

EVALUATION OF MITRAL STENOSIS PATIENTS WITH ATRIAL FIBRILLATION FOR FACTORS ASSOCIATED WITH LEFT ATRIAL THROMBOSIS.

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ABSTRACT

Introduction: Rheumatic heart disease still remains a common health problem and an important cause of morbidity and mortality in all age group. Mitral stenosis is the most common cardiac valve lesion involved in rheumatic heart disease. This can cause serious complications if left untreated and can lead to enlargement of the left atrium and stasis of blood which increases risk of clot formation in the left atrium and the left atrial appendage. The presence of left atrial thrombi is associated with a threefold increase in embolic events.

In clinical practice we frequently come across patients of mitral stenosis with atrial fibrillation, this study will enlighten the practicing physicians about the magnitude of the problem of LA thrombus in patients with mitral stenosis having atrial fibrillation and will help them to modify their management protocol accordingly to prevent the fatal complications of Thromboembolism.

Objectives: To determine the prevalence of Left Atrial thrombus in mitral stenosis patients with atrial fibrillation. To study the association of Left Atrial Size, gender, LASEC (Left Atrial Spontaneous Echo Contrast) and severity of Mitral Stenosis with LA clot formation in mitral stenosis patients with atrial fibrillation.

Methods: A cross sectional descriptive type study was conducted in the Echocardiography department of the cardiology Department Lady Reading Hospital Peshawar from March 23, 2010 to September 22, 2010. A total of 152 consecutive patients with severe and moderate Mitral stenosis (MS) and Atrial Fibrillation (AF) were included in this study. 12-lead Electrocardiography was done once clinical and echocardiographic features revealed moderate and severe MS. Patients with signs of AF were selected and both Transthoracic Echocardiography (TTE) and Transesophageal echocardiography (TEE) was performed on all patients to detect Left atrial clot.

Results: Among 152 patients studied; there were 65 males and 87 females. TTE and TEE was performed in all patients and TTE detected LA thrombus in 3 patients while TEE detected LA thrombus in 41 patients. Among them, 6 patients had clots in LA body while LA appendage clots were found in 32 patients. Left atrial dimension was found to be relevant (P-value = 0.004) with the presence of thrombus in patients with moderate and severe mitral stenosis associated with atrial fibrillation. Moderate MS was present in 28 (18.4%) patients while severe MS was present in 124 (81.6%) patients. Female to male ratio was 1.6 but there was no statistically association with LA thrombus (P value=0.1363). Left atrial spontaneous echo contrast (LASEC) was found in 54% and its association was statistically significant (P value <0.001)

Conclusion: Left atrial thrombus was present in 27% patients with mitral stenosis associated with atrial fibrillation. All patients who underwent TTE and are found having larger LA diameter and LASEC must undergo TEE to exclude LA thrombus as TTE is having very low sensitivity for LA thrombus.

Keywords: Left Atrial Thrombus, Mitral Stenosis, Atrial Fibrillation, Rheumatic heart disease.

INTRODUCTION

Rheumatic heart disease still remains a common health problem and an important cause of morbidity and mortality in all age group¹. Mitral stenosis is the most common cardiac valve lesion involved in rheumatic heart disease². This can cause serious complications if left untreated and can lead to enlargement of the left atrium and stasis of blood which increases risk of clot formation in the left atrium and the left atrial appendage. The presence of left atrial (LA) thrombi is associated with a threefold increase in embolic events³.

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The prevalence of atrial fibrillation in mitral stenosis is related to the severity of valve obstruction and age of the patient. It is 17% in the age of 21-30 years age group, 60% in the age of 31-50 years and 80% in the age more than 51 years age group⁴. Prevalence left atrial thrombus in patients of mitral stenosis with atrial fibrillation is 26.1% whereas 13.5% in patients of mitral stenosis with normal sinus rhythm⁵.

Left atrial thrombus can be detected by various modalities like Transthoracic echocardiography (TTE), Transesophageal echocardiography (TEE) or coronary angiography. The sensitivity of TTE is 28%, specificity 99%; sensitivity of TEE is 100% and specificity is 99%. TEE provides better images of the mitral valve and is more sensitive way to detect atrial thrombus^{6,7}.

In clinical practice we frequently come across patients of mitral stenosis with atrial fibrillation, this study will enlighten the practicing physicians about the magnitude of the problem of LA thrombus in patients with mitral stenosis having atrial fibrillation and its association with the variables like LA size, gender, LASEC, Severity of Mitral Stenosis and will also help in prevention of complications by early intervention.

OBJECTIVES

To determine the prevalence of Left Atrial thrombus in mitral stenosis patients with atrial fibrillation.

To study the association of Left Atrial Size, gender, LASEC and severity of Mitral Stenosis with LA clot formation in mitral stenosis patients with atrial fibrillation.

OPERATIONAL DEFINITIONS

MODERATE MITRAL STENOSIS

This will be defined as mitral valve area 1-1.5cm² on 2D echocardiography by planimetry method at the end of diastole and mitral valve gradient 5-10 mmHg on continuous wave spectral display of transmitral flow with peak and mean gradient derived from planimetry of wave form upon Doppler echocardiography.

SEVERE MITRAL STENOSIS

This will be defined as mitral valve area $\leq 1\text{cm}^2$ on 2D echocardiography by planimetry method at the end of diastole and mitral valve gradient ≥ 10 mmHg on continuous wave spectral display of transmitral flow with peak and mean gradient derived from planimetry of wave form upon Doppler echocardiography.

ATRIAL FIBRILLATION

This will be defined as absent P waves and irregularly irregular QRS complexes on surface electrocardiography using rhythm strip of lead II of electrocardiogram.

LEFT ATRIAL THROMBUS

This will be defined as echo dense mass of any size with independent motion relative to chamber wall, found in the left atrial cavity or left atrial appendage using first TTE and if thrombus not detected then TEE will be performed.

LEFT ATRIAL SIZE

This will be defined maximum edge to edge dimensions in Parasternal long axis view using M-Mode.

MATERIAL AND METHODS

STUDY DESIGN

Descriptive cross sectional study

SETTING

Department of Cardiology, Post graduate Medical Institute Govt. Lady Reading Hospital Peshawar

DURATION OF THE STUDY

Six months, from March 2010 to September 2010.

SAMPLE SIZE

Sample size was calculated by using WHO sample size formula using prevalence of left atrial thrombus in patients of mitral stenosis with atrial fibrillation to be 26.1% with confidence interval 95% and absolute precision 7%, a sample size of 152 patients was taken.

SAMPLING TECHNIQUE

Non probability purposive.

SAMPLE SELECTION

INCLUSION CRITERIA

Patients of age ≥ 20 years and both gender with moderate to severe mitral stenosis and atrial fibrillation.

EXCLUSION CRITERIA

Patients with mitral stenosis and with no documented atrial fibrillation.

Moderate to severe mitral regurgitation.

Congestive heart failure.

The above mentioned cases will be excluded from the study because they will act as confounders and will introduce bias in the study results.

DATA COLLECTION PROCEDURE

The study was approved by the Hospital Ethical Committee. Patients who are admitted to Cardiology unit Lady Reading Hospital through OPD or casualty department were included. An informed consent was obtained. Patients of mitral stenosis were diagnosed on Transthoracic echocardiographic assessment using Acuson CV 70 Siemens using planimetry and Doppler method. Mitral valve will be graded as moderate when valve area is 1-1.5cm² and a transmitral valve pressure gradient 5-10mmHg and severe when valve area is $\leq 1\text{cm}^2$ and transmitral valve pressure gradient of $\geq 10\text{mmHg}$. An electrocardiogram was done on these patients and atrial fibrillation was diagnosed as absent P waves and irregularly irregular QRS complexes by me after diagnosed by consultant cardiologist.

Atrial thrombus is detected using both Transthoracic echocardiography (TTE) and Transesophageal echocardiography. Both atrial cavity and appendage are evaluated for thrombus and Frequency of left atrial thrombus was recorded.

Confounding variables like severe mitral regurgitation and congestive heart failure was excluded following exclusion criteria. Echocardiography was done on same machine performed by two operators to avoid operator bias, by the findings upon which both operators agree.

DATA ANALYSIS:

The statistical analysis was performed using the statistical software for social sciences (SPSS Ver. 10.0). Categorical variables like gender, moderate mitral stenosis, severe mitral stenosis and left atrial thrombus presented in the form of frequencies and percentages. Numerical variables like age presented as means \pm SD. Chi-square with Yates correction and student t-test is used to compare means while finding association.

Data is presented as tables and graphs

RESULTS

Out of 152 patients screened for left atrial clot fulfilling all criteria were included in the study. Table 01 shows descriptive statistics of Gender and Age.

All patients presented with history of palpitation and shortness of breath on exertion (NYHA class II – III). Figure 01 shows patients data with presenting symptoms.

Most of our patients presented with Severe Mitral stenosis. Figure 02 shows the Pie Chart of Mitral Stenosis severity among our patients.

All the patients underwent Transthoracic echocardiography that revealed thrombi in 3 patients. Remaining 149 patients underwent TEE that revealed thrombi in 38 patients. Table 04 shows the Frequency of Left Atrial Clot.

Among all 41 patients who were having LA Clot, 28 were females and 13 were males. A ratio between male and female was 1:1.6 but the result was not statistically significant with P value of 0.094. Table 05 shows the 2X2 table for association of LA clot with Gender.

Our study showed that LA thrombus is associated with the LA size. Mean LA size in patients with LA thrombus was 63.53 ± 15.79 mm when compared with patient with no thrombus where mean LA size was 55.55 ± 10.94 mm. t-test showed statistical significance with P value =0.004 . Table 06 shows the Association between LA thrombus and LA size.

TTE of 152 patients showed LA clot in 3 patients while TEE showed that 41 patients were having LA clot. Assuming TEE as gold standard, Sensitivity and Specificity for TTE is calculated. Table 07 shows the Sensitivity and Specificity of TTE.

The study also showed that 29% of Severe MS

Table 01: Descriptive Statistics Of Gender and Age

Sample Size	152	100%
Male	65	42.76%
Female	87	57.23%
Mean Age (in years)	36.93 \pm 12.72	-

Table 03 shows Descriptive statistics of Echocardiographic Variables of our study.

Echo Parameter	Mean
Mitral Valve Area	0.81 \pm 0.14 cm ²
Pressure Half Time	266.62 \pm 43.83 ms
LA Diameter	60.58 \pm 13.50 mm

Table 04: Frequency of LA Clot

LA Thrombus	Number of patients	Percentage
Present	41	26.97%
Absent	111	73.03%

Table 05: Association of LA Thrombus with Gender:

Gender	LA Clot Present	LA clot Absent	Total
Male	13	52	65
Female	28	59	87
Total	41	111	152

Chi squared equals 2.219 with 1 degrees of freedom. The two-tailed P value equals 0.1363

Table 06: Association between LA Thrombus an LA size

LA Thrombus	Mean LA Size
Present	63.53 \pm 15.79 mm
Absent	55.55 \pm 10.94 mm

T-test showed statistical significance with P value =0.004

Table 07: Sensitivity and Specificity of TTE for LA thrombus

Thrombus de-tection by TEE	Thrombus Detected by TTE	Thrombus not Detected by TTE
Present	3 (True Positive)	38 (False Negative)
Absent	0 (False Positive)	111 (True Neg-atives)

Sensitivity=7.31% , Specificity=100%

Table 08: Association of LA Thrombus with Severity of MS

MS Severity	LA Clot Present	LA clot Absent	Total
Severe MS	36	88	124
Moderate MS	5	23	28
Total	41	111	152

Chi squared equals 0.936. The two-tailed P value equals 0.3332

Table 09: Association of LASEC with LA thrombus

LASEC	LA Clot Present	LA clot Absent	Total
Present	28	26	54
Absent	13	85	98
Total	41	111	152

Chi squared equals 24.394. The two-tailed P value is less than 0.0001

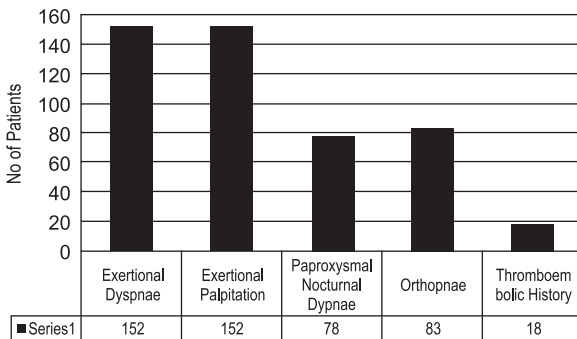


Figure 01: Pateints Presenting Symptoms

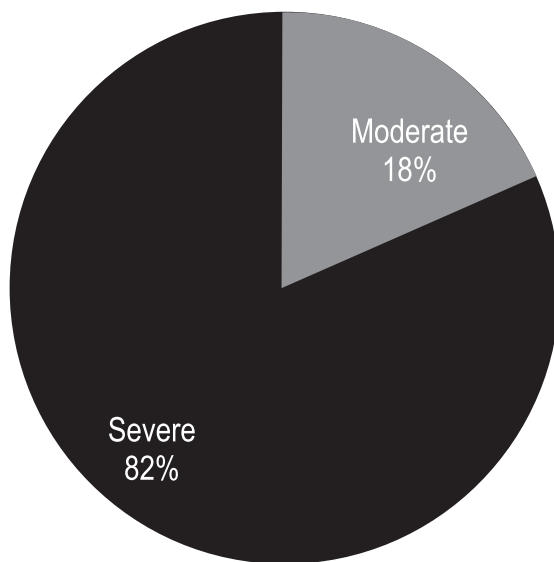


Figure 02: Severity of Mitral Stenosis

patients had LA Clot versus 18% patients of Moderate MS. The difference was not statistically significant with P value=0.2288. Table 08 shows the 2X2 table for the association of LA thrombus with severity of MS.

DISCUSSION

Rheumatic mitral stenosis with atrial fibrillation is a common clinical problem in Pakistan^{8,10}. It is a potential source of thrombus formation and associated with a very high risk of embolic cerebro-vascular accidents, which is reported to be as much as seventeen times greater than in unaffected controls¹¹.

TEE is well established as the gold standard for detecting thrombi in the left atrium and the LA appendage. The sensitivity and the specificity of TEE are reported to be 100% and 99%, respectively⁷. Though it is known that thrombi are common in patients with MS and AF, until recently only small studies have documented the exact frequency of occurrence of these thrombi. In a small group of 50 patients with MS and AF, Hwang et al¹² observed an LA thrombus in 28 patients (56%) by TEE. In another small study of 22 patients with MS and AF, Karatasakis et al¹³ observed an LA thrombus in 12 patients (54%). A study performed in NICVD Karachi found 38% with sever mitral stenosis and atrial fibrillation¹³.

However, recently Srimannarayana J et al¹⁴ studied 490 patients with severe MS and AF and observed LA thrombi in 163 (33.5%) patients. We found LA thrombus in 27% patients in a group of 152 consecutive patients. Considering the size of the study group though the number of patients in our study group is little less for the prevalence of LA thrombi in patients with moderate and severe MS and AF, but our results were comparable. Thus, it can be stated that 1 out of every 4 patients with MS and AF will have an LA thrombus.

Another important finding emerged in our study is male to female ratio of disease Male: Female = 1: 1.6. but the results were not statistically significant (P value =0.1363) . The results are in accordance to Mahmood ul Hasaan et al¹⁵ findings (P value=0.42).

Our study showed that LA size is relevant with the presence of LA thrombus (63.53 ± 15.79 mm versus 55.55 ± 10.94 mm, P = 0.004). This means that larger the atrial size greater the chances of presence of LA thrombus in patients with severity of MS and AF. While describing clinical risk factors for thrombus formation among patients with severe MS Goswami et al¹⁶ documented the same finding.

Apart from LA diameter Goswami et al¹⁶ found that longer duration of symptoms and more frequent atrial fibrillation with spontaneous echo contrast (LASEC) were independent risk factors for LA thrombus formation. Our Study also showed a strong statistically significant association between LASEC and LA thrombus with P value=0.000002. Our study showed 51.85% of

patients with LASEC are having LA thrombus confirming Goswami et al¹⁶ finding where he observed 53.5% of patients with LASEC are having LA thrombus.

However, at least it can be said that larger LA diameter is an alarming sign and one has to carefully look for LA thrombus in these patients. A P value=0.004 suggest a strong association between LA size and LA thrombus. So we can conclude that all patients who underwent TTE and are found having enlarged LA must undergo TEE to exclude LA thrombus as according to our study sensitivity of TTE for LA thrombus detection is very low i.e. 7.3%.

The Study also showed there is no association between Severity of MS and LA thrombus (P value=0.332). The reason could be that there are very less patients (28 patients) with Moderate MS are enrolled in the study as compare to Severe MS (124 patients).

CONCLUSION

The proportion of patients with LA thrombi in patients suffering from severe and moderate MS and AF observed in this study was 27%. Therefore it can be stated that more than one fourth of the patients with severe and moderate rheumatic MS and AF will have LA thrombi. Larger LA diameter was observed statistically significant as far as the presence of LA thrombus was concerned.

Therefore, larger the LA size in patients with severe MS and AF greater the frequency of having LA thrombus is expected. Hence, it is prudent to anticoagulate this high-risk group of patients to prevent them from serious implications of systemic thrombo-embolism.

Furthermore those patients who undergo TTE and are found with increase LA size must opted for TEE as there is very high risk of LA thrombus in these patients. One should not rely on TTE for LA clot as sensitivity is very low for LA thrombus. But high specificity shows that there is no need of TEE for those patients who are having LA clot detected on TTE.

Study Limitation

The present study was conducted at Cardiology Unit Lady Reading Hospital, one of the largest tertiary care centers of densely populated city of Peshawar. This center receives patients from almost every part of the province and neighboring Afghanistan hence results of our study reflect the diseased status of both KPK and Afghanistan. There is need of same study for KPK Province Only to better understand the prevalence of the LA thrombus in respected study group. To learn about the exact prevalence of the disease, a multi-center study should be conducted.

There were less patients with Moderate MS are included as compare to Severe MS which might have affected our results while association between Severity

of MS and LA thrombus.

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