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Study of Left Atrial Appendage Function in Patients of Severe Rheumatic Mitral Stenosis and Effect of Successful PTMC on SEC Grading

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Abstract: Background: Left Atrial Appendage (LAA) dysfunction is common in patients of Mitral stenosis (MS). In the present study we compared the LAA function amongst patients of severe rheumatic MS with particular reference to spontaneous echo contrast (SEC) and evaluated the effect of successful Percutaneous Transvenous Mitral Commissurotomy (PTMC) on SEC grading. Methods: It was a single centre prospective descriptive type of study. Total 75 cases were included during the study period from 2016 to 2020. Symptomatic patients with severe rheumatic mitral stenosis (MVA<1.5cm^2) in sinus rhythm fulfilling the elective PTMC intervention criteria and those who had a successful intervention only were included. All the patients underwent Clinical examination, ECG, detailed TTE and TEE before, Immediately after (within 24hrs) & after 6 months of PTMC. Results: In the present study mean LAAAC% and LAA PW Doppler velocities were significantly less in patients of severe rheumatic Mitral Stenosis having SEC than patients without SEC, implying more severe LAA dysfunction in patients with SEC. LAA Tissue Doppler velocities were also less in patients with SEC compared to patients without SEC but it was statistically not significant. There was a significant negative correlation between SEC grading and LAAAC (%) and LAA PW Doppler velocities (LAAEDE Velocity, LAALDE Velocity and LAAF velocity), i.e. greater the degree of SEC lesser was the LAAAC (%), LAAEDE Velocity, LAALDE Velocity and LAAF velocity, suggesting more severe LAA dysfunction in patients with greater degree of SEC. There was also negative correlation between SEC grading and LAA Tissue Doppler velocities (E_{LAA} Velocity, A_{LAA} Velocity, S_{LAA} Velocity) but it was statistically not significant. Successful PTMC resulted in significant decrease in SEC grading. Conclusion: Among the patients of severe rheumatic mitral stenosis, presence of SEC implies severe LAA dysfunction, greater the intensity of SEC, greater would be the severity of LAA dysfunction and successful PTMC results in improvement of SEC grading.

Keywords: PTMC, Left Atrial Appendage, Mitral Stenosis, Transesophageal Echocardiography, Spontaneous Echo Contrast

1. Introduction

Although mitral stenosis is now rare in developed countries, it has been recognised for more than 300 years. Vieussens described the disease in 1705 and has provided major milestones in cardiology. It was the first disease to be diagnosed with echocardiography, and the first valve lesion to be successfully treated by surgery or percutaneous balloon valvuloplasty.

For suitable valve Percutaneous Transvenous Mitral Commissurotomy (PTMC) is safe and effective treatment for

rheumatic mitral Stenosis with results similar to surgical valvotomy [1].

Contrary to earlier belief, the Left Atrial Appendage (LAA) is now thought to play an important role in normal cardiac hemodynamics. The appendage, being more compliant than LA, acts as a reservoir to attenuate the rise in intra-atrial pressure in response to various hemodynamic factors [2]. LAA is a highly contractile muscular sac that obliterates its apex during atrial systole. In Mitral Stenosis (MS) due to chronic pressure and volume overload there occurs gradual left atrial (LA) and Left Atrial Appendage (LAA) dilatation and dysfunction leading to reduced blood flow velocities which predisposes to thrombus formation and thromboembolic episodes [3]. Hence in patients of MS study of LAA emptying and filling velocities are helpful in predicting the risk of thrombus formation. Echocardiography, particularly transesophageal echocardiography (TEE), is currently the modality of choice for evaluation of the LAA [4]. In addition to delineation of thrombus, TEE is helpful in detection of LAA spontaneous echo contrast (SEC). SEC is a smoke-like swirling pattern seen on two- dimensional imaging, it indicates the presence of blood stagnation and is a precursor of thrombus formation [5]. In this study we compared the LAA function in patients of severe rheumatic MS with and without SEC and correlated degree of SEC with LAA function and evaluated the effect of PTMC on SEC grading.

2. Methods

It was a single centre prospective descriptive type of study. Total 75 cases were included during the study period from 2016 to 2020.

2.1. Inclusion Criteria

Symptomatic patients with severe rheumatic mitral stenosis (MVA<1.5cm^2) in sinus rhythm fulfilling the elective PTMC intervention criteria and those who had a successful intervention only were included. Successful PTMC was defined as patients who had MVA>1.5cm^2 without increase in MR more than grade 1 and LA mean pressure less than 18 mmHg in absence of complications.

2.2. Exclusion Criteria

1. Patients in Atrial Fibrillation,
2. LA or LAA thrombus,
3. Concomitant significant Aortic valve disease,
4. Associated congenital heart disease,
5. Organic tricuspid involvement like tricuspid stenosis
6. Any disease that could affect the myocardial function (coronary artery disease, chronic lung disease, cardiomyopathy)
7. Critically ill patients, NYHA functional class IV,
8. Past PTMC or surgical valvulotomy,
9. Pregnancy.
10. Patients who did not give consent

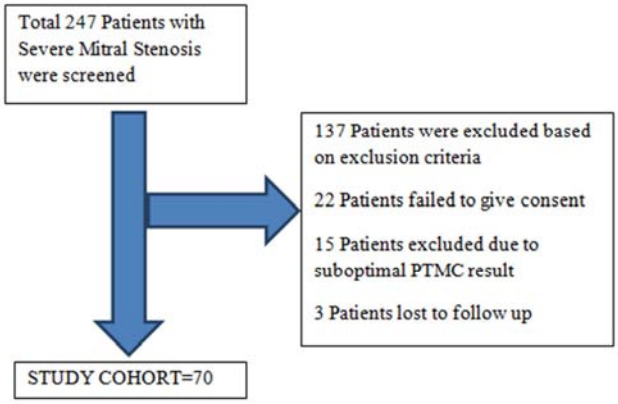

Figure 1. *Study sample.*

All the patients underwent Clinical examination, ECG, detailed Transthoracic echocardiography (TTE) and Transesophageal echocardiography (TEE) before, Immediately after (within 24hrs) & after 6months of PTMC using available equipment (Philips IE33 Vision 2007 system, Bothell, WA, U.S.A).

2.3. Following LAA Function Parameters Were Studied on TEE

Two-Dimensional- LAA fractional area change (LAAAC%)

PW Doppler Velocities

1. LAA early diastolic emptying (LAAEDE) velocity
2. LAA late diastolic emptying (LAALDE) velocity
3. LAA filling (LAAF) velocity

Tissue Doppler Velocities-

1. E_{LAA} velocity
2. A_{LAA} velocity
3. S_{LAA} velocity

2.3.1. LAA Fractional Area Change% [6]

LAA maximal and minimal areas are obtained by tracing the entire endocardial border of LAA at end diastole and end systole respectively by correlating with ECG. LAA fractional area change percentage (LAAAC%) is calculated according to the formula:

$$\left(\frac{MaximalLAAArea - MinimalLAAarea}{MaximalLAAarea}\right) \text{ x } 100$$

2.3.2. LAA PW Doppler Velocity [4]

LAA PW Doppler velocities were obtained by keeping the sample volume in the middle third of LAA cavity without wall artifacts as shown in figure 2.

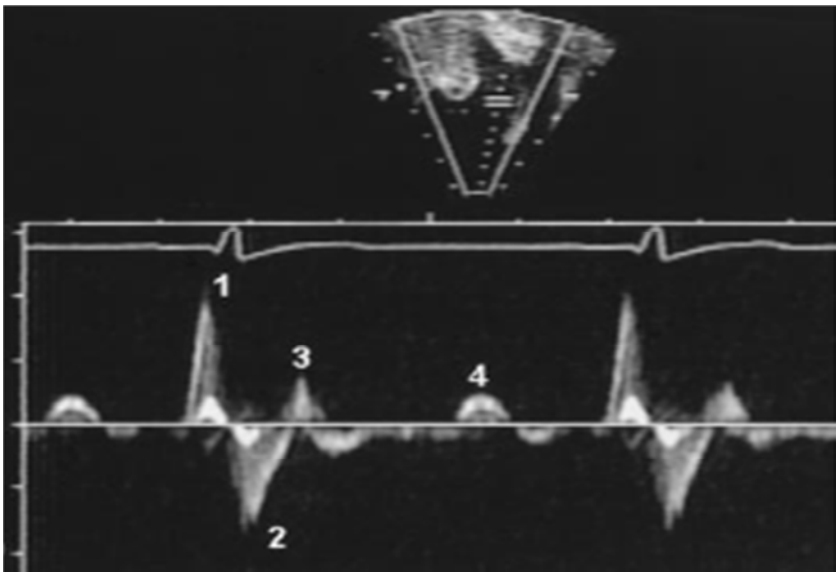

Figure 2. *LAA flow velocity by Pulsed Wave Doppler. 1-LAA late diastolic emptying (LAALDE), 2- LAA filling (LAAF) velocity, 3-systolic reflection waves (positive and negative), 4-LAA early diastolic emptying (LAAEDE) velocity.*

2.3.3. LAA Tissue Doppler Velocity [6]

LAA Tissue Doppler velocities were obtained by placing the spectral mode of PW Doppler sample volume on LAA lateral wall midway between the LAA tip and outlet (figure 3).

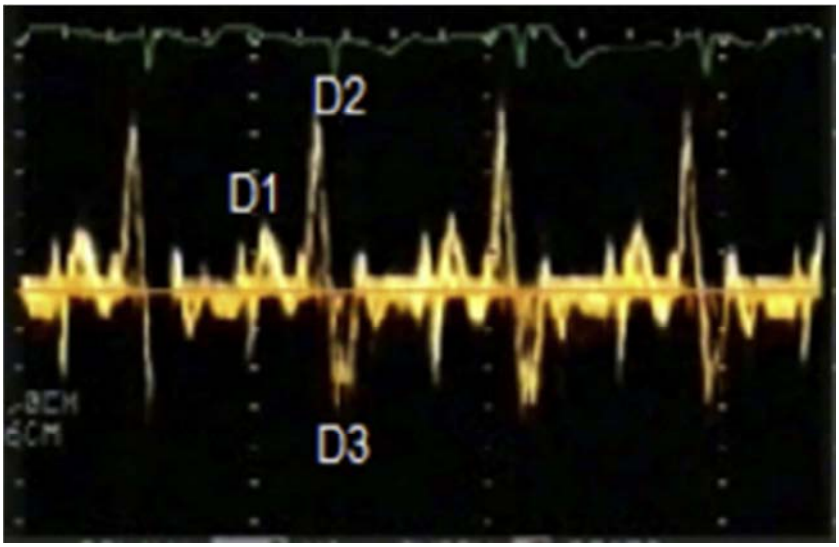

Figure 3. *LAA flow velocity by Tissue Doppler. D1-E_{LAA} velocity, D2-A_{LAA} velocity, D3-S_{LAA} velocity.*

SEC grading was done as per scheme proposed for semi-quantitative grading of the severity of SEC on echocardiography (Table 1) (Figure 4) [7].

Table 1. *Grading of spontaneous echo contrast on echocardiography.*

Grade	Definition
0	None (absence of echogenicity)
1+	Mild (minimal echogenicity located in the LA appendage or sparely distributed in the main cavity of the left atrium; may be detectable only transiently during the cardiac cycle; imperceptible at operating gain settings for two dimensional echocardiographic analysis)
2+	Mild to moderate (more dense swirling pattern than grade 1+ but with similar distribution; detectable without increased gain settings)
3+	Moderate (dense swirling pattern in the LAA, generally associated with somewhat lesser intensity in the main cavity; may fluctuate in intensity but detectable constantly throughout the cardiac cycle)
4+	Severe (intense echo density and very slow swirling patterns in the LAA, usually with similar density in the main cavity)

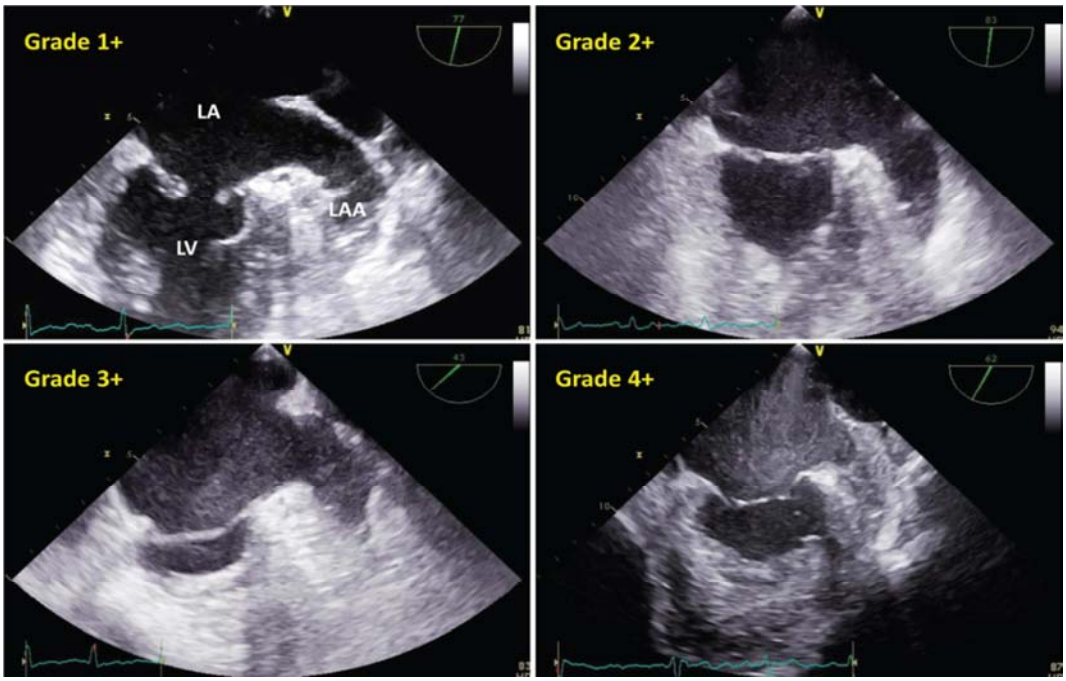

Figure 4. *TEE images showing SEC grads 1+ to 4+ in four cases.*

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.

2.4. Statistical Methods

The data was analyzed by using statistical soft ware SPSS Version 17. Results were presented as tables and charts. Continuous variables were presented as mean±SD and categorical variables as percentages. Non parametric continuous variables were tested with paired sample t-test. Spearman's correlation coefficient was used to assess the correlation between SEC grading and LA appendage function.

Probability less than 0.05 was considered as significant.

Microsoft excel 2013 was used to generate the graphs.

3. Results & Observations

Table 2 summarizes the baseline characteristics of the patient population.

Table 2. *Baseline characteristics of the patient population.*

Characteristics	
Mean AGE	32.83±8.75years
SEX	
MALE	20 (29.33%)
FEMALE	55 (73.33%)
Mean BMI	19.78±3.42Kg/m^2
Mean WILKINS SCORE	9.69±0.96
Mean SBP	109.26±10.21mmHg
Mean DBP	70.51±7.78mmHg
Mean HR	77.2±11.39beats/min
NYHA functional class	40 (53.33%) NYHA class II and 35 (46.66%) NYHA class III

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

Total 75 cases were enrolled, mean age among the cases was 32.83±8.75 years. 20 (29.33%) were male and 55 (73.33%) were female. Mean BMI was 19.78±3.42 Kg/m^2. Mean wilkins score was 9.69±0.96. Mean SBP was 109.26±10.21 mmHg, mean DBP was 70.51±7.78 mmHg and Mean HR was 77.2±11.39 beats/min. Among the cases 40 (53.33%) had NYHA class II symptoms and 35 (46.66%) had NYHA class III symptoms.

Table 3. *Comparison of Left Atrial Appendage Function amongst Patients With and Without SEC.*

Sr. No.	**Variables**	**Pts. with no SEC0 [N-25]**		**Pts. with SEC+ [N-50]**		**'t' test**	**'p' value**	**Significance**
		Mean	**SD**	**Mean**	**SD**			
1.	LAAAC%	52.95	1.48	46.75	33.75	7.31	0.001	Significant
2.	LAAEDE Velocity (cm/s)	13.93	1.25	11.02	1.96	6.25	0.001	Significant

Sr. No.	Variables	Pts. with no SEC0 [N-25]		Pts. with SEC+ [N-50]		't' test	'p' value	Significance
		Mean	SD	Mean	SD			
3.	LAALDE Velocity (cm/s)	25.15	3.42	21.73	4.96	2.87	0.005	Significant
4.	LAAF Velocity (cm/s)	33.2	4.35	28.84	6.06	2.98	0.004	Significant
5.	E_{LAA} Velocity (cm/s)	6.80	1.67	6.2	1.48	1.51	0.13	Not Significant
6.	A_{LAA} Velocity (cm/s)	12.27	2.58	11.41	2.24	1.4	0.16	Not Significant
7.	S_{LAA} Velocity (cm/s)	9.33	1.77	8.98	1.2	0.74	0.45	Not Significant

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

Table 3 and Figure 5 shows comparison of left atrial appendage function in patients with and without SEC before PTMC.

Among the cases, 21 subjects had no SEC and 49 subjects had SEC on TEE. LAAAC (%) and PW Doppler velocities [LAAEDE Velocity (cm/s), LAALDE Velocity (cm/s), LAAF Velocity (cm/s)] were significantly less in patients who had SEC than patients who do not had SEC ($p<0.05$).

LAA Tissue Doppler velocities [E_{LAA} Velocity (cm/s), A_{LAA} Velocity (cm/s), S_{LAA} Velocity (cm/s)] were also less in patients who had SEC than patients without SEC but it was statistically not significant ($p>0.05$).

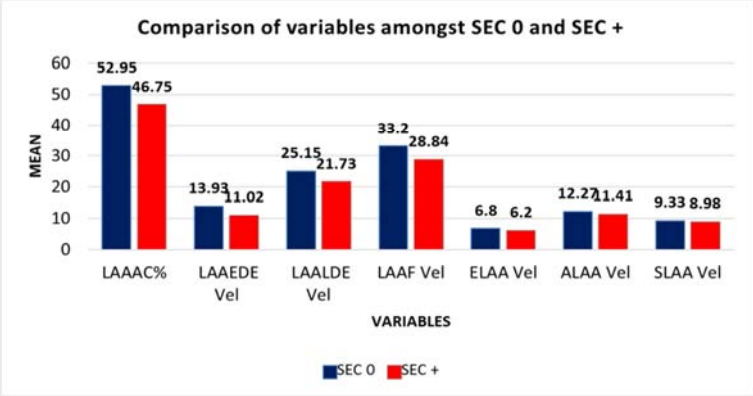

Figure 5. *Comparison of LAA function in patients with and without SEC.*

Table 4. *Correlation between SEC grading and Left Atrial Appendage Function Parameters among the cases.*

Sr. No.	SECgrading and LAAparameters	CorrelationCoefficient	Pvalue	Significance
1.	SEC and LAAAC (%)	-0.838	<0.001	Significant
2.	SEC and LAAEDE Velocity (cm/s)	-0.816	<0.001	Significant
3.	SEC and LAALDE Velocity (cm/s)	-0.582	<0.001	Significant
4.	SEC and LAAF velocity (cm/s)	-0.45	<0.001	Significant
5.	SEC and E_{LAA}-(cm/s)	-0.23	0.55	Not Significant
6.	SEC and A_{LAA} (cm/s)	-0.21	0.8	Not Significant
7.	SEC and S_{LAA} (cm/s)	-0.072	0.55	Not Significant

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

Table 4 shows correlation between SEC grading and LAA function among the cases before PTMC.

There was a significant negative correlation between SEC grading and LAAAC (%) and LAA PW Doppler velocities (LAAEDE Velocity, LAALDE Velocity and LAAF velocity) ($p<0.001$), i.e. greater the degree of SEC, lesser was the LAAAC (%), LAAEDE Velocity, LAALDE Velocity and LAAF velocity.

There was also negative correlation between SEC grading and LAA Tissue Doppler velocities (E_{LAA} Velocity, A_{LAA} Velocity, S_{LAA} Velocity) but it was statistically not significant ($p>0.05$).

Table 5. *Effect of PTMC on SEC grading among the study subjects.*

Sr. No.	SEC Grading	Pre PTMC	Immediately Post PTMC	6 months Post PTMC
1.	SEC0	25	44	50
2.	SEC1+	18	24	22
3.	SEC2+	25	07	03
4.	SEC3+	5	00	00
5.	SEC4+	2	00	00
Total		75	75	75

SEC- Spontaneous echo contrast; PTMC- Percutaneous Transvenous Mitral Commissurotomy.

Table 5 shows effect of PTMC on SEC grading among the study subjects.

PrePTMC, 25 subjects had no SEC, 18 subjects had SEC1+, 25 subjects had SEC2+, 5 subjects had SEC3+ and 2 subjects had SEC4+. Immediately PostPTMC prevalence of SEC reduced so that 44 subjects had no SEC, 24 subjects had SEC1+, only 7 subjects had SEC2+ and none of the subjects had SEC3+ or 4+. 6months Post PTMC prevalence of SEC further reduced, 50 subjects had no SEC, 22 subjects had SEC1+, only 3 subjects had SEC2+ and none of the subjects had SEC3+ or 4+.

4. Discussion

In 1983, Sigel *et al*. found in their experimental study that SEC indicated red cell aggregation by demonstrating that SEC severity, as determined by the video densitometric method, correlated positively with hematocrit and fibrinogen concentration, and inversely with shear stress [8-10]. Black *et al*. confirmed the relationship between SEC and blood components in patients with atrial fibrillation (AF), and found that LA SEC appeared in relation to hematocrit, fibrinogen concentration and LA dimension, but not to platelet count [11]. In patients with MS, due to low flow velocity and low shear conditions, RBC aggregates form by noncovalent binding between red cells and plasma proteins. RBC aggregates thus formed lead to increased blood echogenicity causing ultrasonic backscatter and produce a pattern of smoke or SEC in LA. SEC is associated with clot formation and embolic phenomena.

4.1. Comparison of Baseline Left Atrial Appendage Function in Patients with and Without SEC Before PTMC

In the present study mean LAAAC% and LAA PW Doppler velocities were significantly less in patients with SEC when compared with patients without SEC implying more severe LAA dysfunction in patients with SEC. LAA Tissue Doppler velocities were also less in patients with SEC compared to patients without SEC but it was statistically not significant. Thus presence of SEC could be an indicator of severe LAA dysfunction among patients of severe rheumatic MS, who are at high risk of systemic thromboembolism.

4.2. Correlation of SEC Grading with Left Atrial Appendage Function Before PTMC Among the Cases

In the present study we correlated degree of SEC with LAA function among the cases, there was a significant negative correlation between SEC grading and LAAAC (%) and LAA PW Doppler velocities (LAAEDE Velocity, LAALDE Velocity and LAAF velocity), i.e. greater the intensity of SEC lesser was the LAAAC (%), LAAEDE Velocity, LAALDE Velocity and LAAF velocity, suggesting more severe LAA dysfunction among patients with greater degree of SEC. There was also negative correlation between SEC grading and LAA Tissue Doppler velocities (E_{LAA} Velocity, A_{LAA} Velocity, S_{LAA} Velocity) but it was statistically not significant. Thus greater density of SEC indicates greater severity of LAA dysfunction and higher risk of thrombus formation among patients of severe rheumatic MS.

4.3. Effect of PTMC on SEC Grading

In the present study before PTMC out of 75 cases, SEC was present in 50 (66.66%) cases. Immediately post PTMC SEC completely disappeared in 19 cases and reduced in 31 cases. At 6months follow up SEC completely disappeared in 25 cases and reduced in another 25 cases, hence successful PTMC results in gradual improvement of SEC by improving LAA function and may reduce future risk of thromboembolism. This result was similar to previous studies [6, 12-16].

5. Conclusions

Among the patients of severe rheumatic MS, presence of SEC is an indirect evidence of severe LAA dysfunction, greater the intensity of SEC, greater would be the severity of LAA dysfunction and higher risk of systemic thromboembolism even in patients who are in sinus rhythm and successful PTMC results in gradual improvement of SEC, hence relief of MS by PTMC not only provide hemodynamic benefits with symptomatic improvement but also reduces the future risk of thromboembolism by decreasing SEC formation which is the harbinger of thrombus formation.

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

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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