ORIGINAL RESEARCH PAPER

Cardiology

KEY WORDS: RHD rheumatic heart disease, MS mitral stenosis, LA left atrium, LAA left atrial appendage, SEC spontaneous echo contrast, SR sinus rhythm and AF atrial fibrillation.

STUDY OF PREVALENCE AND FACTORS INFLUENCING THE OCCURRENCE OF LEFT ATRIAL/ LEFT ATRIAL APPENDAGE CLOT IN PATIENTS WITH RHEUMATIC HEART DISEASE & MITRAL STENOSIS IN SINUS RHYTHM VS ATRIAL FIBRILLATION.

Dr. Ashish Chauhan* DM Cardiology, SMS Medical College, Jaipur.*Corresponding Author

Dr. Rajeev Kumar Gupta DM Cardiology Resident, Christian Medical College and Hospital, Ludhiana.

Dr. V.V. Agarwal Professor, Department Of Cardiology, SMS Medical College, Jaipur.

ABSTRACT

BACKGROUND: The purpose of this study was to prospectively evaluate a large group of consecutive, non-anticoagulated patients with RHD (rheumatic mitral stenosis) and to analyze the left atrial appendage function in relation to left atrial appendage clot and spontaneous echo contrast formation in patients who were in SR vs. in AF. **METHODS AND RESULTS:** This is a hospital based observational study conducted in department of cardiology, S. M. S. MEDICAL COLLEGE and associated hospital, Jaipur, Rajasthan; between march 2016 to august 2017. We prospectively studied clinical and echocardiographic parameters of LA/LAA in 303 consecutive patients with mitral stenosis who underwent trans-esophageal echocardiography and correlated it with spontaneous echo contrast and left atrial appendage clot. The mean age of the patients was 32.94 years. One hundred thirty seven (45.21%) patients were in atrial fibrillation and 166 (54.79%) patients were in sinu rhythm. We found a statistically significant difference in the age of presentation (29.16/33.93/36.68 Yr; P =0.006/<0.001), MVA (1.17/0.8/0.69 cm2; P=<0.001/0.024), LA diameter (39/47.24/50 cm; P=<0.001/<0.001), LAA emptying velocity (45/26.43/15 cm/sec; P=<0.001/<0.001) and EF (37.49/30.67/23.7%; P=<0.001/0.001) among the patients without spontaneous echo contrast /clot vs. with spontaneous echo contrast vs. with spontaneous echo contrast & clot. By using student t-test, we found that there was a statistically significant difference in age of presentation, BMI, MDG, LA diameter, LAA emptying velocity and EF in patients who were in sinus rhythm vs. atrial fibrillation (P<0.05). Incidence of spontaneous echo contrast was 68.67% vs. 91.97% in patients in sinus rhythm vs atrial fibrillation, while that of SEC & CLOT both was 4.22% vs. 33.58% in patients in SR vs AF. In a subgroup of the patients with LA/LAA clot, the LA diameter (55.14 : 49.98 CM; P=0.057) and the LAA emptying velocity (15.14 : 15.26 CM/Sec; P=0.923) were not significantly different among patients in SR vs in AF. **CONCLUSION:** In the patients with severe mitral stenosis, besides atrial fibrillation, a subgroup of patients in normal sinus rhythm with depressed left atrial appendage function had a higher risk of clot formation in left atrial appendage and these patients should be routinely anticoagulated for prevention of clot formation.

INTRODUCTION:

Mitral stenosis is a huge burden in third world countries because of increased prevalence of rheumatic heart disease. The predominant cause of MS is rheumatic fever, with rheumatic changes present in 99% of stenotic mitral valves excised at the time of mitral valve replacement[1]. Although effective antibiotic treatment substantially reduces the risk for rheumatic fever, in situations of untreated epidemic GAS pharyngitis, the disease develops in up to 3% of patients[2]. Mitral valve is solely affected in 25% and is affected in combination with other valves in 40% patients. Mitral stenosis (MS) is a common finding in rheumatic heart disease and can lead to enlargement of the left atrium and stasis of blood in this heart chamber[3]. This can lead to an increased risk of clot formation in the left atrium and the left atrial appendage.

The frequency of LA thrombi is 20-33% in different studies[4,5,6] and is frequently associated with embolic episodes. Systemic arterial embolism is one of the most important complications in patients with mitral stenosis, and has been reported in 10–45% of them. Although systemic embolization most often occurs in patients with AF, 20% of patients with MS and a systemic embolic event are in sinus rhythm. In patients with rheumatic heart disease, 50% of thrombi and in patients with non-valvular AF 90% of LA thrombi are located in LA appendage.

Spontaneous echo contrast is seen in about 50% of atrial fibrillation patients and in more than 80 percent of those with AF and left or right atrial appendage thrombi[7,8].

The most common complication of MS is AF. The prevalence of AF in patients with MS is related to the severity of valve obstruction and patient age and varies from 17-80% with age 21-30 yrs. to >50 yrs. The frequency of LA thrombus in patients with mitral stenosis is 13.5% (in SR) to 33% (in AF)[4,5,9]. However, up to 45% of patients with MS who are in normal sinus rhythm demonstrate prominent spontaneous left atrial contrast (a marker of embolic risk) on TEE.

The sensitivity and specificity of TEE for left atrium and the left atrial appendage thrombi are reported to be 100% and 99%, respectively[10]. Studies have showed that presence of spontaneous echo contrast (SEC)/ thrombus in LAA is associated with increased risk of thromboembolism. In numerous studies to date, various precipitating factors for the formation of a clot inside the left atrium have been identified, including atrial fibrillation (AF) rhythm, left atrial size, duration of symptoms, advanced age, and severity of MS. Furthermore, mitral regurgitation (MR) in conjunction with MS has been mentioned as a factor which reduces the risk of left atrial clot formation.

However there are limited studies evaluating the relationship between LA morphology & function, prevalence of LA clot in MS patients who are in sinus rhythm. So this study is planned to determine the prevalence of LA/LAA clot in the MS patients who are in sinus rhythm/AF and to determine the factors influencing the formation of LA clot.

AIMS AND OBJECTIVES:

1. To know the prevalence of LA clot in patients of RHD with MS who are in sinus rhythm/AF.
2. To know the factors influencing the occurrence of LA clot in these patients.

MATERIAL AND METHOD:

1. STUDY PROTOCOL:

This is a hospital based observational study, conducted at department of cardiology S. M. S. medical college and associated hospital, Jaipur, Rajasthan. Three hundred three consecutive patients of mitral stenosis who presented to cardiology department for further management were included in the study. Sampling technique was non-probability consecutive sampling. All clinical and echocardiographic data were collected prospectively. Patients with associated > 2/4 mitral regurgitation, significant aortic valve disease, previous closed mitral valvotomy/MV repair/MVR, patient with non-valvular AF, patient with history of CVA/TIA and those on anticoagulation or antiplatelet therapy were excluded.

2.METHOD: All the consecutive patients who meet the inclusion criteria were enrolled in the study.

Transthoracic echocardiography (TTE): The Trans-thoracic studies were done as per the ASE guidelines using PHILIPS iE-33 with 5MHz to evaluate MVA (by planimetry and continuous wave Doppler using the pressure half time method), mean trans-mitral gradient, for the presence of MR/ other valvular involvement and to assess LVEF by standard techniques.

Left atrial diameter was taken in the parasternal long axis view in M-mode at end-systole.

Trans-esophageal echocardiography (TEE): TEE was performed after TTE in the left lateral decubitus position using PHILIPS XL-2t with 11 MHz multi-plane transducer. All patients were in fasting condition for at least 4 hours and had received local pharyngeal anesthesia with 2% lidocaine spray/ jelly immediately before probe insertion. TEE probe was introduced with the patient lying in left lateral position. The LA was be scanned in long axis view. With a counterclockwise rotation of the probe at the level of aortic valve, the LA appendage was visualized and by using pulsed doppler imaging with sample volume positioned at mouth of the appendage the maximal velocity during atrial contraction was be measured.

Patients were examined using standard protocol to assess the presence of LA clot and to assess the morphology & function of left atrium. In patients with normal sinus rhythm, the maximum area of LAA (LAA max) was measured just before the P wave and minimum area of LAA (LAA min) was measured at or just after the QRS complex at the end of LAA systole, by planimetry. The perimeter extended from the tip of the limbus between the upper left pulmonary vein along a straight line drawn to the aorta at its shortest point at the base of LAA. In patients with AF the maximum and minimum appendage area were not related to QRS. In these cases maximum and minimum areas were obtained independent of the electrocardiogram (ECG) in each cardiac cycle. An average of 5 readings was taken in patients with AF and 3 for normal sinus rhythm (NSR).

LAA ejection fraction = (LAAmax – LAAmin)/ LAAmax
LAA clot was diagnosed by the presence of clearly defined echogenic intra-cavitary mass with an echo texture different from that of the underlying endocardium.
LA thrombus based on their location, extension, and mobility as assessed by TTE/TEE were classified by Manjunath. et. al.[11] as follows:
Type Ia: LA appendage clot confined to appendage.
Type Ib: LA appendage clot protruding into LA cavity.
Type IIa: LA roof clot limited to a plane above the plane of fossa ovalis.
Type IIb: LA roof clot extending below the plane of fossa ovalis.
Type III: Layered clot over the interatrial septum (IAS).
Type IV: Mobile clot which is attached to LA free wall or roof or IAS.
TypeV: Ball valve thrombus (Free Floating).

Spontaneous echo contrast was diagnosed by the presence of dynamic smoke-like echoes in the LAA with a characteristic swirling motion distinct from white noise artifact after properly adjusting the gain settings. All studies were reviewed independently by two experienced observers and any discrepancy was resolved by consensus.

STATISTICAL ANALYSIS:

Data are presented as mean ± SD. For comparison, unpaired student's *t* test was used for continuous variables and Chi-square test for categorical variables and values were considered significant when p value was <0.05. Univariate, multivariate logistic regression analysis and discriminant function analysis were done for all the variables to determine the factors that independently predict the presence of clot and spontaneous echo contrast.

RESULTS:

The mean age of the patients was 32.94y (range from 18-60 yrs.). The female patients made 58% (N=176) of cases. The baseline patient characteristics are shown in Table-1.

BASELINE PARAMETERS OF THE PATIENTS OF RHD WITH MITRAL STENOSIS (TABLE-1, FIGURE 1)

The mean MVA was 0.88 cm^2 and 0.98 cm^2 by planimetry and PHT respectively. The mean MDG was 13.44 mmHg and mean EDG was 4.01 mmHg. The mean Wilkins score was 7.28. The mean LA diameter, LAA velocity were 45.52 mm and 30.54 cm/sec respectively and the mean LAA-EF was 35.62%.

N		Minimum	Maximum	Mean
AGE in years	303	18	60	32.94
BMI	303	17.80	23.70	20.3403
MVA BY PLANIMETRY (cm2)	303	0.56	1.60	0.8838
MVA BY PHT (cm2)	303	.60	1.64	0.9779
WILKINS SCORE	303	6	9	7.28
MDG in mmHg	303	4	35	13.44
EDG in mmHg	303	2	11	4.01
LA DIAMETER (in mm)	303	34	65	45.52
LAA VELOCITY (in cm/sec)	303	12	67	30.34
LAA EF(%)	303	21	42	35.62

Figure 1.Baseline parameters of the patients of Rheumatic Heart Disease with mitral stenosis.

CLINICAL VARIABLES AND ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS WITHOUT LA/LAA-SEC/CLOT, PATIENTS WITH LA/LAA-SEC AND PATIENTS WITH LA/LAA-SEC & CLOT (table-2):

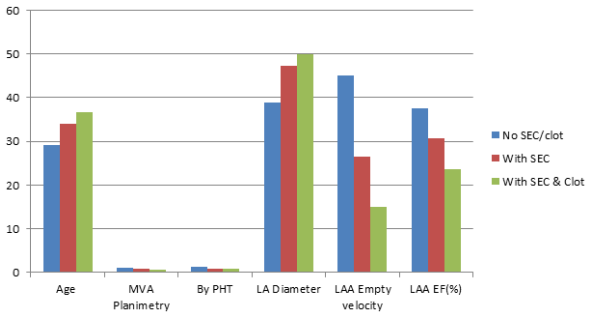
We found a statistically significant difference in the age of presentation, MVA, LA diameter, LAA emptying velocity and EF among the patients without SEC/clot vs. with SEC vs. with SEC/clot.

TABLE 2.

VARIABLES	NO SEC/CLOT (N=63)	WITH SEC (N=240)	WITH SEC & CLOT (N=53)	P-VALUE
AGE (YEARS)	29.16	33.93	36.68	0.006/<0.001
MVA (BY PLAIMETRY / PHT IN cm^2)	1.17/1.26	0.8/0.9	0.69/0.79	<0.001/0.024
LA DIAMETER (in mm)	39	47.24	50	<0.001/<0.001

LAA EMPTYING VELOCITY (cm/sec)	45	26.43	15	<0.001/<0.001
LAA EF (%)	37.49	30.67	23.7	<0.001/<0.001

FIGURE 2. CLINICAL VARIABLES AND ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS WITHOUT LA/LAA-SEC/CLOT, PATIENTS WITH LA/LAA-SEC AND PATIENTS WITH LA/LAA-SEC & CLOT.



CLINICAL VARIABLES AND ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS IN SR AND IN AF (TABLE-3):

The mean age, MDG, LA diameter, LAA velocity, and LAA- EF were significantly different in patients of SR vs. patients in AF.

TABLE-3.

	RHYTHM	N	Mean	Std. Deviation	Std. Error Mean	p value
AGE in years	SR	166	30.42	7.057	.548	<0.001
	AF	137	36.00	6.694	.572	
BMI	SR	166	20.1500	1.35193	.10493	0.016
	AF	137	20.5708	1.60908	.13747	
MVA BY PLANIMETRY (in cm^2)	SR	166	.8936	.24792	.01924	0.465
	AF	137	.8718	.26637	.02276	
MVA BY PHT (in cm^2)	SR	166	.9867	.25631	.01989	0.511
	AF	137	.9672	.25604	.02187	
WILKINS SCORE	SR	166	7.25	.822	.064	0.572
	AF	137	7.31	.819	.070	
MDG in mmHg	SR	166	14.60	6.412	.498	<0.001

PREVELANCE OF LA/LAA-SEC/CLOT IN PATIENTS OF RHD WITH MS IN SR AND AF (TABLE-4, FIGURE 3):

TABLE-4.

	SR (N=166,%)	AF (N=137,%)	P-VALUE
NO LA/LAA-SEC/CLOT (N=63)	52(31.33%)	11(8.03%)	<0.001
LA/LAA-SEC (N=240)	114(68.67%)	126(91.97%)	<0.001
LA/LAA-SEC & CLOT (N=53)	7(4.22%)	46(33.58%)	<0.001

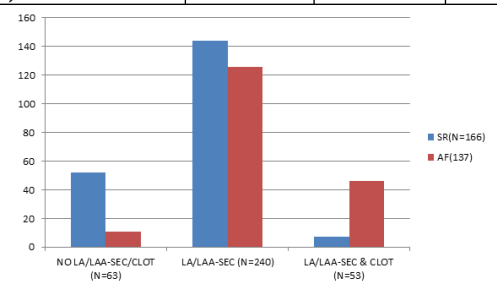


FIGURE-3. PREVELANCE OF LA/LAA-SEC/CLOT IN PATIENTS OF RHD WITH MS IN SR AND AF.

In our study we found prevalence of LA/LAA- SEC in 68.67% vs. 91.97% of patients in sinus rhythm vs. AF, while the prevalence of clot was 4.22% vs. 33.58% in sinus rhythm and AF.

TABLE-5.Patients with SEC Independent Sample t-test

	RHYTHM	N	Mean	Std. Deviation	Std. Error Mean	p value
LA DIAMETER (in mm)	SR	114	44.70	5.333	.499	<0.001
	AF	126	49.53	4.880	.435	
LAA VELOSITY (incm/sec)	SR	114	32.75	11.970	1.121	<0.001
	AF	126	20.71	5.809	.518	
MDG in mmHg	SR	114	16.34	6.032	.565	<0.001
	AF	126	12.40	3.765	.335	
EDG in mmHg	SR	114	4.85	1.854	.174	<0.001
	AF	126	3.96	1.311	.117	

TABLE- 6. Patients with Clot Independent Sample t-test.

	RHYTHM	N	Mean	Std. Deviation	Std. Error Mean	p value
LA DIAMETER (in mm)	SR	7	55.14	12.294	4.647	0.057
	AF	46	49.98	5.335	.787	
LAA VELOSITY (in cm/sec)	SR	7	15.14	2.673	1.010	0.923
	AF	46	15.26	3.029	.447	
MDG in mmHg	SR	7	23.43	14.432	5.455	<0.001
	AF	46	13.15	2.494	.368	
EDG in mmHg	SR	7	7.86	2.673	1.010	<0.001
	AF	46	4.33	1.851	.273	

The table 5 & 6 suggests that in patients with LA/LAA clot the LA diameter and LAA emptying velocities are not different in patients in SR vs in AF.

DISCUSSION

Various studies have shown that LAA is the major site of clot formation, especially in patients with mitral stenosis. It is assumed that the larger size and poor contraction of LAA in mitral stenosis, which is reflected by a decrease in ejection fraction, and reduced filling and emptying velocities, leads to stasis of blood, which helps in formation of clot. Its long, narrow, tubular structure with a narrow tip and muscular ridges inside the lumen also make it more vulnerable for clot formation.

After the introduction of TEE, which enables the cardiac chambers to be examined in more detail than with TTE, the interest to evaluate the role of LAA contractile function has increased and many reports on various heart diseases have shown its correlation with presence of clot and spontaneous echo contrast formation in LA or LAA. Among all the cardiovascular diseases, mitral stenosis had the highest incidence of clot formation in LAA. However, there are not enough studies properly evaluating LAA function in a large number of patients with severe mitral stenosis.

In the present study we prospectively evaluated LAA function in 303 consecutive patients with mitral stenosis and compare their clinical and echocardiographic characters in patient who were in SR or in AF.

The incidence of rheumatic heart disease is still high in the developing countries and the majority of the patients who need anticoagulation were not receiving it because of the delay in diagnosis, poor drug compliance and lack of facilities to monitor the pro- thrombin time in the remote areas. So we were able to collect a large number of patients

with mitral stenosis who were not on any anticoagulation despite being in AF.

LAA flow pattern and its correlation with LAA function and clot formation: In our study we consistently found that LAA emptying velocity was significantly less in MS patients, which was reported in the previous studies. This difference in velocities was because of the fact that in patients with severe mitral stenosis the elevated LA pressure favors the filling waves while opposing the emptying waves thus increasing the velocity of filling waves and decreasing the velocity of emptying waves, which may not be true in patients with non-rheumatic AF and other diseases with normal LA pressure. We consistently found that patients with lower LAA emptying velocity had significantly larger LA and LAA sizes, lower LAA ejection fraction than normal.

There was fewer previous studies, these studies had smaller number of patients and did not evaluate all LAA function parameters and flow patterns with respect to clot and spontaneous echo contrast formation.

Garcia-Fernandez et al.[12] studied 27 patients with rheumatic valvular heart disease (not isolated mitral stenosis) and found that patients with low LAA emptying velocity had highest incidence of LAA clot and spontaneous echo contrast as compared to those with normal flow; however, they did not correlate the type of flow pattern with other LAA function parameters.

Porte et al.[13]reported that patients with mitral stenosis having low LAA emptying velocity (n=37), had larger LA and LAA sizes, lower LAA ejection fractions, as compared to those with normal flow velocity, but they did not correlate the LAA flow patterns with LAA clot and spontaneous echo contrast.

LAA function and LAA SEC/clot:
In the patients with severe mitral stenosis we found significantly larger LAA size, lower LAA ejection fraction and lower emptying velocities than normal. In the present study LAA size was significantly more and ejection fraction was significantly less in patients with AF. The LA size, LAA -EF, LAA emptying velocities were also significantly less in the patients with SEC/clot. The higher incidence of clot in patients with larger and poorly functioning LAA with decreased ejection fraction, and emptying velocities favors the hypothesis of stasis of blood in this chamber leading to increased incidence of clot formation. After multivariate logistic regression analysis LAA emptying velocity, LAA ejection fraction along with AF were found to be independently correlated with presence of clot.

Pollick et al.[14] were the first to assess the LAA flow patterns and the effect of LAA function on LAA clot formation in a different subgroup of patients (for evaluation of prosthetic valve, stroke and endocarditis). They found that patients with sinus rhythm and LAA clot had increased LAA size as compared to patients without clot. The LAA ejection fraction and LAA velocities were also significantly less in patients with clot as compared to patients without clot. Patients with AF and clot or spontaneous echo contrast had larger LAA area as compared to patients with AF but without clot or spontaneous echo contrast.

STUDY LIMITATION:
The possibility of intermittent AF in the patients with normal sinus rhythm could not be ruled out, thus not strictly isolating the patients with true normal sinus rhythm.

This study only highlights the patients with severe mitral stenosis (only very few patients were in the range of progressive MS; N=6); the patients with mild to moderate mitral stenosis need to be further examined.

CONCLUSION:
In the patients with severe mitral stenosis, AF, LA size, LAA emptying velocity and LAA ejection fraction appear to be independent predictors of clot and spontaneous echo contrast formation in LAA. In a subgroup of patients with spontaneous echo contrast , patients had larger LA diameter, lower LAA emptying velocity and ejection fraction than patients without SEC/clot. In patients with mitral stenosis the emptying velocity was consistently lower even in patients who were in SR and had SEC; so lower LAA emptying velocity and LAA-EF appeared to be the predictors for spontaneous echo contrast formation in LAA. Large studies are needed to suggest that these patients should be anti-coagulated for prevention of clot formation.

REFERENCES :

1. Chambers JB, Bridgewater B: Epidemiology of valvular heart disease. In Otto CM, Bonow RO (eds): Valvular Heart Disease: A Companion to Braunwald's Heart Disease. 4th ed. Philadelphia, Saunders, 2013, pp 1–13.
2. Robertson KA, Volmink JA, Mayosi BM: Antibiotics for the primary prevention of acute rheumatic fever: A meta-analysis. BMC Cardiovasc Disord 5:11, 2005.
3. Olson LJ, Subramanian R, Ackermann DM. Surgical pathology of the mitral valve: a study of 712 cases spanning 21 years. Mayo Clin Proc 1987;62:22-7.
4. Goswami KC, Yadav R, Rao BM, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic stenosis: a prospective study in 200 patients by transesophageal echocardiography. Int J Cardiol 2000;73:273-9.
5. Srimannarayana J, Varma 34.7%. In a small group of 50 patients with mitral stenosis RS, Anilkumar R, Balachnander J. Prevalence of left atrial thrombus in rheumatic mitral stenosis with atrial fibrillation and its response to anticoagulation: a transesophageal echocardiographic study. Indian Heart J 2003;55:358-61.
6. Kronzon I, Tunick PA, Charney LH. Echocardiography as a tool in the evaluation of conditions with a high likelihood of cardiogenic embolism. Isr Med Assoc J 2006;8:768-72.
7. Echocardiographic predictors of stroke in patients with atrial fibrillation: a prospective study of 1066 patients from 3 clinical trials. Arch Intern Med 1998;158:1316-21.
8. Chambers JB, Bridgewater B: Epidemiology of valvular heart disease. In Otto CM, Bonow RO (eds): Valvular Heart Disease: A Companion to Braunwald's Heart Disease. 4th ed. Philadelphia, Saunders, 2013, pp 1–13
9. Robertson KA, Volmink JA, Mayosi BM: Antibiotics for the primary prevention of acute rheumatic fever: A meta-analysis. BMC Cardiovasc Disord 5:11, 2005.
10. Olson LJ, Subramanian R, Ackermann DM. Surgical pathology of the mitral valve: a study of 712 cases spanning 21 years. Mayo Clin Proc 1987;62:22-7.
11. Goswami KC, Yadav R, Rao BM, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic stenosis: a prospective study in 200 patients by transesophageal echocardiography. Int J Cardiol 2000;73:273-9.
12. Srimannarayana J, Varma 34.7%. In a small group of 50 patients with mitral stenosis RS, Anilkumar R, Balachnander J. Prevalence of left atrial thrombus in rheumatic mitral stenosis with atrial fibrillation and its response to anticoagulation: a transesophageal echocardiographic study. Indian Heart J 2003;55:358-61.
13. Kronzon I, Tunick PA, Charney LH. Echocardiography as a tool in the evaluation of conditions with a high likelihood of cardiogenic embolism. Isr Med Assoc J 2006;8:768-72.
14. Echocardiographic predictors of stroke in patients with atrial fibrillation: a prospective study of 1066 patients from 3 clinical trials. Arch Intern Med 1998;158:1316-21.
15. de Divitiis M, Omran H, Rabahieh R, Rang B, Illien S, Schimpf R, et al. Right atrial appendage thrombosis in atrial fibrillation: its frequency and its clinical predictors. Am J Cardiol 1999;84:1023-8.
16. Chiag CW, Lo SK, Ko YS, Cheng NJ, Lin PJ, Chang CH. Predictor of systemic embolization in patients with mitral stenosis: a prospective study. Ann Intern Med 1998;128:885-9.
17. Manning WJ, Weintraub RM, Waksmonski CA, Haering JM, Rooney PS, Maslow AD, et al. Accuracy of transesophageal echocardiography for identifying left atrial thrombi. Ann Intern Med 1995;123:817-22.
18. Manjunath CN, Srinivasa KH, Panneerselvam A, Prabhavathi B,Ravindranath KS, Rangan K, et al. Incidence and predictors of left atrial thrombus in patients with rheumatic mitral stenosis and sinus rhythm: a transesophageal echocardiographic study. Echocardiography. 2011;28(4):457– 60.
19. Garcia-Fernandez MA, Torrecilla EG, San Roman D, Azevedo J, Bueno H, Moreno MM, et al. Left atrial appendage Doppler flow patterns:implications on thrombus formation. Am Heart J 1992; 124:955–961.
20. Porte JM, Cormier B, Iung B, Dadez E, Starkman C, Nallet O, et al. Early assessment by transesophageal echocardiography of left atrial appendage function after percutaneous mitral commissurotomy. Am J Cardiol 1996; 77: 72–76.
21. Pollick C, Taylor D. Assessment of left atrial appendage function by transesophageal echocardiography : implications for development of thrombus. Circulation 1991;84:223–231.