

Predictors of Left Atrial Thrombus in Patients with Severe Mitral Stenosis

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Left Atrial Thrombus in Severe Mitral Stenosis

ABSTRACT

Objective: To evaluate the trans esophageal echocardiography (TEE) findings in patients of mitral stenosis and to determine the risk factors associated with Left atrial (LA) thrombus in this disease.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Medicine & Cardiology/CCU DG Khan Medical College & Teaching Hospital, DG Khan from May 2019 to April 2020 in one year duration.

Materials and Methods: A total of hundred patients selected in this study. Patients aged 15 or above with any gender having severe mitral stenosis eligible for percutaneous trans venous mitral commissurotomy (PTMC) on the basis of trans esophageal echocardiography (TEE) were selected for this study. SPSS version 23 was used for data analysis. Test of significant were applied and p value ≥ 0.05 was taken as significant.

Results: Considering demographics, the mean age of the patients was 33.4 ± 16.56 years and majority of females 89% in our study. LA thrombus formation was cross tabulated against 7 clinical and echocardiographic parameters and their association with LA clot formation was evaluated with Pearson chi square test. These variables were Age, Atrial fibrillation, mitral valve area, mitral regurgitation, Wilkins score, pulmonary hypertension and LA size. Out of these parameters; atrial fibrillation, Wilkin's score, LA size and pulmonary hypertension were significantly associated with LA clot formation with asymptotic significance of 0.000, 0.000, 0.007 and 0.034 respectively.

Conclusion: Rheumatic Mitral stenosis is a major public health concern in our country. Management of these patients is complicated by LA thrombus and systemic embolism. This study showed presence of AF, enlarged LA, severe pulmonary hypertension and high Wilkin's score to be the predictor of LA thrombus.

Key Words: Rheumatic heart disease (RHD), Left atrial thrombus, Mitral stenosis, Transesophageal echocardiography

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INTRODUCTION

Rheumatic fever licks at the joints, but bites at the heart, this is an old saying by Laseque in 1884. Rheumatic heart disease (RHD) is caused by Group A Streptococci that initially causes innocuous looking sore throat which leads to Rheumatic fever that in some patients ends up crippling the heart. In the USA in the 1920s, Rheumatic fever was the leading cause of death in individuals between 5 and 20 years of age¹. The discovery of Penicillin in 1928 by Alexander Fleming exponentially reduced mortality and morbidity associated with Rheumatic Fever.

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However, it still remains a public health problem in developing countries especially in sub Oceania, Saharan Africa and South Asia.

In 2015, a total of 33.41 Million cases of rheumatic heart disease occurred in the world with estimated age-standardized prevalence of 444 cases per 100,000 populations for countries with an endemic pattern². In Pakistan in 2015, there were 2.25 Million cases of RHD with 18900 deaths².

Mitral valve is most commonly involved in RHD either in isolation or in combination and the most common lesion is mitral stenosis. Mitral stenosis is often complicated by enlargement of Left Atrium (LA) and presence of Atrial Fibrillation (AF) which not only worsen heart failure but also is a major cause of thromboembolism in Rheumatic Mitral Stenosis. Clinical deterioration occurs because of the loss of atrial contraction and increase in heart rate, resulting in reduced cardiac output and functional capacity³.

TEE is mandatory before PTMC not to rule out LA clot but also to reassess mitral valve anatomy and to exclude MR. The standard of care in severe mitral stenosis is percutaneous trans septal mitral commissurotomy. In this procedure, a balloon is placed across Mitral Valve through Atrial septal puncture and expanded at high pressure which results in splitting of commissures and

fracture of calcium. This increases the Mitral valve area and results in relief of symptoms. However, success and freedom from complications in this procedure depends upon proper selection of Patients. LA thrombus, more than mild Mitral regurgitation and poor valve anatomy with heavy calcification and high Wilkins score constitute contraindication to this procedure⁴. Wilkins Scoring system is being used for assessment of pliability of Mitral valve for PTMC. This scoring system includes four grades that is mobility, thickening, calcification and sub-valvar disease. Total score is 16. Score ≤ 8 is pliable for PTMC⁵⁻⁶.

MATERIALS AND METHODS

This prospective study was conducted at Medicine & Cardiology/CCU DG Khan Medical College & Teaching Hospital, DG Khan from 1ST May 2019 to 30th April 2020 in one-year duration. A total of hundred patients having age ≥ 15 years with both gender having severe mitral stenosis eligible for PTMC on the basis of TEE were included. The patients having severe mitral regurgitation, contraindications to PTMC/TEE, multivalvular involvement and concomitant coronary artery disease were excluded. All Patients eligible for PTMC were involved in this study after informed consent. ECG was evaluated for presence of AF which is defined as irregularly irregular rhythm on ECG with absent P waves and fibrillatory f waves. Severe Mitral stenosis is defined as mitral valve area less than or equal to 1.5 cm^2 as measured by planimetry or pressure half time more than or equal to 150 milli seconds and less than or equal to 1.0 cm^2 as measured by planimetry or pressure half time more than or equal to 220 milli seconds defined as very severe mitral stenosis.

Transthoracic echocardiogram (TTE) was performed for measurement of Wilkin's score, LA size, pulmonary hypertension and Mitral regurgitation. Left Atrial size is measured in TTE in PLAX view at end systole either in M mode or 2D echo with normal size 40mm or less, mild enlargement defined as 41-45 mm, moderate enlargement described as 46-50mm and severe enlargement described as $>50\text{mm}$. Mitral Regurgitation (MR) is seen on TTE in PLAX and A4C views. Mild MR described as regurgitation fraction filling $< 20\%$ of LA on color Doppler and vena contract of $< 3\text{mm}$. Moderate MR is described as regurgitation fraction filling 20-40% of LA on color Doppler with VC of 3-6mm. Pulmonary Hypertension is based on measurement of estimated Pulmonary artery systolic pressures which is measured by Tricuspid calve pressure gradient and estimated Right atrial pressure on the basis of IVC size and respiratory variations. Mild, moderate and severe pulmonary hypertension (PH) are categorized as 40-50 mmHg, 51-60 mmHg and >60 mmHg respectively. TEE was carried out to evaluate LA and LAA for Thrombus. Findings along with demographical data was noted on given Performa. All

the data was analyzed by using computer software SPSS version-23. Mean and standard deviation were calculated for quantitative variables like age. Frequency and percentage calculated for all qualitative variables i.e. LA clot, AF etc. Pearson chi square test was used for association of different parameters with LA thrombus formation.

RESULTS

Hundred patients participated in this study. Considering demographics, the mean age of the patients was 33.4 ± 16.56 years. A total of 49 patients were 30 years or younger, 35 patients were aged 31 to 45 years and only 16 patients were older than 45 years. Women formed the bulk of our patient cohort with 89% being female and only 11% male. Sixty-eight patients were married and 32 patients were unmarried.

Regarding clinical characteristics, 26 people had clot in left atrium or Left atrial appendage, while rest of the 74 patients had no LA or LAA thrombus. Atrial Fibrillation was present in only 11 patients. Only seven patients had normal sized LA i.e. less than 40mm, while rest of 93 patients had varying degrees of LA enlargement. Thirty-three patients had mild LA enlargement i.e. 41-45mm, 34 patients had moderate LA enlargement i.e., 46-50mm while 26 patients had severe LA enlargement i.e. more than 50mm. Regarding Mitral Valve area, 81 patients had very severe MS i.e. MVA less than 1 cm^2 and 19 patients had severe MS i.e. MVA 1- 1.5 cm^2 . Surprisingly only 11 patients had atrial fibrillation while 89 patients had normal sinus rhythm. Mitral regurgitation was absent in 77 patients while Mild MR was present in 17 patients and 6 patients had moderate MR. There were no patients with severe MR as they were excluded from study design. Wilkins score was calculated in each patient on TTE. The mean Wilkin's score was 7.10 ± 1.90 with median score of 7. The patients clustered around score of 6 (27%) and 7 (35%). Seventy-nine patients had Wilkins score of 8 or below while rest of 21 patients had high Wilkin's score. Mean LA size in our study was 47 ± 50 mm while mean Mitral valve area was $0.86 \pm .22 \text{ cm}^2$ Regarding pulmonary hypertension (PH), Mild PH was present in 32 patients, Moderate PH in 24 patients and Severe PH in 44 patients.

LA thrombus formation was cross tabulated against 7 clinical and echocardiographic parameters and their association with LA clot formation was evaluated with Pearson chi square test. These variables were Age, Atrial fibrillation, Mitral Valve area, Mitral regurgitation, Wilkins score, pulmonary hypertension and LA size. Out of these parameters; atrial fibrillation, Wilkin's score, LA size and pulmonary hypertension were significantly associated with LA clot formation with asymptotic significance of 0.000, 0.000, 0.007 and

0.034 respectively. On the other hand, age, mitral valve area and mild to moderate mitral regurgitation were not significantly associated with LA thrombus (Table-1).

Table No.1: Predictors of LA thrombus

Parameter		Absent	Present	Significance (Pearson Chi square test)
Atrial Fibrillation	Absent	73	16	0.001
	Present	1	10	
Age	Less than 30 years	35	14	0.837
	31-45 years	27	8	
	More than 46 years	12	4	
Wilkins Score	4-8	68	11	0.000
	9 or above	6	15	
Mitral Valve Area	Less than 1cm ²	58	23	0.260
	1-1.5cm ²	16	3	
Left Atrial size	Below 40mm	7	0	0.007
	40-45mm	30	3	
	46-50mm	21	13	
	Above 50mm	16	10	
Mitral Regurgitation	Absent	57	20	0.895
	Mild	13	4	
	Moderate	4	2	
Pulmonary Hypertension	Mild	29	3	0.034
	Moderate	16	8	
	Severe	29	15	

DISCUSSION

Both male and female patients were selected in this study however 89% of patients with Mitral stenosis were females. This female preponderance regarding acute rheumatic fever and rheumatic heart disease has been documented in literature from all over the world. A study evaluating incidence and progression of RHD in Australia showed 65% of patients suffering from RHD were females⁸. The reason for this female dominance is not completely understood but may relate to reduced access to health care facility to females in developing and underdeveloped countries and increased likelihood of disease becoming symptomatic during pregnancy especially mitral stenosis. As ARF is a disease of children and teenagers and because Pakistan is an endemic area for RHD², most of our disease burden of Rheumatic MS is shared by relatively younger individuals as evidenced in this study by 49% of patients below 30 years of age and while 84% of patients below 45 years.

Left Atrial thrombus was found in 26% of patients or roughly one in four patients with severe Mitral stenosis. An Indian study showed the presence of LA clot in 33% of patients which is marginally higher than our study⁹. A recent study (2020) in Karachi showed the prevalence of LA clot to be 25 % that is similar to our study¹⁰. Another study from Quetta in 2018 showed the

prevalence of LA clot to be 27% but in this study all the patient had AF in addition to Mitral stenosis¹¹. Atrial fibrillation was present in 11% of patients. The world prevalence of AF in general population is 0.4-0.5%¹². This prevalence is much lower in general population as Mitral valve obstruction exposes LA to high pressure which causes wear and tear in LA eventually culminating into AF. A study from Lahore showed the frequency of AF in mitral stenosis at 25%¹³. This number is roughly double the frequency seen in our study likely due to selection bias as patients with moderate MS, severe MR and those patients who were advised surgical procedure were excluded from our study.

As already discussed a total of 7 variables (2 clinical i.e. age, atrial fibrillation and 5 TTE i.e. LA size, MVA, mild to moderate MR, Wilkins score and pulmonary hypertension) were assessed for association with LA clot formation. Four of these variables i.e. LA size, AF, Wilkins score and pulmonary hypertension were significantly associated with LA clot with p value <0.05. On the other hand, Age, mild to moderate MR and Mitral valve area were not significantly associated with LA thrombus. A study conducted in 2011 in India found 3 variables associated with LA thrombus formation i.e. Age >44 years, LA infer superior dimension >6.9 cm and mean mitral gradient >18 mmHg¹⁴. An older study of LA thrombus risk factors in

mitral valve disease found female gender, prior history of embolism, prior anticoagulant therapy, mitral stenosis and atrial fibrillation to be significantly associated with LA thrombosis on univariate analysis. However, on logistic regression analysis only MS and AF were significantly associated with LA thrombosis¹⁵. A study from Thailand found atrial fibrillation, male sex, left atrial enlargement by electrocardiogram, left atrial diameter, left atrial volume, Ejection fraction by Teichholz method, EF by Biplane method, tricuspid regurgitation, mitral regurgitation and Right ventricular systolic pressure as significant predictors of LA thrombus¹⁶. A study from Lahore found frequency of left atrial thrombus formation is increased in patients of rheumatic mitral stenosis with low left atrial appendage flow velocities, atrial fibrillation and smaller mitral valve area¹⁷.

Another study from Lahore showed atrial fibrillation, large left atrial size and old age to be significantly associated with LA thrombus¹⁸.

Logistic regression analysis showed maximum strength of association for Wilkins score and atrial fibrillation followed by LA size and pulmonary hypertension. On the basis of univariate analysis, a risk score is proposed in Table 4. Cut off value of 6 is selected with patient having a score of 6 or more deemed to be at high risk for clot formation. This cutoff value of 6 gives a Specificity of 87.84% and sensitivity of 61.54%, positive predictive value of 64% and negative predictive value of 86.67 % and accuracy of 81%. This simple score can be calculated easily with TTE and can help in predicting the presence of thrombosis in patients with Severe MS.

CONCLUSION

Rheumatic Mitral stenosis is a major public health concern in our country. Management of these patients is complicated by LA thrombus and systemic embolism. This study showed presence of AF, enlarged LA, severe pulmonary hypertension and high Wilkin's score to be the predictor of LA thrombus. On the basis of these parameters, a simple scoring system is proposed for risk stratification of such patients.

Author's Contribution:

Concept & Design of Study:	Imran Javaid
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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