

Incidence of Left Atrial Appendage Clot in Patients of Severe Mitral Stenosis - A Large Observational Study at a Tertiary Level Cardiac Centre In India

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Abstract

Mitral stenosis (MS) is constriction of mitral valve orifice area due to structural abnormality of the mitral valve apparatus. Most commonly it is because of chronic sequel of acute rheumatic fever. Normal valve area of mitral valve orifice is in between 4 - 6 cm². To maintain proper flow of blood from left atria to left ventricle with decrease in mitral valve area, pressure in left atria and gradient across the valve increases according to Poiseuille's law. Progressive narrowing resulting in mitral valve area of less than 1 - 1.5 cm², termed as severe mitral stenosis. Critical mitral orifice stenosis and raised left atrial pressure result in dilation of left atrial cavity and onset of atrial fibrillation. Due to stasis of blood, sluggish flow of blood and atrial fibrillation, thrombus formation occurs in left atria/left atrial appendage (LA/LAA). The aims and objectives of this study was to see the frequency of left atrial and appendage clot formation on trans-esophageal echocardiography in symptomatic severe mitral stenosis patients planned for percutaneous mitral balloon valvotomy and relation of this thrombus formation with atrial fibrillation, spontaneous ECHO contrast (SEC) and LAA emptying velocity. This is first largest ever study done in patients with rheumatic heart disease from an endemic country comprising of 2000 subjects. On analyzing results it was reported that the frequency of left atrial and appendage clots on trans-esophageal echocardiography in patients with severe mitral stenosis is much higher as reported and more frequent in patients with AF (33%) and LAA emptying velocity < 25 cm/sec (60%), but patients with normal sinus rhythm are also at increased risk.

Keywords: Left Atrial Appendage Clot; Mitral Stenosis; Rheumatic Heart Disease; Left Atrial Emptying Velocity; Atrial Fibrillation

Abbreviation

AF: Atrial Fibrillation; RHD: Rheumatic Heart Disease; LA: Left Atria; LAA: Left Atrial Appendage; SEC: Spontaneous ECHO Contrast; PTMC: Percutaneous Trans Mitral Commissurotomy; TEE: Trans Esophageal Echocardiography; ECHO: Echocardiography; IAS: Inter Atrial Septum; MS: Mitral Stenosis

Introduction

Mitral stenosis (MS) is narrowing of mitral valve area because of progressive inflammatory damage to the mitral valve apparatus. Most commonly in more than 90% of cases it is because of chronic sequel of acute rheumatic fever. Other less common non rheumatic causes of

mitral stenosis reported in literature are left atrial tumor particularly myxoma, infective endocarditis with large vegetation in left atrium (LA), ball valve thrombus in LA, presence of congenital membrane in the left atrium (Cor triatriatum) and extensive calcification of mitral annulus in the old age leading to mitral valve obstruction. Normal valve area of mitral valve orifice is in between 4 - 6 cm². To maintain proper flow of blood from left atria to left ventricle with decrease in mitral valve area, pressure in left atria and gradient across the valve increases according to Poiseuille's law. Progressive narrowing resulting in valve area of less than 1 - 1.5 cm², termed as severe mitral stenosis. Due to progressive inflammatory response over the time, the mitral valve apparatus becomes calcified, thickened and contracted causing anterolateral and posterolateral commissural adhesion which ultimately result in more severe stenosis. Continuous turbulent blood flow and ongoing inflammatory damage due to rheumatic activity lead to critical mitral valve stenosis. Critical mitral orifice stenosis and raised left atrial pressure result in dilation of left atrial cavity and onset of atrial fibrillation. Due to stasis of blood, sluggish blood flow and atrial fibrillation, thrombus formation occurs in left atria/left atrial appendage (LA/LAA) [1-3].

The most common site for thrombus formation is the left atrial appendage since it is a natural out pouching acting as a capacitance chamber though it can form anywhere in the LA cavity [1,2]. So, it is important to carefully visualize the entire LA including LA appendage during trans esophageal echocardiography to exclude the thrombus. There is no doubt that left atrial/appendage thrombus is common in patients with severe mitral stenosis and more so in presence of atrial fibrillation; but till date there was no new large scale study to report incidence of LA/LAA thrombus in patients of rheumatic severe Mitral stenosis and its association with rhythm disturbance in Indian population, prior studies done were old and of small scale in spite of endemic nature of disease so their data did not match the real current scenario. This is first new large scale study data from rheumatic heart disease endemic country India comprising of 2000 subjects.

Aims and Objectives of the Study

The aims and objectives of this study was to see the frequency of left atrial and left atrial appendage clot formation on trans-esophageal echocardiography in symptomatic severe mitral stenosis patients planned for percutaneous mitral balloon valvotomy and relation of this thrombus formation with atrial fibrillation, spontaneous ECHO contrast (SEC) and LAA emptying velocity.

Methods

In this observational study 2000 patients with severe MS presented first time at our centre LPS Institute of Cardiology, Kanpur, UP, India over a period of 30 months (from February 2017 to July 2019) either in OPD or in emergency department and found to be suitable for percutaneous mitral balloon commissurotomy (PTMC) on 2D Echocardiography, were taken for TEE procedure to rule out LA/LAA clot as a prerequisite for PTMC as per institutional protocol irrespective of their prior anticoagulation status.

TEE is an invasive procedure and require proper evaluation regarding contraindications. As per our institutional policy patients having AF, history of prior thromboembolic episode and history of previous clot in LA on 2D ECHO are anti coagulated with vitamin K antagonist with monitoring and maintenance of therapeutic INR between 2 - 3. As per literature TEE can be performed on full therapeutic anticoagulation so there is no need to stop anticoagulant for TEE only. However, this policy can vary from center to center as per operator comfort and institutional protocol. In our center too, we stop anticoagulant on day of performing TEE in view of subsequent PTMC if found suitable. In remaining cases we used to start it 12 hour post TEE procedure. After exclusion of all possible contraindications, patients were kept empty stomach 6 hours prior to the procedure. Xylocaine spray was given to gargle just few seconds before the procedure. To prevent damage to probe due to teeth bite a stop block is placed in patient's mouth. Xylocaine jelly was applied over lower end of TEE probe to reduce patient sensation during probe insertion. To avoid aspiration, patient was instructed to lie in left lateral decubitus position, while examiner stand on patient's left side. The probe should be in unlocked position at the time of insertion. At the time of probe insertion instruct the patient to swallow or act like drinking water and at the same time operator carefully advanced it to the back of pharynx with

slight ante flexion and slowly into the esophagus. Sometimes in case of difficult insertion, guide the probe with insertion of your two fingers in patient mouth. Never ever forcefully push the probe to avoid injury.

LA/LAA imaging

Left atrial appendage (LAA) imaged in upper esophageal 5 chamber view (5 CH UE) at 0 degree while at 90 - 110 degree angulation in mid esophageal view. Emptying velocity was calculated in mid esophageal 4 chamber view between 90 - 110 degree angulation views with the help of pulse Doppler.

Classification of LA/LAA clot done as follows [7,8]:

- **Type Ia:** Clot confined to left atrial appendage.
- **Type Ib:** Clot protruding into left atrial cavity from appendage.
- **Type IIa:** Clot attached to left atrial roof and restricted above the plane of fossa ovalis.
- **Type IIb:** Clot attached to left atrial roof and extending below the plane of fossa ovalis.
- **Type III:** Clot layered over the inter atrial septum.
- **Type IV:** Clot which is mobile and attached to left atrial free wall or left atrial roof or over inter atrial septum.
- **Type V:** Left atrial clot which is free floating in LA cavity (Ball valve thrombus).

All data recorded on Microsoft excel sheet. As an institutional policy post procedure (post TEE) patients were advised not to eat anything for 4 hours and warm eatables up to 24 hours. Those who had LA/LAA clot were advised either anticoagulant therapy followed by repeat TEE after 3 months or surgical management for mitral valve stenosis in place of PTMC on case to case basis.

Results

Out of 2000 patients of severe mitral stenosis on the basis of transthoracic echocardiography (TTE), 1300 (65%) were female and 700 (35%) were Male (p value < 0.0001). Overall mean age was 30.84 +/- 12.6 years. Mean age of males was 30.56 +/- 13.1 years and females were 31.02 +/- 12.6 years. Minimum age was 4 years and maximum was 65 years (Table 1).

S. No	Sex	Number of pts (n 2000)	Percentage	P value
1	Male	700	35%	
2	Female	1300	65%	< 0.0001

Table 1: Distribution of sex.

Out of 2000 patients, those having atrial fibrillation were 660 (33%) and those in sinus rhythm were 1340 (67%) (p value < 0.0001) (Table 2 and figure 1, 2).

Rhythm	Number of pts (n 2000)	Percentage	P value
AF	660	33%	
Sinus	1340	67%	< 0.0001

Table 2: Incidence of atrial fibrillation.

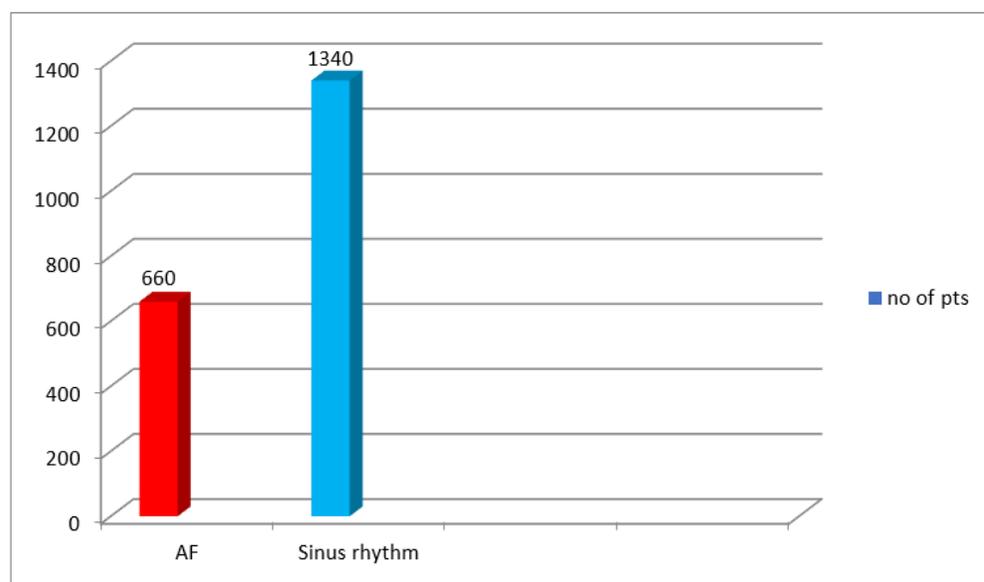


Figure 1: Incidence of atrial fibrillation.

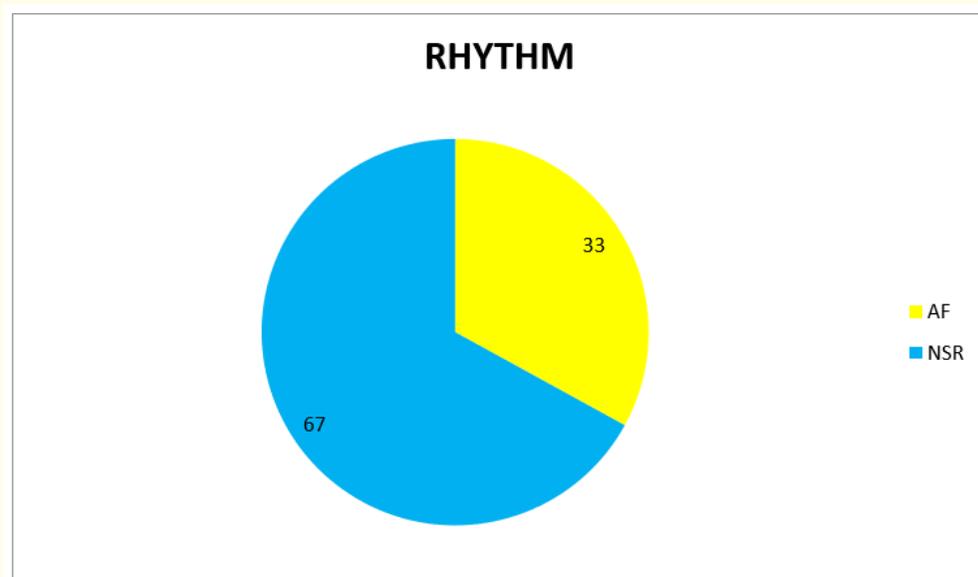


Figure 2: Incidence of atrial fibrillation in patients with Rheumatic severe MS.

On performing TEE on these patients it was reported that out of 2000 patients 37% i.e. 740 patients had clear cut LA/LAA clot while 61% i.e. 1220 patients had spontaneous ECHO contrast. While 2% i.e. 40 patients had clear LA/LAA (Table 3 and figure 3).

TEE Finding	No of pts (n 2000)	Percentage	P value
LA/LAA clot	740	37%	
SEC	1220	61%	P < 0.0001
Clear LAA	40	2%	

Table 3: TEE finding of LA/LAA clot.

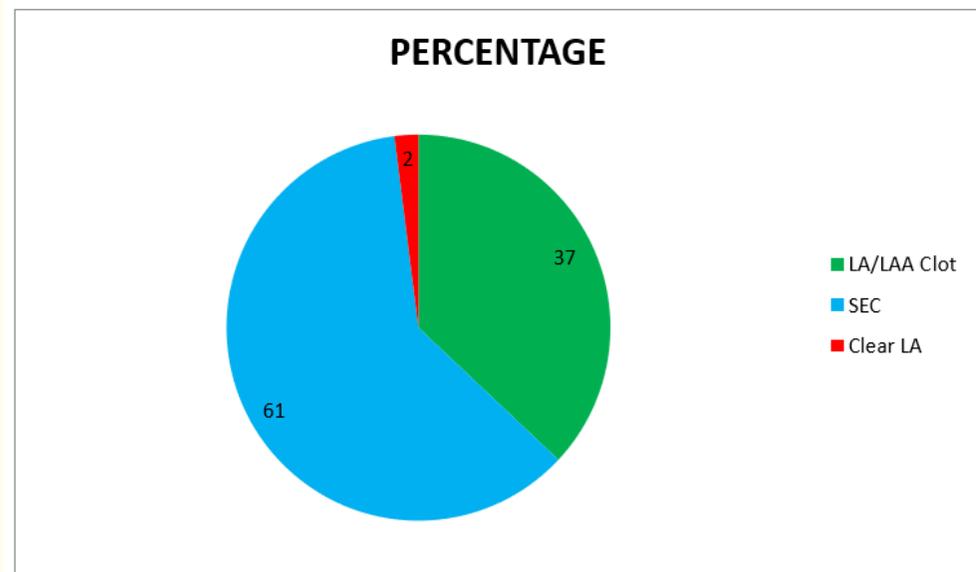


Figure 3: TEE finding of LA/LAA clot.

In 740 patients with LA/LAA clot, it was reported that 480 (65%) patients have AF and 260 (35%) patients have sinus rhythm (Table 4 and figure 4).

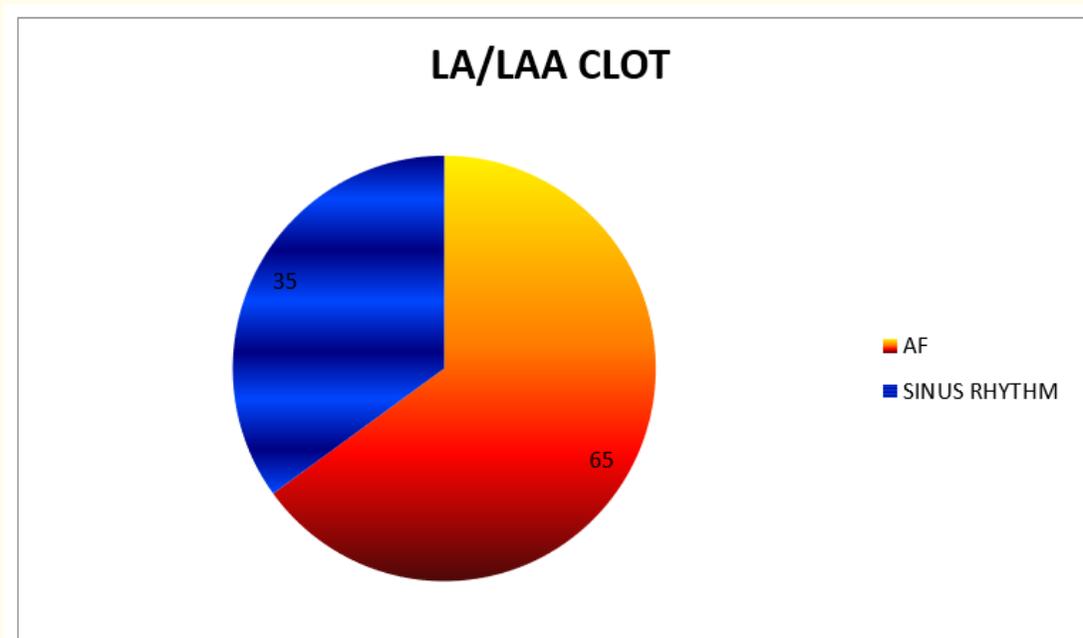


Figure 4: Rhythm and incidence of LA/LAA clot.

S. No.	Rhythm	LA/LAA clot	Percentage	P value
1	AF	480	65%	< 0.0001
2	Sinus rhythm	260	35%	

Table 4: Rhythm and incidence of LA/LAA clot.

In 1220 patients with spontaneous ECHO Contrast, 560 (46%) patients have AF and 660 (54%) patients have sinus rhythm (p value 0.0001) (Table 5 and figure 5).

S. No	Rhythm	SEC	Percentage	P value
1	AF	560	46%	
2	Sinus rhythm	660	54%	0.0001

Table 5: Rhythm and incidence of SEC in LA.

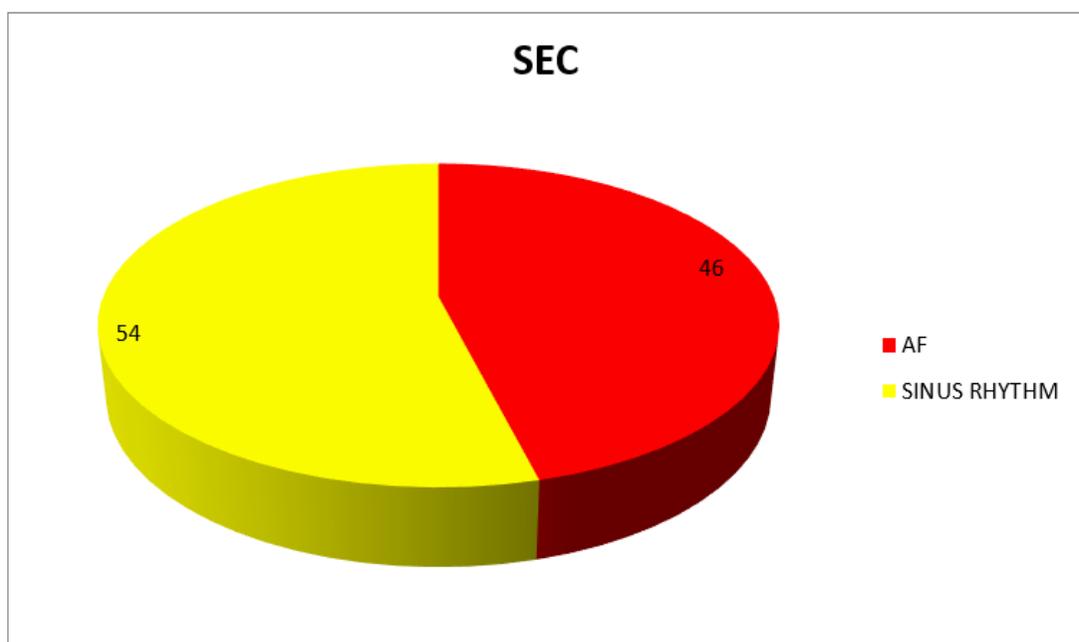


Figure 5: Rhythm and incidence of SEC in LA.

According to Manjunath classification of LA/LAA clot it was reported that type Ia (60%) and Ib (22%) thrombus were seen in majority of the patients who had thrombus (Table 6 and figure 6-8).

Type of LAA clot	Number of pts	Percentage
Type Ia	444	60%
Type Ib	163	22%
Type IIa	111	15%
Type IIb	4	0.5%
Type III	4	0.5%
Type IV	14	2%
Type V	0	0%

Table 6: Type of LA/LAA clot as Manjunath classification.

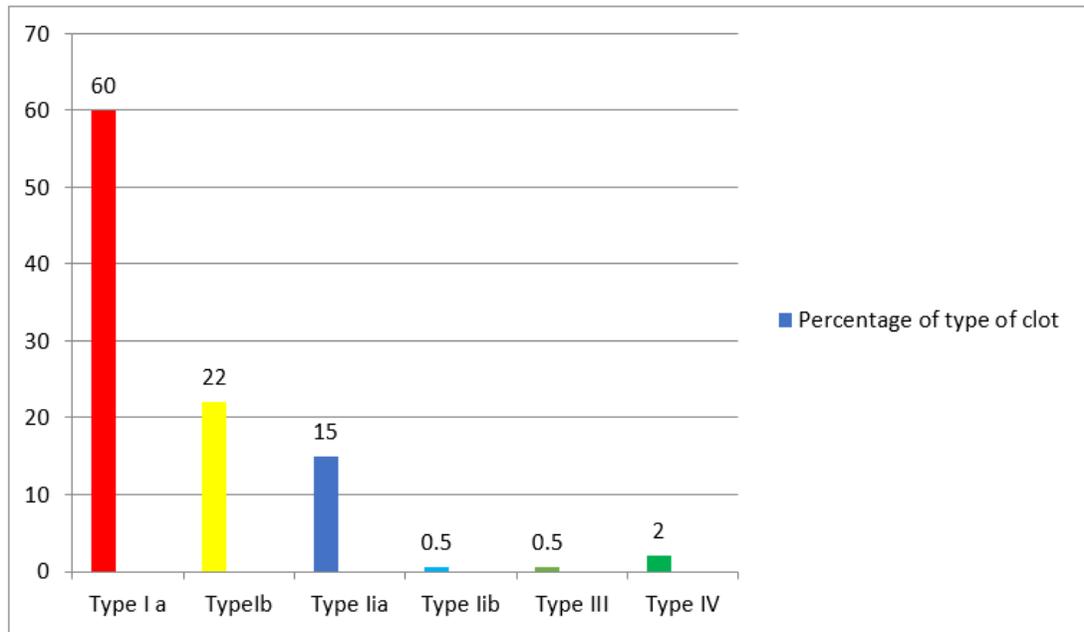


Figure 6: Type of LA/LAA clot as Manjunath classification.



Figure 7: Type 1b LAA clot on TEE.



Figure 8: Type IV LAA clot on TEE.

On assessing LAA emptying velocity impaired LAA emptying velocity was reported in 1240 (62%) of patients while normal LAA emptying velocity was seen in 760 (38%) of patients. (p value < 0.0001) (Table 7).

S. No	LAA emptying velocity	Number of patients	Percentage	P value
1	< 25 cm/sec	1240	62%	< 0.0001
2	> 25 cm/sec	760	38%	

Table 7: LAA emptying velocity.

In 1240 patients having LAA emptying velocity < 25 cm/sec, 740 (60%) patients had LA/LAA thrombus and 500 (40%) patients had SEC in LA (Table 8 and figure 9).

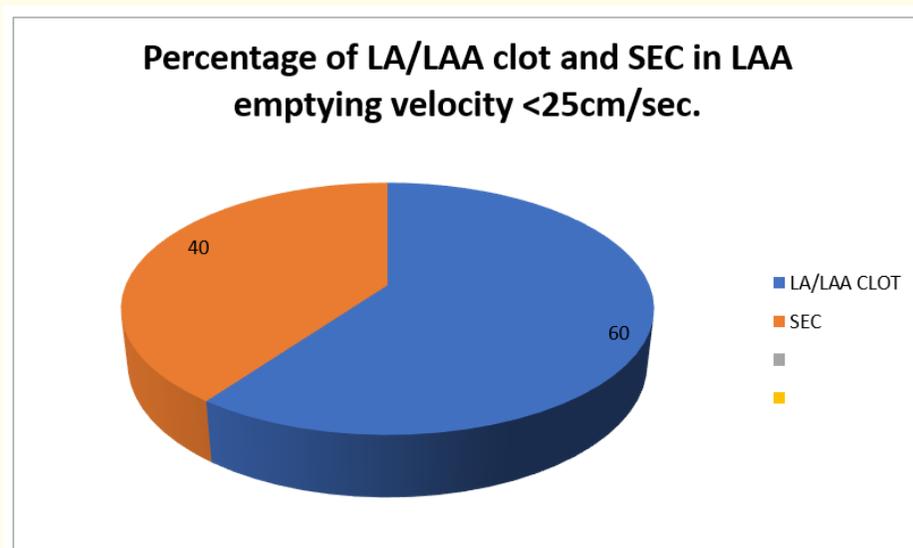


Figure 9: Correlation of LAA emptying velocity with thrombus.

S. No	LAA emptying velocity < 25 cm/sec	Number of pts (n 1240)	Percentage	P value
1	LA/LAA Clot	740	60%	< 0.0001
2	SEC	500	40%	

Table 8: Correlation of LAA emptying velocity with thrombus.

Discussion

In studies done by Srimannarayana, *et al.* and Saidi SJ, *et al.* it was noticed that Rheumatic MS is associated with LA thrombus both in patients with sinus rhythm (3% - 13%) [1,2] and in patients with AF (~33%) [3]. The incidence of LA/LAA thrombus resulting in cerebrovascular accidents was more in patients of AF in our study which was done on large number of patients i.e. 2000 with Rheumatic severe mitral stenosis it was reported that LA /LAA thrombus was present in 37% of severe stenosis patients, out of which 65% were in AF, which is clinically significant while 35% of patients were in sinus rhythm. As compared to different studies done by Davison, Saidi and Srimannarayana frequency of LA thrombus in our study is much higher in both group of patients. Frequency of thrombus formation in AF patients was more than two times as compared to previous small studies done on this topic. It showed that the actual incidence of LA/LAA clot is much more in real world as expected on the basis of prior studies. In patients of severe mitral stenosis with sinus rhythm, incidence of LA/LAA clot were 35%. Higher frequency of thrombus formation in sinus rhythm clearly indicates that parameters other than AF are also important in formation of LA/LAA thrombus and threshold to start anticoagulant should be low in patients with dilated LA (4.5 C.M.) and patients with SEC in LA. As per classification given by Manjunath it was reported that type Ia (60%) and Ib (22%) thrombus were of maximum frequency in our study too. Type IV thrombus were also reported in 2% of patients. These findings were similar to original studies done by Manjunath *et al* which showed that the incidence of type of LA thrombus reported were Type Ia (64% - 76%), Type Ib (9% - 32%), Type IIa (3.6% - 12.5%), and Type IIb (2%) [7,8].

In our study other important parameter i.e. SEC which is assumed to be precursor of thrombus formation was well studied and it was seen that 61% of total patients had SEC on TEE. Out of these 46% were in AF and 54% were in sinus rhythm, this is also suggestive that patients with normal sinus rhythm should not be ignored and be evaluated properly.

To diagnose LAA clot accurately TEE is most sensitive investigation with sensitivity of 97% [4,5]. To detect tiny clots, contrast study can be done in which filling defects are suggestive of clots [6].

In our study it was seen that thrombus formation is more in patients with AF (65%) and LAA emptying velocity less than 25 cm/sec (60%). While presence of sinus rhythm did not exclude the possibility of LA/LAA clot. In accordance with our study, in other studies too it was observed that except AF other factors responsible for clot formation were previous history of embolic episodes, LA dimension > 4.5 cm, mean LAA emptying velocity < 20 cm/s and SEC [7,8].

Regarding anticoagulation in our patients, prior to this study our institute protocol was to anti coagulate patients with AF, prior history of thromboembolic episode and history of clot in LA/LAA. But after results of this study we also included patients with dense spontaneous ECHO contrast in LA and LAA emptying velocity < 25 cm/sec in the list of anticoagulation. Main anticoagulant agent of choice used in our institute are Vitamin K antagonist (warfarin and acenocoumarol) with dose adjustment as per INR monitoring (INR between 2 - 3). More than 25 - 30% of these patients are non-adherent to anticoagulant therapy due to poverty and lack of awareness. Though no study was done on this topic, it is only an observational figure. In our study there was no definite correlation was seen between severity of MS and thrombus formation as in about in about 2% (40 patients), LA/LAA was clear inspite of severe MS.

Conclusion

The frequency of left atrial and left atrial appendage clots on trans-esophageal echocardiography in patients with severe mitral stenosis is more common than reported in previous studies. And more frequent in patients with AF and LAA emptying velocity < 25 cm/sec, but patients with normal sinus rhythm are also at increased risk.

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Conflict of Interest

No conflict of interest.

Ethical Approval

Not required.

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