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ORIGINAL ARTICLE

Echocardiographic Predictors of Left Atrial Appendage Thrombi in Non-Valvular Atrial Fibrillation Patients

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ABSTRACT

Background: Non-valvular atrial fibrillation (NVAF) increases stroke risk, primarily from left atrial appendage (LAA) thrombi. Although TEE is superior for detection, transthoracic echocardiography (TTE) measures like atrial size may help early risk assessment. The predictive role of transthoracic echocardiography (TTE) parameters and related biomarkers remains uncertain. This study aimed to assess whether TTE-derived measures together with laboratory markers, can predict LAA thrombus and spontaneous echo contrast in NVAF patients efficiently.

Methods: This cross-sectional study at cardio department of Zagazig University Hospital involved 26 NVAF patients underwent clinical evaluation, lab tests, TTE for LA measurements, TEE and Doppler techniques for comprehensive thromboembolic risk evaluation. Data were analyzed using SPSS v20.0. Means, percentages, and standard deviations were reported. Appropriate parametric and non-parametric tests, along with logistic regression, were used. Significance was set at $p < 0.05$.

Results: The mean age was 63.2±17.1 years, with 50% males; hypertension was most common (69.2%). LAA thrombus was linked to older age (P=0.0208) and higher AST (P=0.0329). Thrombus patients had higher LAESV, LAEDV, lower EF, and reduced LAA velocity (P<0.05). Positive associations existed with D-dimer (P<0.0001, CI:0.242–0.469), ALT (P=0.004, CI:0.013–0.061), LAESV (P<0.0001, CI:0.019–0.037), LAEDV (P=0.029, CI:0.001–0.018); negative with albumin (P=0.022, CI:-1.127–-0.097), EF (P=0.001, CI:-0.068–-0.02), and LAA velocity (P=0.002, CI:-0.041–-0.011).

Conclusion: Transthoracic echocardiography offers non-invasive indicators of LAA thrombus risk in NVAF, including atrial volumes, ejection fraction, and LAA velocity, supported by biomarkers like D-dimer and albumin. Though TEE is definitive, these parameters aid early risk stratification and anticoagulation decisions.

Keywords: Non-valvular atrial fibrillation; Echocardiography; Left atrium; Left atrial appendage thrombi.

INTRODUCTION

Non-valvular atrial fibrillation (NVAF) is a common arrhythmia associated with ischemic stroke, primarily due to thromboembolic events originating from the left atrial appendage (LAA) [1,2]. Its prevalence in the general population is approximately 0.4–1%, increasing to 7.2%

in individuals over 65 and 10.3% in those older than 75 years [3]. NVAF symptoms include palpitations, chest discomfort, lightheadedness, and shortness of breath [3]. Patients with NVAF have a fivefold higher risk of ischemic stroke compared to those in sinus rhythm, with over 90% of embolic strokes in NVAF attributed to thrombi from the LAA [4].

The LAA's anatomy—a long, narrow, wavy, multi-lobed structure with a crenellated lumen—promotes blood stasis and thrombus formation, especially in atrial fibrillation. Thrombus appears on transesophageal echocardiography (TEE) as a hyperechogenic, non-muscular, non-endocardial mass in multiple imaging planes, while spontaneous echo contrast (SEC) appears as persistent, smoke-like swirling material [5]. The presence of thrombus, SEC in the left atrium or LAA, or low LAA emptying velocity are strong indicators of thromboembolic risk in NVAF.

While Transesophageal echocardiography (TEE) is the gold standard for detecting left atrial appendage (LAA) thrombus in non-valvular atrial fibrillation (NVAF), alternatives like transthoracic echocardiography (TTE) are gaining traction due to TEE's invasiveness and limited availability [3].

TTE is widely used for initial evaluation due to its non-invasiveness and accessibility, its sensitivity for detecting LAA thrombi and SEC is limited compared to TEE, which remains the gold standard [6]. Nevertheless, certain TTE-derived parameters can help predict LAA thrombus and SEC. Left atrial enlargement, which reflects the severity and chronicity of NVAF, is associated with elevated thromboembolic risk. Moreover, specific LAA morphologies (e.g., narrow orifice or complex lobes) and reduced LAA emptying velocity contribute to increased risk due to impaired blood flow and stasis [3,7].

Although TTE is widely accessible, its role in predicting LAA thrombus and SEC using volumetric and functional indices has not been fully established. Furthermore, the combined use of echocardiographic parameters with circulating biomarkers has not been sufficiently investigated. Identifying TTE-based predictors of LAA thrombosis may improve early risk stratification and guide management strategies in NVAF patients, even though TEE remains essential for definitive diagnosis [8-11].

We hypothesize that TTE findings can predict left atrial appendage thrombi and spontaneous echocardiographic contrast in non-valvular atrial fibrillation patients, as confirmed by transesophageal echocardiography.

The aim of this study was to evaluate the effectiveness of transthoracic echocardiography in predicting left atrial appendage thrombi and spontaneous echocardiographic contrast in patients with non-valvular atrial fibrillation, approaching its results with those of transesophageal echocardiography. The objectives were to identify transthoracic echocardiographic predictors for left atrial appendage thrombi and to assess the association between transthoracic echocardiographic findings and the presence of spontaneous echocardiographic contrast in these patients.

METHODS

This prospective cross-sectional study was conducted at the Cardiology Clinic of Zagazig University Hospital. The sample size was calculated using the OPEN-EPI program with a 95% confidence interval and 80% power, based on prior findings showing a mean left atrial (LA) diameter on transthoracic echocardiography (TTE) of 46.7 ± 3.91 mm in atrial fibrillation patients with appendage thrombi, compared to 41 ± 5.94 mm in those without [3]. Accordingly, the required sample size was

determined to be 26 patients. Ethical approval code: ZU-IRB # 453 / 23 -June-2024.

The study population consisted of patients aged 18 years or older who were diagnosed with non-valvular atrial fibrillation (NVAF) based on electrocardiographic evidence. Individuals were excluded if they had known valvular heart disease, such as mitral stenosis or mechanical heart valves, or a history of recent myocardial infarction or cardiac surgery. Patients with significant comorbidities that could affect cardiac structure or function, including severe heart failure or cardiomyopathy, were also excluded. Additionally, pregnant or breastfeeding patients, those with active infections or inflammatory conditions potentially impacting cardiac function, and individuals with advanced renal or hepatic impairment were not included in the study.

Study procedures

This prospective study involved a detailed clinical and echocardiographic evaluation of patients with non-valvular atrial fibrillation (NVAF) attending the Cardiology Clinic at Zagazig University Hospital. All enrolled patients underwent thorough clinical assessment, beginning with detailed history taking and a complete physical examination, with particular focus on vital signs including blood pressure, heart rate, and respiratory rate. Local cardiac examination was performed to assess structural and functional cardiac abnormalities.

Laboratory investigations

Laboratory tests were conducted to evaluate systemic and organ-specific status. Complete blood count (CBC) was measured using the automated Sysmex XN-1000 analyzer (Japan), which provided data on red blood cell (RBC) count, hemoglobin concentration (Hb%), white blood cell (WBC) count, and platelet count (Plts). D-dimer levels, a marker of thrombotic activity, were measured using enzyme-linked immunosorbent assay (ELISA) kits (Catalog No. SG-00493, SinoGeneClon Biotech, Hangzhou, China). Renal function was assessed through serum creatinine, blood urea nitrogen (BUN), and serum uric acid levels using the Roche Cobas 6000 platform (Switzerland). Liver function tests—alanine aminotransferase (ALT) and aspartate aminotransferase (AST)—were performed using the Abbott Architect C16000 analyzer (USA), ensuring exclusion of patients with significant hepatic impairment.

Echocardiographic assessment

All patients underwent transthoracic echocardiography (TTE) using the Vivid 9 system (GE Vingmed, Norway) equipped with a harmonic M5S variable-frequency (1.7–4 MHz) probe. The examination was conducted in the left lateral decubitus position following standard echocardiographic protocols. The left atrial diameter (LAD) and left atrial volume (LAV) were measured from standard apical four-, two-, and three-chamber views corresponding to 0°–30°, 60°–90°, and 120°–150° angles, respectively. The LAD was measured about 1 cm above the mitral annulus in two- and four-chamber views, while the end-systolic and end-diastolic LAD in the three-chamber view was assessed from the posterior aortic root to the posterior LA wall, as recommended by Lang et al. (2006) [12]. M-mode tracing from the parasternal long-axis view was used to measure LA anteroposterior diameter. LA volume was calculated using the biplane area-length formula: $LAV = 8 \times A1 \times A2 / 3\pi L$, where A1 and A2 represent the maximal planimetered LA area in apical 4- and 2-chamber views, and L is the LA length measured at ventricular end-systole [13].

Transesophageal echocardiography (TEE)

All patients were further assessed using transesophageal echocardiography (TEE) as per standard protocols [14]. TEE was performed using a 6T phased-array multiplane probe capable of 0° to 180° imaging, offering superior resolution to TTE for detecting intracardiac thrombi. Multiplane views enabled comprehensive visualization of the left atrium and especially the left atrial appendage (LAA), where thrombus typically forms in NVAF patients. Thrombus was defined as a soft, echo-dense mass with clear borders distinct from the pectinate muscles, visible in more than one tomographic plane.

The LAA was evaluated for structural morphology, orifice area, and anatomical variants using Doppler pulsed wave and multiplane imaging. LAA emptying velocity was assessed using spectral Doppler, averaging 20 cardiac cycles and applying four analytical methods to ensure accurate detection of spontaneous echocardiographic contrast (SEC): (1) average of the three highest diastolic velocities, (2) average of ten consecutive systolic and diastolic velocities, (3) average of ten consecutive diastolic velocities, and (4) average of the ten highest diastolic velocities. SEC was defined as a swirling, smoke-like echo density within the LA or LAA, persisting at low gain settings, and LAA thrombus was identified as a discrete mass with consistent echogenicity in multiple views.

This rigorous multi-modality assessment allowed for accurate correlation between transthoracic and transesophageal findings regarding the presence of LAA thrombi and SEC, as well as detailed measurement of structural and functional parameters that may serve as predictive markers in NVAF.

The primary outcome of the study was to evaluate the predictive value of various transthoracic echocardiography (TTE) parameters in detecting left atrial appendage (LAA) thrombus or spontaneous echo contrast, with confirmation provided by transesophageal echocardiography (TEE). The secondary outcome is to assess the association between TTE parameters and laboratory biomarkers in relation to the presence of LAA thrombus.

STATISTICAL ANALYSIS

Data were processed and analyzed using SPSS version 20.0, with qualitative variables presented as numbers and percentages, and quantitative data as mean ± standard deviation (SD). The arithmetic mean was used to describe the central tendency, while SD measured dispersion around the mean. The Student's t-test was employed to compare means between two independent groups, and the Mann-Whitney test was used for non-normally distributed data. Fisher's exact test replaced the chi-square test for non-parametric data, and the chi-square test (X^2) assessed associations between variables. Univariate logistic regression analysis identified significant correlations. Statistical significance was determined at a 5% level ($p < 0.05$).

RESULTS

A total of 26 patients (mean age 63.2 ± 17.1 years) were included; 50% were male. Smoking status: 30.8% current, 23.1% ex-smokers. Histories of similar attacks of arrythmia were present in 34.6% and 26.9%, respectively. Hypertension was the most common comorbidity (69.2%), followed by dyslipidemia (30.8%) and diabetes (11.5%). Positive family history was reported in 19.2%. No statistically significant differences were found (all $p > 0.05$). Table 1.

Patients with LAA thrombus had a statistically significant higher mean age (77.5 ± 7.0 vs. 60.6 ± 17.2 years, $P = 0.0208$). No significant differences were found regarding sex, smoking status, prior attacks, arrhythmia, comorbidities (hypertension, diabetes, dyslipidemia), or family history ($P > 0.05$ for all). Table 2.

AST was statistically significant higher in patients with thrombus (30.28 ± 6.59 vs. 23.59 ± 6.89 U/L, P = 0.0329). All other laboratory parameters, including RBCs, hemoglobin, WBCs, platelets, D-dimer, renal function tests, ALT, and albumin, showed no statistically significant differences (P > 0.05). Table 3.

Patients with thrombus had statistically significant higher LAESV (74 ± 2.35 vs. 51.05 ± 6.68 mm³, P < 0.0001) and LAEDV (95.25 ± 8.67 vs. 75.91 ± 15.62 mm³, P = 0.0178), and lower EF (57.75 ± 1.48% vs. 66.32 ± 4.29%, P < 0.0001). LAA velocity was also Statistically significant reduced (25.5 ± 8.5 vs. 38.5 ± 6.16 cm/s, P = 0.0498). Other structural parameters showed no significant differences (P > 0.05). Table 4.

There were significant positive associations between LAA thrombus formation and D-dimer (P < 0.0001), ALT (P = 0.004), LAESV (P < 0.0001) and LAEDV (P = 0.029). While there were significant negative associations between LAA thrombus formation and albumin (P = 0.022), EF (P = 0.001) and LAA velocity (P = 0.002). Table 5**.**

TABLE (1): Demographic data and basal characteristics among included subjects

	Value (N = 26)
Age (Years)	63.23 ± 17.14
Sex	
• Male	13 (50%)
• Female	13 (50%)
Smoking status	22 (84.62%)
• Smoker	8 (30.77%)
• Ex-smoker	6 (23.08%)
• Non-smoker	12 (46.15%)
Clinical history	
• Similar attacks	9 (34.62%)
• Arrythmia	7 (26.92%)
Comorbidities	
• Hypertension	18 (69.23%)
• DM	3 (11.54%)
• Dyslipidemia	8 (30.77%)
Family history	5 (19.23%)

TABLE (2): Comparison between Cases with and without thrombus formation regarding demographic data and basal characteristics

	Cases without thrombus (N = 22)	**Cases with thrombus (N = 4)**	**P. Value**
Age (Years)	60.64 ± 17.16	77.5 ± 6.98	0.0208*[MWU]
Sex			
• Male	12 (54.55%)	1 (25%)	0.2957[X]
• Female	10 (45.45%)	3 (75%)	0.2957[X]
Smoking status			
• Smoker	7 (31.82%)	1 (25%)	0.7959[X]
• Ex-smoker	5 (22.73%)	1 (25%)	0.9248[X]

	Cases without thrombus (N = 22)	Cases with thrombus (N = 4)	P. Value
• Non-smoker	10 (45.45%)	2 (50%)	0.8732[X]
Clinical history			
• Similar attacks	7 (31.82%)	2 (50%)	0.5017[X]
• Arrythmia	6 (27.27%)	1 (25%)	0.9286[X]
Comorbidities			
• Hypertension	16 (72.73%)	2 (50%)	0.3852[X]
• DM	2 (9.09%)	1 (25%)	0.3798[X]
• Dyslipidemia	7 (31.82%)	1 (25%)	0.7959[X]
Family history	5 (22.73%)	0 (0%)	0.5552[f]

TABLE (3): Comparison between Cases with and without thrombus formation regarding Laboratory investigations

	Cases without thrombus (N = 22)	Cases with thrombus (N = 4)	P. Value
Laboratory investigations			
RBCs (×10^6 / mcl)	4.81 ± 0.5	4.85 ± 0.4	0.99[MWU]
Hb (g/dL)	13.57 ± 1.73	13.73 ± 0.78	0.9148[MWU]
WBC (×10^3/mcl)	7.35 ± 2.16	8.35 ± 1.97	0.2553[MWU]
PLTs (×10^3/mcl)	241.96 ± 43.74	244.75 ± 17.67	0.8461[s.t]
D.Dimer (mg/L FEU)	0.78 ± 0.25	2.57 ± 1.1	0.0672[w.t]
BUN (mg/dL)	20.93 ± 8.7	20.38 ± 3.6	0.9151[MWU]
Serum creatinine (mg/dL)	1.03 ± 0.18	1.1 ± 0.07	0.2411[w.t]
AST (U/L)	23.59 ± 6.89	30.28 ± 6.59	0.0329*[MWU]
ALT (U/L)	18.49 ± 4.06	26.5 ± 6.32	0.1129[w.t]
Albumin (g/dL)	4.18 ± 0.21	3.85 ± 0.36	0.2107[w.t]

TABLE (4): Comparison between Cases with and without thrombus formation regarding Echo data

	Cases without thrombus (N = 22)	Cases with thrombus (N = 4)	P. Value
Echo			
LASD (mm)	43.09 ± 4.09	46.75 ± 5.02	0.3009[s.t]
LADD (mm)	46.68 ± 5.05	49.25 ± 4.6	0.4213[s.t]
LA anteroposterior diameter (mm)	44.86 ± 5.59	45.5 ± 7.57	0.8961[s.t]
LAESV (mm^3)	51.05 ± 6.68	74 ± 2.35	<0.0001*[s.t]
LAEDV (mm^3)	75.91 ± 15.62	95.25 ± 8.67	0.0178*[s.t]
EF (%)	66.32 ± 4.29	57.75 ± 1.48	<0.0001*[w.t]
TEE			
LAA velocity (cm/s)	38.5 ± 6.16	25.5 ± 8.5	0.0498*[MWU]

TABLE (5): Univariable regression analysis between LAA thrombus and possible risk factors:

	Unstandardized Coefficients		OR	Test value	P. Value	95% CI	
	B	Std. Error				Lower Bound	Upper Bound
(Constant)	-0.319	0.263				-0.862	0.225
Age	0.007	0.004	1.007	1.86	0.075	-0.001	0.016
Male	-0.154	0.144	0.8573	-1.069	0.296	-0.451	0.143
Female	0.154	0.144	1.1665	1.069	0.296	-0.143	0.451
Smoker	-0.042	0.159	0.9589	-0.261	0.796	-0.371	0.287
Similar attacks	0.105	0.153	1.1107	0.682	0.502	-0.212	0.421
Arrythmia	-0.015	0.166	0.9851	-0.091	0.929	-0.358	0.328
Hypertension	-0.139	0.157	0.8702	-0.884	0.385	-0.463	0.185
DM	0.203	0.227	1.2251	0.895	0.38	-0.265	0.671
Dyslipidemia	-0.042	0.159	0.9589	-0.261	0.796	-0.371	0.287
Family history	-0.19	0.183	0.827	-1.042	0.308	-0.568	0.187
RBCs	0.023	0.152	1.0233	0.151	0.881	-0.291	0.337
Hb	0.008	0.045	1.008	0.166	0.869	-0.086	0.101
WBC	0.028	0.034	1.0284	0.829	0.415	-0.041	0.097
PLTs	0	0.002	1	0.121	0.905	-0.004	0.004
D. Dimer	0.355	0.055	1.4262	6.448	<0.0001*	0.242	0.469
BUN	-0.001	0.009	0.999	-0.12	0.905	-0.02	0.018
Serum creatinine	0.314	0.425	1.3689	0.739	0.467	-0.563	1.191
AST	0.017	0.01	1.0171	1.727	0.097	-0.003	0.036
ALT	0.037	0.012	1.0377	3.159	0.004*	0.013	0.061
Albumin	-0.612	0.25	0.5423	-2.451	0.022*	-1.127	-0.097
LASD	0.024	0.016	1.0243	1.524	0.141	-0.009	0.057
LADD	0.013	0.014	1.0131	0.911	0.371	-0.016	0.043
LA anteroposterior diameter	0.002	0.012	1.002	0.19	0.851	-0.023	0.028
LAESV	0.028	0.004	1.0284	6.526	<0.0001*	0.019	0.037
LAEDV	0.009	0.004	1.009	2.315	0.029*	0.001	0.018
EF	-0.044	0.012	0.957	-3.798	0.001*	-0.068	-0.02
LAA velocity	-0.026	0.007	0.9743	-3.497	0.002*	-0.041	-0.011

DISCUSSION

Atrial fibrillation (AF) affects up to 17% of 80-year-olds. Non-valvular atrial fibrillation (NVAF) accounts for most AF cases and is rising due to global aging. Thromboembolic stroke, which accounts for 30% of all ischemic strokes and over 50% in older persons, is the most serious NVAF consequence [15].

NVAF causes left atrial appendage (LAA) thrombosis due to diminished contractility and blood stasis, which greatly enhance thromboembolic risk [16]. In NVAF patients, transesophageal echocardiography (TEE) is the most sensitive and specific method for LAA thrombus and spontaneous echo contrast (SEC) detection [3].

Echocardiographic predictors such as left atrial enlargement (measured by diameter, surface area, or indexed volume) and reduced left ventricular ejection fraction (LVEF) are connected to thrombus formation, but their accuracy is limited [17].

Our study included 26 elderly subjects with a mean age of 63.2 years, evenly split by sex, with hypertension being the most common comorbidity in more than half of patients. Our study revealed that those with LAA thrombus were significantly older, while no notable differences were found in sex, smoking, comorbidities, or clinical history. Hypertension was the most common comorbidity. These findings agree with the Polish LATTEE registry by Gawałko et al. (2021) [18], which reported a higher prevalence of LAA thrombus in patients aged ≥65 years compared to those <65 years (7.7% vs. 4.0%, p < 0.001), although differences between older age subgroups were not statistically significant. Similarly, Ayirala et al. (2011) [19] found no gender or hypertension differences but noted statistically significant higher age (>75 years) and a trend toward increased diabetes in LAA thrombus patients (P=0.07). Our results support the hypothesis that advancing age contributes to thrombus formation through atrial remodeling, decreased contractility, and endothelial dysfunction promoting blood stasis [20, 21].

In contrast, Uziębło-Życzkowska et al. (2022) [22] observed in a younger AF cohort (<65 years) that smokers were statistically significantly more frequent in the LAT-positive group (P=0.004), alongside higher rates of diabetes, previous transient ischemic attack, coronary artery disease, and chronic kidney disease (P<0.05), factors not significant in our study.

The study found statistically significant elevation in AST levels in the thrombus group, while D-dimer levels were higher but not statistically significant. Other laboratory values showed no notable differences.This partially agrees with Cinar et al. (2020) [23], who found no significant difference in hematocrit, hemoglobin, WBC, or platelets between thrombus groups, though creatinine and BUN were higher in thrombus-positive patients; however, they reported no AST or ALT differences. The elevated AST in our patients may indicate atrial myocardial stress or subtle ischemia linked to impaired contractility and blood stasis, contributing to thrombus formation. AST elevation might also reflect hepatic hypoperfusion due to atrial stretch or congestion. Although not significant, raised D-dimer supports increased fibrin turnover and thrombogenesis [24-26].

Conversely, Almorad et al. (2021) [27] reported statistically significant higher D-dimer levels in patients with LA thrombus ($2{,}376 \pm 1{,}081$ ng/L vs. 729 ± 611 ng/L, $p < 0.05$), contrasting our non-significant finding. A meta-analysis of 11 studies involving 4,380 AF patients by Diaz-Arocutipa et al. (2021) [28] found that D-dimer has moderate sensitivity (~50–68%) and high specificity (~73–99%) for ruling out left atrial thrombus at various thresholds. Huang et al. (2023) [29] further showed that doubling plasma D-dimer levels raised intracardiac thrombus risk by over 60%. Rafla and Beshay (2020) [30] observed elevated D-dimer in 26.7% of LAA thrombus patients, with levels and thrombus resolving statistically significantly after 3 to 6 months of warfarin therapy.

Our study highlighted that patients with LAA thrombus had statistically significant high left atrial volumes, reduced ejection fraction, and lower LAA emptying velocity, with strong associations to LAESV and LAEDV. Other atrial dimensions showed no significant differences. These findings agree with Kaufmann et al. (2022) [31], who reported that LA enlargement and reduced LVEF are strongly associated with left atrial appendage thrombosis (LAAT) in real-world AF/AFL patients. Similarly, Dudziñska-Szczerba et al. (2022) [32] identified increased LAA volume as a predictor of thrombus or stroke in AF, while Katic and

Borovac (2023) [33] confirmed that lower LVEF correlates with higher risk of LA/LAA thrombus, especially in heart failure patients. Okada et al. (2024) [34] found that reduced LAA peak flow velocity (<20 cm/s) predicted poor thrombus resolution and adverse outcomes, a conclusion supported by Uziębło-Życzkowska et al. (2024) [35], who highlighted decreased LAAV as a significant thrombus risk factor.

Our study found that the average LAA velocity was 36.5 cm/s, with LAA thrombus identified in 15.38% of patients. This is consistent with Tabak et al. (2025) [36], who reported a mean LAA emptying velocity of 41.6 ± 21.0 cm/s in a large cohort of 995 patients. Yaghi et al. (2015) [37] showed markedly lower LAA contraction velocities in thrombus-positive patients (10 ± 4 cm/s) compared to those without thrombus (22 ± 7 cm/s, $P < 0.001$). Lee et al. (2015) [38] reported thrombus prevalence of ~0.5% among patients with LAA velocities <40 cm/s, with a statistically significant greater thrombus likelihood at lower velocities (~37 ± 19 cm/s in stroke patients vs. ~51 ± 20 cm/s in controls). The relatively low mean LAA velocity in our cohort explains the 15.38% thrombus detection rate, reflecting impaired mechanical function of the LAA. Disorganized atrial contractions in AF reduce appendage contractility and blood flow, fostering stasis and a prothrombotic milieu per Virchow's triad, especially the stasis component [39, 40].

Our study identified key associations between LAA thrombus formation and several factors, including increased D-dimer, ALT, LAESV, and LAEDV, along with decreased albumin, ejection fraction, and LAA velocity. These findings suggest that thrombus formation is influenced by a prothrombotic state, hepatic congestion, and atrial stasis. Almorad et al. (2021) [41] similarly reported an inverse relationship between albumin and D-dimer levels, associating hypoalbuminemia with increased coagulation markers in a Chinese AF cohort (n=909). Cicek et al. (2024) [42] linked low albumin to inflammatory activation and left atrial thrombosis, while a meta-analysis by Wan et al. (2017) [43] (16 studies, n=2,652) found statistically significant higher D-dimer in patients with left atrial thrombus, with a standardized mean difference of approximately 2.34 and a ~3.8-fold increased risk in the upper tertile of D-dimer levels.

The increased left atrial volumes in thrombus cases reflect structural remodeling and impaired atrial emptying, while elevated D-dimer signifies active coagulation. The negative associations with albumin, ejection fraction, and LAA velocity emphasize the role of reduced cardiac output, decreased appendage contractility, and hypoalbuminemia in promoting blood flow stagnation, endothelial dysfunction, and a hypercoagulable state that favor thrombus formation in atrial fibrillation [39, 44, 45].

Clinically, TTE can provide useful non-invasive indicators of thrombus risk in NVAF patients. Enlarged LA volumes, reduced EF, and lower LAA velocity, supported by biomarkers such as D-dimer and albumin, may guide earlier anticoagulation, especially when TEE is not available. In resource-limited settings, a management policy combining TTE with simple biomarkers could support stroke prevention decisions without immediate reliance on TEE. This approach may improve access to timely management and optimize use of healthcare resources.

So theoretically, the association between structural atrial changes and biochemical alterations supports the concept of atrial myopathy as a substrate for thrombus formation. This strengthens the link between impaired atrial mechanics, systemic

biomarkers, and thrombogenesis. However, larger studies are needed to validate these findings and to develop predictive models integrating TTE parameters and biomarkers. Prospective trials should assess whether using these tools for early anticoagulation reduces stroke risk and improves outcomes.

Our study has several limitations, including a small sample size (n=26, with only 4 thrombus cases), which limits statistical power and generalizability. The single-center design introduces potential selection bias, and reliance on TTE instead of direct LAA visualization via TEE restricts definitive thrombus detection. Additionally, unmeasured confounders like anticoagulation adherence and AF duration could influence outcomes, and the cross-sectional nature of the study prevents causal inferences. Larger, multicenter studies with advanced imaging are necessary for validation.

CONCLUSION

Transthoracic echocardiography (TTE) predicts LAA thrombus in NVAF patients by detecting increased LA volumes (LAESV, LAEDV), reduced ejection fraction, and lower LAA emptying velocity. Elevated D-dimer and AST levels, along with decreased albumin, also correlate with thrombus risk. While TEE remains the gold standard, TTE parameters and these biomarkers offer useful, non-invasive risk stratification tools to guide early anticoagulation and stroke prevention when TEE is unavailable.

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