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RESEARCH ARTICLE
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ASSOCIATION BETWEEN LEFT ATRIAL APPENDAGE MORPHOLOGY AND LEFT ATRIAL APPENDAGE THROMBUS FORMATION IN PATIENTS WITH NON-RHEUMATIC ATRIAL FIBRILLATION BY 3D TRANSOESOPHAGEAL ECHOCARDIOGRAPHY

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ABSTRACT:
In patients with atrial fibrillation (AF), most thrombus forms in the left atrial appendage (LAA).[1] However, the relation of LAA morphology with LAA thrombus is unknown**.** In this study we prospectively enrolled 60 patients who had non valvular atrial fibrillation. Transoesophageal echocardiography (TEE) was performed to assess LAA thrombus. LAA structure was assessed by 3-dimensional TEE. LAA volume and number of lobes were measured on reconstructed 3-dimensional images. Clinical characteristics and echocardiographic measures were compared to determine variables predicting LAA thrombus.

BACKGROUND

Atrial fibrillation (AF) occurs in approximately 0.4% to 1% of the general population, increasing with age to >8% in those >80 years of age, with prevalence projected to more than double by 2035.[2] In 1909, Welch 4 noted that cardiovascular stroke associated with AF was due to left atrial appendage (LAA) thrombi and that this was the most common site for thrombus formation in the setting of AF because the saccate and complex morphology of the LAA induces stasis of blood flow[3]. The CHADS2 (Congestive heart failure, Hypertension Age>75, Diabetes mellitus and prior Stroke or transient ischemic attack) and CHA2DS2-VaSc scores are indices of thromboembolic risk for patients with AF.[4] Of the echocardiographic indices, left ventricular systolic dysfunction, dense spontaneous echo contrast (SEC), low LAA peak flow velocities, and complex aortic plaque were reported to be related to thromboembolic risk.[59] However, whether LAA morphology itself is a risk

factor for LAA thrombus formation has not been well studied. Di Biase et al assessed the LAA with computed tomography (CT) or magnetic resonance imaging (MRI) and reported the types of morphology related to thromboembolic risk[6]. That report strongly suggests that LAA morphology is a risk factor for LAA thrombus formation; however, the relation between presence of LAA thrombus and types of LAA morphology has not been established.

Although CT and MRI have been used to assess LAA morphology, initial studies with three-dimensional (3D) transoesophageal echocardiography (TEE) have also shown the potential to assess LAA morphology[78].

Therefore, the aim of this study is to clarify the relation between LAA morphology evaluated with 3D-TEE and LAA thrombus in patients with AF in comparison with conventional indices.

MATERIALS AND METHODS:

It was a prospective Observational study carried out for a period of two years at a tertiary care centre**.**

Inclusion Criteria:

Age > 40 years irrespective of sex

Non-Valvular atrial fibrillation (paroxysmal or non-paroxysmal)

Exclusion criteria:

Age < 40 Years irrespective of age Any patient with valvular heart disease Patient on haemodialysis Patient not on anticoagulation

STUDY PROTOCOL

- Patients were recruited at the time of 0PD consultations or during hospital stay.
- Suitable subjects were asked to give their consents for their potential participation in the study.
- All the subjects underwent transoesophageal echocardiogram as per standard protocol of the institute.
- Ethical approval of the present study was obtained from the institute's. ethical committee

ECHOCARDIOGRAPHIC METHODS

Standard 2D transthoracic echocardiographic examinations were performed with a WIPRO GE VIVID. Left ventricular end-diastolic volume, end-systolic volume, and ejection fraction (LVEF) was measured using the modified Simpson's method from the apical view. The left atrial (LA) volume was measured using the modified Simpson's method from the apical view.

TEE was performed with WIPRO GE VIVID. SEC was visually classified into 4 grades by careful attention to the gain settings adjusted to distinguish background white noise.

The severity of SEC was scored as follows:

0, absence of echogenicity; 1+, mild (minimal echogenicity detectable in only a part of the LA cavity with high gain settings); 2+, moderate (denser swirling during the entire cardiac cycle); and 3+, severe (intense echo density and slow swirling patterns in the LAA usually with similar density in the main cavity) Based on the recommendations from the American Society of Echocardiography, blood stasis was quantified by LAA flow velocities, which were measured at ≈1 cm below the outlet of the LAA cavity using pulsed Doppler.

LAA emptying flow velocity was measured in the basal short-axis view from the transverse scan (45° views). The LAA emptying and filling flow velocities were measured as the average of 3 consecutive cardiac cycles in patients with normal sinus rhythm and 5 consecutive cardiac cycles in patients with AF.

Full-volume mode examinations were performed from 45° views during apnea at end-expiration. To obtain these data sets, 6 sectors were scanned with gating to the electrocardiographic R wave and

were automatically integrated into a wide-angle (76×69 degrees) pyramidal data image covering the entire LAA. The frame rate of each image was set at ≈20 to 30 frames/s. In patients with AF during the examination, zoom mode, which magnified the pyramidal scan by 1 cardiac beat, was used. The frame rate of each image was set at ≈10 frames/s.

Quantification of LAA Morphology

On a 3D image, we measured LAA volume and the number of LAA lobes, which was assessed based on the definitions by Veinot et al29 as follows:

(1) LAA lobe was a visible out-pouching from the main tubular body of the LAA, usually demarcated by an external crease;

(2) it was internally capable of admitting a 2-mm probe (ie, it was not simply a tag of external adipose tissue);

(3) it was occasionally but not necessarily associated with a change in direction of the main tubular body of the LAA;

(4) it could lie in a different anatomic plane than the main tubular body; and

(5) by definition, the LAA must have ≥1 lobe.

Results

TEE examinations were successfully performed in all patients. This study comprised 60 patients. Among them, LAA thrombus was observed in 6 (10%) patients.

Comparisons between patients with and without LAA thrombus are summarized in Table 1. Patients with LAA thrombus had a significantly higher prevalence of non paroxysmal AF (P<0.001). Patients with LAA thrombus were significantly older (P=0.003), and their LVEF was lower (P<0.001) and CHADS2 score higher (P<0.001) than those in patients without LAA thrombus.

In patients with LAA thrombus, LAA volume (P<0.001) and LA volume (P<0.001) were significantly larger. In addition, the number of LAA lobes was significantly higher (P<0.001) than that of the patients without LAA thrombus. Degree of SEC was significantly higher (P<0.001) with lower LAA emptying velocities(P<0.001) compared with those in patients without LAA thrombus.

Table 1. Baseline Characteristics According to Presence of LAA Thrombus

VARIABLES	NO THROMBUS (n=54)	THROMBUS (n=6)	P VALUE
Age, y	64±11	66±8	0.003
AF (NON PAROXYSMAL)	17(3I%)	4(66%)	<0.001
Sex (MALE)	43 (80%)	5 (83%)	0.12
CHADS2	1.07±1.1	2.5±1.3	<0.001
LVEF	60	50±10	<0.001
LA VOLUME, ML	64±26	93±45	<0.001
LAA VOLUME, ML	7.0±7.1	12.3±5.8	<0.001
LAA E VELOCITY, CM/S	45.6±21	28±17	<0.001
SEC	0.35±1.0	2.3±1.1	<0.001
LAA lobe	2.05±0.8	3.3±0.8	<0.001

Risk Factors for LAA Thrombus:

Various factors had a significant relation with the presence of LAA thrombus as shown in Table 2. In a multivariate logistic analysis, number of LAA lobes (odds ratio [OR], 2.469; 95% confidence interval [CI {1.495–4.078}]; *P*<0.001) was identified as an independent risk factor for presence of LAA thrombus, as were CHADS2 score (OR, 1.752; 95% CI [1.237 2.483]; *P*=0.002), LVEF (OR, 0.962; 95% CI [0.934–0.992]; *P*=0.01), LA volume (OR, 1.018; 95% CI [1.003–1.032]; *P*=0.02),

and degree of SEC (OR, 1.783; 95% CI [1.102 2.740]; *P*=0.02). The majority of patients with LAA thrombus (5/6, 83.3%) had ≥3 LAA lobes. In contrast, LAA thrombus was observed in only 1 (2.3%) of 43 patients with 1 or 2 lobes. In a multiple logistic regression analysis model, as compared with an LAA with 1 or 2 lobes, an LAA with 3 lobes was 8.6 times (OR, 8.6; 95% CI [1.9–39.8]; *P*=0.006), 4 or 5 lobes was 10 times (OR, 10.0; 95% CI [2.2–42.1]; *P*=0.004), and ≥3 lobes was 9.2 times (OR, 9.2; 95% CI [2.0–41.1]; *P*=0.004) more likely to have thrombus**.** In patients with ≥3 LAA lobes, a higher degree of SEC and lower LAA emptying velocity were observed as compared with those in patients with 1 or 2 LAA lobes.

Table 2. Univariate and Multivariate Analyses for Presence of LAA Thrombus

Variable	Univariate		Multivariate	
	OR (95% CI)	P Value	OR (95% CI)	P value
AF (NON PAROXYSMAL)	4.785 (2.26–10.10)	<0.001	.....	0.41
CHADS2	4.785 (2.26–10.10)	<0.001	1.752 (1.237–2.483)	0.002
LVEF	1.915 (1.486–2.467)	<0.001	0.962 (0.934–0.992)	0.01
LA VOLUME, ML	0.935 (0.914–0.956)	<0.001	1.018 (1.003–1.032)	0.02
LAA VOLUME, ML	1.031 (1.021–1.041)	0.02	.....	0.60
LAA E VELOCITY , CM/S	1.038 (1.007–1.070)	<0.001	.....	0.86
LAA E VELOCITY , CM/**S**	0.947 (0.925–0.970)	<0.001	1.783 (1.102–2.740)	0.02
SEC	3.128 (2.262–4.326)	<0.001	2.469 (1.495–4.078)	<0.001
LAA LOBE	3.318 (2.179–5.052)	<0.001	1.752 (1.237–2.483)	0.41

Study Limitations:

From the statistical aspect, there is a great difference between the number of patients with thrombus (n=54) and without thrombus (n=6). Therefore, comparisons between the 2 groups are limited statistically. Furthermore, our study was a single-centre study.

CONCLUSION:

Complex LAA morphology that was characterized by an increased number of LAA lobes was associated with the presence of LAA thrombus, independently of clinical risk and blood stasis. Our study suggested that LAA morphology might be a congenital risk factor for LAA thrombus formation in patients with AF. Accordingly, analysis of LAA morphology may provide additional information in the diagnosis of LAA thrombus and in decision making and formulation of medical strategies including anticoagulation management**.**

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