Original Article

Clinical and Echocardiographic Predictors of Left Atrial Thrombus in Rheumatic Mitral Stenosis

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Objectives: To evaluate various clinical and echocardiographic predictors of left atrial (LA) thrombus in patients with severe mitral stenosis and to determine the utility of transesophageal (TEE) as compared to transthoracic echocardiography (TTE) in detection of thrombus in LA.

Place and Duration of Study: Department of Echocardiography and Out Patient Department of Punjab Institute of Cardiology, Lahore from January 2007 to April 2007.

Study Design: It was an observational analytical study.

Patients and Methods: In this study left atrial (LA) thrombus and spontaneous echo contrast were evaluated by both TTE and subsequent TEE in 100 patients with rheumatic mitral stenosis. The study population was divided into two groups: Group I consisted of 38 (15.2%) patients having thrombus in LA and Group II consisting of 212 (84.8%) patients with no thrombus in LA. Various clinical and echocardiographic variables were compared in these two groups.

Results: Two hundred and fifty consecutive patients having tight rheumatic mitral stenosis were studied. The mean age of the study population was 26.9 ± 7.5 years. There were more female 128 (51.2%) patients than males 122 (48.8%). Atrial fibrillation (AF) was present less frequently in the study as 33 (13.2%) patients had AF as compared to 217 (86.8%) patients having sinus rhythm. AF was more significantly associated with thrombus formation with 23 (60.5%) patients having thrombus as compared to 15 (39.5%) patients in sinus rhythm having thrombus $p < 0.0001$. Thrombus in LA was more commonly visualized on TEE as compared to TTE ($X^2=242.3$, $p=0.0001$) and was mostly detected in left atrial appendage ($X^2=211.2$, $p=0.0001$). Spontaneous echo contrast was visualized more frequently on TEE as compared to TTE in both the groups $p<0.001$.

Conclusion: TEE is better than conventional TTE in detecting left atrial thrombi in patients with severe mitral stenosis having AF. Patients with rheumatic mitral stenosis having atrial fibrillation, large left atrial size and old age are more prone to have LA thrombus.

Key Words: Atrial thrombus, transesophageal echocardiography (TEE), transthoracic echocardiography (TTE).

Introduction

Mitral stenosis is one of the commonest long term complications of rheumatic fever and can lead to enlargement of the LA leading to increased risk of thrombus formation.[1] LA thrombi are reported to occur in 26-33% of patients with severe mitral stenosis.[2,3] LA thrombi were found in 20% of patients who underwent surgery for mitral stenosis.[4] The presence of LA thrombi was associated with a threefold increase in embolic events.[4] Fifty percent of LA thrombi in patients with rheumatic valvular disease, and nearly 90% of LA thrombi in patients with non-valvular AF are limited to the LA appendage.[4]

Various factors determine the individual risk of LA thrombus in patients with rheumatic heart disease which include AF, LA size, older age, and severity of mitral stenosis.[5] The presence of spontaneous echo contrast is frequently observed by TEE in patients with rheumatic heart disease and has been associated with increased risk of thrombus formation in LA.[5] The incidence of thromboembolic complications is higher in patients with rheumatic mitral stenosis especially in those with AF.[5,6]

TEE is the gold standard for detecting thrombi in the LA and the LA appendage. The sensitivity and specificity of TEE are reported to be 100% and 99%, respectively.[7]

The accessibility of the left atrial appendage by TEE is better than TTE in detection of thrombi.[8] TTE does not demonstrate the majority of LA appendage thrombi, since the appendage is frequently not well seen on TTE.[4]

Ahmad et al have reported that AF and LA dilatation are frequent associations of LA thrombus.[9] We designed this study to evaluate various clinical and echocardiographic predictors of LA thrombi in patients with severe mitral stenosis and to determine the usefulness of TEE as compared to TTE in detection of thrombus in LA.

Material and Methods

Two hundred and fifty consecutive patients of severe mitral stenosis were studied in the Department of Echocardio-

graphy, Punjab Institute of Cardiology, Lahore from 1st of January 2007 till 30th April 2007. Informed consent was obtained from each patient before inclusion in the study. Clinical and echocardiographic data was collected prospectively on a pre-designed proforma. Patients with mild mitral regurgitation, significant aortic valve disease, previous closed mitral valvotomy and currently taking anticoagulation or antiplatelet therapy were excluded from study. Symptoms were inquired from all patients and functional status assessed by New York Heart Association class.[10] Presence of atrial fibrillation was demonstrated in every individual case on baseline electrocardiogram. All patients after clinical assessment were subjected first to TTE and then to TEE. Variables like LA size, mitral valve area (MVA), mitral valve mean pressure gradient (MVMPG), spontaneous echo contrast (SEC) on TTE, spontaneous echo contrast (SEC) on TEE, thrombus on TEE vs TTE, and thrombus in LA appendage were noted on the proforma for each patient.

Transthoracic Echocardiography

Transthoracic studies were done by a standard technique using Vivid 7 BT6 GE (USA). M-mode measurements were recorded according to American Society of Echocardiography criteria.[11] The mitral valve area was measured by continuous wave Doppler using the pressure half time method. The mean transmitral diastolic pressure was estimated from the maximal transmitral flow velocity using a modified Bernoulli equation. LA diameter was taken in the parasternal long axis view in M-mode at end systole. Measurements were taken in three beats in patients with normal sinus rhythm and in ten beats in atrial fibrillation and the mean values were taken for analysis. To maximize the transthoracic visualization of LA thrombus, the LA was examined in standard parasternal long axis, apical, subcostal and parasternal short axis views with angulation of transducer to enhance the imaging of LA appendage.

Transesophageal Echocardiography

TEE was performed after TTE in all cases. A 5-MHz transducer multiplane probe was used. All patients were given local pharyngeal anaesthesia (1% lidocaine spray) and intravenous diazepam 3mg. During the study heart rate, blood pressure, single lead ECG and pulse oximetry were monitored. TEE probe was introduced with the patient lying supine in left lateral position. The LA was scanned in short axis view and bicaval view. With a counterclockwise rotation of the probe at the level of aortic valve, the LA appendage was visualized. LA thrombus was diagnosed by the presence of well defined echogenic intracavity mass with an echotexture different from that of underlying endocardium and not due to pectinate muscle. LA spontaneous echo contrast was diagnosed by the presence of dynamic smoke like echoes in the LA cavity and LA appendage with swirling motion distinct from white noise artifact after adjusting the gain setting properly.

After completion of TEE, patients were observed in the ward for 2 hours prior to discharge.

Statistical Analysis

All the data were analyzed by SPSS (Statistical Package for Social Sciences) Version 15.0 for Windows. Categorical variables were expressed as numbers and percentages while continuous variables were expressed as mean ± SD (Standard deviations). The study population was divided into two groups i.e. Group I (LA thrombus group) and Group II (No LA thrombus group) and influence of various predictors of LA thrombus formation were investigated using Pearson Chi-square and Contingency Coefficient values. The factors considered were age, sex, New York Heart Association (NYHA) class, AF, LA size, mitral valve area (MVA), Mitral valve mean pressure gradient (MVMPG), spontaneous echo contrast on TTE, spontaneous echo contrast on TEE, thrombus on TEE vs TTE, thrombus in LA appendage. 5% level of significance was used. All tests applied were two tailed.

Table 1: *Baseline Characteristics.*

Characteristics	Total N = 250	Group I N = 38	Group II N = 212	P-value
Age mean years	26.9 ± 7.5	29.6 ± 9.6	26.4 ± 7.05	<0.02
Gender				
Male	122 (48.8%)	14 (38.8%)	108 (50.9%)	<0.109
Female	128 (51.2%)	24 (63.2%)	104 (49.1%)	
Symptoms				
NYHA II	69 (27.6%)	5 (13.2%)	64 (30.2%)	<0.032
NYHA III	164 (65.6%)	32 (84.2%)	132 (62.3%)	
NYHA IV	17 (6.8%)	1 (2.6%)	16 (7.5%)	
Rhythm				
Sinus	217 (86.8%)	15 (39.5%)	202 (95.3%)	<0.0001
Atrial fibrillation	33 (13.2%)	23 (60.5%)	10 (4.7%)	

NYHA=New York Heart Association Class.

Results

After fulfilling the inclusion criteria, 250 patients of severe mitral stenosis were studied. Group I (LA thrombus group) consisted of 38 (15.2%) patients and Group II (No LA thrombus group) of 212 (84.8%) patients.

The mean age of the study population was 26.9 ± 7.5 years. Mean age was similar in both the groups. There were more females 128 (51.2%) than males 122 (48.8%); this trend persisted in the two groups. Majority of the patients 164 (65.5%) had New York Heart Association (NYHA) Class III symptoms at the time of study followed by 69 (27.6%) patients in NYHA

class II and 17 (6.8%) patient in NYHA class IV symptoms. In both the groups majority of patients had NYHA class III symptoms (Table 1).

AF was present less frequently in the study as 33 (13.2%) patients had AF as compared to 217 (86.8%) patients having sinus rhythm. AF was more significantly associated with thrombus formation with 23 (60.5%) patients having thrombi as compared to 15 (39.5%) patients in sinus rhythm having thrombus ($p < 0.0001$). Mean LA size was 50.7 ± 4.9 mm. LA chamber was larger in patients with Group I as compared to Group II ($p < 0.001$). Mean mitral valve area of the study population was 0.84 ± 0.13 Cm^2. Mitral valve area was larger in the Group II as compared to Group I ($p < 0.074$). Mitral valve MVMPG was 20.3 ± 4.2 mm Hg. MVMPG was more in Group I as compared to Group II ($p < 0.187$). Spontaneous echo contrast was visualized more frequently on TEE as compared to TTE in both the groups ($p < 0.001$). More patients in Group I had thrombus visualized on TEE than on TTE. Thrombus was visualized in 5 (2%) patients on both TTE and TEE in the Group I while on TEE 38 (100%) patients had thrombus in LA or LA appendage. Among these 28 (73.7%) patients had thrombus in LA appendage, 9 (23.7%) patients had thrombus in LA and 1 (2.6%) patient had thrombus in both LA and LA appendage.

Table 2: *Echocardiographic Findings.*

Characteristics	Total N = 250	Group I N = 38	Group II N = 212	P value
LA size mean mm	50.7 ± 4.9	53.6 ± 5.9	50.3 ± 4.5	<0.001
MVA Cm^2	0.84 ± 0.13	0.78 ± 0.14	0.85 ± 0.13	<0.074
MVPG mean mm Hg	20.3 ± 4.2	20.6 ± 4.4	18.6 ± 4.73	<0.187
Spontaneous echo contrast				
TTE	7 (2.8%)	4 (10.5%)	3 (1.4%)	<0.002
TEE	79 (31.6%)	28 (73.7%)	51 (24.1%)	<0.0001
Thrombus Visualized on				
TTE	5 (2%)	5 (13.2%)	---	---
TEE	38 (15.2%)	38 (100%)	---	---

LA= Left Atrium; **LAA=** Left Atrial appendage; **MVA=** Mitral valve area; **MVPG=** Mitral valve pressure gradient; **TTE=**Transthoracic echocardiography; **TEE=**Trans esophageal echocardiography.

Table 3: *Independent clinical predictors of LA thrombus formation.*

Variable	Chi-square value	P value (2-sided)	Contingency Coefficient
Thrombus on TEE vs TTE	242.3	0.0001	0.707
Thrombus in LAA	211.2	0.0001	0.677
Atrial fibrillation	81.1	0.0001	0.495
LA size	50.6	0.003	0.411
Age	50.44	0.02	0.415
SEC on TEE	34.4	0.001	0.348
MVPG mean	23.1	0.187	0.291
SEC on TTE	10.2	0.001	0.198
MVA	9.91	0.078	0.195
NYHA class	8.4	0.015	0.180
Sex	2.56	0.148	0.091

LA= Left Atrium; **LAA=** Left Atrial appendage; **MVA=** Mitral valve area; **MVPG=** Mitral valve pressure gradient; **TTE=**Transthoracic echocardiography; **TEE=**Trans esophageal echocardiography.

In order to see the independent clinical predictors of LA thrombus, all variables were analyzed by using Chi-square and their association was checked by using Contingency coefficient (Table 3). Thrombus in LA was most commonly visualized on TEE as compared to TTE ($X^2 = 242.3$, $p = 0.0001$) and was mostly detected in LA appendage ($X^2 = 211.2$, $p = 0.0001$). Following these significant Chi-square values were observed for AF ($X^2 = 81.1$, $p = 0.0001$) and older age ($X^2 = 50.4$, $p = 0.02$). Contingency coefficient value for all variables in relation to LA thrombus was noted. Thrombus detection on TEE vs TTE had the highest value of 0.707 followed by LA appendage thrombus location 0.677, AF 0.495, older age 0.415 and LA size 0.411.

Discussion

LA thrombus formation is a complication frequently encountered in patients with severe mitral stenosis with a higher chance of systemic embolization leading to higher morbidity and mortality in this subgroup of patients.[12] Mitral stenosis is more commonly associated with thrombus formation in

the LA than mitral regurgitation; furthermore the increasing severity of mitral stenosis is significantly correlated with increased incidence of thrombus in the LA and LA appendage.[13] Fifty percent of LA thrombi in patients with rheumatic valvular disease, and nearly 90% of LA thrombi in patients with non-valvular AF are limited to the LA appendage.[4] TEE is superior to TTE in the evaluation of LA thrombi.[4] TTE does not demonstrate the majority of LA appendage thrombi, since the appendage is frequently not well seen on TTE. TEE, on the other hand, is a very reliable tool for evaluating LA thrombi.[4] In a group of patients who underwent both TTE and TEE prior to cardiac surgery, TTE sensitivity for the presence of LA thrombi was 59% compared to 100% for TEE.[4]

In the present prospective study we evaluated 250 patients of severe mitral stenosis for presence of thrombi in LA and various clinical and echocardiographic predictors of thrombus formation. Our patient population was younger and majority was in sinus rhythm. The incidence of LA thrombus was 14.8% in our study. In various earlier studies, the incidence has varied from 26-33%.

Goswami et al[2] studied 200 consecutive patients of severe mitral stenosis. In their study the patients with AF had higher incidence of thrombus as compared to the patients with normal sinus rhythm. Patients with thrombus were older, had longer duration of symptoms, there was more frequent occurrence of AF and spontaneous echo contrast and larger LA diameter as compared to patients without thrombus. In their study, AF and LA diameter were independent predictors of LA thrombus formation. This study supports our findings as we observed more frequent occurrence of LA thrombus in patients with AF patients as compared to patients in sinus rhythm.

Saidi et al[4] studied 203 patients with mitral stenosis who presented for percutaneous mitral valvuloplasty or mitral valve surgery. 52.7% had normal sinus rhythm and 47.3% had AF. In sinus rhythm group 13.5% patients had a thrombus in LA. While the prevalence of LA thrombus in AF group was 26.1%; the difference between sinus rhythm and AF groups was significant. They did not observe meaningful relation between LA size and the presence of thrombus in the LA, or between age and thrombus formation. In our study there was a significant Chi Square association between LA thrombus and age of patients and LA size. Similarly Contingency coefficient value for thrombus detection on TEE vs TTE and LA appendage thrombus location had the highest value of 0.707 and 0.677 respectively followed by AF 0.495, older age 0.415 and LA size 0.411.

Ahmad et al[9] in a prospective study of 26 patients of mitral stenosis with LA thrombus observed that 18 (70%) patients were in AF and 5 (20%) had spontaneous echo contrast on echocardiography. They observed that TEE is superior in detecting thrombi in LA appendage, however 26 of their cases had thrombi clearly visible in LA cavity on TTE and TEE was not needed in those cases for the purpose of study. In our study we performed TTE and TEE for all patients and observed that TEE is more significantly associated with detection of LA thrombus.

Rao et al[15] performed TEE and compared its results with those of TTE in a series of 120 patients with rheumatic mitral stenosis. Their aim was to study the usefulness of TEE as compared to TTE in the detection of thrombus in LA. LA thrombus was imaged in 34/120 TEE studies as compared to 21/120 TTE studies. They concluded that TEE is a safe and valuable adjunct to TTE with better diagnostic ability for the detection of LA thrombus and should be performed in all patients with mitral stenosis in whom a thrombus in LA is suspected or needs to be excluded. In our study LA thrombus was imaged in 33/250 TEE studies as compared to 5/250 TTE studies which also supports the accuracy of TEE over TTE in detecting LA thrombus.

Thomas et al[16] assessed the relative merits of TTE and TEE before balloon dilatation of mitral valve. In their study, in 35 patients being considered for balloon dilatation of mitral valve, LA thrombus was detected in 1/35 patients by TTE studies compared with 6/35 by TEE.

Srimannarayana et al[3] in their study of 490 patients undergoing TEE noted that LA thrombi were present in 163 (33.2%). Isolated LA appendage thrombi were found in 88 (18%) patients. Isolated LA body thrombi or LA appendage thrombi extending into the LA body were found in 75 (15.3%) patients. These findings are consistent with our study in which out of 38 thrombi, 28 (73.7%) were present in LA appendage, 9 (23.7%) patients had thrombi in LA and 1 (2.6%) patient had thrombi in both LA and LA appendage.

There are few reports on the prevalence of LA body and LA appendage thrombi in patients with severe mitral stenosis and AF. In a small group of 50 patients with mitral stenosis and AF, Hwang et al[17] observed an LA thrombus in 28 patients (56%) by TEE. In another small study of 22 patients with mitral stenosis and AF Karatasakis et al[18] observed an LA thrombus in 12 patients (54%). In the study of Srimannarayana et al[3] the prevalence was 33.5%. Considering the size of study group, this can be considered a representative figure for the prevalence of LA thrombi in patients with severe mitral stenosis and AF. Thus it can be stated that 1 out of every three patients with severe mitral stenosis and AF will have an LA thrombus.

Conclusion

TEE is better than conventional TTE in detecting left atrial thrombi in patients with severe mitral stenosis having AF. Patients with rheumatic mitral stenosis having atrial fibrillation, large left atrial size and old age are more prone to have LA thrombus. TEE should be performed in all patients with mitral stenosis in whom a thrombus in LA is suspected or needs to be excluded regardless of rhythm. Because of the potential risk of embolization, TEE is recommended in all candidates for balloon mitral valvuloplasty.

Study Limitations

This study was carried out in a relatively small number of patients and it is possible that just one false positive result might change the level of significance while comparing the two groups. Hence, in order to obtain more accurate results, larger groups of patients should be included in any future study.

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