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Correlation between Mitral Annular Systolic Velocity and Left Atrial Appendage Function in Mitral Stenosis.

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ABSTRACT

Background: The left atrial appendage is a long, tubular and trabecular structure and has a narrow junction with the left atrium. The left atrial appendage has been the focus of clinicians' interests, because it is a potential site for the development of thrombus in several diseases. Aim: To study the correlation between mitral annular systolic velocity and left atrial appendage function in mitral stenosis. **Methods:** 60 patient with moderate to severe Mitral Stenosis with MVO <1.5 cm2 were included in the study. All eligible patients underwent a detailed history and clinical examination. A 12 lead electrocardiogram was taken. Echocardiographic evaluation was done for all patients Atrial fibrillation diagnosis was based on the electrocardiogram. **Result:** There was a positive correlation between these two variables which are statistically significant. (r=0.944, p-value<0.001). There was a positive correlation between left atrial appendage emptying velocity and mitral annular late diastolic velocity in patients in sinus rhythm. (r=0.695(p<0.001) The cut off value of peak annulus systolic velocity which is derived from the analysis of the receiver operator characteristic curve is 13.5cm/sec. The area under the curve is 0.840 with confidence interval 0.689 to 0.936 and the p-value<0.001. This value predicts inactive LAA (Laaev<25cm/sec) with a sensitivity of 92% and specificity of 96.5%. **Conclusion:** The systolic and diastolic annular velocities obtained by Doppler tissue imaging are reduced in patients with mitral stenosis. There is a positive correlation between annular systolic and left atrial appendage emptying velocities in mitral stenosis. The annular systolic velocity is an independent predictor for the presence of inactive left atrial appendage in mitral stenosis patients with sinus rhythm.

Keywords: Mitral stenosis, left atrial appendage function, annular systolic velocity

INTRODUCTION

The appendage of the left atrium is a bulbar structure which is long with a narrow junction at its meeting point with the left atrium. In many diseases the left atrial appendage is clinically important because of the propensity for the development of thrombus.[1,2] Being a dynamic structure, the stasis of blood is prevented, but when its function is impaired, stasis will increase. This may lead to the development of spontaneous echo contrast and thrombus formation. Moreover an inactive left atrial appendage is an independent predictor of thromboembolism. Hence the decision for anticoagulant therapy can be made on the basis of the presence of inactive left atrial appendage.In patients with rheumatic mitral stenosis, left atrial appendage velocities are reduced. Also in mitral stenosis, the annular velocities calculated by Doppler tissue imaging are reduced.[3,4] The lateral mitral annulus and the left atrial appendage has a close functional and anatomic relation and hence the velocities obtained from the annulus by Doppler tissue imaging may reflect left atrial appendage functions. Echocardiography is used to detect thrombi in the left atrium and its appendage. Transthoracic echocardiography is 50% sensitive in detecting left atrial and left atrial appendage thrombi. Transesophageal echocardiography (TOE) is superior to transthoracic echocardiography and has high sensitivity and specificity for the detection of left atrial and left atrial appendage thrombi. The individual valve lesion severity can be assessed by echocardiography in patients with rheumatic heart disease and can be matched with left atrial dimensions and hence used for risk stratification from thromboembolism.[5]

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Aim

To study the correlation between mitral annular systolic velocity and left atrial appendage function in mitral stenosis.

MATERIALS AND METHODS

The present study was a prospective study based on a semi-invasive procedure conducted in the department of cardiology in Madras Medical College and Rajiv Gandhi Government General Hospital. The total number of patients selected for the study was 60.Inclusion Criteria: Patient with moderate to severe Mitral Stenosis with MVO <1.5 cm2 were included in the study. Exclusion Criteria: Mitral regurgitation – Moderate and severe, Aortic regurgitation – Moderate and severe, Aortic stenosis, Post PTMC or CMC, Congestive heart failure, Patients on oral anticoagulants, Hypertension, Hyperthyroidism, Diabetes mellitus, Coronary artery disease, Patient unwilling for transesophageal echocardiography, Pregnancy and Puerperium. All eligible patients underwent a detailed history and clinical examination. A 12 lead electrocardiogram was taken. Atrial fibrillation diagnosis was based on the electrocardiogram. Echocardiographic evaluation was done for all patients with Phillips HD 7XE echocardiographic machine. For transthoracic echo imaging a 2 Megahertz probe and for transesophageal echocardiography 5Megahertz multi-plane probe was used.

RESULTS

Among 60 patients, 40 were in sinus rhythm constituting 66.7 % of the study population and 20 were in atrial fibrillation constituting 33.3 %. Hence patients were divided into 2 groups, Group A – sinus rhythm patients and Group B – patients with atrial fibrillation. Among group A, 14 patients were males and 6 patients were females. In the atrial fibrillation group, 14 patients were females and 6 patients were males. The mean left atrial diameter for Group A patients was 45.7 mm and Group B was 54.5 mm. The difference in LA diameter between the two groups is statistically significant. (p <0.001). Mean mitral valve area is smaller in Group B with a mean of 0.76 cm2 compared to Group A with a mean of 1.07 cm2. The difference between both groups is statistically significant. (p <0.001). Left ventricular ejection fraction is similar in both groups and does not achieve statistical significance. Mean gradient (MG) across the mitral valve hada mean of 15 mmHg in Group A whereas in Group B it is 11.5 mmHg. The difference in means of the mean gradient is statistically significant. (p = 0.009). The difference between peak gradients in both groups was not statistically significant. Peak annular systolic velocity (S') is statistically significant between Group A and Group B. (p<0.0001). Mean Sm velocity in Group A is 17.1 cm/sec and in Group B is 12. 3 cm/sec. Mean early diastolic annular velocity (Em) is 13.8 cm/sec in Group A and 12.7 cm/sec in Group B. The difference between the 2 groups is statistically not significant. Mean late diastolic annular velocity in Group A is 14.8 cm/sec. Group B patients do not have late diastolic velocity as Am wave is absent in atrial fibrillation patients. Left atrial appendage emptying velocity is different between both groups. In Group A patients the mean Laaev is 24.3 cm/sec and in Group B patients the mean Laaev is 4.5 cm/sec. The difference between both groups is statistically significant. (p< 0.001).

22 patients of Group A were having spontaneous echo contrast (SEC) constituting 55 % of that population. All 20 patients in Group B had spontaneous echo contrast. The difference is statistically significant. (p< 0.001). Left atrial appendage thrombus was found in 2 persons in Group A and 11 persons in Group B which corresponds to 5 % and 55 % of the study groups respectively. The difference in the occurrence of thrombus is statistically significant. (p<0.001). 18 patients in Group A did not show any spontaneous echo contrast in contrary to Group B patients in whom no one was free of spontaneous echo contrast. In Group B patients, the number of patients is increasing in an ascending pattern as the grade of the density of spontaneous echo contrast is increased. In Group A one patientare having grade 4 SEC whereas in Group B 8 patients are having grade 4 SEC. The differences between both groups regarding the presence of various grades of SEC are statistically significant. (p< 0.001). The Group A is further subdivided into 2 groups depending upon left atrial appendage emptying velocity. Group A1 is having left atrial appendage emptying velocity ≥ 25 cm/sec and Group A2 patients were having left atrial emptying velocity < 25 cm/sec. Group B (Atrial Fibrillation group) is kept as such and not subdivided as the Laaev< 25 cm/sec in all cases. The subgroups are compared within for statistical significance as follows.

P1 – Comparison between Group A1 and A2
P2 – Comparison between Group A1 and B
P3 – Comparison between Group A2 and B

The distribution of gender and age groups between all 3 subgroups are not statistically significant when they are compared within them. The mean left atrial dimension was 40.1 mm in Group A1, 50.7 mm in Group A2 and 54.5 mm in Group B. The difference is statistically significant between Group A1 and A2, Groups A1 and B. The difference between Groups A2 and B (P3) is not statistically significant. (p3 = 0.162). There is also a progressive increase in LA dimension when we move from Group A1 to Group A2 to Group B. Comparing tissue Doppler imaging parameters, the mean peak mitral annular systolic velocity (S wave) is 19.4 cm/sec in Group A1, 15.1 in Group A2 and 12.3 cm/sec in Group B. The differences between these 3 groups are statistically significant. There is a progressive decreasing trend in S wave velocity when we move from Group A1 to Group A2 to Group B. There are no statistically significant variations between early diastolic

velocities (Em) of mitral annulus in between subgroups.

As the late diastolic mitral annular velocity (Am) is absent in Groups B (presence of atrial fibrillation abolishes Am wave), it is only compared within Group A1 and A2. The mean Am velocity is 16.1 cm /sec in Group A1 and 13.5 cm/sec in A2. The difference in means and standard deviation between these groups is statistically significant.

The mean left atrial appendage emptying velocity in Group A1 is 31.7 cm/sec, in Group A2 is 17.5 cm/sec and in Group B is 4.5 cm/sec. There is a statistically significant difference between subgroups when analyzed. There is also a progressive decreasing trend when we move from Group A1 to Group A2 to Group 3. The decreasing trend in Sm wave, Am wave and Laaevare depicted in the figure below.

Mean mitral valve area is 1.22 cm2 in Group A1, 0.94 cm2 in Group A2 and 0.76 cm2 in Group B. The inter differences between the three groups is statistically significant. Stenosis severity is progressively increasing from Group A1 to Group A2 to Group B. Left ventricular ejection fraction does not vary significantly between groups.

Mean gradient and peak gradient were statistically significant between groups. Mean and Peak gradients increase progressively as we move from Group A1 to Group A2. The Peak and mean gradient in Group B is lesser than that of Group A2.

Table 1: Baseline Characteristics.

Characteristics	Group A	Group B	p-Value	Significance
	Mean ± SD	Mean ± SD		
Age (yrs)	26.73 ± 5.6	29.36 ± 5.7	0.098	NS
Sex (M / F)	14 / 26	6 / 14	0.699	NS
LAD (mm)	45.7 ± 9.1	54.5 ± 7.2	< 0.001	Sig
MVA (cm2)	1.07 ± 0.18	0.76 ± 0.22	< 0.001	Sig
Ejection Fraction (%)	63.3 ± 2.1	65.1± 1.2	0.087	NS
Mean Gradient (mmHg)	15.0 ± 7.3	11.5 ± 2.5	0.009	Sig
Peak Gradient (mmHg)	22. 5 ± 8.4	21.3 ± 2.7	0.406	NS

Table 2: Patient Groups Characteristics – TTE.

Variable	Group A1	Group A2	Group B	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD			
Age (Years)	26.74 ± 5.32	27.86 ± 6.3	29.35 ± 5.76	0.539	0.150	0.424
Sex (M / F)	7 / 12	7 / 14	6 / 14	0.816	0.651	0.819
LAD (mm)	40.1 ± 3.2	50.7 ± 9.8	54.5 ± 7.2	< 0.001	< 0.001	0.162
MVA (cm2)	1.22 ± 0.15	0.94 ± 0.09	0.76 ± 0.20	< 0.001	< 0.001	0.004
EF (%)	63.6 ± 2.5	63.0 ± 1.8	65.1 ± 1.3	0.410	0.082	0.203
MG (mmHg)	8.84 ± 2.1	20.6 ± 5.4	11.5 ± 2.5	< 0.001	< 0.001	< 0.001
PG (mmHg)	15.4 ± 4.0	29.0 ± 5.7	21.3 ± 2.7	< 0.001	< 0.001	< 0.001

Table 3: Patient Groups Characteristics – TDI & TEE

Variable	Group A1	Group A2	Group B	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD			
S Wave (cm/s)	19.4 ± 3.5	15.1 ±2.6	12.3 ± 1.0	< 0.001	< 0.001	< 0.001
Em (cm/s)	14.3 ± 1.7	13.3 ±1.8	12.7 ± 2.3	0.120	0.072	0.312
Am (cm/s)	16.1 ± 2.2	13.5 ± 2.6	-	0.002	-	-
Laaev (cm/s)	31.7 ± 7.2	17.5 ± 5.2	4.5 ± 2.2	< 0.001	< 0.001	<0.001
% of patients with SEC	3 (15.7 %)	19 (90.4 %)	20 (100 %)	< 0.001	< 0.001	0.157
% of patients with Thrombus	0	2 (9.5 %)	11 (55%)	0.168	< 0.001	0.002

Table 4: Spontaneous Echo contrast density grading within Groups

SEC	Group A1	Group A2	Group B	p1	p2	p3
Grade 0	16	2	0	< 0.001	< 0.001	0.049
Grade 1	2	6	4			
Grade 2	1	7	3			
Grade 3	0	5	5			
Grade 4	0	1	8			
Total	19	21	20			

3 patients in Group A1 had spontaneous echo contrast constituting 15.7 % of that population, Group A2 had 19 patients had SEC constituting 90.4 %. In Group B, all the patients had spontaneous echo contrast. The difference between Groups A1 and A2 and between Group A1 and Group B is statistically significant. The difference between Group A2 and Group B is not statistically significant. (p = 0.157). No patients in Group A1 had any thrombus whereas 2 patients in Group A2 had thrombus. 11 patients in Group B had thrombus as already discussed above. The difference between

Group A1 and A2 is statistically not significant (p= 0.168). The difference between Groups A1 & B and Groups A2 & B were statistically significant. 16 patients in Group A1 did not show any spontaneous echo contrast, in Group A2 two persons does not have any spontaneous echo contrast in contrary to Group B patients in whom no one was free of spontaneous echo contrast. Grade 3 and Grade 4 SEC is absent in Group A1 patients whereas 5 persons in Group A2 & Group B had Grade 3 spontaneous echo contrast. Grade 4 spontaneous echo contrast is present in only one patient in Group A2 whereas 8 persons in Group B had Grade 4 SEC. The relationship between left atrial appendage emptying velocity and peak annular systolic velocity was studied using Pearson correlation. There was a positive correlation between these two variables which are statistically significant. (Pearson correlation coefficient r = 0.944, p-value< 0.001).

There was a positive correlation between left atrial appendage emptying velocity and mitral annular late diastolic velocity in patients in sinus rhythm. The Pearson Correlation coefficient r = 0.695 (p < 0.001).

The cutoff value of peak annulus systolic velocity which is derived from the analysis of the receiver operator characteristic curve is 13.5 cm/sec. The area under the curve is 0.840 with confidence interval 0.689 to 0.936 and the p-value< 0.001. This value predicts inactive LAA (Laaev< 25 cm/sec) with a sensitivity of 92 % and specificity of 96.5 %.

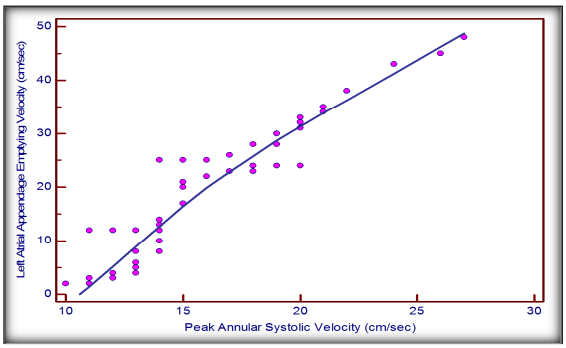

Figure 1: Correlation between Laaev and S wave

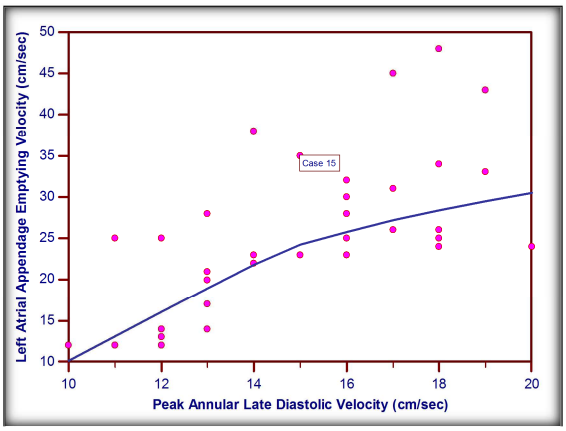

Figure 2: Correlation between Laaev and S wave

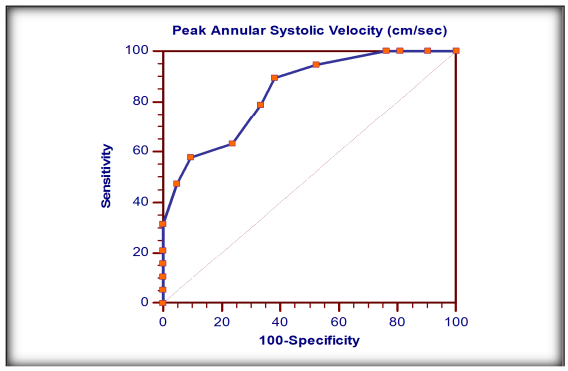

Figure 3: ROC Curve

DISCUSSION

Rheumatic heart disease and the long term consequence of mitral stenosis is a major challenge in many developing countries like India. Over the years a lot of research has been done to understand the pathophysiology and complication of this chronic disorder. Though there has been good progress, a lot of questions still remain unanswered and contributing to the morbidity associated with this condition. The major morbidity and mortality in patient with mitral stenosis were due to thromboembolism. Thromboembolic events are more common in patient with mitral stenosis and atrial fibrillation. Patient in sinus rhythm was also at increased risk. Recently much attention has been focused on LA appendage and its emptying velocity. Anti-coagulants therapy is not introduced for all patients in sinus rhythm. High-risk individuals only need anticoagulation treatment. In patients with mitral stenosis the movement of the mitral annulus is decreased due to scarring and inflammatory process. In a study done by Ozer N et al showed that patients with mitral stenosis long axis function of left ventricle measured by TDI were reduced. In our study also the annular velocities obtained by tissue Doppler were reduced.[6] The mean age of the patient in our study was 28 years which is in concordance with the world literature. The study population was predominantly female, which is also consistent with the epidemiology of the disease. The average age of patients in various studies ranges from 28 – 34 years, with the less predominance of patients over the age of 30 years. In our study positive correlation exists between annular systolic velocity and LAA emptying velocity. In those patients with reduced annular systolic velocities, the left atrial appendage emptying velocity was also reduced. In those patients with reduced annular systolic velocity the spontaneous echo contrast, frequency and density were also increased. In a study done by Hoiat et al, the left atrial appendage flow velocity was evaluated by altering the loading conditions on the left atrium and they showed that the early emptying velocity was reduced significantly. They also found that the left ventricular systolic function is an important

causal factor in the late emptying velocity of the appendage.[7] In a study published in the Journal of American Society of Echocardiography by Tabata et al, showed that in patients with sinus rhythm elevated left atrial pressures will decrease left atrial appendage emptying velocity and predisposes to thrombus formation.8In our study patients with left atrial appendage emptying velocity less than 25 cm/s have smaller MVA, higher gradients across the mitral valve and reduction in the annular velocities than patients who have emptying velocities more than 25 cm/s. In a study done by SaitMesut et al, they also demonstrated decreased peak mitral annular systolic velocities in patients with mitral stenosis. But they did not compare the annular velocities with emptying velocities. Instead they suggested it could be an early sign of myocardial abnormality.[9] Previously reported studies showed a negative correlation between systolic annular velocity and mitral valve area. But our study showeda positive correlation between systolic annular velocity and mitral valve area. In a study by Bilge et al showed that left atrial emptying velocity was reduced in patients with untreated hypertension. They showed if an elevated after the load was imposed on left atrium and appendage, the emptying velocity of the appendage was also reduced. They also demonstrated spontaneous echo contrast and thrombus in those patients.[10] In a study by Golbasi et al which was done in patients with mitral stenosis and sinus rhythm, left atrial appendage contractile dysfunction is more common in those patients with spontaneous echo contrast.[11] Our study also showed that group A2 patients with emptying velocity less than 25 cm/s also had increased frequency spontaneous echo contrast and thrombus formation. Cayli et al also showed in patients with mitral stenosis in sinus rhythm, the presence of spontaneous echo contrast is directly related to the lower annular systolic velocity.[12] The reported incidence of thrombus in the studies done in the past ranges from 0 to 14% in patients with mitral stenosis and sinus rhythm. In our study of 21 patients in group A2, two patients had left atrial appendage thrombus. A smaller percentage of thrombus in sinus rhythm patients could be related to our smaller study group. In our study there was no correlation between Em velocity and left atrial appendage emptying velocity but there is a correlation between Laaev and Am velocity in sinus rhythm patients. Multivariate regression analysis showed that the annular systolic velocity alone is an independent predictor of the inactive left atrial appendage. This result showed that long axis function was diminished in mitral stenosis patients and could be the most significant factor contributing to the appendage dysfunction in mitral stenosis patients with sinus rhythm. Cut off value obtained by ROC curve for annular systolic velocity is 13.5 cm/sec and this predicts inactive left atrial appendage in mitral stenosis patients. These patients had narrower mitral valve area and larger left atrial size as compared to group A patients. Also these patients had lower annular systolic velocities and lower emptying velocities of the left atrial appendage. This finding will explain the increased prevalence of spontaneous echo contrast and thrombus in these group B patients due to significant stasis in the appendage. In Framingham Heart Study, patients with mitral stenosis and atrial fibrillation have 17 fold increased risk of cerebrovascular events than control population.[13]

CONCLUSION

In patients with mitral stenosis annular systolic and diastolic velocities acquired by Doppler tissue imaging were reduced. A positive correlation is found between mitral annular systolic velocity and left atrial appendage emptying velocity. In mitral stenosis patients with sinus rhythm, the systolic annular velocity is an independent predictor of the contractile function of LAA. In mitral stenosis with sinus rhythm lower annular systolic velocity can be given consideration for anticoagulation. Patients in AF also have reduced mitral annular systolic velocity and LAA contractile function which predicts the higher incidence of SEC and thrombus formation in those patients.

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