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Atrial thrombus detection on transoesophageal echocardiography in patients with atrial fibrillation undergoing cardioversion or catheter ablation: A pooled analysis of rates and predictors

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Abstract

Objective: To summarize data on the rates and predictors of left atrial thrombus/left atrial appendage thrombus (LAT/LAAT) detection by transoesophageal echocardiography (TEE) before electrical cardioversion (ECV) or catheter ablation (CA) for atrial fibrillation (AF).

Methods: EMBASE, MEDLINE, and Web of Science Core Collection were searched to identify all studies providing relevant data and published by October 7, 2020. A random-effects meta-analysis method was used to pool effect size estimates.

Results: A total of 85 studies were included, reporting data from 56 660 patients with AF. In patients undergoing CA and ECV, the pooled prevalence of LAT/LAAT was 1.8% and 7.5% in those not on oral anticoagulation (OAC), 1.8% and 5.5% in those taking OAC, and 1.3% and 4.9% in case of adequate OAC, respectively. According to the type of OAC, the prevalence was 2.0% and 7.6% for vitamin K antagonist, 1.3% and 3.5% for direct oral anticoagulant. Predictors of LAT/LAAT detection were nonparoxysmal AF (odds ratio [OR]: 3.6, 95% confidence interval: 2.4–5.2), hypertension (OR: 2.9, 1.2–7.0), previous stroke (OR: 3.0, 1.6–5.63), heart failure (OR: 4.3, 2.7–6.8), and $CHADS_2$ score ≥2 (OR: 3.3, 1.9–5.8) for patients undergoing CA; and heart failure (OR: 2.8, 1.3–6.2) and the CHA_2DS_2-VASc score (OR: 2.55, 1.5–4.5) for those undergoing ECV.

Conclusion: The prevalence of LAT/LAAT in AF patients undergoing ECV or CA varies widely, mainly due to differences in patient risk profiles and OAC types. Further research should determine whether the predictors of LAT/LAAT detection identified by this study could be used to select patients who require pre-procedural TEE.

KEYWORDS

ablation, atrial fibrillation, cardioversion, echocardiography, thrombus

Abbreviations: AF, atrial fibrillation; CA, catheter ablation; CV, cardioversion; DOAC, direct oral anticoagulant; LAAT, left atrial appendage thrombus; LAT, left atrial thrombus; OAC, oral anticoagulation; TEE, transoesophageal echocardiography; VKA, vitamin K antagonist.

1 | INTRODUCTION

Electrical cardioversion (ECV) and catheter ablation (CA) are commonly used rhythm control modalities for symptomatic atrial fibrillation (AF).[1] Restoration of sinus rhythm after ECV or CA is sometimes associated with embolization of left atrial (LA) or left atrial appendage (LAA) thrombi to the brain, leading to either stroke or asymptomatic cerebral emboli.[2] Transoesophageal echocardiography (TEE) is the reference standard to identify LA and LAA thrombus in routine clinical practice. The presence of left atrial thrombus (LAT) or left atrial appendage thrombus (LAAT) is a contraindication to ECV and CA.

To reduce the incidence of cardioembolic stroke associated with ECV and CA, current guidelines recommend for AF patients who present in sinus rhythm either at least 3 weeks of adequate anticoagulation or a TEE before the procedure (class IIa).[2] For those who are in AF on a presentation for CA, systematic TEE should be performed even if they have been receiving anticoagulation therapeutically for 3 weeks or longer (class IIa).[2] However, the patterns of TEE use before ECV or CA for AF vary significantly across different settings. For instance, a survey of the writing group members of the 2018 Heart Rhythm Society consensus statement on catheter and surgical ablation of AF showed that 51% of them performed a TEE in all patients undergoing AF ablation, regardless of the presenting rhythm and anticoagulation status.[2] This suggests that for a significant proportion of clinicians, the decision to perform a TEE before CA is influenced by considerations other than the current guidelines, such as the patients' risk profiles.

Some studies have suggested that factors such as LA dilatation, reduced left ventricular ejection fraction (LVEF), and increased CHA_2DS_2-VASc score (≥2) and $CHADS_2$ score (≥1) are potential predictors for LAT/LAAT detection on TEE.[3-6] Few other studies have reported conflicting results.[7,8] Therefore, it remains unclear whether additional clinical criteria could help the selection of patients who are likely to be diagnosed with LAT/LAAT on TEE. Hence, this systematic review and meta-analysis aimed to summarize data on the rates and predictors of LAT/LAAT detection by TEE performed before ECV and CA for AF. Such data may help in refining the screening strategy for LAT/LAAT before these procedures and improve the cost–benefit of preprocedural TEE.

2 | METHODS

This review is reported in accordance with the meta-analyses of observational studies in epidemiology guidelines.[9] It was registered with PROSPERO (CRD42020212084).

2.1 | Literature search

PubMed/MEDLINE, Excerpta Medica Database (EMBASE), and Web of Science Core Collection were searched by one investigator (J. J. N.) to identify all studies reporting primary data on the prevalence of predictors of LAT or LAAT, as well as spontaneous echo contrast (SEC) or sludge using TEE done before ECV or CA for AF, published and included in these bibliographic databases from inception through October 7, 2020 (date of the last search), irrespective of the language. The search strategy was built based on the combination of relevant terms related to "atrial fibrillation," "transoesophageal echocardiography," "thrombus," "echo contrast," "sludge," "cardioversion," "ablation," and their bibliographic synonyms (Table S1). The reference lists of eligible articles were also scrutinized to identify potential additional data sources.

2.2 | Selection of studies to include in the review

We included cross-sectional or cohort studies and randomized controlled trials reporting on the prevalence or predictors of LAT or LAAT, SEC, or sludge identified using TEE done before ECV or CA in patients with AF, or enough data to compute these estimates. We excluded studies not reporting primary data or with an unclear description of the methods, and those with a sample size less than 100. For studies reporting data from the same primary study or registry (duplicates), we included the single most comprehensive (i.e., reporting the largest sample size), or articles presenting complementary data (each article having original information not included in the others). After screening the titles and abstracts of records from bibliographic searches, the full texts of articles deemed potentially eligible were reviewed for final inclusion. Study selection was conducted independently by two investigators (J. J. N. and T. A. A.), with discrepancies resolved via discussion and consensus.

2.3 | Data extraction and management

Data were extracted using a preconceived and standardized data abstraction form, by two investigators (A. L. N. and T. A. A.), and crosschecked by a third one (J. J. N.). These data included the first author, year of publication, recruitment period, country, design (cohort, cross-sectional, or randomized controlled trial), sampling method, timing of data collection (retrospective collection of data from a registry or prospective collection from patients), selection criteria, type of procedure (ECV or CA), total sample size, mean age, proportion of males, proportions of patients on anticoagulation in general, and on a specific anticoagulant (warfarin, rivaroxaban, endoxaban, apixaban, and dabigatran), minimum duration on anticoagulation, proportions of patients with various cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity, smoking, and valvular heart disease), proportions with different types of AF according to duration (paroxysmal, persistent, or permanent), number of participants with LAT or LAAT, SEC, or sludge, and risk estimate (odds ratio [OR] or relative risk) with the 95% confidence interval (95% CI) for each variable assessed as a potential predictor of thrombus. Adequate or good oral anticoagulation (OAC) was defined as either at least 3 weeks of either vitamin K antagonist (VKA) with confirmed international normalized ratio (INR) 2–3 or direct oral anticoagulant (DOAC) with compliance. The risk of bias in included

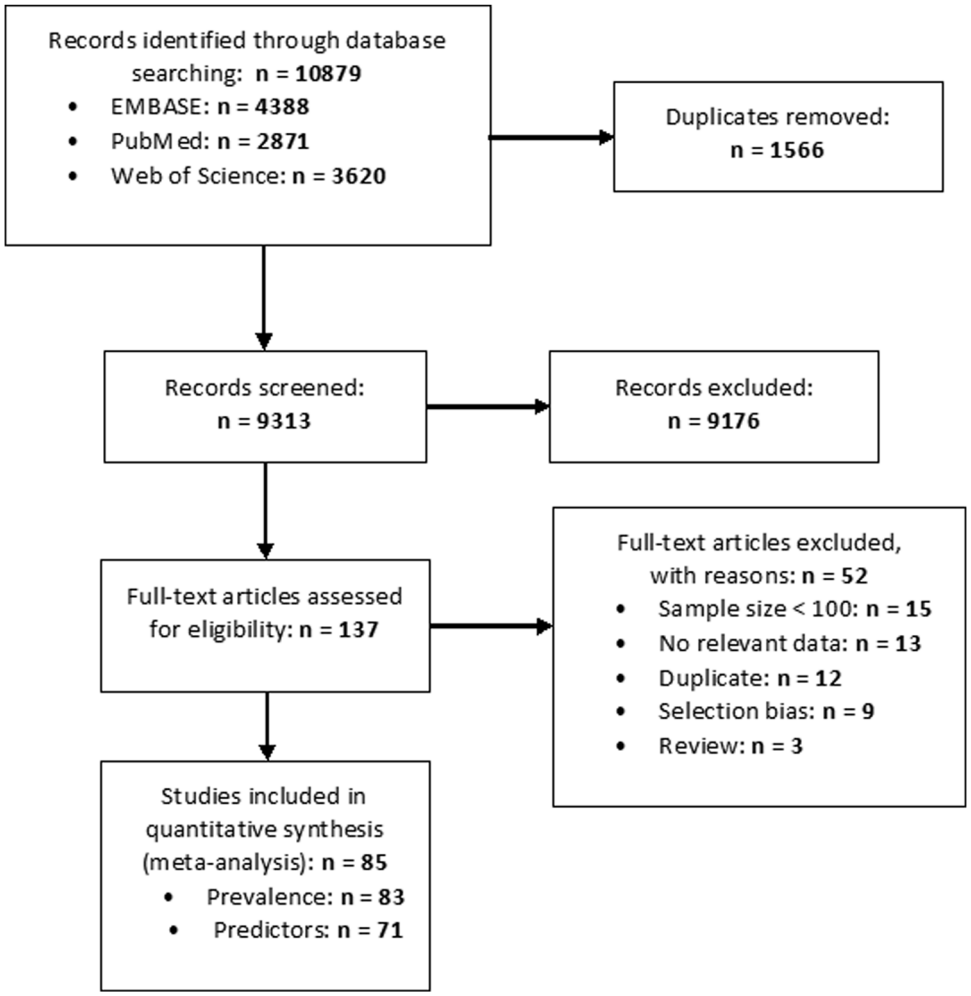


FIGURE 1 PRISMA flowchart of study selection

studies was assessed using an adapted version of the tool developed by Hoy et al.[10]

2.4 | Statistical analysis

All analyses were conducted using the R statistical software (version 3.6.2, The R Foundation for Statistical Computing, Vienna, Austria). We performed a random-effects meta-analysis of proportion using the inverse variance model, with variance stabilizing transformation done via the Freeman–Tukey double-arcsine transformation.[11] Potential clinical conditions contributing to the variance in the estimation were evaluated by means of meta-regression. Heterogeneity was assessed by the χ^2 test on Cochrane's Q statistic,[12] which was quantified by I^2 values, assuming I^2 values of 25%, 50%, and 75%, respectively, representing low, medium, and high heterogeneity.[13] Heterogeneity across studies was further explored using the outlier analysis to detect extreme effect sizes. The influence of each study on the overall estimates and heterogeneity was assessed through the *Leave-One-Out* influencer analysis model. We assessed the small-study effect by funnel plots and tests of funnel plot asymmetry (Egger's linear regression test and Trim-and-fill analysis). Next, univariable and multivariable random-effects meta-analyses were performed on predictors of thrombus. For univariable analyses, continuous variables reported as mean and standard deviations (*SD*) were first transformed to a standardized scale and rescaled to OR per *SD* change in the variable. We characterized statistical significance using a two-tailed *p* value of ≤.05.

2.5 | Ethics committee approval

This is a systematic review using published data. Ethical approval is not required.

2.6 | Patient and public involvement

This is not applicable to this systematic review that used published data.

3 | RESULTS

In total, we identified 10 879 records from bibliographic searches, from which 85 articles were finally included (Figure 1), reporting on a pooled population of 56 660 patients with AF. The list of included studies and their characteristics (Tables S2 and S5) are presented in the appendix. Most studies (75%, $n = 64$) had a low risk of bias.

3.1 | Meta-analysis of thrombus prevalence

3.1.1 | Patients undergoing CA

Forty-two studies reported prevalence data in patients undergoing CA (not mixed with those undergoing ECV), with a pooled sample of 26 806 patients. The overall pooled prevalence of LAT/LAAT was 1.8% (95% CI: 1.4%–2.1% [Figure S1 and Table 1]). It was 1.8% in patients not on OAC and in those taking OAC (Figures S2 and S3 and Table 1). The pooled prevalence was 1.6% in patients who were on OAC for a minimum of 3 weeks, and 1.3% in those with OAC considered as adequate (Figures S4 and S5 and Table 1). When considering the type of OAC used, the prevalence of LAT/LAAT was 2.0% in patients on the VKA warfarin, compared with 1.3% in patients on DOAC (Figures S6 and S7 and Table 1). Specifically, the prevalence was 0.7% for rivaroxaban, 1.3% for apixaban, and 1.0% for patients taking dabigatran (Table 1 and Figures S8–S10). There was evidence of publication bias by funnel plot analysis and by Egger's test ($p < .01$) in the overall, OAC, and VKA analyses, but not in the no OAC and DOAC analyses (Figures S11–S15 and Table 1). There was significant heterogeneity in most analyses.

3.1.2 | Before CV

Thirty-two studies reported on patients undergoing ECV alone (not mixed with those undergoing CA), with a pooled sample of 17 710 patients. The overall pooled prevalence of LAT/LAAT was 8.1% (95% CI: 6.8%–9.3%). It was 7.5% in patients not on OAC, compared with 5.5% in those taking OAC (Figures S17 and S18 and Table 1). The pooled prevalence was 5.2% in patients who were on OAC for a minimum of 3 weeks, and 4.9% in those with OAC considered as adequate (Figures S19 and S20 and Table 1). When considering the type of OAC used, the prevalence of LAT/LAAT was 7.6% in patients on the VKA warfarin, compared with 3.5% in patients on DOAC (Figures S21 and S22 and Table 1). Specifically, the prevalence was 2.5% in patients taking dabigatran (Table 1 and Figures S23). There was evidence of publication bias by funnel plot analysis and by Egger's test ($p < .01$) only in the overall analyses, but not in the no OAC, OAC, VKA, or DOAC analyses (Figures S24–S28 and Table 1). There was significant heterogeneity in most analyses.

3.1.3 | Before CA or CV

Eleven studies reported data on populations including both patients undergoing CA and patients undergoing ECV, with a pooled sample of 9772 patients. The overall pooled prevalence of LAT/LAAT was 4.7% (95% CI: 3.0%–6.4%), with 6.7% in those taking OAC (Figures S29 and S30 and Table 1). It was 5.3% in patients who were on OAC for a minimum of 3 weeks (Figures S31 and Table 1). When considering the type of OAC used, the prevalence of LAT/LAAT was 12.4% in patients on the VKA warfarin, compared with 4.7% in patients on DOAC ($p = .13$; Figures S32 and S33 and Table 1). Specifically, the prevalence was 3.7% in patients taking rivaroxaban, 5.7% in those on dabigatran, respectively (Table 1 and Figures S34 and S35). There was evidence of publication bias by funnel plot analysis and by Egger's test ($p < .01$) only in the overall analyses, but not in the no OAC, OAC VKA, or DOAC analyses (Figures S36–S39 and Table 1). There was significant heterogeneity in most analyses.

3.1.4 | Meta-analysis of SEC and sludge prevalence

The pooled prevalence of SEC was 9.7% in studies focusing on patients undergoing CA, 36.8% in those focusing on patients undergoing ECV, and 8.0% in those including both patients undergoing CA and patients undergoing CA (Figures S40–S42 and Table S6). The prevalence rate of sludge was 1.0% and 3.4% in patients undergoing CA and ECV, respectively.

3.1.5 | Meta-analysis of predictors of thrombus detection

Catheter ablation

Pooled univariable correlates of LAT/LAAT detection on TEE before CA included age ≥75 years, AF type, previous stroke, heart failure, vascular disease, hypertension, diabetes, CAD, $CHADS_2$ and CHA_2DS_2-VASc scores, LA dimension, left ventricular (LV) dysfunction (Figure 2A). In multivariable analyses, nonparoxysmal AF, hypertension, previous stroke, heart failure, and the $CHADS_2$ score were associated with LAT/LAAT detection, whereas diabetes, age, and LA were not (Figure 3A).

Cardioversion

Pooled univariable correlates of LAT/LAAT detection on TEE before ECV included age, age ≥75 years, AF type, previous stroke, heart failure, vascular disease, LA dimension, LVEF, $CHADS_2$ and CHA_2DS_2-VASc scores, and DOAC use are presented in (Figure 2B). In multivariable analyses, only heart failure and the CHA_2DS_2-VASc score were predictors of LAT/LAAT detection (Figure 3B).

CA and/or CV

Pooled univariable and multivariable analyses done on data from studies conducted in patients undergoing or CV are presented in the

TABLE 1 Meta-analysis of thrombus prevalence on transoesophageal echocardiography in patients with atrial fibrillation, by subgroups

Parameter	Number of studies	Sample size	Cases	Prevalence		Heterogeneity		Egger's test (*p* value)
				Rate (%)	95% CI	I^2	*p* Value	
Thrombus before catheter ablation								
Overall	42	26 806	502	1.75	1.41–2.10	84.8%	<.001	<.001
By OAC status								
OAC	31	18 631	327	1.84	1.36–2.38	82.9%	<.001	.010
No OAC	5	1922	37	1.84	0.00–6.53	95.9%	<.001	.266
By adequacy of OAC								
≥3 weeks OAC	20	11 788	192	1.60	1.09–2.19	78.8%	<.001	.186
Good OAC	11	5658	78	1.27	0.79–1.85	64.3%	.002	.715
By type of OAC								
VKA	18	7459	151	1.99	1.28–2.84	81.4%	<.001	.042
DOAC	7	4042	58	1.32	0.38–2.74	89.8%	<.001	.364
By type of DOAC								
Apixaban	2	529	7	1.30	0.45–2.50	0.0%	.622	ND
Dabigatran	4	664	8	0.99	0.00–3.14	71.3%	.015	.290
Rivaroxaban	6	1441	17	0.74	0.00–2.24	78.7%	<.001	.852
Thrombus before cardioversion								
Overall	32	17 710	1,367	8.07	6.83–9.32	90.6%	<.001	.002
By OAC status								
OAC	12	5470	320	5.54	3.65–7.78	89.7%	<.001	.785
No OAC	4	1319	100	7.50	6.13–9.01	0.0%	.564	.948
By adequacy of OAC								
≥3 weeks OAC	7	2342	106	5.19	3.03–7.86	81.0%	<.001	.214
Good OAC	2	203	10	4.86	2.20–8.38	0.0%	.514	ND
By type of OAC								
VKA	5	2064	162	7.55	4.06–12.0	91.0%	<.001	.806
DOAC	5	1760	64	3.46	1.98–5.31	69.1%	.012	.864
By type of DOAC								
Dabigatran	3	631	16	2.51	1.07–4.46	37.7%	.201	.545
Thrombus before catheter ablation or cardioversion								
Overall	9	9772	311	4.67	3.04–6.29	95.4%	<.001	.001
By OAC status								
OAC	5	2652	164	6.73	4.2–9.67	84.4%	<.001	.390
By adequacy of OAC								
≥3 weeks OAC	2	1956	104	4.95	4.12–5.86	54.5%	.138	ND
By type of OAC								
VKA	3	671	68	12.40	5.30–21.84	88.1%	<.001	.243
DOAC	4	2001	96	4.72	3.82–5.71	0.0%	.405	.902

(Continues)

TABLE 1 (Continued)

Parameter	Number of studies	Sample size	Cases	Prevalence		Heterogeneity		Egger's test (*p* value)
				Rate (%)	95% CI	I^2	*p* Value	
By type of DOAC								
Dabigatran	2	743	43	5.73	4.15–7.54	0.0%	.456	ND
Rivaroxaban	2	826	31	3.72	2.51–5.14	0.0%	.538	ND

Note: Good OAC: either at least 3 weeks of either VKA with confirmed INR 2–3 or DOAC with compliance.

Abbreviations: CI, confidence interval; DOAC, direct oral anticoagulants; INR, international normalized ratio; OAC, oral anticoagulants; VKA, vitamin K antagonist.

appendix (Figures S43 and 3). Findings were mostly similar to those from studies focusing on pre-CA TEE or focusing on pre-ECV TEE presented above.

4 | DISCUSSION

This comprehensive systematic review and meta-analysis show LAT/LAAT detection rates on preprocedural TEE of 1.8% and 8.1% in AF patients undergoing CA and ECV, respectively. These rates were lower in patients on OAC before TEE, especially those on at least 3 weeks of OAC, with the lowest rates in those in whom anticoagulation was considered as adequate. Detections rates were also much lower in patients taking DOAC compared to those taking VKA. In general, there was a marked variation in LAT/LAAT rates in patients on OAC across studies, both in patients undergoing CA and those undergoing ECV. Several factors, such as non-paroxysmal AF, OAC use, age ≥75 years, hypertension, previous stroke, heart failure, cardiomyopathy, LA dilatation or LVEF less than 40%, were associated with LAT/LAAT detection.

The disparities in LAT/LAAT detection rate in the included studies are mainly attributable to differences in the clinical characteristics of patients, and to variations in OAC practices across settings. Indeed, the proportions of known risk factors for thromboembolism varied widely between studies, and meta-regression analyses showed that some of these risk factors explained a substantial proportion of the variations in the LAT/LAAT detection rates across studies. Furthermore, these detection rates were consistently higher in patients undergoing ECV compared to those undergoing CA. This is most likely due to the fact that ECV is often an emergency procedure, and patients are less likely to have received OAC for enough time to prevent thrombus formation. On the opposite, CA is usually an elective and well-prepared procedure, done in patients who are mostly chronically anticoagulated.

Although the LAT/LAAT rates were lower in patients on OAC, especially on at least 3 weeks of OAC or OAC considered as being adequate, compared to those not on OAC, it is clear that being on OAC does not abolish the risk of thrombus formation. There are several possible explanations for the presence of LAT/LAAT despite OAC. First, OAC might be ineffective due to reduced bioavailability from noncompliance, inappropriate mode of administration in relation to food intake leading to decreased drug intestinal absorption.[14] Indeed, lower time in therapeutic range (TTR) is associated with higher rates of thromboembolism in patients on warfarin.[15] In one of the studies included in this meta-analysis, in AF patients on warfarin undergoing CV or CA, the TTR was 36.8% in those found to have LAAT compared to 52.7% in those without LAAT.[16] Moreover, the extent of atrial cardiomyopathy, as well as other risk factors, can contribute to atrial thrombosis despite OAC.[17] The prevalence of LAT/LAAT was much higher in patients on VKA than those on DOAC. Higher compliance, lesser drug-food interactions, and no requirement for INR testing are potential reasons for the observed lower atrial thrombus rates associated with DOAC use compared to VKA.

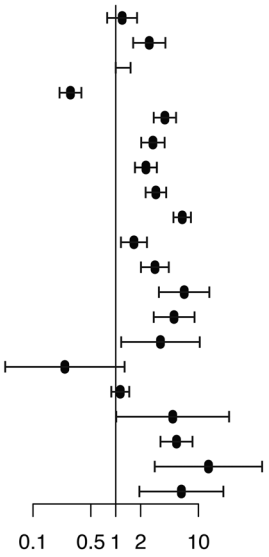
Predictors of LAT/LAAT included age ≥75 years, nonparoxysmal AF, hypertension, previous stroke, heart failure, $CHADS_2$ and CHA_2DS_2-VASc scores, LA dilatation, and LVEF less than 40%. The identification of such predictors has important clinical implications. Although TEE is highly accurate in identifying LAAT, it is an invasive procedure that is associated with discomfort, the need for general anesthesia in some patients, and some potential complications. In one study, the frequency of TEE-related complications, although mostly minor, exceeded that of detected LAAT.[18] Furthermore, routine use of TEE before ECV or CA could be resource-demanding and associated with high expenditure. For instance, using decision analysis and microsimulation model, a study showed that that routine use of TEE in an unselected population anticoagulated with warfarin before pulmonary vein isolation reduced the incidence of cerebral thromboembolic events but at a cost of $226 608 per quality-adjusted life-year.[19] Hence, a strategy allocating preprocedural TEE to patients who have a high probability of LAT/LAAT detection might be more cost-effective and practical, especially in resource-limited settings, than routine TEE in almost all patients before ECV or CA.

The $CHADS_2$ and CHA_2DS_2-VASc scores were already known for their potential value in predicting LAT/LAAT before AF ablation. In fact, a trial showed that a CHA_2DS_2-VASc score ≤1 ruled out LAAT with 100% sensitivity, 100% negative predictive value, but with very low positive predictive value, overall due to low event rates (13 cases of LAAT in 1658 patients).[6] Other risk stratification schemes such as the CHADS-65 score endorsed by the Canadian Cardiovascular Society and the Canadian Heart Rhythm Society could also be useful.[20,21] A risk stratification score integrating nonparoxysmal AF, OAC use, age ≥75 years, hypertension, previous stroke, heart failure,

(A)

Univariate Correlates of Thrombus before Ablation

Correlates	Studies	Patients	OR	[95% CI]	P–value	I–square
Age (per SD increase)	24	18,084	1.20	[0.77; 1.86]	0.42	80.65
Age ≥75 years	8	5,920	2.54	[1.58; 4.09]	0.00	0.00
Female	24	18,084	1.23	[0.98; 1.55]	0.08	0.00
PAF	19	15,997	0.28	[0.20; 0.39]	0.00	27.62
NPAF	23	17,892	3.93	[2.81; 5.50]	0.00	40.52
Diabetes	24	18,073	2.82	[1.99; 3.98]	0.00	39.40
Hypertension	25	18,481	2.32	[1.67; 3.21]	0.00	43.65
Previous stroke	24	18,073	3.06	[2.24; 4.17]	0.00	13.01
Heart failure	19	14,743	6.38	[4.88; 8.33]	0.00	0.00
CAD	12	7,609	1.66	[1.12; 2.45]	0.01	0.00
Vascular disease	8	6,166	2.98	[1.97; 4.50]	0.00	0.00
$CHADS_2$ score	8	3,363	6.74	[3.26; 13.92]	0.00	75.58
CHA_2DS_2Vasc score	11	6,815	5.07	[2.80; 9.17]	0.00	72.50
OAC use	15	16,392	3.47	[1.13; 10.64]	0.03	84.14
DOAC use	6	6,033	0.24	[0.05; 1.31]	0.10	86.32
Mean INR (per SD increase)	5	4,729	1.14	[0.86; 1.49]	0.37	0.27
Mean eGFR (per SD decrease)	4	4,921	4.89	[0.99; 24.16]	0.00	0.00
LA diameter	14	10,170	5.44	[3.40; 8.69]	0.00	66.96
LVEF (per SD decrease)	21	16,083	13.24	[2.90; 60.53]	0.00	78.13
LV dysfunction	2	1,010	6.22	[1.89; 20.47]	0.00	0.00



(B)

Univariate Correlates of Thrombus before Electrical Cardioversion

Correlates	Studies	Patients	OR	[95% CI]	P–value	I–square
Age (per SD increase year)	12	6,318	1.37	[1.15; 1.64]	0.00	20.1
Age ≥65 years	2	1,242	1.48	[0.99; 2.22]	0.05	0.0
Age ≥75 years	4	2,219	1.67	[1.22; 2.28]	0.00	0.0
Female	15	8,201	0.71	[0.37; 1.36]	0.30	93.3
PAF	3	1,987	0.57	[0.36; 0.91]	0.02	19.0
NPAF	3	2,691	1.74	[1.15; 2.61]	0.01	14.8
Diabetes	9	4,324	1.21	[0.90; 1.62]	0.21	31.4
Hypertension	11	6,259	1.11	[0.85; 1.46]	0.45	33.0
Previous stroke	12	5,285	1.94	[1.27; 2.95]	0.00	53.6
Heart failure	7	3,081	2.90	[1.72; 4.89]	0.00	62.0
CAD	7	4,739	1.71	[0.94; 3.09]	0.08	82.9
Vascular disease	3	1,885	1.93	[1.29; 2.88]	0.00	0.0
$CHADS_2$ score	3	1,208	2.78	[1.95; 3.96]	0.00	0.0
CHA_2DS_2Vasc score	4	2,267	1.65	[1.22; 2.23]	0.00	72.5
OAC use	3	3,708	0.88	[0.49; 1.57]	0.66	63.4
DOAC use	4	3,475	0.56	[0.32; 0.97]	0.04	61.9
Mean INR	5	2,650	1.13	[0.94; 1.37]	0.18	0.5
LA Diameter	10	4,830	2.28	[1.80; 2.88]	0.00	42.1
LVEF (per SD decrease)	7	4,005	6.67	[1.15; 38.72]	0.00	0.0

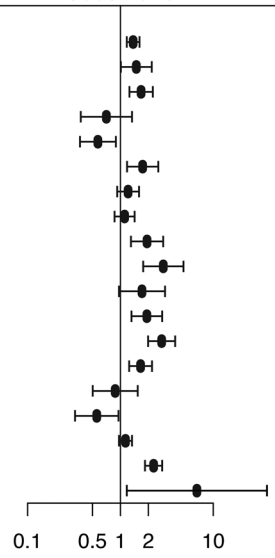


FIGURE 2 Univariable correlates of thrombus detection on transoesophageal echocardiography in patients with atrial fibrillation. 95% CI, 95% confidence interval; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; INR, international normalized ratio; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; NPAF, nonparoxysmal atrial fibrillation; OR, odds ratio; PAF, paroxysmal atrial fibrillation; $CHADS_2$ and CHA_2DS_2-VASc scores are as per *SD* increase

cardiomyopathy, LA dilatation, or LVEF less than 40% on prior transthoracic echocardiography might show good performance in selecting patients who require a preprocedural TEE. Such a score should ideally be tested in a large clinical trial. But due to contemporaneous low rates of LAT/LAAT detection and of postprocedural cerebrovascular embolic events, it might be difficult to appropriately power a trial of preprocedural TEE strategies. An alternative is to test a proposed risk stratification score in existing registries, although this comes with its own limitations, including selection bias. Nevertheless, there is increasing evidence suggesting that performing AF ablation while on uninterrupted DOAC without TEE is feasible and safe,[22,23] with rates of periprocedural cerebrovascular events reported at 0.02% (from 6186 patients) and 0.3% (from 900 patients) in two studies.[22,23]

Our study has some limitations. The numbers of studies and participants vary substantially across analyses. This is due to the fact

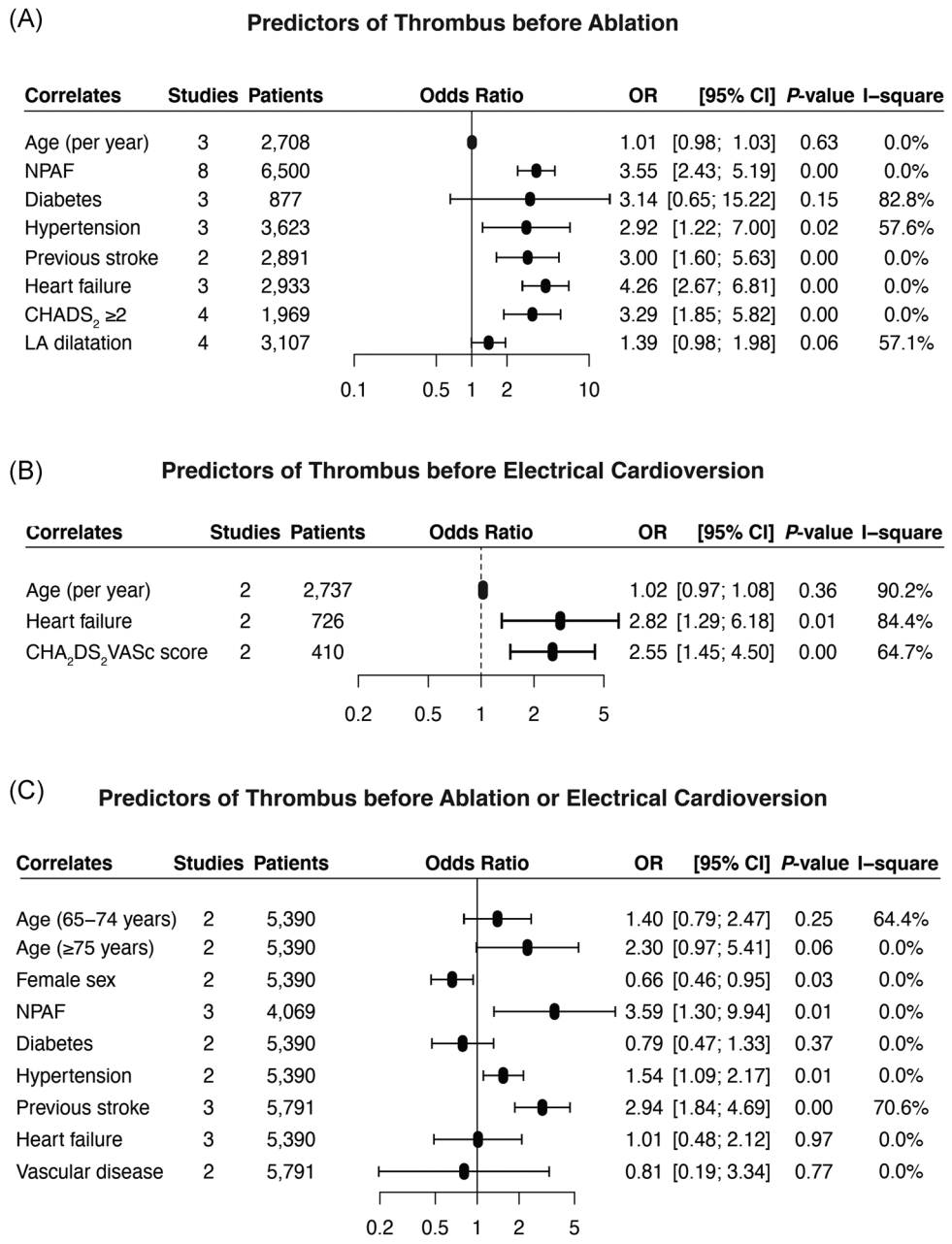


FIGURE 3 Multivariable predictors of thrombus detection on transoesophageal echocardiography in patients with atrial fibrillation. 95% CI, 95% confidence interval; LA, left atrial; NPAF, nonparoxysmal atrial fibrillation; OR, odds ratio; PAF, paroxysmal atrial fibrillation; CHA_2DS_2-VASc scores are: as per 1-point increase

that we performed several subgroup analyses separately in patients undergoing ECV and those undergoing CA, with more studies contributing to some subgroup analyses than others. About half of the studies included in this review were retrospective, leading to potentially significant reporting bias. Although the high heterogeneity of pooled analysis of LAT/LAAT detection rates was partly explained by differences in the distribution of thromboembolic risk factors across studies, the difference in diagnostic accuracy due to interobserver variability and inconsistent TEE screening strategies between settings is also a potentially important source of bias and heterogeneity. For instance, per physician preference, some patients deemed at low risk were probably excluded in some studies, leading to selection bias and overestimation of LAT/LAAT detection rates. Furthermore, we were not able to capture some details about periprocedural OAC strategies for most studies, including OAC interruption or continuity and bridging therapy, and to evaluate their impact on LAT/LAAT occurrence. Some emerging prothrombotic factors such as LA morphology or a persistent prothrombotic state (as evidenced by increased platelet activation and thrombin formation, decreased fibrinolysis, enhanced inflammation, and endothelial dysfunction)[24] are not covered here because they were not reported in the primary studies included in this review. Finally, our study did

not investigate the relationship between LAT detection on preprocedural TEE and the occurrence of periprocedural cerebrovascular events.

5 | CONCLUSION

This study shows that the prevalence of LAT/LAAT in AF patients undergoing CA or ECV varies widely, mainly due to differences in patient risk profiles and OAC types. The rates of LAT/LAAT were relatively low, especially in patients taking DOAC (1.3% and 3.5% for CA and ECV, respectively). This suggests that preprocedural TEE could be avoided in a large proportion of patients, especially those undergoing CA and who are on DOAC. A risk stratification based on predictors of LAT/LAAT detection identified in this study (nonparoxysmal AF, age ≥75 years, hypertension, previous stroke, heart failure, cardiomyopathy, LA dilatation, or LVEF less than 40%) might help in identifying patients who really need a preprocedural TEE based on a high pretest probability.

AUTHOR CONTRIBUTIONS

Conception and design: Jean Jacques Noubiap. *Search strategy*: Jean Jacques Noubiap. *Studies selection*: Jean Jacques Noubiap and Thomas A. Agbaedeng. *Data extraction*: Aude Laetitia Ndoadoumgue, Thomas A. Agbaedeng, and Jean Jacques Noubiap. *Data synthesis*: Thomas A. Agbaedeng and Jean Jacques Noubiap. *Data interpretation*: Jean Jacques Noubiap and Thomas A. Agbaedeng. *Manuscript drafting*: Jean Jacques Noubiap and Thomas A. Agbaedeng. *Manuscript revision*: Jean Jacques Noubiap, Thomas A. Agbaedeng, Aude Laetitia Ndoadoumgue, Ulrich Flore Nyaga, and Andre Pascal Kengne. *Approval of the final manuscript*: Jean Jacques Noubiap, Thomas A. Agbaedeng, Aude Laetitia Ndoadoumgue, Ulrich Flore Nyaga, and Andre Pascal Kengne. *Guarantor of the review*: Jean Jacques Noubiap.

DATA AVAILABILITY STATEMENT

All data generated or analyzed in this study are included in the published article and the supplementary files.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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