



## Echocardiographic Predictors of Left Atrial Appendage Thrombus in Patients with Atrial Fibrillation and CHADS<sub>2</sub> ≤1

<b>Adikesava Naidu Otikunta</b>	Associate Professor, Department of Cardiology, Osmania General Hospital and Osmania Medical College, Hyderabad - 500012, India
<b>Naveen Kumar Cheruku</b>	Senior Resident, Department of Cardiology, Osmania General Hospital and Osmania Medical College, Hyderabad - 500012, India
<b>Y.V. Subba Reddy</b>	Professor and Head, Department of Cardiology, Osmania General Hospital and Osmania Medical College, Hyderabad - 500012, India
<b>Ravi Srinivas</b>	Assistant Professor, Department of Cardiology, Osmania General Hospital and Osmania Medical College, Hyderabad - 500012, India

### ABSTRACT

**Objective:** To evaluate the role of transthoracic echocardiographic (TTE) parameters in predicting left atrial appendage (LAA) thrombus, confirmed by transesophageal echocardiography (TEE), in patients with atrial fibrillation (AF).

**Methods:** A total of 25 patients with non-valvular AF and CHADS<sub>2</sub> ≤1 were evaluated using TTE and tissue Doppler imaging. Presence of LAA thrombus was confirmed using TEE.

**Results:** Left atrial thrombus index (LATI) <1.7, mitral e' velocity >10 cm/sec, and E/e' ratio >11 were found as significant predictors of LAA thrombus. Other parameters, including left atrial size >5 cm, left atrium volume index >28 mL/m<sup>2</sup>, LAA E' velocity <9.7 cm/s, and LAA velocity <40 cm/s did not show significant association in predicting LAA thrombus.

**Conclusion:** Embolic events in AF patients with CHADS<sub>2</sub> ≤1 can be predicted with TTE examination of LATI, E/e', and mitral e' velocity. These predictors may help in decision-making for early initiation of anticoagulation therapy to reduce morbidity and mortality among them.

### KEYWORDS

Atrial fibrillation; Left atrial appendage; Left atrial thrombus index; Transesophageal echocardiography; Transthoracic echocardiography

### INTRODUCTION

The prevalence of non-valvular atrial fibrillation, the most common form of cardiac arrhythmia, is increasing worldwide.<sup>1,2</sup> Patients with atrial fibrillation are associated with an increased risk of stroke, heart failure, and cardiovascular mortality.<sup>3</sup> However, the most dreaded complication of atrial fibrillation involves an increased risk of thromboembolic events, particularly in cardiac chambers. Of them, left atrial appendage (LAA) thrombi are most frequent among patients with atrial fibrillation.<sup>1</sup> While transesophageal echocardiography (TEE) is considered as the definitive imaging technique for the identification of LAA thrombus, the predictive value of various transthoracic echocardiographic (TTE) parameters for this purpose are rarely investigated.<sup>4</sup> Nevertheless, several recent studies have hypothesized that left atrial thrombus index, a relatively new echocardiographic parameter, could have significant value in predicting LAA thrombus in patients with atrial fibrillation.<sup>1,4</sup> Such predictors may help in decision-making for early initiation of anticoagulation therapy to reduce morbidity and mortality among them.<sup>1</sup> With this background, we conducted the present study to investigate the predictive value of certain TTE parameters including left atrial thrombus index in detecting LAA thrombus, confirmed by TEE examination, in patients with atrial fibrillation.

### METHODS

#### Study design and patient population

In this prospective cohort study, 25 patients with non-valvular atrial fibrillation and CHADS<sub>2</sub> ≤1, who were referred for echo-

cardiographic examinations at the Osmania General Hospital, Hyderabad, India between January-2013 and January-2014, were examined. Inclusion criteria included (a) presentation of non-valvular atrial fibrillation; (b) CHADS<sub>2</sub> ≤1; and (c) undergoing echocardiographic examination for the detection of LAA thrombus. Patients with CHADS<sub>2</sub> >1 were excluded. The study protocol was approved by our Institutional Review Board. A signed informed consent was obtained from each enrolled patient.

#### Data collection

Demographic and medical data including age, gender, height, weight, and history of diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, rheumatic heart disease, stroke, transient ischemic attack (TIA), thromboembolism, smoking, and alcoholism were obtained from past medical records or interviews with patients at the time of presentation. Accordingly, a CHADS<sub>2</sub> score for each patient was calculated as: congestive heart failure = 1 point; hypertension = 1 point; age 75 years or older = 1 point; diabetes mellitus = 1 point; and history of stroke including transient ischemic attack or systemic embolism = 2 points. Subsequently, all patients underwent 2D-TTE examination by an experienced cardiologist, who was blinded to the clinical data. Patients were evaluated for left atrium (LA) dimensions including size and area. Left atrial volume was measured using the biplane area-length method. Left atrial volume index (LAVI) was calculated by dividing left atrial volume with body surface area. Dop-

pler assessment of mitral flow velocities and Doppler tissue imaging of the medial mitral valve annulus were evaluated in the apical four-chamber view. Subsequently, Early transmitral flow velocity (E), early diastolic septal mitral annulus velocity (e'), and E/e' were estimated. In addition, LAA flow velocities were measured using tissue Doppler. Left ventricular ejection fraction (LVEF) was measured using the modified Simpson's method. Left atrial thrombus index (LATI) was defined as the ratio of LVEF to LAVI. Presence of LAA thrombus was evaluated by TEE examination.

**Statistical analysis**

Continuous data are expressed as mean ± standard deviation and are compared using the Mann Whitney U test. Categorical data are presented as frequencies and percentages and are compared using the Chi-square test or Fisher exact test. P value of <0.05 was considered as statistically significant. The role of TTE-based echocardiographic parameters as a predictor of TEE-based diagnosis of LAA thrombus was evaluated using the Chi-square test for association of variables. Here, the presence of LAA thrombus was compared between patients with (a) Left atrial size: <5 cm vs. ≥5 cm; (b) LAVI: <28 mL/m<sup>2</sup> vs. ≥28 mL/m<sup>2</sup>; (c) LATI: >1.7 vs. (normal) vs. ≤1.7 (abnormal); (d) Mitral e' velocity: <10 cm/s vs. ≥10 cm/s; (e) E/e': <11 vs. ≥11; (f) LAA E' velocity: >9.7 cm/s vs. ≤9.7 cm/s; and (g) LAA velocity: >40 cm/s (normal); vs. ≤40 cm/s (abnormal). The Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15 was used for statistical analysis.

**RESULTS**

**Baseline demographics**

The demographic characteristics of enrolled 25 patients with non-valvular atrial fibrillation and CHADS<sub>2</sub> ≤1 are given in **Table 1**. In brief, the mean age of enrolled patients was 55.36 ± 9.19 and 13 (52%) of them were males. TEE examination indicated that 9 (36%) patients had LAA thrombus. Comparison of demographic variables between patients with and without LAA thrombus revealed that patients with LAA thrombus were significantly younger (P=0.114), while other characteristics including body-mass index, female gender, obesity, diabetes mellitus, hypertension, congestive heart failure, coronary artery disease, prior stroke, TIA, thromboembolism, alcoholism, smoking, and CHADS<sub>2</sub> score were comparable.

**Table 1: Demographic characteristics of patients included in the study**

Characteristics	Overall patients (n=25)	Patients with LAA clot (n=9)	Patients without LAA clot (n=16)	Statistical significance
Age (years), mean±SD	55.36 ± 9.19	50.44 ± 8.20	58.13 ± 8.75	P=0.014
Female gender, n (%)	12 (48%)	6 (66.7%)	6 (37.5%)	P=0.161
Body-mass index (kg/m <sup>2</sup> ), mean±SD	23.85 ± 2.91	25.23 ± 2.48	23.07 ± 2.91	P=0.051
Obesity, n (%)	8 (32%)	4 (44.4%)	4 (25.0%)	P=0.317
Diabetes mellitus, n (%)	3 (12%)	2 (22.2%)	1 (6.3%)	P=0.405
Hypertension, n (%)	5 (20%)	1 (11.1%)	4 (25%)	P=0.835
Congestive heart failure, n (%)	4 (16%)	1 (11.1%)	3 (18.8%)	P=0.617
Coronary artery disease, n (%)	3 (12%)	1 (11.1%)	2 (12.5%)	P=0.918
Prior stroke, TIA, or thromboembolism, n (%)	0 (0%)	0 (0%)	0 (0%)	-
Alcohol, n (%)	1 (4%)	0 (0%)	1 (6.3%)	P=0.444
Smoking, n (%)	5 (20%)	2 (22.2%)	3 (18.8%)	P=0.835
CHADS <sub>2</sub> score = 0	11 (44%)	4 (44.4%)	7 (43.8%)	P=0.973
CHADS <sub>2</sub> score = 1	14 (52%)	5 (55.5%)	9 (56.3%)	

**Transthoracic echocardiographic characteristics**

The TTE characteristics of 25 patients with non-valvular atrial fibrillation and CHADS<sub>2</sub> ≤1 are described in **Table 2**, along with the comparison of TTE variables between patients with and without LAA thrombus. Findings revealed that patients with LAA thrombus displayed significantly higher LA size (P=0.002), LA area (P=0.001), LA volume (P<0.001), LAVI (P<0.001), and E/e' (P=0.010) as compared to that in patients without LAA thrombus. In addition, patients with LAA thrombus exhibited significantly lower LVEF (P=0.003), LATI (P<0.001), and Mitral e' (P=0.020) as compared to that in patients without LAA thrombus. No significant difference was observed between two groups for LAA apical E', LAA anterior S', and LAA flow velocity.

**Table 2: Transthoracic echocardiographic characteristics of patients included in the study**

Characteristics	Overall patients (n=25)	Patients with LAA clot (n=9)	Patients without LAA clot (n=16)	Statistical significance
LA size (cm), mean±SD	5.73 ± 0.97	6.42 ± 0.89	5.34 ± 0.80	P=0.002
LA area (cm <sup>2</sup> ), mean±SD	25.30 ± 8.85	32.02 ± 10.42	21.51 ± 4.99	P=0.001
LA volume	71.24 ± 27.59	100.78 ± 18.28	54.62 ± 14.88	P<0.001
LA volume index, mean±SD	45.10 ± 19.09	64.88 ± 15.60	33.96 ± 9.28	P<0.001
LVEF (%), mean±SD	59.72 ± 9.36	52.33 ± 9.61	63.89 ± 6.32	P=0.003
LATI, mean±SD	1.60 ± 0.78	0.84 ± 0.26	2.03 ± 0.63	P<0.001
Mitral S, mean±SD	8.72 ± 3.10	8.13 ± 2.43	9.06 ± 3.45	P=0.760
Mitral e', mean±SD	9.58 ± 4.01	7.30 ± 2.16	10.86 ± 4.29	P=0.020
E/e', mean±SD	12.39 ± 4.14	15.44 ± 3.44	10.67 ± 3.51	P=0.010
LAA apical E', mean±SD	7.81 ± 2.79	8.21 ± 3.32	7.58 ± 2.54	P=0.718
LAA anterior S', mean±SD	9.41 ± 3.17	9.73 ± 2.74	9.23 ± 3.45	P=0.388
LAA flow velocity (cm/s), mean±SD	34.65 ± 11.30	29.47 ± 8.18	37.57 ± 11.97	P=0.095

E: Early transmitral flow velocity; e': Early diastolic septal mitral annulus velocity; S: Early systolic mitral annular velocity; LA: left atrium; LAA: left atrial appendage; LATI: Left atrial thrombus index; LAVI: Left atrium volume index; LVEF: Left ventricular ejection fraction.

**Predictors of LAA thrombus**

The significant values of various TTE parameters as predictors of LAA thrombus are described in **Table 3**. It was observed that LATI <1.7 was a significant predictor of LAA thrombus (P<0.001). Other echo parameters like mitral e' velocity >10 cm/s (P=0.027) and E/e' ratio >11 (P=0.027) were predictive of LAA thrombus. Other routine parameters, including LA size >5 cm, LAVI >28 mL/m<sup>2</sup>, LAA E' velocity <9.7 cm/s, and LAA velocity <40 cm/s, showed numerical but not statistically significant association in predicting LAA thrombus.

**Table 3: Analysis of association between echocardiographic parameters and LAA clot**

Characteristics	Overall patients (n=25)	Patients with LAA clot (n=9)	Patients without LAA clot (n=16)	Statistical significance
LA size	≥5 cm	19 (76%)	8 (88.9%)	P=0.258
	<5 cm	6 (24%)	1 (11.1%)	
LAVI	≥28 mL/m <sup>2</sup>	21 (84%)	9 (100%)	P=0.102
	<28 mL/m <sup>2</sup>	4 (16%)	0 (0%)	
LATI	≤1.7	12 (48%)	9 (100%)	P<0.001
	>1.7	13 (52%)	0 (0%)	
Mitral e' velocity	≥10 cm/s	15 (60%)	8 (88.9%)	P=0.027
	<10 cm/s	10 (40%)	1 (11.1%)	
E/e'	≥11	15 (60%)	8 (88.9%)	P=0.027
	<11	10 (40%)	1 (11.1%)	

LAA E'	≤9.7 cm/s	17 (68%)	7 (77.8%)	10 (62.5%)	P=0.432
velocity	>9.7 cm/s	8 (32%)	2 (22.2%)	6 (37.5%)	
LAA	<40 cm/s	15 (60%)	7 (77.8%)	8 (50%)	P=0.174
velocity	>40 cm/s	10 (40%)	2 (22.2%)	8 (50%)	

E: Early transmitral flow velocity; e': Early diastolic septal mitral annulus velocity; LA: left atrium; LAA:

left atrium appendage; LATI: Left atrium thrombus index; LAVI: Left atrium volume index; LVEF: Left ventricular ejection fraction.

## DISCUSSION

Atrial fibrillation and associated cardio-embolic events are major healthcare problems worldwide.<sup>1,5</sup> TEE is considered the gold standard modality in detecting LAA thrombi in AF patients because it provides superior visualization of posterior structures, such as the left atrium and LAA, when compared with transthoracic echocardiography (TTE).<sup>3,6</sup> Further, large-scale prospective studies have found that TEE is an accurate modality for LAA thrombi detection, with 93.3–100% sensitivity, 99–100% specificity, 86–100% positive predictive value, and 98.9–100% positive predictive value.<sup>7,8</sup> Nevertheless, TEE examination remains time-consuming, carries physical discomfort, is not readily available at all times, and is associated, although rarely, with potential life-threatening complications. Therefore, the role of TTE along with tissue Doppler imaging becomes vital. The traditionally important TEE-based echocardiographic parameters associated with an increased risk of LAA thrombi are increased left atrial dimension and decreased LA appendage flow velocity.<sup>3</sup> In recent years, interest has been shifted on evaluation of LAVI and LATI as a marker of LAA thrombi in patients with atrial fibrillation. The initial results have been encouraging.<sup>1,4</sup>

The present prospective, cohort study demonstrates that LATI <1.7, mitral e' velocity >10 cm/s, and E/e' ratio >11 are significant predictors of LAA thrombus patients with non-valvular atrial fibrillation and CHADS<sub>2</sub> ≤1. Other parameters, including left atrial size >5 cm, left atrium volume index >28 mL/m<sup>2</sup>, LAA E' velocity <9.7 cm/s, and LAA velocity <40 cm/s did not show significant association in predicting LAA thrombus. Earlier, Ayirala et al.<sup>4</sup> in USA had investigated 368 consecutive patients with atrial fibrillation and CHADS<sub>2</sub> ≤1. They found that LATI was a significant marker as the LATI ≤1.7 produced 100% sensitivity for detection of LAA thrombus in AF patients with a CHADS<sub>2</sub> score ≤1. Findings of our study are in lines with this study, which suggests that LATI could be a valuable marker in Indian setting too. We are of opinion that early diagnosis/prediction of LAA thrombus may have major therapeutic implications in patients with atrial fibrillation. In particular, it may help in decision-making for early initiation of anticoagulation therapy to reduce morbidity and mortality among them.

## Study limitations

The present study has several limitations. It is a single-center study; hence, scope of the finding might be limited. Further, the findings of the study were substantiated from comparatively smaller sample-size data. Therefore, we recommend fellow researchers to conduct a multi-center study involving large-sample size for further investigation and confirmation of present findings.

## CONCLUSION

TTE can be a reliable alternative imaging modality to TEE for the detection of LAA thrombi in patients with atrial fibrillation. Here, we found that LATI <1.7, mitral e' velocity >10 cm/sec, and E/e' ratio >11 are significant predictors of LAA thrombus patients with non-valvular AF and CHADS<sub>2</sub> ≤1. These predictors may help in decision-making for early initiation of anti-coagulation therapy to reduce morbidity and mortality among them.

## REFERENCES

1. Doukky R, Khandelwal A, Garcia-Sayan E, Gage H. External validation of a novel transthoracic echocardiographic tool in predicting left atrial appendage thrombus formation in patients with nonvalvular atrial fibrillation. *European Heart Journal-Cardiovascular Imaging*. 2013;14(9):876-81.

2. Stoddard MF, Dawkins PR, Prince CR, Ammass NM. Left atrial appendage thrombus is not uncommon in patients with acute atrial fibrillation and a recent embolic event: A transesophageal echocardiographics study. *Journal of the American College of Cardiology*. 1995;25(2):452-9.
3. Hsu PC, Lee WH, Chu CY, Lee HH, Lee CS, Yen HW, Lin TH, Voon WC, Lai WT, Sheu SH, Su HM. Prognostic role of left atrial strain and its combination index with transmitral E-wave velocity in patients with atrial fibrillation. *Scientific Reports*. 2016;6.
4. Ayirala SR, Kumar S, O'Sullivan D, Silverman D. Left atrial (LA) thrombus index is a sensitive test for the detection of left atrial appendage (LAA) thrombus in atrial fibrillation (AF) patients with CHADS<sub>2</sub> scores ≤1. *Journal of the American College of Cardiology*. 2011;57(14):E64.
5. Romero J, Husain SA, Kelesidis I, Sanz J, Medina HM, Garcia MJ. Detection of left atrial appendage thrombus by cardiac computed tomography in patients with atrial fibrillation: a meta-analysis. *Circulation: Cardiovascular Imaging*. 2013;6(2):185-94.
6. Decker J, Madder R, Hickman L, Marinescu V, Marandici A, Raheem S, Carlyle LM, Van Dam R, Boura JA, Haines DE. CHADS<sub>2</sub> score is predictive of left atrial thrombus on precardioversion transesophageal echocardiography in atrial fibrillation. *American Journal Cardiovascular Diseases*. 2011;1(2):159-65.
7. Kim YY, Klein AL, Halliburton SS, Popovic ZB, Kuzmiak SA, Sola S, Garcia MJ, Schoenhagen P, Natale A, Desai MY. Left atrial appendage filling defects identified by multidetector computed tomography in patients undergoing radiofrequency pulmonary vein antral isolation: a comparison with transesophageal echocardiography. *American Heart Journal*. 2007;154(6):1199-205.
8. Kapa S, Martinez MW, Williamson EE, Ommen SR, Syed IS, Feng D, Packer DL, Brady PA. ECG-gated dual-source CT for detection of left atrial appendage thrombus in patients undergoing catheter ablation for atrial fibrillation. *Journal of Interventional Cardiac Electrophysiology*. 2010;29(2):75-81.