted within the framework of the LATTEE registry and focuses on a cohort of patients with nonvalvular AF and on chronic anticoagulation who were scheduled for elective AF/AFL CA. Chronic anticoagulation was defined as the uninterrupted use of direct oral anticoagulants (DOACs) or vitamin K antagonists (VKAs) for a minimum of 3 weeks before the TEE study. Nonvalvular AF definition excluded patients with AF due to moderate-severe mitral stenosis of rheumatic origin and those with mechanical prosthetic valves.

Data collection and study endpoint

Data were collected prospectively and encompassed detailed demographics, medical history, comorbidities, calculation of CHA_2DS_2-VASc score, pharmacotherapy, and results of routine laboratory blood tests. Patients received treatment with a DOAC using standard dosing protocols based on their weight, age, estimated glomerular filtration rate, concomitant medications, and bleeding risk, and the dosage of VKA drugs was adjusted so that the international normalized ratio was in the range of 2–3. Trained echocardiographers conducted all echocardiographic studies under the predefined protocol [16]. Performing a TEE was imperative for study inclusion, involving the assessment of parameters such as the presence and location of LAT, the presence of spontaneous echocardiographic contrast, and left atrial appendage outflow velocity. Transthoracic echocardiography (TTE) was performed in the majority of participants and involved obtaining data on LVEF, left atrial diameter (LAD), LAA, left atrial volume (LAV), and LAVI, which was calculated as the ratio of left atrial volume to body surface area. In addition, based on the results of our previous study [15], the ratios of LVEF and left atrial parameters, namely LVEF/LAD, LVEF/LAA, and LVEF/LAVI, were investigated. The study endpoint was the determination of echocardiographic cut-off values identifying LAT-free patients.

Statistical analysis

Continuous data were reported as medians with 25^{th}–75^{th} percentiles while categorical data were presented as numbers (n) and percentages (%). Differences between the LAT+ and LAT– groups were assessed using the Mann-Whitney U-test for continuous variables and the χ^2 or Fisher's test for categorical variables. The accuracy of pre-specified cut-off values for the analyzed parameters and their association as potential predictors of LAT-free outcomes was assessed using the area under the receiver operating characteristic curve. In the context of specificity, sensitivity, positive predictive value, and NPV analysis for the absence of LAT, a detailed assessment of the diagnostic effectiveness of the investigated predictors was conducted. Cut-off values were determined specifically to achieve 100% sensitivity and 100% NPV. All the results were considered statistically significant at *P*-value <0.05. The statistical analysis was performed using the R 4.0.5 environment (R Core Team, Vienna, Austria).

RESULTS

Study population

Of 3109 participants of the LATTEE registry, a total of 1346 patients with nonvalvular AF, on chronic anticoagulation treatment, hospitalized for the scheduled CA procedure were included in this study. The prevalence of LAT was 3.3%. The median age of the enrolled patients was 63 years; 34% were female, 865 (64%) patients had paroxysmal AF, and 678 (53%) had sinus rhythm during the TEE study. In conjunction with AF, patients commonly presented comorbidities such as hypertension (72%), heart failure (24%), and vascular disease (23%). Furthermore, nearly one-third of the subjects were either current smokers or had a history of smoking cigarettes. The median CHA_2DS_2-VASc score for the study population was 2 (1–3). Most patients (88%) were on DOAC, with rivaroxaban accounting for 41% of cases, dabigatran for 36%, and apixaban for 11%. The remaining participants (167 patients) were on VKA, with acenocoumarol accounting for 7% and warfarin for 5% of the cases. Accurate data are presented in Table 1.

Clinical parameters

LAT-free patients tended to be younger (63 vs. 65 years old), more likely to have paroxysmal AF (65% vs. 32%), less likely to have AF during TEE (43% vs. 84%) and comorbidities such as heart failure (23% vs. 43%), diabetes (17% vs. 29%),

Table 1. Comparison of clinical characteristics between LAT– and LAT+ patients

Variable	Overall (n = 1346)	LAT– (n = 1302)	LAT+ (n = 44)	*P*-value
Demographics				
Age, years, median, Q1–Q3	63 (65–69)	63 (55–69)	65 (61–73)	0.03
Female sex, n (%)	457 (34)	446 (34)	11 (25)	0.26
BMI, kg/m^2, median, Q1–Q3	29 (26–33)	29 (26–33)	30 (28–33)	0.18
AF/AFL type and rhythm				
AF/AFL paroxysmal, n (%)	865 (64)	851 (65)	14 (32)	<0.001
AF/AFL non-paroxysmal, n (%)	479 (36)	449 (34)	30 (68)	
AF rhythm during TEE, n (%)	601 (47)	564 (43)	37 (84)	<0.001
Sinus rhythm during TEE, n (%)	678 (53)	672 (52)	6 (13)	<0.001
Comorbidities				
Hypertension, n (%)	967 (72)	934 (72)	33 (75)	0.61
Myocardial infarction, n (%)	107 (8)	102 (8)	5 (11)	0.38
Vascular disease, n (%)	309 (23)	294 (23)	15 (34)	0.07
HF, n (%)	319 (24)	300 (23)	19 (43)	0.003
HFrEF, n (%)	106 (8)	94 (7)	12 (27)	<0.001
ICD/CRT-D, n (%)	28 (2)	24 (2)	4 (9)	0.012
Previous ischemic stroke/TIA/systemic embolism, n (%)	81 (6)	78 (6)	3 (7)	0.74
Diabetes mellitus, n (%)	241 (18)	228 (17)	13 (29)	0.04
Systemic connective tissue disease, n (%)	25 (2)	22 (2)	3 (7)	0.04
CKD with GFR <50 ml/min/1.73 m^2, n (%)	107 (8)	103 (8)	4 (9)	0.77
COPD, n (%)	43 (3)	39 (3)	4 (9)	0.045
Tobacco users current/in the past, n (%)	424 (31)	402 (31)	22 (50)	0.003
Thromboembolic risk and indications for chronic OAC				
CHA_2DS_2-VASc score, median, Q1–Q3	2 (1–3)	2 (1–3)	2 (2–4)	0.03
Class I indications to OAC[a], n (%)	790 (56)	757 (58)	33 (75)	0.02
Class IIa indications[b], n (%)	354 (27)	348 (27)	6 (14)	
No indications for chronic OAC[c], n (%)	189 (3)	187 (14)	2 (4)	
Antithrombotic therapy				
DOACs, n (%)	1179 (88)	1146 (88)	33 (75)	0.02
VKAs, n (%)	167 (12)	156 (12)	11 (25)	

[a]CHA_2DS_2-VASc score ≥2 for men and ≥3 for women. [b]CHA_2DS_2-VASc score 1 for men and 2 for women. [c]CHA_2DS_2-VASc score 0 for men and 1 for women

Abbreviations: AF, atrial fibrillation; AFL, atrial flutter; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DOACs, direct oral anticoagulants; GFR, glomerular filtration rate; LAT, left atrial thrombus; OAC, oral anticoagulant, VKAs, vitamin K antagonists

systemic connective tissue disease (2% vs. 7%), and chronic obstructive pulmonary disease (3% vs. 9%). These patients also had lower CHA_2DS_2-VASc scores and were less likely to be smokers. The incidence of LAT was significantly lower in patients receiving DOACs compared to those receiving VKAs, 2.7% vs. 6.6%, respectively ($P = 0.02$).

Echocardiographic parameters

Transthoracic echocardiography was performed in 1087 patients, representing 81% of the study sample (Table 2). Patients without LAT exhibited higher LVEF and lower LAD, LAA, LAV, and LAVI values compared to those with LAT. The echocardiographic indices showed significant differences between the compared groups. Specifically, LAT– patients had higher values of LVEF to left atrial ratios: LVEF/LAD 1.3 (1.1–1.5) vs. 0.9 (0.7–1.2) (P <0.001), LVEF/LAA 2.3 (1.8––2.8) vs. 1.5 (1.1–1.9) (P <0.001), and LVEF/LAVI 1.4 (1.1–1.8) vs. 0.8 (0.5–1.3), respectively (P <0.001), as shown in Table 2.

Echocardiographic predictors of LAT-free outcome

To identify LAT-free patients, cut-off values were determined for echocardiographic parameters and indices that achieved 100% sensitivity and 100% NPV; the results are outlined in Table 3. The number of patients identified through "single" echocardiographic parameters and indices was then calculated, as depicted in Figure 1.

A total of 417 patients met at least one of the single echocardiographic parameters, including LVEF >65%, LAD <40 mm, LAA <20 cm^2, LAV <113 ml, LAVI <51 ml/m^2, while additional 57 patients were identified by using echocardiographic indices such as LVEF/LAD ≥1.4, LVEF/LAVI ≥1.6. and LVEF/LAA ≥2.7. Consequently, a total of 474 patients, representing 35% of the study population, fulfilled at least one of the echocardiographic criteria outlined in Table 3. As a result, in over one-third of the study participants, the presence of LAT could be excluded with 100% sensitivity and 100% NPV.

Table 2. Comparison of LVEF, LA parameters, and ratios in LAT– and LAT+ patients

Variable	Overall	LAT–	LAT+	*P*-value
LVEF (%), median, Q1–Q3	57 (50–60)	57 (50–60)	44 (35–60)	<0.001
LAD (mm), median, Q1–Q3	44 (48–48)	44 (40–47)	49 (45–52)	<0.001
LAA (cm^2), median, Q1–Q3	25 (21–29)	24 (21–28)	31 (26–34)	<0.001
LAV (ml), median, Q1–Q3	82 (66–104)	81 (65–102)	116 (92–135)	<0.001
LAVI (ml/m^2), median, Q1–Q3	41 (33–49)	41 (33–49)	55 (43–69)	<0.001
LVEF/LAD ratio, median, Q1–Q3	1.3 (1.1–1.5)	1.3 (1.1–1.5)	0.9 (0.7–1.2)	<0.001
LVEF/LAA ratio, median, Q1–Q3	2.3 (1.8–2.7)	2.3 (1.8–2.8)	1.5 (1.1–1.9)	<0.001
LVEF/LAVI ratio, median, Q1–Q3	1.4 (1.1–1.7)	1.4 (1.1–1.8)	0.8 (0.5–1.3)	<0.001

Abbreviations: LAA, left atrial area; LAD, left atrial diameter; LAV, left atrial volume; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; other — see Table 1

Table 3. Cut-off values of analyzed echocardiographic parameters for LAT-free outcomes with 100% sensitivity and negative predictive value

Parameter	AUC	Characteristics (%)		Predictive value (%)	
		Sensitivity	Specificity	Positive	Negative
LVEF >65%	0.69	100	4	3	100
LAD <40 mm	0.75	100	30	4	100
LAA <20 cm^2	0.76	100	22	4	100
LAVI <51 ml/m^2	0.76	100	24	5	100
LVEF/LAD ratio ≥1.4	0.79	100	28	4	100
LVEF/LAA ratio ≥2.7	0.80	100	25	4	100
LVEF/LAVI ratio ≥1.6	0.76	100	31	5	100

Abbreviations: AUC, area under the curve; CI, confidence interval; other — see Table 2

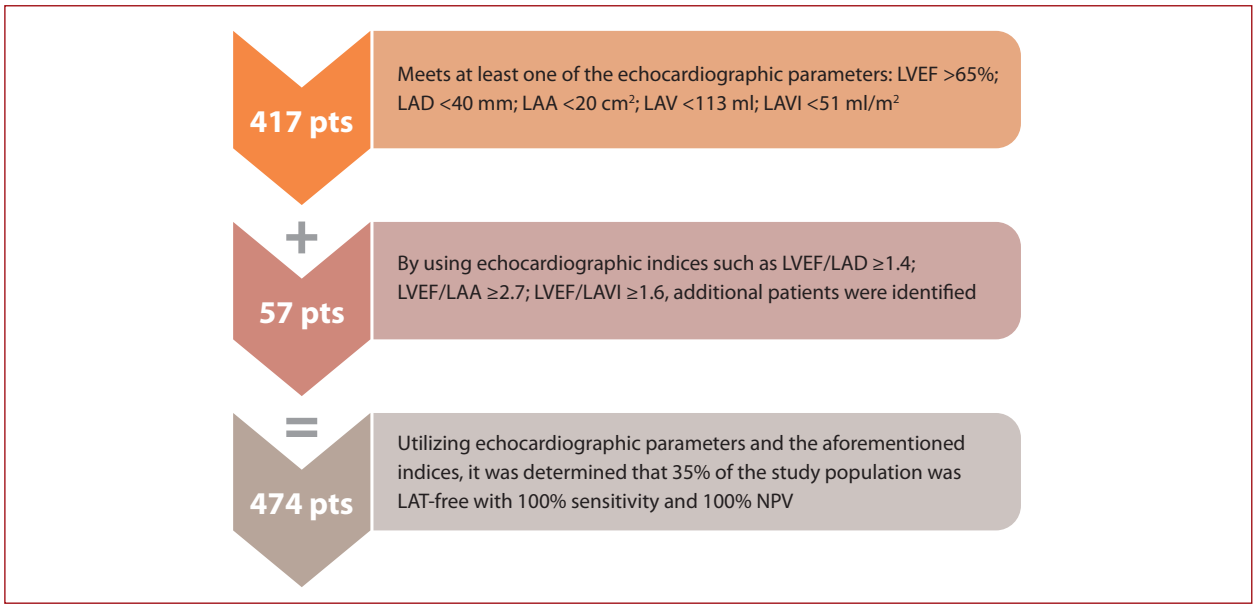

Figure 1. Diagram showing the number of patients meeting at least one echocardiographic criterion associated with LAT-free outcomes
Abbreviations: NPV, negative predictive value; pts, patients; other — see Table 2

DISCUSSION

The primary accomplishment of the presented sub-analysis involves identifying cut-off values of echocardiographic parameters, which demonstrated 100% sensitivity and 100% NPV for detecting LAT absence, thereby enabling the potential exclusion of TEE before CA in patients with AF/AFL.

Current AF management guidelines, both European and American, do not require mandatory TEE study before AF/AFL CA in patients on optimal chronic anticoagulation [1, 4]. There are notable disparities concerning the routine use of TEE before the AF/AFL CA procedure. Certain centers continue to employ TEE as a standard procedure for all patients undergoing AF/AFL CA [17, 18], which indicates lack of consensus and adherence to relevant guidelines, potentially leading to excessive utilization of this diagnostic modality. As stated in the introduction, the available data regarding the incidence of LAT in patients receiving chronic anticoagulant therapy are mutually exclusive [5–9]. On the one hand, there are studies indicating a notable occurrence of LAT before scheduled AF/AFL CA. For instance,

a meta-analysis conducted by Lurie et al. [5] encompassing a sample size of 14 653 patients on anticoagulant treatment for a minimum duration of 3 weeks and undergoing TEE revealed the presence of LAT in 2.73% of cases. Similarly, a study by Di Minno et al. [6] involving a large cohort of 20 516 patients diagnosed with AF reported a weighted mean prevalence of LAT of 3.4% in the subpopulation on chronic anticoagulation. The results of our investigation align with the previously referenced research, revealing a comparable 3.3% prevalence of LAT among patients under long-term anticoagulation therapy. On the other hand, Patel et al. found no incidence of LAT in their prospective multicenter registry involving 6186 patients with AF, on uninterrupted DOACs, undergoing radiofrequency CA, with intracardiac echocardiography guidance, despite a mean CHA_2DS_2-VASc score of 2.86 ± 1.58 [9]. Likewise, in the study by Di Biase et al. [19] with 970 patients on chronic anticoagulation therapy and a mean CHA_2DS_2-VASc score of 3.01 ± 1.3, no LAT was observed, before AF CA in patients on uninterrupted DOAC regimen. It is important to highlight that, in the two aforementioned studies where LAT was not observed, patients received exclusively DOACs, and the CA procedures were carried out without halting anticoagulation treatment, setting them apart from investigations reporting LAT, wherein a subset of patients were on VKAs and procedures were conducted following temporary cessation of anticoagulation and, in some cases, with or without heparin bridging therapy. Given the variability in reported rates of LAT incidence among patients in question, it is crucial, from a clinical perspective, to identify non-invasive parameters that can effectively identify individuals with an exceptionally low risk of LAT.

Thus far, numerous risk stratification methods have been devised to accurately predict the presence or absence of LAT in patients affected by AF/AFL. In-depth academic exploration has highlighted the essential contribution of various echocardiographic parameters, complemented by clinical factors, in enhancing the predictive capacity for LAT in both the population of patients before CA [7, 10] or in the mixed population of patients undergoing cardioversion and CA [12–14, 20]. Notably, our previous research extensively examined the assessment of echocardiographic indices, encompassing parameters such as LVEF/LAD, LVEF/LAA, and LVEF/LAVI [15]. In another study examining the usefulness of the aforementioned indices conducted by Ayirala et al. [11] and involving a cohort of 334 patients undergoing electrical cardioversion on VKA or VKA and heparin (LAT found in 15.6%), the authors demonstrated that an LVEF/LAVI ratio of <1.5 effectively distinguished patients with and without LAT, serving as a reliable negative predictor of LAA thrombus formation with a sensitivity and NPV of 100% when $CHADS_2$ scores were <1. External validation of the aforementioned study, conducted by Doukky et al. [13], in a group of 215 subjects (LAT found in 8.8%) undergoing electrical cardioversion or CA, reproduced similar results. Our multicenter study, which involved a significant patient sample (n = 1346), reproduced findings that are akin, albeit not identical to those reported by the authors mentioned earlier. In our examination, the threshold value for LVEF/LAVI, yielding both 100% sensitivity and 100% NPV, was determined to be 1.6. It is important to note that our study cohort differed significantly from those examined in the studies conducted by Ayirala et al. [11] and Doukky et al. [13]. First, in our study, all participants were treated with anticoagulants, with a majority (88%) receiving DOACs, and thereby the incidence of LAT was substantially lower at 3.3%, compared to 15.6% in Ayirala et al.'s group and 8.8% in Doukky et al. group. Second, our study covered a considerably larger sample size of n = 1346, in contrast to n = 334 and n = 215 in the aforementioned studies [11, 13]. Finally, we included patients exclusively sheduled for CA, while the authors mentioned above included individuals qualified for both CA and cardioversion.

TEE is regarded as the gold standard for evaluating preexisting LAT [21], yet its semi-invasive nature, potential complications, and associated discomfort not only burden patients but also amplify the workload of echocardiography laboratories, contributing to the overall cost of treatment [22, 23]. Regarding treatment costs, Gula et al. [24] argued that though routine use of TEE before AF/AFL CA may help detect LAT and prevent strokes, the higher incremental cost-effectiveness ratio of $226 608 per quality-adjusted life year for the general population compared to the lower ratio of $2232 per quality-adjusted life year for high-risk patients raises the need for cost-effectiveness considerations in implementing this approach. The findings of our research provide robust backing for the utilization of TTE parameters in clinical practice to effectively rule out the existence of LAT within a population of adequately anticoagulated patients (88% utilizing DOACs a minimum of 3 weeks before the intervention in the study population). It is essential to note that the results presented in our study cannot be extrapolated to the entire population of AF/AFL patients and may not apply to those with an unclear status of anticoagulant treatment, individuals with a history of LAT (in such cases, repeat TEE is suggested), or when the procedure is conducted in an accelerated/urgent manner [1]. Owing to the remarkable sensitivity and NPV of established cut-off values for simple TTE parameters, implementing these in a clinical setting offers many potential advantages. Foremost among these benefits is the substantial reduction in the necessity for TEE (35% of patients were identified as LAT-free using TTE), thereby mitigating associated periprocedural risks and reducing the overall financial outlay required for the intervention.

Study limitations

Our study has several limitations that need to be acknowledged. First, it is important to recognize that the study was based on a registry with certain limitations. Second, the utilization of echocardiographic studies, including TTE,

was dependent on the discretion of attending physicians, resulting in missing data for some patients. Lastly, the TTE and TEE studies were performed using echocardiography devices from various vendors and were analyzed and interpreted at local echocardiography laboratories without central supervision. Additionally, certain promising parameters, such as parameters of left ventricular diastolic dysfunction and peak atrial longitudinal strain, which could potentially identify patients at increased risk of LAT, were not included in the registry methodology [25, 26]. Furthermore, variations in TEE use across participating centers, with some performing TEE selectively based on factors such as anticoagulation status or concerns about non-adherence to DOACs, may have introduced selection bias.

CONCLUSIONS

Simple echocardiographic parameters could help identify, among patients scheduled for elective CA due to atrial arrhythmias, those individuals for whom TEE could be safely omitted. Further research and validation may be necessary to confirm and establish the widespread use of those parameters in clinical practice.

Article information

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