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Relationship between Mitral Annular Velocities and Left Atrial Appendage Emptying Velocity

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Abstract **Original Research Article**

Background: Mitral stenosis (MS) is a prevalent kind of valvular heart disease. Thromboembolism is one of the most severe complications, particularly when it is accompanied with atrial fibrillation (AF). When associated with Left atrial appendage (LAA) dysfunction, patients with sinus rhythm (SR) are also at risk for this condition. In mitral stenosis, LAA dysfunction is an independent predictor of thromboembolism. The aim of the study was to see if there is an association between mitral annular velocities measured with Doppler tissue imaging (DTI) and LAA function measured with transesophageal echocardiography (TEE), and to see if annular velocities can predict the presence of an inactive LAA in MS. ***Methods*****:** This was an observational study carried out by the department of cardiology of the National Institute of Cardiovascular Diseases (NICVD). From January 2006 to December 2007, 60 MS patients were evaluated using transthoracic echocardiography and transesophageal echocardiography. The systolic (S-wave) and diastolic (Em- and Am-waves) annular velocities were measured. Inactive LAA was defined as a velocity of <25 cm/sec for LAA emptying. Patients were divided into three groups. Group A (I) (n = 18): Sinus rhythm (SR) and LAA emptying velocity ≥25 cm/sec, group A (II) (n =22): SR and LAA emptying velocity <25cm/sec and group B (n = 20): atrial fibrillation. ***Results****:* Thrombus was found in 14 patients, and spontaneous echo contrast (SEC) was found in 43. From group A to group B, S-wave and peak LAA emptying velocities decreased while SEC frequency and density increased. There was a positive correlation between LAA emptying versus S-wave & Am wave velocity ($p<0.001$, $r=0.708$ and $p<0.001$, $r=0.495$, respectively). Only S-wave was found to be an independent predictor of inactive LAA in multivariate regression analysis ($p = 0.001$, odds ratio = 0.133, 95%ci =0.032-0.556). The cutoff value of S-wave in patients with SR for predicting the presence of inactive LAA was 14 cm/sec (sensitivity: 92.3%, specificity: 95.3%). ***Conclusions:*** S-wave is a useful parameter in evaluating inactive LAA in MS with SR since it is an independent predictor of inactive LAA.

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

INTRODUCTION

The left atrial appendage (LAA) has been the focus of clinician's interest for long, because it is the potential site for the development of thrombus in several diseases especially in mitral stenosis (MS) [1].Normally, LAA is a highly dynamic structure which prevents stasis. When its function is impaired, stasis will increase, which leads to the formation of spontaneous echo contrast (SEC) and/ or thrombus [2]. The development of Spontaneous echo contrast and/or thrombus is linked to decreased LAA contractility. LAA dysfunction has been found to be an independent predictor of thromboembolic events [3, 4].

The prevalence of spontaneous echo contrast (SEC) varies from 25% to 67% in patients with mitral stenosis. Left atrial SEC is a marker of previous thromboembolism in patients with non-valvular AF, MS or mitral valve prosthesis [5]. It has been demonstrated that >15% of strokes originates from the heart and from the LAA in particular [6]. The previous studies reported that up to 13% of MS patients with sinus rhythm also had thrombi [4, 7]. LA appendage thrombi are associated either with mitral valve disease or LA chamber and appendage dysfunction [8]. So, prediction of LAA dysfunction in such patients is of paramount importance to prevent thromboembolic episode [5]. But, thromboembolic risk stratification of MS patients with sinus rhythm by a sensitive as well as specific tool is yet to be established [7]. The diagnostic procedure of choice for morphological and functional evaluation of LAA is transesophageal echocardiography (TEE). TEE is the best standard for assessing the LAA function [9].

Methods

This was an observational study carried out by the department of cardiology at the National Institute of Cardiovascular Diseases (NICVD). From January 2006 to December 2007, 60 MS patients were transthoracic echocardiography and all patients underwent transesophageal echocardiography as part of the study. The systolic (S-wave) and diastolic (Em- and Am-wave) velocities of the annulus were measured. LAA emptying velocity of <25 cm/sec was considered inactive. Patients were divided into three groups. Group A (I) (n = 18): Sinus rhythm (SR) and LAA emptying velocity ≥25 cm/sec, group A (II) (n =22): SR and LAA emptying velocity <25cm/sec and group B (n = 20): atrial fibrillation: sinus rhythm (SR) and LAA emptying velocity <25 cm/sec. Inclusion Criteria were patients with mitral stenosis of any age. Exclusion Criteria were aortic stenosis, moderate or severe aortic regurgitation, moderate or severe mitral regurgitation, history of mitral commissurotomy or valvuloplasty, uncontrolled congestive heart failure and using antiplatelet or anticoagulant drug. All calculations were performed with Statistical Package for the Social Sciences 24.0 (SPSS 24.0) program. Continuous variables between groups were compared with Student's t test. Categorical variables were tested with the chi-square test. Multivariate, stepwise backward conditional logistic regression analysis was used to determine the relative importance of the independent predictors associated with inactive LAA in MS.

Results

Table 1 shows that the mean age was higher in patients with atrial fibrillation (32.5±8.3) than that of sinus rhythm (28.8±8.1), but the mean difference was not statistically significant (p >0.05). Regarding sex distribution, mean difference between the groups was not significant (p >0.05). The mean mitral valve area was lower in atrial fibrillation (0.77±0.15) than that of sinus rhythm (1.07±0.21) and the mean difference was highly significant (P<0.01). But, mean left atrial dimension was higher in atrial fibrillation (54.2±7.5) than that of sinus rhythm (47.6±10.0) was significant (p<0.05). The mean difference between the ejection fractions was not significant p>0.05). The transmitral mean gradient was higher in sinus rhythm (15.3±5.9) than that of atrial fibrillation (11.1±2.1) and the mean difference is highly significant. Table II shows that among age and sex there was no significant. Mitral valve area was higher in patients in MS with normal LAA function. Similany, MVA was higher in patients of sinus rhythm with LAA dysfunction than that or atrial fibrillation group (0.77±0.15). The mean differences between the three groups were highly significant (p<0.01). Thus, there was progressive decrease or mitral valve area among the three groups. The mean lateral mitral annular systolic velocity (S-wave) in patients of normal LAA function (19.6±2.7) was highest. Patients of SR with LAA dysfunction (15.8±3.8) showed higher S-wave than those of atrial fibrillation (12.0±1.1).Among the groups, they were decreasing progressively. The mean difference between patients of normal LAA function and SR with LAA dysfunction was highly significant, as the difference between normal LAA function and atrial fibrillation was. But, the mean difference between SR with LAA dysfunction and atrial fibrillation was very highly significant. Figure I shows that there is association between LAAEV, S-wave and Am wave. Thus, mitral annular systolic velocity and late diastolic velocity were decreasing progressively with the decrease of left atrial appendage emptying velocity. Table IV shows multivariate regression analysis. Variables included are Age, LAD, MVA, MG, PG, S-wave and Am velocities were evaluated by multivariate regression analysis with backward elimination.. Only S-wave velocity was found to be an independent predictor for the presence of inactive LAA (odds ratio = 0.133, 95% CI = 0.032-0.556).

Table-I: Baseline characteristic of variables in groups (N=60)

	Group A (n=40)	Group B (n=20)	p-value
	Mean±SD	Mean±SD	
Age	28.8±8.1	32.5±8.3	0.100NS
Sex(M/F)	13/27	6/14	0.844NS
MVA(cm2)	1.07±0.21	0.77±0.15	0.0001
LAD(mm)	47.6±10.0	54.2±7.5	0.012
EF%	60.2±5.9	58.1±5.1	0.187
MG(mmHg)	15.3±5.9	58.1±5.1	0.187NS
PG(mmHg)	22.9±8.1	21.2±3.9	0.364NS
S wave(cm/sec)	17.5±3.8	12.0±1.1	0.001
Em(cm/sec)	14.4±3.1	13.3±3.1	0.194NS
Am(cm/sec)	14.5±2.7	-	-
Laaev(cm/sec)	21.6±8.4	3.5±5.8	0.001
Mean SEC density	2.1±1.4	4.6±0.9	0.001
SEC%	23(57.5)	20(100)	0.001
Thrombus%	2(5.0)	12(60.0)	0.001

Table-II: Demographic and Transthoracic Echocardiographic Characteristics in groups: (N=60).

	Group A (I) (n=18)	Group A (II) (n=22)	Group B (n=20)	ρ	ρ2	ρ3
	Mean±SD	Mean±SD	Mean±SD			
Age(year)	30.6±8.0	27.3±8.1	32.5±8.3	0.203^{NS}	0.473^{NS}	0.05^{NS}
Sex(M/F)	5/13	8/14	6/14	0.564^{NS}	0.880^{NS}	0.662^{NS}
MVA(mm2)	1.26±0.15	0.91±0.07	0.77±0.15	0.001	0.001	0.001
LAD(mm)	40.4±3.5	53.4±9.8	54.2±7.5	0.001	0.001	0.787^{NS}
EF%	60.4±5.5	59.8±6.3	58.1±5.1	0.775^{NS}	0.180^{NS}	0.312^{NS}
MG(mmHg)	9.8±3.4	19.9±2.7	11.1±2.1	0.001	0.172^{NS}	0.001
PG9mmHg)	15.4±3.9	29.9±4.6	21.2±3.9	0.001	0.001	0.001

Table- III: Doppler tissue imaging and transoesophageal echocardiograpnic variables in Groups (N=60)

	Group A (I) (n=18)	Group A (II) (n=22)	Group B (n=20)	ρ1	ρ2	ρ3
	Mean±SD	Mean±SD	Mean±SD			
S wave(cm/sec)	19.6±2.7	15.8±3.8	12.0±1.1	0.001	0.001	0.000
Em(cm/sec)	14.3±2.7	14.5±3.3	13.3±3.1	0.807	0.317	0.234
Am(cm/sec)	15.8±1.2	13.4±3.2		0.006		
Laaev(cm/sec)	29.5±5.8	15.1±2.7		0.001		
Mean SEC	1.5±1.1	2.6±1.5	4.6±0.9	0.009	0.001	0.001
density						
SEC%	3(16.7)	20(90.9)	20(100)	0.001	0.001	0.268
Thrombus		2(9.1)	12(60.0)	0.296	0.003	0.002

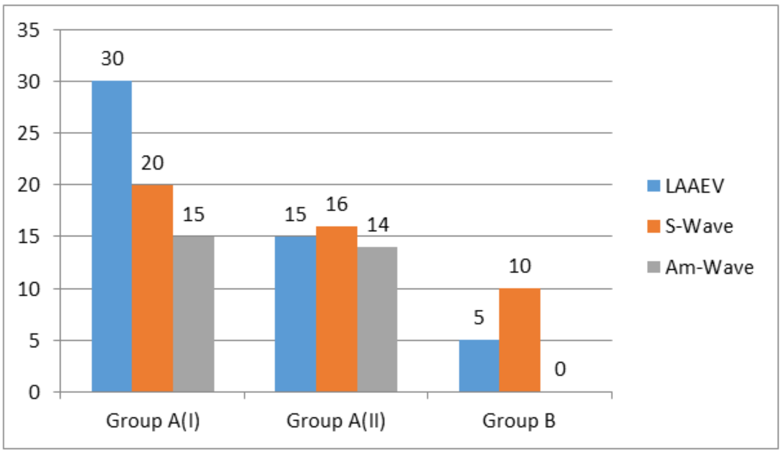

Fig-I: Bar chart showing association between LAAEV, S-wave and Am (cm/sec).

Table: IV- Multivariate regression analysis of the total left atrial appendage emptying velocity (N=60):

Variables	ß	±SE	P value	95%	CI
				Lower	Upper
Age	0.06	9.40	0.417	-0.09	0.22
LAD	-0.28	0.07	0.007	-0.350	-0.061
MVA	0.23	4.44	0.077	-0.930	17.11
MG	-0.27	0.17	0.048	-0.683	-0.003
PG	-0.21	0.10	0.074	-0.393	0.019
S-wave	-0.01	0.11	0.967	-0.407	0.391
Am-wave	0.14	0.22	0.087	-0.058	0.814

CI=Confidence interval

DISCUSSION

Demographic and clinical data showed that there was no significant difference regarding age and sex between groups (SR and AF) and subgroups (A I), (A II) and group B. Cases were double in SR group than in AF group. Total number of women was as twice as those of men. About 60% (n=35) of patients had severe MS and the rest (n=25) had moderate MS. Thus, women are affected more commonly by rheumatic MS. Mitral annular systolic, late diastolic and peak LAA emptying velocities were decreasing, while SEC frequency and density were increasing in group with LAA dysfunction than without. Annular E-wave was similar in both groups. Mitral annular velocities (S-wave & Am) are reduced in MS [10], but Em is unaffected [11]. As LAAEV was decreasing there was reduction of LAA function which was associated with increased frequency and density of SEC [12]. Thrombi were found in patients with inactive LAA, but not in the other group although difference is insignificant probably related to smaller number of cases. Other study supported the fact that LAA dysfunction leads to thrombus formation [13]. We showed that there was a significant positive correlation between LAAEV with both S-wave ($p<0.001$, $r=0.708$) and Am ($p<0.001$, $r=0.495$) and reduction in annular systolic (S-wave) and late diastolic (Am) velocities were corresponded closely with reduction in LAA emptying velocity. A study showed that S-wave is correlated with LAAEV [11]. Diastolic movement of mitral annulus may also be affected by inflammation and scarring [14].

The presence of the inactive LAA in MS patients can be predicted by annular systolic velocity, according to this study. The ROC curve analysis cut-off value for annular S-wave velocity for predicting the presence of inactive LAA was 14cm/sec, with a sensitivity of 92.3% and a specificity of 95.3%. This finding is similar to the one from the prior study [11]. Both sensitivity and specificity with a cut-off value of 14 cm/sec. is very high. Therefore, the annular systolic velocity may be used as a reliable parameter in the estimation of LAA function in MS patients. Late diastolic wave is also correlated to left atrial appendage emptying velocity. This may be related to the fact the most of our cases were severe MS. This is supported by Lin *et al.* (1996) that the lower diastolic augmentation of the LAA outflow velocity at the ventricular diastolic phase might result from interference suction effect of the left ventricular diastole by the stenotic mitral valve [14]. The previous Studies reported that 0-13% of MS patients with SR have thrombi [4, 7]. There were only 22 patients in group AII in this study, and two of them had thrombi. There was no significant difference between groups A and B, which could be due to the smaller number of instances. In AF patients, Garcia-Fernandez *et al*. (1992) identified two forms of LAA flow patterns: active sawtooth pattern and no recognizable wave. They discovered that the second pattern has a greater rate of LAA SEC and thrombus than the sawtooth and SR patterns. In all of the patients with AF, there was no discernible wave pattern. We couldn't find any other pattern, which is likely due to the fact that the majority of the subjects in our study had severe MS. The AF group had a lower mitral valve area, mean gradient of mitral inflow velocity, Am, systolic velocity of lateral mitral annulus, and left atrial appendage emptying velocity than the sinus rhythm group. AF is more frequently linked to severe MS. Severe MS reduces mitral annular long axis movement [10], potentially resulting in decreased S-wave and Am. The diastolic augmentation of LAA flow velocity is lower in patients with rheumatic AF, especially those with significant mitral stenosis [15]. Lower diastolic augmentation of LAA flow velocity may be related to decreased transmitral mean gradient. Furthermore, because LAA contraction is absent in AF, there is a reduction in LAAEV. In comparison to SR patients, the left atrial diameter (LAD), presence of spontaneous echo contrast (percent), SEC density, and thrombus were all considerably larger in the AF group. The underpinnings for the development of AF are structural remodeling and lengthening of atrial muscle fibers produced by bigger LAD [16]. The most common cause of inactive LAA is AF, which results in blood stasis in the LA and the formation of SEC and/or thrombus [1, 17]. For this reason, MS patients with AF have higher thromboembolic risk. Similarly, it was found that patients with MS and AF have a 17-fold increased risk of stroke than age-matched controls in the Framingham Heart study [11].

CONCLUSION

The systolic and diastolic annular velocities are lower in individuals with mitral stenosis. The annular systolic and left atrial appendage emptying velocities have a favorable connection in mitral stenosis. The annular systolic velocity is an independent predictor of the presence of an inactive left atrial appendage in mitral stenosis patients with sinus rhythm. Finally, reduced annular systolic velocity in mitral stenosis patients with sinus rhythm might be considered a reason for anticoagulation.

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