

# Echocardiographic Predictors of Left Atrial Thrombus in Patients With Severe Rheumatismal Mitral Stenosis

Afsoon Fazlinezhad<sup>1,2</sup>; Hamed Golmohammadzadeh<sup>3</sup>; Ali Azari<sup>2,3</sup>; Leila Bigdelu<sup>1,2,4,\*</sup>

<sup>1</sup>Department of Cardiology, Ghaem hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

<sup>2</sup>Cardiovascular Research Center, Ghaem Hospital, School of Medicine, Mashhad University of Medical sciences, Mashhad, IR Iran

<sup>3</sup>Department of Surgery, Ghaem Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

<sup>4</sup>Preventive Cardiovascular Care Research Center, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

\*Corresponding author: Leila Bigdelu, Department of Cardiology, Ghaem Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran. Tel: +98-5118012739, E-mail: bigdelul@mums.ac.ir; bigdelul@gmail.com

Received: October 23, 2013; Revised: December 19, 2013; Accepted: December 22, 2013

**Background:** Rheumatismal mitral stenosis is less common today than it was several decades ago, but it is a common cause of mitral stenosis (MS) in the developing world. Mitral valve stenosis symptoms include fatigue, palpitations, and Shortness of breath especially with exertion.

**Objectives:** The purpose of this prospective study was to determine the incidence of left atrial (LA) thrombus and the predisposing factors predicting its developments in patients with symptomatic rheumatismal mitral stenosis who underwent transesophageal echocardiography (TEE) planned for percutaneous transvenous mitral commissurotomy (PTMC).

**Patients and Methods:** Patients who were referred to perform TEE before mitral balloon valvuloplasty enrolled the study. Data were analyzed by SPSS.

**Results:** Out of 92 patients, females were 68 (73.91%). Mean age was  $43.35 \pm 13.94$ . They were classified into two groups based on the presence or absence of LA thrombus. Group A consisted of 21 patients (seven men and 14 women) with LA thrombus (mean age of  $53.00 \pm 15.70$  years). Group B consisted of 71 patients (17 men and 54 women) without LA thrombus. There were no statistically significant differences between the two groups regarding age, sex, LA diameter, LA area, LA smoke, Trans-mitral mean pressure gradient, systolic pulmonary artery pressure, left ventricular ejection fraction and right ventricular function, but patients with LA clot had more LA appendage dysfunction, more frequent atrial fibrillation rhythm, and smaller mitral valve area ( $P = 0.020, 0.005$  and  $0.020$  respectively) and the prevalence of MR was also lower in this group ( $P = 0.049$ ). In our evaluation there was no statistically significant difference regarding the LA diameter or LA area in patients with or without LA smoke.

**Conclusions:** The frequency of left atrial clots increased with the presence of LAA dysfunction, atrial fibrillation rhythm, and smaller mitral valve area. Presence of MR had protective effects against LA clots.

**Keywords:** Heart Atria; Thrombosis; Mitral Valve Stenosis; Echocardiography, Transesophageal

## 1. Background

Rheumatismal mitral stenosis is less common today than it was several decades ago, but it is a common cause of mitral stenosis (MS) in the developing world. Mitral valve stenosis symptoms include fatigue, palpitations, and Shortness of breath especially with exertion. Left atrial (LA) enlargement and blood stasis in this chamber can lead to increased risk of clot formation and thromboembolic events. Some of the reported risk factors for thrombus formation are advanced age, LA enlargement and low cardiac output state. In this study, we aimed to evaluate echocardiographic predictors of left atrial thrombus formation.

## 2. Objectives

The purpose of this prospective study was to investigate the frequency and the predisposing factors associated with LA thrombus formation in patients with mitral stenosis who underwent transesophageal echocardiography (TEE).

## 3. Patients and Methods

In a prospective study, 92 consecutive patients with mitral stenosis who were referred for performing TEE enrolled in this study. Patients were included in this study if they had mitral stenosis with a mitral valve area less than

### Implication for health policy makers/practice/research/medical education:

LA thrombus is a result of blood stasis secondary to rheumatismal mitral stenosis. Transesophageal echocardiography is a simple, feasible, and reproducible method for the assessment of the presence of LA clot and for prediction of patients who were high risk for it. In our study, the frequency of left atrial clots increased with presence of LAA dysfunction, atrial fibrillation rhythm, and smaller mitral valve area. Presence of MR had protective effects against LA clots.

1.5 cm<sup>2</sup> and were not on anticoagulant therapy. Diagnosis of rheumatic mitral valve involvement was based on echocardiographic findings. Diagnosis of cardiac rhythm was confirmed by 12-lead electrocardiograms in all patients. These Patients were divided into two groups according to the presence or absence of LA clot. The baseline demographic information, electrocardiographic and echocardiographic data were prospectively recorded.

### 3.1. Echocardiographic Examination

A complete resting 2-dimensional (2D) transesophageal echocardiogram was performed in the left lateral decubitus position by an experienced fellowship of echocardiography using VIVID 3 (GE-USA) and 7 MHz multiplane transducer. All patients were in fasting condition for at least 4 hours and had received local pharyngeal anesthesia with 2% lidocaine spray and intravenous sedation by low dose midazolam under tight O<sub>2</sub> saturation control, immediately before probe insertion. Patients were examined using standard protocol. Routine M-mode measurements were obtained according to the recommendations of the American Society of Echocardiography. Left ventricular ejection fraction (LVEF) was calculated by Simpson rule. Systolic pulmonary artery pressure (SPAP) measured with echocardiographic parameters. The mitral valve area (MVA) was measured by continuous-wave Doppler, with pressure half-time method, and by direct planimetry. The mean transmitral pressure gradient was calculated by Doppler method and mitral regurgitation (MR) grade was assessed using the proximal isovelocity surface area (PISA) method, color Doppler flow mapping, jet eccentricity, and integrating jet expansion within the left atrium (jet area to atrial area). We used all standard views and evaluated LA and LA appendage for the presence or absence of thrombus and/or spontaneous echo contrast carefully. We also placed the pulse wave sample volume in the LA appendage cavity near the orifice and determined maximum contraction velocity as the most predictor of LAA function.

### 3.2. Statistical Analysis

All data analyses were performed using SPSS statistics 15 for windows. Data were expressed as a Mean  $\pm$  SD for continuous variables and absolute value and percentage for qualitative variables. Group comparisons were made using Student's t test. Chi-square test was used instead of nominal data. All the used tests were two-sided, and differences were considered statistically significant for  $P < 0.05$ .

## 4. Results

The patients' ages ranged from 15 to 74 years (mean age was  $43.35 \pm 13.94$  years). Sixty eight of patients (73.91%) were women. The incidence of LA thrombus in MS was 22.8%. They were classified into two groups based on the presence or absence of LA thrombus. Group A consisted

of 21 patients (7 men and 14 women) with LA thrombus (mean age of  $53.00 \pm 15.70$  years). Group B consisted of 71 patients (17 men and 54 women), without LA thrombus; a complete TEE was obtained in 92 patients and all data were recorded (Table 1). Patient with LA clot did not differ significantly from the patients without LA clot regarding age, sex, LA diameter, LA area, Transmitral mean pressure gradient, SPAP, LVEF and right ventricular function, but group A patients had more LA appendage dysfunction, more frequent atrial fibrillation rhythm, and smaller mitral valve area (MVA) and the prevalence of MR was also lower in this group (Table 1).

In our evaluation, 81 patients (88.0%) had LA smoke from which 20 patients (22%) had LA thrombus. Among patients without LA smoke, no one had LA thrombus but there was no statistically significant difference between the two groups of patients regarding the presence or absence of LA smoke ( $P = 0.072$ ). From patients with LA smoke, 62 patients (68.1%) had atrial fibrillation (AF) rhythm versus 19 patients with sinus rhythm ( $P = 0.001$ ) but there was no statistically significant difference regarding LA diameter or LA area in patients with or without LA smoke ( $P = 0.380, 0.061$  respectively).

**Table 1.** Comparison Among the Patients With or Without Clot<sup>a,b</sup>

Variable	Group A (With Clot), n = 21	Group B (Without Clot), n = 71	P Value
Age, y	53.00 $\pm$ 15.70	44.58 $\pm$ 13.79	NS
Male	7	17	NS
Normal LVEF	16 (17.4%)	60 (65.2%)	NS
Normal RVF	12 (13%)	54 (58.7%)	NS
LAA function	24.65 $\pm$ 10.35	34.98 $\pm$ 18.51	0.02
Presence of LA smoke	20 (22%)	61 (67%)	NS
MVA, cm <sup>2</sup>	0.81 $\pm$ 0.22	0.91 $\pm$ 0.27	0.02
Mean pressure gradient, mmHg	12.48 $\pm$ 7.34	13.23 $\pm$ 6.98	NS
LA diameter, cm	5.79 $\pm$ 1.06	5.44 $\pm$ 0.81	NS
LA area, cm <sup>2</sup>	40.19 $\pm$ 11.03	37.61 $\pm$ 6.48	NS
AF rhythm	20	45	0.005
Presence of MR	21 (23.1%)	70 (76.9%)	0.049
Mild MR	20 (22%)	53 (75.7%)	
Moderate MR	1 (1.1%)	16 (17.7)	
Severe MR	0	1 (1.1%)	
SPAP, mmHg	61.43 $\pm$ 6.10	56.72 $\pm$ 2.19	NS

<sup>a</sup> Abbreviations: AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LA, Left atrium; LAA, left atrial appendage; MR, mitral regurgitation; MVA, mitral valve area; NS, not significant; RVF, right ventricular function; SPAP, systolic pulmonary artery pressure.

<sup>b</sup> Values are expressed as mean  $\pm$  SD and No. (%).

## 5. Discussion

In our study, patients' age with LA clot was not significantly higher than patients without LA clot. Conradie et al. found the similar result (1). However, some studies showed that with increased age, the risk of thrombus formation was increased significantly. We think this controversy is most probably due to the differences in the study design and population selection. LA echo contrast or spontaneous echo contrast is smoke like echoes in cardiac chambers and it refers to the blood stasis. LA smoke is a common finding in patients with severe MS and the importance of such echocardiographic finding is its association with LA thrombus formation and with subsequent systemic arterial embolization. Li et al. (2) reported that the incidence of LA smoke is higher in patients with atrial fibrillation rhythm in comparison with sinus rhythm even though they had similar mitral valve area. In our study, 81 patients had LA smoke and 68% of them had AF rhythm and LA smoke was significantly lower in patients with sinus rhythm ( $P = 0.001$ ) but LA thrombus formation were not more frequent in patients with LA smoke ( $P = 0.072$ ). Previous investigations on rheumatic MS had emphasized that severe mitral valve stenosis and LA enlargement are two important predisposing factors for LA smoke formation (2, 3) but we did not find any correlation between LA diameter or LA area with LA smoke ( $P = 0.380, 0.061$  respectively). LAA is a common source of cardiac embolism. TEE plays an important role in the assessment of LAA function. Previous study reported that reduced LAA ejection fraction and lower LAA peak emptying velocity increased risk of thrombus formation (3-6). Our findings were compatible with these results and patients who had reduced LAA function had more LA clot ( $P = 0.02$ ).

Our study suggested that mitral valve area (MVA) was significantly smaller in patients with LA clot ( $P = 0.02$ ) but mean pressure gradient was not significantly higher. The study by Golbasi et al. (4) showed that LAA dysfunction is an important risk factor for thrombus formation than MVA alone. Many other studies revealed that MVA did not have a significant relation to the clot formation (7-9). However it is a matter of controversy and Manjunath et al. reported that on multivariate analysis, the LA infero-superior dimension, mean mitral gradient and dense spontaneous echo contrast cannot predict the clot formation in patients with sinus rhythm (8). We found that presence of MR has a protective effect against left atrial clot formation and our result was compatible with other studies (10, 11). The frequency of left atrial clots increased with the presence of LAA dysfunction, atrial fibrillation rhythm, and smaller mitral valve area. Presence of MR had protective effects against LA clots.

### 5.1. Study limitations

Our study was conducted on small group and it may affect the results. We also evaluated all patients with sinus

rhythm and atrial fibrillation together. However, it is better to study in separate groups.

## Acknowledgements

We are grateful to the staff of echocardiography department of Ghaem Cardiovascular Medical and Research Center who did favours throughout this project. The authors also appreciate the efforts of Dr Habibolah Esmaili for data analysis.

## Authors' Contribution

Data collection and acquisition: Dr Fazlinezhad, Study concept and design: Dr Fazlinezhad, Dr Azari, and Dr Bigdelu. Analysis and interpretation of data: Dr Golmohammadzadeh, Dr Azari, and Dr Bigdelu. Drafting of the manuscript: Dr Bigdelu. Critical revision of the manuscript for important intellectual content: Dr Fazlinezhad and Dr Bigdelu. Statistical analysis: Dr Golmohammadzade and Dr Esmaili.

## Financial Disclosure

The authors declare that they have no conflicts of interest.

## Funding/Support

There were not any supports for performing of this study. This manuscript is the result of dissertation for the degree of M.D. (thesis No: 6085).

## References

- Conradie C, Schall R, Marx JD. Echocardiographic study of left atrial thrombi in mitral stenosis. *Clin Cardiol.* 1993;**16**(10):729-31.
- Li YH, Hwang JJ, Ko YL, Lin JL, Tseng YZ, Kuan P, et al. Left Atrial Spontaneous Echo Contrast in Patients With Rheumatic Mitral Valve Disease in Sinus Rhythm Implication of an Altered Left Atrial Appendage Function in Its Formation. *Chest J.* 1995;**108**(1):99-103.
- Zoppo F, Brandolino G, Berton A, Frigato N, Michieletto M, Zanolto A, et al. Predictors of left atrium appendage clot detection despite on-target warfarin prevention for atrial fibrillation. *J Interv Card Electrophysiol.* 2012;**35**(2):151-8.
- Golbasi Z, Cicek D, Canbay A, Ucar O, Bayol H, Aydogdu S. Left atrial appendage function in patients with mitral stenosis in sinus rhythm. *Eur J Echocardiogr.* 2002;**3**(1):39-43.
- Goswami KC, Yadav R, Rao MB, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic mitral stenosis: a prospective study in 200 patients by transesophageal echocardiography. *Int J Cardiol.* 2000;**73**(3):273-9.
- Kaya MG, Akpek M, Elcik D, Kalay N, Yarlioglu M, Koc F, et al. Relation of left atrial spontaneous echocardiographic contrast in patients with mitral stenosis to inflammatory markers. *Am J Cardiol.* 2012;**109**(6):851-5.
- Saidi SJ, Motamedi MH. Incidence and factors influencing left atrial clot in patients with mitral stenosis and normal sinus rhythm. *Heart.* 2004;**90**(11):1342-3.
- 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.
- Srimannarayana J, Varma RS, Sathesh S, Anilkumar R, Balachan-

- der 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**(4):358-61.
10. Karatasakis GT, Gotsis AC, Cokkinos DV. Influence of mitral regurgitation on left atrial thrombus and spontaneous echocardiographic contrast in patients with rheumatic mitral valve disease. *Am J Cardiol.* 1995;**76**(4):279-81.
  11. Kranidis A, Koulouris S, Filippatos G, Kappos K, Tsilias K, Karvounis H, et al. Mitral regurgitation protects from left atrial thrombogenesis in patients with mitral valve disease and atrial fibrillation. *Pacing Clin Electrophysiol.* 2000;**23**(11 Pt 2):1863-6.