



Original Article

Study of immediate and late effects of successful PTMC on left atrial appendage function in patients with severe rheumatic mitral stenosis IN SINUS rhythm

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ABSTRACT

Introduction: Since its introduction in 1984, Percutaneous Transvenous Mitral Commissurotomy (PTMC) has become established as a safe and effective treatment for rheumatic Mitral Stenosis (MS). (Ben Farhat et al., 1998) 1 Chronic pressure and volume overload imposed by MS causes left atrial (LA) and Left Atrial Appendage (LAA) dysfunction. Risk of cerebrovascular accident (CVA) is increased approximately 17-fold in patients of MS in Atrial Fibrillation (AF) and is present even in patients of MS in sinus rhythm (SR). This study was undertaken to evaluate the effect of PTMC on LAA function by Trans-esophageal echocardiography (TEE) Doppler and Doppler Tissue Imaging (DTI).

Methods: Total 70 cases were enrolled in this study. Patients with symptomatic severe MS (Mitral Valve Area <1.5cm²), in SR, who underwent a successful PTMC during the period from May 2016 to May 2019 were selected. All the patients underwent Clinical examination, ECG, detailed TTE and TEE before, immediately after (within 24 h) & after 6 months of PTMC.

Results: There was non significant improvement in Left Atrial appendage fractional area change {LAAAC (%)} immediately Post PTMC but there was significant improvement at 6 months Post PTMC. There was significant increase in LAA PW Doppler velocities (LAAEDE, LAALDE and LAAF velocity) immediately Post PTMC which got further improved significantly at 6 months of follow up. There was significant increase in LAA DTI velocities (E_{LAA}, A_{LAA} and S_{LAA} velocity) immediately Post PTMC which got further improved significantly at 6 months of follow up.

Conclusion: PTMC improves left atrial appendage function in patients with mitral stenosis.

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1. Introduction

Since its introduction in 1984, Percutaneous Transvenous Mitral Commissurotomy (PTMC) has become established as a safe and effective treatment for rheumatic Mitral Stenosis (MS) with results equivalent to surgical valvotomy.¹ Chronic pressure and volume overload imposed by MS causes left atrial (LA) and Left Atrial Appendage (LAA) dysfunction leading to reduced blood flow velocities thereby producing stasis of blood, reduced LA and LAA ejection fraction and atrial fibrillation (AF).² These factors predispose to formation of LA and LAA thrombi in MS and result in thromboembolic episodes.³ Risk of cerebrovascular accident (CVA)

is increased approximately five-fold in non-rheumatic AF and 17-fold in patients with MS with AF.⁴ Even patients of MS in sinus rhythm with depressed LA and LAA function are at increased risk of CVA.⁵ Assessment of LAA function is helpful in predicting the risk of thromboembolism.

Echocardiography, particularly transesophageal echocardiography (TEE), is currently the modality of choice for evaluation of the LAA.⁶ Transesophageal echocardiography (TEE) allows semi-invasive, highly accurate imaging of the functional efficiency of LAA by LAA Doppler and Doppler tissue imaging (DTI) flow profile.⁵ MS causes decreased LAA Doppler and DTI velocities in patients even with sinus rhythm.^{2,7} Very few studies in the literature have evaluated the impact of PTMC on LAA function so far. So, this study was undertaken to evaluate the immediate and late effect of successful PTMC on LAA function by TEE Doppler and DTI.

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2. Methods

It was a single centre prospective observational study. Total 70 cases were enrolled in this study. Patients with symptomatic severe MS (Mitral Valve Area <1.5cm²), in sinus rhythm, who underwent a successful PTMC during the period from May 2016 to May 2019 were selected. Successful PTMC was defined as patients who had MVA >1.5 cm² without increase in MR more than grade 1 and LA mean pressure less than 18 mmHg in absence of complications.

□ Exclusion Criteria

- > AF,
- > LA or LAA thrombus,
- > Concomitant significant Aortic valve disease,
- > Associated congenital disease,
- > NYHA functional class IV,
- > Past PTMC or surgical valvulotomy, &
- > Pregnancy.

All the patients underwent Clinical examination, ECG, detailed Transthoracic echocardiography (TTE) and Transesophageal echocardiography (TEE) before, immediately after (within 24 h) & after 6 months of PTMC.

□ Following parameters of LAA function were assessed on TEE

- > Two-Dimensional- LAA fractional area change (LAAAC%)
- > PW Doppler - LAA early diastolic emptying (LAAEDE) velocity
 - LAA late diastolic emptying (LAALDE) velocity
 - LAA filling (LAAF) velocity
- > Doppler Tissue Imaging - E_{LAA} velocity
 - A_{LAA} velocity
 - S_{LAA} velocity

2.1. LAA fractional area change %⁸

LAA maximal and minimal areas are traced by drawing a line from the top of the limbus of the left upper pulmonary vein along the entire endocardial border of LAA at end diastole and end systole by correlating with ECG as shown in Fig. 1. LAA fractional area change percentage (LAAAC %) is calculated according to the formula:

$$\left(\frac{\text{Maximal LAA Area} - \text{Minimal LAA area}}{\text{Maximal LAA area}} \right) \times 100$$

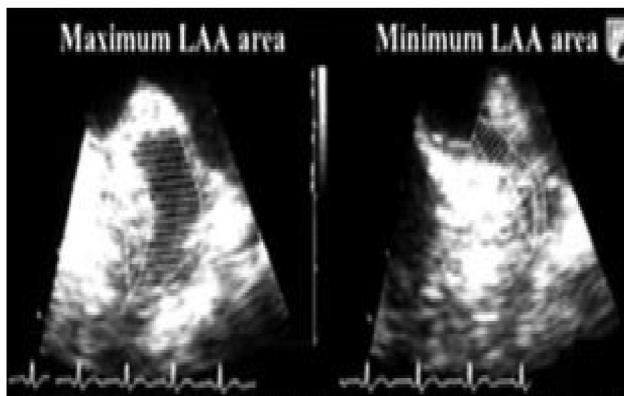


Fig. 1. LAA fractional area change.

2.2. LAA PW Doppler flow profile⁶

After suitable gain and filter adjustments, LAA Doppler flow velocities were obtained by using Pulsed wave (PW) Doppler from a site approximately 1 cm below the LAA outlet cavity from the middle third of LAA with no wall artifacts as shown in Fig. 2.

2.3. Doppler tissue examination of LAA⁸

By placing the spectral mode of PW Doppler sample volume on LAA lateral wall midway between the LAA tip and outlet; DTI velocities were obtained after suitable gain adjustments. While recording, Doppler beam was kept as parallel as possible to myocardial wall (Fig. 3).

PTMC Procedure: PTMC was performed using a standard transseptal approach with an Accura balloon. Written informed consent was obtained from all subjects before enrollment in the study. The study protocol was approved by the institutional ethics committee.

3. Statistical methods

The data was analyzed by using statistical software SPSS Version 17. Data is expressed in terms of absolute numbers and percentages in simple frequency distribution tables. Mean and standard deviation used to summarize the data. For repeated measurements one way ANOVA was used to assess the difference between the cardiac variables. Mauchly's test was used to test the sphericity. If the assumption of Sphericity was violated Greenhouse-Geisser correction was used. Post hoc analysis was done wherever the ANOVA was found to be significant. Tukey's post hoc test was used to see the difference between two means.

Probability less than 0.05 was considered as significant. Microsoft excel 2013 was used to generate the graphs.

4. Results & observations

Table 1 summarizes the baseline characteristics of the patient population. Total of 70 cases were enrolled, mean age among the cases was 31.83 ± 8.85 years. 19 (27.14%) were male and 51 (72.86%) were female. Mean BMI was 18.78 ± 3.32. Mean wilkins score was 9.89 ± 0.96. Mean SBP was 108.26 ± 11.21 mm Hg, mean DBP was 69.51 ± 7.68 mm Hg and Mean HR was 76.2 ± 13.39 beats/min.

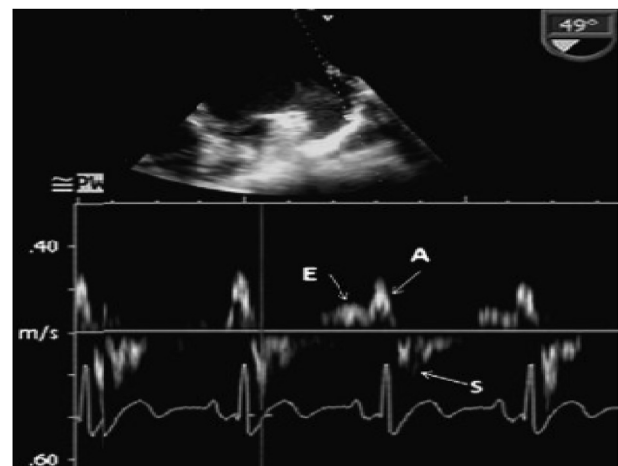


Fig. 2. LAA flow velocity by Pulsed Wave Doppler.

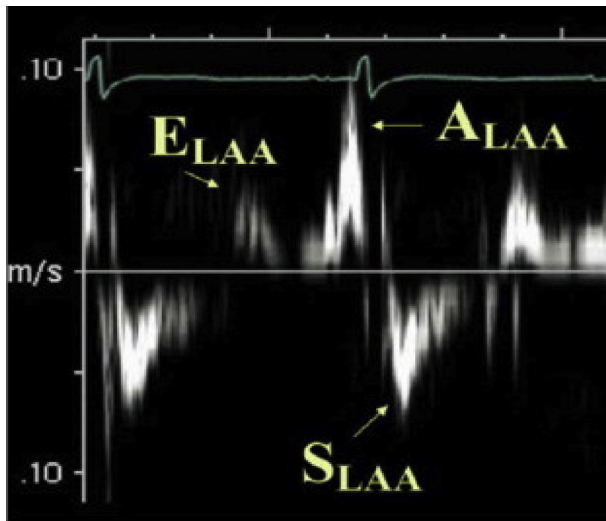


Fig. 3. LAA flow velocity by Tissue Doppler.

Table 1
Baseline characteristics of the patient population.

Characteristics	
Mean AGE	31.83 ± 8.85 years
SEX	
MALE	19 (27.14%)
FEMALE	51 (72.86%)
Mean BMI	18.78 ± 3.32 Kg/m ²
Mean WILKINS SCORE	9.89 ± 0.96
Mean SBP	108.26 ± 11.21 mm Hg
Mean DBP	69.51 ± 7.68 mm Hg
Mean HR	76.2 ± 13.39 beats/min
NYHA functional class	38 (54.29%) NYHA class II and 32 (45.71%) NYHA class III

BMI-Body mass index, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, HR-Heart rate, NYHA-New York heart association.

Among the cases 38 (54.29%) had NYHA class II symptoms and 32 (45.71%) had NYHA class III symptoms.

Table 2 summarizes the effect of PTMC on Transthoracic echocardiographic parameters.

PTMC was successful in all enrolled patients.

There was significant increase in Mitral Valve Area (MVA) after PTMC (0.87 ± 0.21 to 1.70 ± 0.18 cm², $P < .001$).

There were significant decreases in MV Peak Gradient (30.51 ± 9.28 to 11.64 ± 4.81 mmHg, $P < .001$) and MV Mean Gradient (21.34 ± 7.8 to 6.12 ± 3.62 mmHg, $P < .001$) after PTMC which got further decreased significantly to 10.97 ± 3.40 and 5.59 ± 2.54 respectively at 6 months follow up.

There was significant decrease in Left Atrial Volume Index (LAVI) after PTMC (49.04 ± 6.47 to 46.47 ± 6.04 ml/m², $P < .001$) which got further decreased significantly at 6 months follow up to 44.75 ± 5.95 , $P < .001$.

Table 2
Transthoracic echocardiographic parameters.

Variables	Pre PTMC	Immediate Post PTMC	6 months Post PTMC	P(Pre vs Immediate Post PTMC)	P(Pre vs 6 months Post PTMC)	P(Immediate Post vs 6 months Post PTMC)
MVA (cm ²)	0.87 ± 0.21	1.70 ± 0.18	1.69 ± 0.17	<0.001	<0.001	0.164
MV Peak Gradient (mmHg)	30.51 ± 9.28	11.64 ± 4.81	10.97 ± 3.40	<0.001	<0.001	0.03
MV Mean Gradient (mmHg)	21.34 ± 7.8	6.12 ± 3.62	5.59 ± 2.54	<0.001	<0.001	0.007
LAVI (ml/m ²)	49.04 ± 6.47	46.47 ± 6.04	44.75 ± 5.95	<0.001	<0.001	<0.001
PASP (mmHg)	57.93 ± 22.72	34.89 ± 11.66	34 ± 10.09	<0.001	<0.001	0.223

MVA-Mitral valve area, MV-Mitral valve, LAVI-Left atrial volume index, PASP-Pulmonary artery systolic pressure.

There was significant decrease in Pulmonary Artery systolic pressure (PASP) (57.93 ± 22.72 to 34.89 ± 11.66 mmHg, $P < .001$) after PTMC.

Table 3 summarizes the effect of PTMC on Transesophageal echocardiographic parameters.

There was non significant improvement in LAA fractional area change (LAAAC%) immediately after PTMC (48.6 ± 4.28 to 48.79 ± 4.29 , $p > .05$) but at 6 months follow up there was significant improvement to 49.12 ± 4.29 , $p < .001$.

There were significant increases in all pulsed-wave flow velocities of the LAA for the LAAEDE velocity, 11.9 ± 2.20 to 14.86 ± 2.29 to 15.1 ± 2.25 cm/s ($P < .01$); for the LAALDE Velocity, 22.76 ± 4.76 to 28.26 ± 5.23 to 28.65 ± 5.03 cm/s ($P < .001$); for the LAAF Velocity 30.15 ± 5.88 to 33.56 ± 5.65 to 34.3 ± 5.40 cm/s ($P < .001$).

Similarly, there were significant increases in Tissue Doppler velocities of the LAA for E_{LAA} , 6.38 ± 1.55 to 9.52 ± 1.98 to 9.71 ± 2.01 cm/s ($P < .01$); and for A_{LAA} , 11.67 ± 2.35 to 19.48 ± 3.77 to 19.85 ± 3.70 cm/s ($P < .001$); for S_{LAA} , 9.08 ± 1.77 to 13.02 ± 2.21 to 13.25 ± 2.13 cm/s ($P < .001$).

5. Discussion

In the present study we evaluated the effect of relief of mitral stenosis by PTMC on Left atrial appendage function in patients with severe symptomatic mitral stenosis in sinus rhythm.

Total 70 cases were enrolled in the present study. All patients were in sinus rhythm and underwent successful PTMC.

In the present study successful PTMC resulted in significant increase in the MVA and significant reduction in peak and mean MV gradient and PASP. There was a significant decrease in LAVI immediately after PTMC which got further decreased significantly at 6 months follow up. Normal indexed LA volume has been determined to be 22 ± 6 ml/m² using the preferred biplane techniques (area-length or method of disks) in a number of studies involving several hundred patients.⁶ Larger LA volume has been associated with a higher risk of AF and thromboembolism.¹⁸ In the present study before PTMC mean LAVI was 49.04 ± 6.47 ml/m². Immediately Post PTMC it reduced to 46.47 ± 6.04 ml/m². 6 months Post PTMC it further reduced to mean value of 44.75 ± 5.95 ml/m².

5.1. Effect of PTMC on left atrial appendage fractional area change (LAAAC %)

LAA is a highly contractile muscular sac that obliterates its apex during atrial systole. In patients with MS due to chronic pressure and volume overload there occurs gradual LAA dilatation and reduced contractility and high risk of SEC and thrombus formation. Measurement of the LAAAC % is prone to observer variability, as demonstrated in the reproducibility study. This, in part, likely reflects the irregularity of the LAA cavity, the arbitrary definition of the upper border with the left atrium, and some interbeat variability. Maintaining the same landmarks of the left atrial cavity

Table 3
Transesophageal echocardiographic parameters.

Variables	Pre PTMC	Immediate Post PTMC	6 months Post PTMC	P(Pre vs Immediate Post PTMC)	P(Pre vs 6 months Post PTMC)	P(Immediate Post vs 6 months Post PTMC)
LAAAC (%)	48.6 ± 4.28	48.79 ± 4.29	49.12 ± 4.29	0.06	<0.001	<0.001
LAAEDE Velocity (cm/s)	11.9 ± 2.20	14.86 ± 2.29	15.1 ± 2.25	<0.001	<0.001	0.003
LAALDE Velocity (cm/s)	22.76 ± 4.76	28.26 ± 5.23	28.65 ± 5.03	<0.001	<0.001	0.001
LAAF Velocity (cm/s)	30.15 ± 5.88	33.56 ± 5.65	34.3 ± 5.40	<0.001	<0.001	<0.001
E _{LAA} Velocity (cm/s)	6.38 ± 1.55	9.52 ± 1.98	9.71 ± 2.01	<0.001	<0.001	0.002
A _{LAA} Velocity (cm/s)	11.67 ± 2.35	19.48 ± 3.77	19.85 ± 3.70	<0.001	<0.001	<0.001
S _{LAA} Velocity (cm/s)	9.08 ± 1.77	13.02 ± 2.21	13.25 ± 2.13	<0.001	<0.001	0.003

LAAAC%-LAA fractional area change; LAAEDE-LAA early diastolic emptying velocity; LAALDE-LAA late diastolic emptying velocity; LAAF-LAA filling velocity.

for LAAmax and LAAmin should help to make the measurements as accurate as possible. Also, the simultaneous use of pulsed Doppler and color flow imaging can ensure that the LAA pattern represents contraction and not translocation of the LAA during the cardiac cycle.¹⁹ In the present study there was non significant improvement in LAAAC (%) immediately Post PTMC but there was significant improvement at 6 months Post PTMC. This result was similar to the previous studies who found non significant improvement in LAAAC (%) immediately post PTMC.^{8,9,11,13,14} But at 6 months F/U we found significant improvement in LAAAC (%). This might be due to chronic reduction in afterload after successful PTMC which led to gradual improvement in LAA contractile function and hence LAAAC (%).

5.2. Effect of PTMC on left atrial appendage PW Doppler velocities

In the study of Tenekecioglu et al. LAA Pulsed wave Doppler emptying and filling velocities were >60 cm/s in normal healthy controls.¹⁶ Sahin et al compared LAA velocities among healthy controls in sinus rhythm v/s patients with MS in AF (peak ejection velocity - 61 ± 16 cm/s versus 24 ± 6 cm/s, Peak filling velocity - 50 ± 9 cm/s versus 24 ± 7 cm/s). Thus LAA Doppler velocities were significantly depressed in MS patients in their study.¹⁷ In the present study also baseline LAA Doppler velocities were significantly low and there was a significant increase in LAA Doppler velocities (LAAEDE, LAALDE and LAAF velocity) immediately post PTMC which got further improved significantly at 6 months follow up. This result was similar to the previous studies.^{9,10,11,13,14}

5.3. Effect of PTMC on left atrial appendage DTI velocities

Contraction of LAA causes displacement toward the base of heart and is displayed as positive wave (A_{LAA}) on TEE DTI velocity profile. LAA does not move during LV isovolumic contraction. So after a brief delay, LAA moves toward the LV apex and is displayed as negative peak velocity (S_{LAA}), coincides with the LV contraction (T-wave on the ECG). During isovolumic relaxation LAA remains immobile and then moves again toward the base of heart. This velocity E_{LAA} corresponds to LV relaxation. Tenekecioglu et al demonstrated A_{LAA} tissue velocity of 33 ± 4.1 cm/s in normotensive healthy controls.¹⁶ Sahin et al demonstrated LAA DTI velocities in healthy controls in sinus rhythm and in patients with MS in AF (E_{LAA} velocity - 14.9 ± 5.9 cm/s versus 4.2 ± 1.3 cm/s and S_{LAA} velocity - 11.4 ± 5.1 cm/s versus 5.6 ± 1.3 cm/s).¹⁷ In the present study also baseline LAA DTI velocities were significantly low and there was significant increase in systolic and diastolic LAA DTI velocities (E_{LAA}, A_{LAA} and S_{LAA} velocity) immediately Post PTMC which got further improved significantly at 6 months follow up. This result was similar to the previous studies who found significant improvement in LAA DTI velocities after PTMC.^{8,9,10}

6. Conclusions

Successful PTMC results in improvement of LAA performance including LAAAC%, LAA PW Doppler and DTI velocities and further improvement was observed at 6-months of follow-up, suggesting continuous structural remodeling of the LAA after successful PTMC, leading to improved global and regional LA and LAA function. So, relief of MS by PTMC may not only confer hemodynamic benefits for symptomatic improvement but also may have a favorable influence on future thromboembolism risk by improving LA and LAA function. However, these findings should be confirmed by further large-scale studies and long-term follow-up.

7. Limitation

Our study was based on single center with limited number of patients. In addition, we provided no normal control group and failed to provide long-term follow-up. Routine TEE in clinical practice is difficult and it is not possible to get good LAA function assessment by TTE.

Conflicts of interest

All authors have none to declare.

Source of funding

The entire study was done using available resources at our institute, no external funds were sought/utilized.

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