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The Relationship Between Left Atrial Appendage Morphology and Thrombus presence in Patients with Atrial Fibrillation, Evaluated by Transesophageal Echocardiography

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ABSTRACT

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Background: Atrial fibrillation [AF] significantly increases the risk of thrombus formation in the left atrial appendage [LAA]. The morphology of the LAA has been suggested to play a crucial role in thrombus presence, yet its relationship remains unclear. Transesophageal echocardiography [TEE] is instrumental in evaluating LAA characteristics.

The aim of the work: This study aims to investigate the relationship between the morphology of the left atrial appendage and the presence of thrombus in patients with atrial fibrillation, utilizing transesophageal echocardiography for detailed assessment.

Patients and Methods: Fifty people with a documented medical necessity for Echocardiography due to atrial fibrillation were enrolled. LAA morphology was classified into different types [commonly categorized as Cactus, Chicken Wing, and Bowtie] based on echocardiographic findings. The presence of thrombus was assessed by TEE findings. Statistical analyses were performed to evaluate the association between LAA morphology and thrombus formation.

Results: Average age was 57.5 ± 11.2 [with a range of 41 to 80 years old]. Each person had at least one established cardiovascular disease risk factor. we discovered a strong correlation between the cauliflower shape of LAA and the formation of thrombi. Statistical analysis revealed a negative correlation among LAA empty velocity and thrombus formation.

Conclusion: We concluded that RT3DTEE is technically feasible, provides accurate results, and additional diagnostic capability in the differential diagnosis of certain cases involving suspected LAA thrombi. More thorough researches are needed to confirm our findings.

Keywords: Left Atrium; Thrombus; Atrial Fibrillation; Transesophageal Echocardiography.

INTRODUCTION

Due to its complicated, pliable structure and massive pectinate muscles, the left atrial appendage [LAA] is a common site for thrombi formation in people with non-valvular atrial fibrillation [AF]. In non-valvular AF, thromboembolic events are caused by structurally altered LAA, leading to a swirling blood pattern and a sluggish LAA empty velocity, which together account for more than 90% of cardiogenic causes of all thromboembolic events [1].

When it comes to assessing and interpreting LAA morphology and architecture, 2D transesophageal echocardiography [2D TEE] is the gold standard because to its higher accuracy and precision. Several aspects of cardiac hemodynamics can be evaluated with the help of 2D transesophageal echocardiography [2D TEE], including flow pattern across the LAA orifice, peak velocity, sludge status, spontaneous echocardiographic contrast [SEC], and thrombus formation. If just 2D TEE is used, misdiagnoses of pectinate muscle instead of LAA thrombus may occur. This is due to the fact that 2D TEE has drawbacks, such as being unable to simultaneously scan the LAA in more than one plane [2].

Due to the fact that RT-3D TEE imaging maintains spatial and temporal resolution, it is feasible to see complex 3D structures in real time, such as the LAA. Compared to 2D imaging, it is a safer, more accurate, and more reproducible method of assessing heart function and architecture in a variety of cardiac diseases. Studies have indicated that 3D echocardiography is more accurate than 2D methods for calculating left ventricular volume and function and evaluating heart valves, especially the mitral and aortic valves; By combining TEE technology with RT-3D TEE, echo image quality and visualization of the cardiac structure can be enhanced [3]. RT-3D TEE allows for multi-beam scanning in any cardiac plane.

Although 3D TEE has been used to assess LAA function and thrombi, few studies have done so, and those that have did not provide a clear anatomical description of LAA or information on the various groups of AF cases [4]. The study's goals included determining whether or not all persons with AF had thrombi in their pectinate muscles and gaining a better understanding of the anatomy and physiology of the left atrial appendage [LAA].

PATIENTS AND METHODS

This research was conducted at Bab Al-Shaaria Hospital, Al-Azhar University. The research included [50] cases with atrial fibrillation with clinical indication for Echocardiography.

Inclusion criteria: All cases with non-valvular AF.

Exclusion criteria: Poor image quality and cases with contraindication to TEE.

Methods

All cases were subjected to: Verbal permission, a full history [including family history, medical history, and the commencement of any symptoms], a thorough physical examination [including a resting 12-lead ECG], and any other relevant diagnostic tests. The patient's HR, systolic BP, and diastolic BP were recorded. CHA2DS2-VASc score consisted of assessing congestive heart failure, hypertension, age ≥ 75 [doubled], diabetes mellitus, stroke [doubled], vascular disease, age 65 – 74, and female gender; HAS-BLED score consisted of HTN, abnormal renal and/or liver function, stroke, bleeding, labile INR, age ≥ 65, and alcohol use.

Laboratory analyses: PT & INR if on VKA, Viral marker & Creatinine.

Radiological investigation

Echocardiography: Every subject in the study underwent echocardiographic image acquisitions without exception.

I. Transthoracic Echocardiography

Two-Dimensional Echocardiography and Measurements:

All patients were positioned in the left lateral decubitus position for examination. Echocardiographic images were obtained from standard views, including the parasternal long-axis, parasternal short axis at the level of the great vessels, apical four-chambers, apical five-chambers, and apical two-chambers. Recordings and calculations of various cardiac chambers and ejection fractions were performed following the guidelines recommended by the American Society of Echocardiography. The measurements of end-systolic and end-diastolic left atrial volumes were conducted using a modified Simpson's method in both the apical 4-chamber and 2-chamber views. Additionally, conventional diastolic transthoracic echocardiographic parameters were assessed, including trans-mitral inflow Doppler patterns and tissue inflow Doppler patterns in the apical 4-chamber view. These parameters consisted of the E wave, e' septal wave, e' lateral wave, and E/e' ratio.

Transesophageal Echocardiography and Measurements

Transesophageal echocardiography images were acquired by using live 3D TEE transducer. Prior to the TEE procedure, patients underwent a 12-hour fasting period. The TEE was performed under local superficial anesthesia of the pharynx and larynx using lidocaine mucilage. Throughout the procedure, close monitoring of blood pressure, heart rate, electrocardiogram, and finger vein blood oxygen saturation was conducted. The acquisition of 2D and 3D TEE images followed the standard protocol set by the American Society of Echocardiography [ASE]. Optimal 2D TEE and Color Doppler TEE images were obtained. Maximal emptying flow velocity at the proximal end or orifice of LAA was measured using pulse wave Doppler. Finally, the average value of LAAeV observed over five cardiac cycles was considered representative of LAA function. LAA volume was determined by utilizing computer software, which involved tracing the endocardium of the LAA in different planes during end-diastole and end-systole. The LAA depth was measured from the orifice to a lobe tip at the end-systole of the left ventricle. Furthermore, the LAA orifice diameter was measured at 45º during both the end-systole and end-diastole of the left ventricle During the 3D imaging analysis, the x-axis plane and the perpendicular y-axis plane were positioned to intersect the longitudinal section of the LAA. To visualize the maximum area of the LAA in one of these planes, the image was rotated accordingly. For the assessment of SEC [spontaneous echo contrast] and thrombi, the 2D TEE simultaneous X-plane mode, which provides orthogonal images, was employed and thrombi. We acquired, stored, and analyzed 3D TEE pyramidal full volume images and a 3D TEE zoom dataset of the entire LAA for each patient.

Ethical Consideration: Information about the participants is kept confidential. No one involved in this study would be identified in any written product that comes out of it. Before enrolling in this study, participants received comprehensive information on the study's aims, methods, potential risks, and benefits. Authorization following completion of suitable training.

Statistical Analysis: Data was reviewed, submitted & analyzed using SPSS for data processing. Both quantitative data [mean + SD] and qualitative data [numbers, percentages] were presented. The relationships between categorical variables were assessed using the Chi-square test. To evaluate the strength and direction of associations between continuous variables, Spearman correlation coefficients were calculated. Odds ratios (OR) were computed to determine the likelihood of certain outcomes occurring in relation to predictor variables. Confidence intervals for odds ratios were set at 95%. The overall significance level for all tests was set at $p < 0.05$.

RESULTS

The mean age was 57.5 ± 11.2 years old [range, 41 – 80 years old]. cases were classified into 3 age groups: less than 50 [n = 13], among 50 & 60 [n = 22], and more than sixty years old [n = 15]. Regarding gender distribution, 24 [48%] cases were women, while 26 [52%] cases were males. A minimum of one cardiovascular risk factor was reported by each participant. Ten had diabetes, twenty-seven had hypertension, eleven had ischemic heart disease eleven had heart failure, and seven had a history of stroke or TIA [Table 1].

The mean empty left atrial appendage velocity was 25.5 ± 5.6 cm/s, ranging from 16 to 35 cm/s. The mean systolic volume of left atrial appendage was 20.1 ± 5.8 ml, ranging from 10 to 30 ml. The mean ejection fraction of left atrial appendage was 49.2 ± 5.3 %, ranging from 40 to 59 %. Spontaneous echo contrast was observed in 13 [26%] cases [Table 2].

Left atrial appendage depth was on average 29.3± 6.3 mm [range: 20-40 mm]. The 45-degree view reveals a left atrial appendage with a mean systolic orifice diameter of 21.1± 4.7 mm [range: 12–29 mm] and a mean diastolic orifice diameter of 15.9± 4.1 mm [range: 10–22 mm]. Eighty-eight percent of cases had at least 2 lobes, with only six [12%] having only one [Table 3].

A statistically significant association was found among cauliflower type and thrombus formation [Chi-square test, P = .001] [Table 4].

The mean LAA empty velocity in cases with thrombus formation was 21.3 ± 4.9 cm/sec, while the mean LAA empty velocity in patients without thrombus formation was 28.1± 4.4 cm/sec. The generation of thrombi and the empty velocity of the LAA was found to have a statistically substantial inverse relationship [r = -0.601, P = .000] [Ta.

The empty velocity of the LAA were found to be negatively correlated with the morphology of the LAA [r = -0.446 & -0.456, *P* < .05]. The Cauliflower pattern was associated with the lowest LAA empty velocity, whereas cactus morphology was associated with the highest LAA empty velocity [Table 6].

Table [1]: Demographic Data

	No.	%	Mean ± SD	Range
Age, y	-	-	57.5 ± 11.2	41 – 80
Sex			-	-
Male	26	52		
Female	24	48		
Body mass index, Kg/m^2	-	-	36.5 ± 4.5	30.2 – 45
Body surface area, m^2	-	-	2 ± 0.96	1.51 – 2.47
Cardiovascular Risk Factors			-	-
Diabetes mellitus	10	20		
Hypertension	27	54		
Ischemic heart disease	11	22		
Heart Failure	11	22		
Prior Stroke/transient ischemic attack	7	14		
CHADS2-VASc Score	-	-	2.3 ± 0.7	0 – 6
HAS-BLED Score	-	-	1.6 ± 0.5	0 – 5

Table [2]: 2D TEE Findings

	Mean	SD	Minimum	Maximum
LAA Empty Velocity	25.5	5.6	16	35
Systolic LAA Volume, ml	20.1	5.8	10	30

Table [3]: 3D TEE Findings

	Mean	SD	Minimum	Maximum
LAA Depth, mm	29.3	6.3	20	40
Systolic LAA Orifice Diameter 45°, mm	21.1	4.7	12	29
Diastolic LAA Orifice Diameter 45°, mm	15.9	4.1	10	22
No. Lobes	2.2	0.6	1	3

3D TEE: three-dimensional transesophageal echocardiography; LAA: left atrial appendage.

Table [4]: Diagnostic ability of WBCs, CRP, bilirubin in differentiating normal and diseased participants

	No. [%]	Odds Ratio	95% Confidence Interval		P value*
			Lower	Upper	
Cactus [n = 20]	4 [20%]	0.250	0.068	0.925	.032
Chickenwing [n = 6]	1 [16.7%]	0.289	0.031	2.685	.251
Windsock [n = 8]	2 [25%]	0.490	0.088	2.723	.409
Cauliflower [n = 16]	12 [75%]	11.571	2.842	47.118	.000

3D TEE: three-dimensional transesophageal echocardiography; LAA: left atrial appendage. * Chi-square test.

Table [5]: Relation Between Thrombus Formation and LAA Empty Velocity

	Mean	SD	Minimum	Maximum
Thrombus	21.3	4.9	16	35
No Thrombus	28.1	4.4	16	35
Correlation Coefficient	- 0.601			
P value	.000			

Table [6]: Relation among Morphology and LAA Empty Velocity

	LAA Empty Velocity	
	Mean	**SD**
Morphology		
Cactus [n = 20]	28.1	5.5
Chicken-wing [n = 6]	26.5	6.9
Windsock [n = 8]	24.3	5.4
Cauliflower [n = 16]	22.5	4.0
Correlation Coefficient	- 0.446	
P value	0.001	

DISCUSSION

The saccate and complicated architecture of the LAA produces stasis of blood flow, making it a prime location for thrombus development in individuals with atrial fibrillation [AF] [6].

The average age of the individuals who participated in the current investigation was 57.5± 11.2 [range, 41–80] years old. Individuals were divided into three groups based on age: those under the age of 50 [n = 13], those among the ages of 50 and 60 [n = 22], and those over the age of 60 [n = 15]. There were 24 female individuals [48%], whereas there were 26 male participants [52%]. In addition, the average body surface area was 2.08 ± 0.96 m^2 [range: 1.51-2.47 m2]. Average body mass index was 36.5 ± 4.5 Kg/m^2 [range: 30.2-45]. All of the individuals in the investigation were overweight. Of those examined, 22 [44%] as class I obese, 14 [28%] were classified as class II obesity and 14 [28%] as class III obese.

Our findings corroborated those of **Dentamaro *et al.*** [7], who set out to compare the efficacy of transthoracic and real-time 3D transesophageal echocardiography in assessing left atrial appendage function and thrombi among individuals with atrial fibrillation. There were 93 individuals with non-valvular atrial fibrillation analyzed [60 men, mean age = 67.1 ± 14.2 years].

Every individual in the present research reported having at least one of several potential cardiovascular risk factors. Ten individuals [20%] were diabetic, twenty-seven patients [54%] were hypertensive, eleven patients [22%] were diagnosed with ischemic heart disease [IHD], eleven individuals [22%] were diagnosed with heart failure, and seven individuals [14%] had a history of stroke or TIA.

Deng *et al.* [8] found that compared to individuals with long-term AF, those with paroxysmal AF were more likely to have hypertension, diabetes, ischemic heart disease, congestive heart failure [CHF], and a history of stroke or transient ischemic attack [TIA], with 63.6%, 12.7%, 7.4%, 14.5%, 14.9%, and 5.4%, respectively. Ischemic heart disease and stroke were more common in the control group, although hypertension, type 2 diabetes mellitus, and heart failure were no different among the two groups.

Arterial hypertension [67 sufferers; 72%], valvular heart disease [30 patients; 32.3%], diabetes mellitus [14 patients; 15%], and ischemic heart disease [12 individuals; 12.9%] were also the most commonly reported diseases by **Dentamaro *et al.*** [7].

The results of our analysis revealed a mean CHADS2-VASc Score of 2.3± 0.7 [range: 0-6]. The mean HAS-BLED Score was 1.6 ± 0.5 [range, 0 – 5].

The findings we obtained mirrored those of Deng et al. To do so, they utilized the CHA2DS2-VASc and HAS-BLED scoring systems. Patients with long-term AF had a high thromboembolic risk [CHA2DS2-VASc =3.21.8] and a moderate hemorrhagic risk [HAS-BLED = 2.61.1], while those with paroxysmal AF had a lower risk of both complications [8].

Our results showed that the left atrium anteroposterior diameter averaged 42.4 ± 4.4 mm, with a range of 35-50 mm. Systolic left atrial volume was calculated to be 70.3 ± 6.1 ml and diastolic left atrial volume was calculated to be 47.8 ± 4.5 ml. E waves traveled at an average speed of 78.9 ± 4.7 cm/s; e' septal waves averaged 5.8± 1.9 cm/s; and e' lateral waves traveled at a speed of 10.3 ± 3.2 cm/s.

This resulted in an average E/e' ratio of 15.4 ± 5.8. The left ventricular ejection fraction ranges from 40 to 70, with a mean value of 56.8%.

The average left atrial volume in the individuals we studied was 63± 29 ml, and the average left ventricular ejection fraction was 56.8 ± 6.1. These numbers are very comparable to those found by **Yamamoto *et al.*** [6].

The average velocity of the empty left atrial appendage was found to be 25.5± 5.6 cm/s, with a range of 16–35 cm/s. Systolic left atrial appendage volume was on average 20.1 ± 5.8 ml, with a range of 10-30 ml. A total of eighteen individuals [or 36%] had spontaneous echo contrast.

Dentamaro *et al.* [7] found that only 59/93 [63% of the total] participants were able to have a reliable measurement of LAA emptying velocity [LAAeV] using TTE before cardioversion. Despite this, all 49/93 [53%] individuals with malfunctioning LAA [LAAeV 40 cm/s] got a high-quality TEE LAAeV. Of the 69 individuals who underwent successful cardioversion, 5 [7.2%] showed chronic dysfunction [measured by LAAeV values 40 cm/s on the TEE post-CV]. TEE revealed a bilobed structure in forty-five patients [48.4%], while 23 patients [23.7%] showed evidence of three lobes.

Our data showed that the depth of the left atrial appendage, on average, was 29.3 ± 6.3 mm [range: 20-40 mm]. The 45-degree view reveals a left atrial appendage with a mean systolic orifice diameter of 21.1 ± 4.7 mm [range: 12–29 mm] and a mean diastolic orifice diameter of 15.9 ± 4.1 mm [range: 10–22 mm]. Eighty-eight percent of individuals had at least two lobes, with only six [12%] having only one.

Our findings corroborated those of **Deng *et al.***, who used RT-3D TEE to collect and compare additional data on LAA morphological characteristics. The LAA orifice was observed to be significantly larger in the chronic group than in the paroxysmal AF group. Multiple views, including 45 and 135 degrees, were used to precisely measure the LAA orifice's diameter. In the 135-degree view, the systolic inner diameter of the LAA opening was 23.9± 8.4 mm in the paroxysmal group and 28.7± 7.6 mm in the long-standing group [P=0.03]. The inner diameter of the LAA opening during diastole was 19.3± 8.9 mm in the paroxysmal group and 24.010.1 mm in the long-term group [P=0.04]. The diameter of the LAA orifice did not vary substantially [P=0.05 during systole and P=0.13 during diastole] when seen at 45 degrees. Both the systolic and diastolic values of LAA area were significantly higher in the long-term AF group than in the paroxysmal group [P<0.01]. There was no statistically significant distinction among the two groups with regard to LAA depth [30.2± 13.6 vs. 32.4± 15.8, P=0.43] [8].

Our analysis of 3D TEE images revealed four distinct morphological categories for the left atrial appendage. Twenty individuals [40%] had the cactus morphology, making it the most prevalent. Cauliflower morphology was the second most common kind, observed in 16 cases [32%]. Six [12%] and eight [16%] individuals had the chickenwing type, windsock type respectively.

Our findings corroborated those of **Deng et al.** [8] who reported Cactus type [46%], cauliflower type [19%], chicken wing type [20%], and windsock type [15%] were the most common LAA morphology types in the paroxysmal AF group, while in the long-standing AF group, these proportions were as follows: cactus type [40%], cauliflower type [32%], chicken wing type [16%], and windsock type [12%]. When comparing the long-term AF group to the paroxysmal AF group, the percentage of cauliflower-type LAAs increased significantly [P<0.001], while the percentage of non-cauliflower-type LAAs fell marginally [P0.05].

In our Study Thrombus was present in 19 of the participants [38%]. Thrombosis occurred at varying rates in each of the four distinct morphologies. The risk of thrombus formation in patients with cauliflower type was increased by a factor of 12. Patients with the cactus, chicken-wing, and windsock blood types, on the other hand, were 4, 3.5, and 2 times less likely to develop a thrombus, respectively. Thrombus development was observed to be correlated with cauliflower phenotype [Chi-square test, P <.001]. Our data showed that 32 patients [64% of the total] had a grade 0 SEC signal. There were Thirteen individuals [26%] individuals suffering from grade 1 or 2 SEC and Five [10%] with grade 3 or 4 SEC

The left atrium protrudes slightly, like a finger, in AA. It has a complicated and very changeable anatomical structure. Cactus [30%], Chicken Wing [48%], Windsock [19%], and Cauliflower [3%] are the diverse types of LAA that have been recently classified using CT. Different morphologies were shown to have varying risks of stroke and TIA [9].

According to our findings, the average empty velocity of the LAA was 21.3± 4.9 cm/sec in individuals who developed thrombus, while it was 28.1± 4.4 cm/sec in those who did not. The generation of thrombi and the empty velocity of the LAA were found to be negatively correlated [r = -0.601, P< .001].

One of the strongest independent predictors of increased thromboembolic risk is a decreased peak flow velocity in the LAA, as documented by **Takada et al**. [10].

The results of our analysis indicated a negative association among LAA morphology and LAA empty velocity [r = -0.446 and -0.456, P< .05]. Cactus morphology was linked to the highest LAA empty velocity, whereas the Cauliflower pattern was linked to the lowest.

Our findings were consistent with those of Pourkia et al., who used 3D TEE to describe morphologic and functional aspects of the LAA in the Iranian population, although few features of the LAA have been documented in Asian populations [11].

Only a small number of isolated occurrences have been recorded for thrombus diagnosis, as shown by research from 2011 by Matyal et al., which detailed the reliability of RT-3D TEE for spotting anatomic variations and LAA thrombi during cardiac surgery and other settings [12].

Several writers have shown the great benefit of this method before and after operations like electrical cardioversion for individuals with anatomical variances [pectinate muscles, multiple lobes], as well as thrombi [13].

This manuscript acknowledges several limitations that may impact the findings. Firstly, while 2D and 3D transesophageal echocardiography [TEE] are valuable imaging modalities, there is currently no universally accepted gold standard technique, such as cardiac MRI, to definitively compare the results obtained from 3D

TEE. This absence of a definitive reference point may result in discrepancies when interpreting LAA morphology and thrombus assessment, potentially affecting the validity of the conclusions drawn.

Additionally, potential observer variability in interpreting the echocardiographic images and the inherent limitations of TEE in visualizing certain anatomical structures may contribute to uncertainties in the measurements and morphological classifications. These factors underline the need for cautious interpretation of the results and further research to establish more standardized evaluation criteria in assessing LAA morphology and thrombus presence.

Conclusion: Based on our findings, we can say that RT3DTEE can be performed successfully, provides reliable results, and demonstrates an increased capacity for differential diagnosis in some situations with suspected LAA thrombi. Our findings need to be confirmed by larger-scale trials.

Conflict of interest and financial disclosure: none

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