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Effect of oral anticoagulation on left atrial appendage thrombus resolution in patients with rheumatic mitral stenosis: A prospective observational study.

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Abstract

Background:
Rheumatic mitral stenosis (MS) remains a major cause of cardiovascular morbidity in developing countries and is frequently complicated by atrial fibrillation and left atrial appendage (LAA) thrombus formation. The presence of LAA thrombus significantly increases thromboembolic risk and contraindicates interventional procedures such as percutaneous transvenous mitral commissurotomy (PTMC).

Objectives:
To evaluate the effect of oral anticoagulation on the resolution of left atrial appendage thrombus in patients with rheumatic mitral stenosis and to identify clinical and echocardiographic predictors of thrombus clearance.

Methods:
This prospective hospital-based observational study was conducted in the Department of Cardiology, Indira Gandhi Institute of Medical Sciences, Patna. Thirty patients with severe isolated rheumatic mitral stenosis and documented LAA thrombus on transesophageal echocardiography (TEE) were enrolled. All patients received oral anticoagulation with acenocoumarol and were followed for 12 weeks with weekly INR monitoring, targeting a therapeutic range of 2.0–2.5.

Results:
Most patients were young adults with a female predominance, and atrial fibrillation was present in 73.3%. Oral anticoagulation led to a significant reduction in mean LAA thrombus size from 5.34 ± 4.42 cm^2 at baseline to 3.82 ± 4.03 cm^2 after treatment. A substantial proportion of patients achieved complete thrombus resolution, while others demonstrated partial clearance. Reduction in spontaneous echo contrast intensity was also observed. Thrombus resolution was more likely in patients with smaller baseline thrombus size, sinus rhythm, lower left atrial dimensions, higher LAA emptying velocities, and sustained therapeutic INR levels.

Conclusion:
Oral anticoagulation with acenocoumarol is effective in achieving complete or partial resolution of left atrial appendage thrombus in patients with rheumatic mitral stenosis. Adequate INR control and favorable echocardiographic parameters play a critical role in thrombus clearance.

Recommendation:
Structured vitamin K antagonist therapy with strict INR monitoring and repeat transesophageal echocardiography should be routinely employed before considering interventional procedures in this high-risk population.

Keywords: *Rheumatic mitral stenosis; Left atrial appendage thrombus; Oral anticoagulation; Transesophageal echocardiography; Acenocoumarol*
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Introduction

Rheumatic heart disease (RHD) remains a major public health problem in low- and middle-income countries, despite a marked decline in its incidence in developed nations [1]. It is a chronic sequela of acute rheumatic fever following Group A β-hemolytic streptococcal infection. Among the valvular lesions caused by RHD, rheumatic mitral stenosis (MS) is the most prevalent and clinically significant, contributing substantially to morbidity and mortality in endemic regions [2].

Progressive narrowing of the mitral valve orifice in rheumatic MS leads to chronically elevated left atrial pressure, atrial dilatation, and structural remodeling. These changes predispose patients to atrial fibrillation and intracardiac thrombus formation, particularly within the left atrial appendage (LAA) [3]. The LAA is especially prone to thrombus formation due to its trabeculated anatomy, reduced contractility, and low flow velocities, conditions that are further exacerbated by atrial fibrillation and severe mitral obstruction [4]. Studies have reported left atrial thrombus in 10–30% of patients with rheumatic MS, with over 90% of thrombi located in the LAA [5].

The presence of LAA thrombus has major clinical implications. It markedly increases the risk of systemic thromboembolism, especially ischemic stroke, which is associated with high mortality and long-term disability [6]. Conventional stroke risk stratification tools, such as the CHA_2DS_2-VASc score, underestimate thromboembolic risk in rheumatic MS, making anticoagulation decisions largely independent of these scores [7]. Furthermore, LAA thrombus is an absolute contraindication to procedures such as percutaneous transvenous mitral commissurotomy, cardioversion, and catheter-based rhythm control, due to the risk of catastrophic embolization [8].

Transesophageal echocardiography (TEE) is the gold standard for detecting LAA thrombus and spontaneous echo contrast, offering superior sensitivity compared to transthoracic echocardiography and allowing functional assessment of the LAA [9,10]. Oral anticoagulation with vitamin K antagonists remains the recommended therapy for patients with rheumatic MS, as direct oral anticoagulants are contraindicated in this population [11]. Sustained therapeutic anticoagulation has been shown to promote partial or complete thrombus resolution; however, reported outcomes vary widely and depend on factors such as thrombus size, atrial rhythm, left atrial dimensions, and adequacy of INR control [12].

Despite the high burden of rheumatic MS in India, prospective data evaluating the effectiveness of oral anticoagulation in resolving LAA thrombus using serial echocardiographic assessment are limited. Therefore, this study aimed to evaluate the effect of oral anticoagulation on left atrial appendage thrombus resolution in patients with rheumatic mitral stenosis and to identify clinical and echocardiographic predictors of thrombus clearance.

Materials & Methods

Study Design and Setting

Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, is a tertiary care referral center catering to patients from Bihar and neighboring states. The study was conducted in the Department of Cardiology. After receiving approval from the Institutional Ethics Committee of IGIMS, Patna, the study was conducted within the time frame stated in the approved DM Cardiology thesis.

Study Population and Sample Size

A **consecutive sampling technique** was used, and all eligible patients meeting the inclusion criteria during the study period were enrolled. The sample size of 30 patients was determined based on the availability of eligible patients with documented left atrial appendage thrombus during the study period, in accordance with the approved DM Cardiology thesis protocol. The study included thirty patients with documented left atrial appendage (LAA) thrombus and severe isolated rheumatic mitral stenosis. All eligible patients who met the inclusion criteria and presented throughout the study period were included in the sample size, which was established in accordance with the thesis procedure.

Inclusion Criteria

Patients were included in the study if they met all of the following criteria:

- Diagnosis of severe rheumatic mitral stenosis, confirmed by transthoracic echocardiography
- Mitral valve anatomy suitable for percutaneous transvenous mitral commissurotomy (PTMC)
- Presence of left atrial appendage thrombus detected on transesophageal echocardiography

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- NYHA functional class I to III
- Patients newly initiated on oral anticoagulation and not on prior long-term anticoagulant therapy
- Willingness to provide written informed consent

Exclusion Criteria

Patients were excluded if they had:

- NYHA functional class IV symptoms
- Moderate to severe mitral valve calcification
- Left atrial body thrombus (outside the appendage)
- Moderate to severe mitral regurgitation or significant involvement of other cardiac valves
- Major systemic comorbidities such as chronic kidney disease, liver dysfunction, or malignancy
- History of previous cardiac surgery, including closed or open mitral valvotomy
- Pregnancy or puerperium
- Refusal to give informed consent

Baseline Clinical Evaluation

All enrolled patients underwent a detailed clinical assessment at baseline. This included:

- Demographic data (age, sex, socioeconomic status)
- Symptom evaluation, including dyspnea, orthopnea, paroxysmal nocturnal dyspnea, palpitations, chest pain, and hemoptysis
- Functional assessment using the New York Heart Association (NYHA) classification
- History of prior thromboembolic events
- Comprehensive physical examination with emphasis on cardiovascular and respiratory systems

Electrocardiographic and Radiological Assessment

A 12-lead electrocardiogram (ECG) was performed in all patients to document cardiac rhythm, with particular attention to the presence of atrial fibrillation. Chest radiography was obtained to assess cardiac size and pulmonary vasculature. Repeat ECGs were performed during follow-up if rhythm changes were suspected.

Echocardiographic Evaluation

All patients underwent baseline transthoracic echocardiography (TTE) followed by transesophageal echocardiography (TEE) [13].

TTE assessment included:

- Mitral valve area by planimetry
- Peak and mean transmitral gradients
- Wilkins score
- Left atrial dimension and volume
- Pulmonary artery systolic pressure

The TEE assessment focused on:

- Presence, size, and morphology of LAA thrombus
- Measurement of thrombus dimensions
- Presence and severity of left atrial spontaneous echo contrast (SEC)
- Left atrial appendage area
- Left atrial appendage ejection fraction
- Left atrial appendage emptying velocity

Anticoagulation Protocol

All patients were initiated on oral anticoagulation with acenocoumarol (Acitrom) at a starting dose of 2–3 mg daily. The dosage was titrated based on weekly prothrombin time and international normalized ratio (INR) monitoring [14].

- Target INR range: 2.0 to 2.5
- Patients were followed weekly for 12 weeks
- INR values, symptoms, adverse events, and compliance were documented at each visit

Concomitant medical therapy included beta-blockers, diuretics, digoxin, and penicillin prophylaxis as clinically indicated.

Follow-Up and Outcome Assessment

After 8 weeks of continuous therapeutic anticoagulation, repeat TTE and TEE were performed in all patients. The following outcomes were assessed:

- **Complete resolution**, partial resolution, or persistence of LAA thrombus
- Change in thrombus size compared to baseline
- Change in the presence or severity of left atrial spontaneous echo contrast
- Suitability for PTMC following thrombus resolution

Patients were also monitored for anticoagulation-related complications, including bleeding and thromboembolic events [15].

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Statistical Analysis

IBM SPSS Statistics for Windows, Version 21.0, was used to evaluate the data once it had been entered into Microsoft Excel.

- Frequencies and percentages were used to express categorical data, whereas mean ± standard deviation (SD) was used to express continuous variables.
- Based on the distribution of the data, the proper statistical tests were used.
- A statistically significant p-value was less than 0.05.

Bias control

To minimize selection and measurement bias, standardized inclusion criteria were applied, all echocardiographic examinations were performed using uniform protocols, and follow-up imaging was conducted by experienced cardiologists blinded to baseline thrombus measurements.

Results

Demographic Characteristics

The investigation comprised thirty individuals with documented left atrial appendage (LAA) thrombosis and rheumatic mitral stenosis. With 50% of patients in the 21–30 age range and 23.3% in the 31–40 age range, the study population was primarily young. The early disease burden of rheumatic mitral stenosis in the study population is highlighted by the fact that only 10% of patients were over 40.

Table 1. Age-wise distribution of patients

Age group (years)	Frequency	Percentage
≤20	5	16.7%
21–30	15	50.0%
31–40	7	23.3%
>40	3	10.0%
Total	**30**	**100%**

There was a definite female preponderance (66.7%), which is in line with the rheumatic heart disease epidemiology in emerging nations.

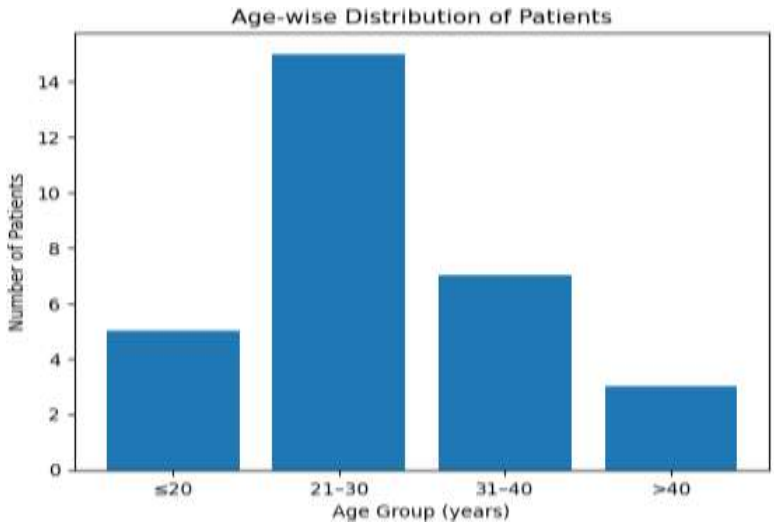

Figure 1: Age-wise distribution of patients with rheumatic mitral stenosis and left atrial appendage thrombus.

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Table 2. Sex-wise distribution

Sex	Frequency	Percentage
Female	20	66.7%
Male	10	33.3%
Total	30	100%

Clinical Profile

The most frequent symptom that appeared was dyspnea. At presentation, nearly 80% of patients had moderate to severe dyspnea, indicating extensive hemodynamic compromise.

Table 3. Severity of shortness of breath

Severity	Frequency	Percentage
Mild	6	20.0%
Moderate	14	46.7%
Severe	10	33.3%
Total	30	100%

NYHA class II was the most prevalent category (53.3%), followed by class III (26.7%), according to the functional status evaluation. According to the exclusion criteria, no patients were in NYHA class IV.

Table 4. NYHA functional class distribution

NYHA Class	Frequency	Percentage
Class I	6	20.0%
Class II	16	53.3%
Class III	8	26.7%
Total	30	100%

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43.3% of patients had orthopnea or paroxysmal nocturnal dyspnea, which suggests a substantial increase in left atrial pressure.

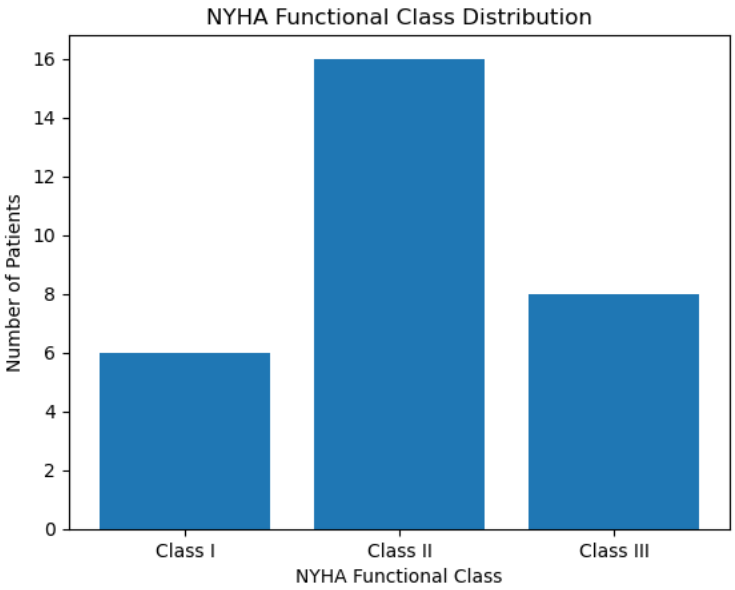

Figure 2: Distribution of NYHA functional class in the study population.

Table 5. Orthopnea/PND distribution

Symptom	Frequency	Percentage
Present	13	43.3%
Absent	17	56.7%
Total	30	100%

Socioeconomic and Electrocardiographic Findings

The majority of patients (86.7%) were from lower socioeconomic groups, highlighting the substantial correlation between socioeconomic hardship and rheumatic heart disease.

Table 6. Socioeconomic status

Status	Frequency	Percentage
Lower	26	86.7%
Middle	4	13.3%
Total	30	100%

Atrial fibrillation was found in 73.3% of patients by electrocardiographic examination, confirming its high correlation with LAA thrombus development in rheumatic mitral stenosis.

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Table 7. ECG rhythm distribution

Rhythm	Frequency	Percentage
Atrial fibrillation	22	73.3%
Sinus rhythm	8	26.7%
Total	30	100%

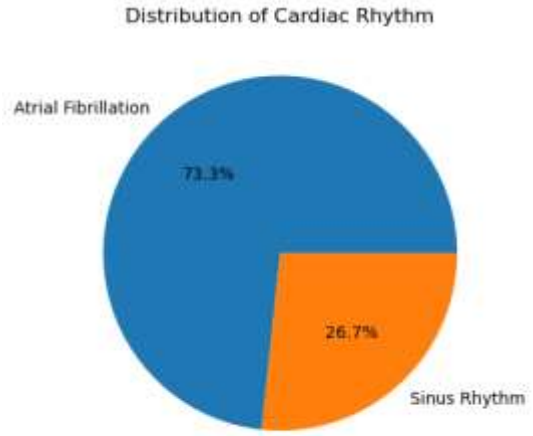

Figure 3: Distribution of cardiac rhythm among patients with left atrial appendage thrombus.

Baseline Echocardiographic and Hemodynamic Parameters

With a mean mitral valve size of 0.98 ± 0.25 cm², the baseline echocardiogram showed significant mitral stenosis. Chronic pressure overload was indicated by significantly enlarged left atrial volumes and dimensions. In line with a high-risk thrombogenic environment, LAA functional metrics revealed decreased appendage function, low emptying velocities, and a decreased ejection fraction.

Table 8. Baseline clinical and echocardiographic parameters

Parameter	Mean ± SD
PT/INR	2.29 ± 0.49
Mitral valve area (cm²)	0.98 ± 0.25
Peak MV gradient (mmHg)	24.47 ± 2.86
Mean MV gradient (mmHg)	13.97 ± 1.71
Wilkins score	7.20 ± 1.27
LA dimension (cm)	4.97 ± 0.74
LA volume (ml)	166.47 ± 27.27
LAA area (cm²)	6.00 ± 1.27
LAA ejection fraction (%)	19.60 ± 4.79
LAA emptying velocity (cm/s)	22.70 ± 14.97

Effect of Oral Anticoagulation on LAA Thrombus

LAA thrombus size was significantly reduced with oral anticoagulation therapy with acenocoumarol and maintenance of therapeutic INR. After 12 weeks of treatment, the mean thrombus size dropped from 5.34 ± 4.42 cm² to 3.82 ± 4.03 cm².

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Table 9. Change in LAA thrombus size

Thrombus Size	Mean ± SD (cm²)
Pre-anticoagulation	5.34 ± 4.42
Post-anticoagulation (12 weeks)	3.82 ± 4.03

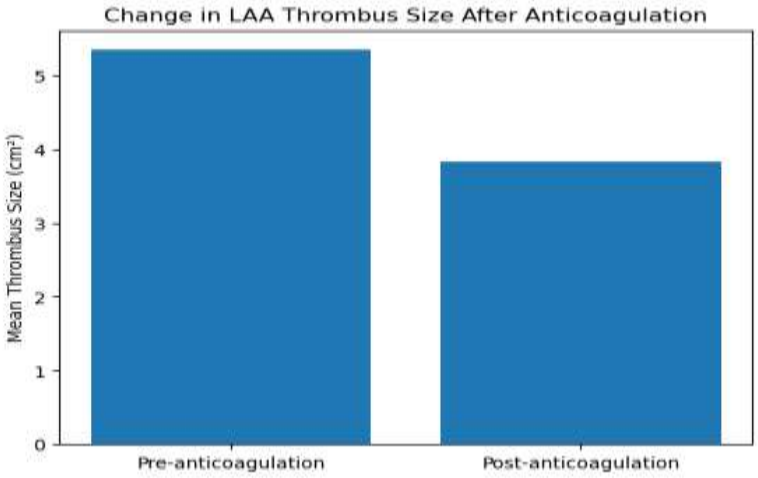

Figure 4: Reduction in left atrial appendage thrombus size following oral anticoagulation therapy.

Some patients had partial thrombus clearance, whereas others showed complete resolution. Patients with atrial fibrillation, bigger left atrial size, and lower LAA emptying velocities were more likely to have persistent thrombus.

Effect on Left Atrial Spontaneous Echo Contrast

96.7% of patients had left atrial spontaneous echo contrast (SEC) on TEE at baseline. There was a discernible decrease in SEC intensity after anticoagulant treatment, which coincided with improvements in appendage flow dynamics and a decrease in thrombus size.

Table 10. Presence of spontaneous echo contrast

SEC Status	Baseline (%)	Post-anticoagulation (%)
Present	96.7%	Reduced in the majority
Absent	3.3%	Increased proportion

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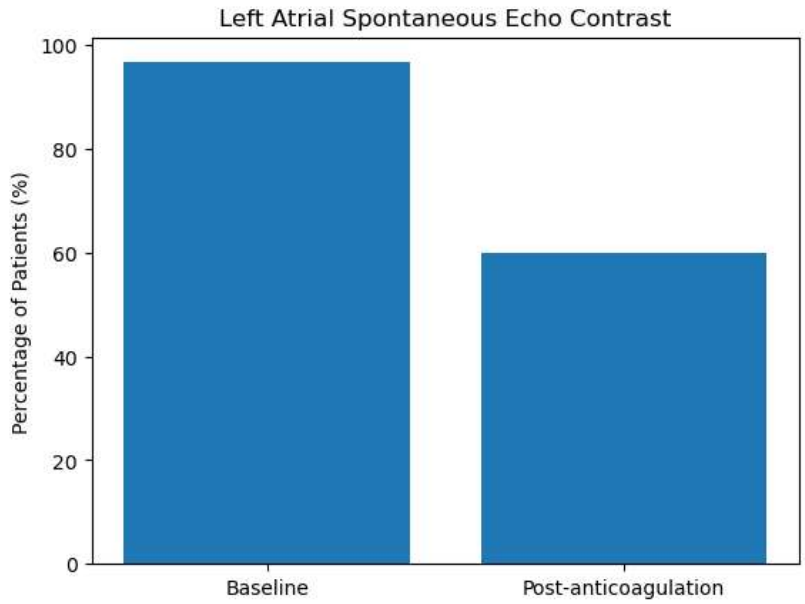

Figure 5: Change in left atrial spontaneous echo contrast following anticoagulation therapy.

Predictors of LAA Thrombus Resolution

Complete thrombus resolution was more frequently observed in patients with sinus rhythm, smaller baseline thrombus size, lower left atrial dimension, higher left atrial appendage emptying velocity, and sustained therapeutic INR levels throughout follow-up. Persistent thrombus was commonly associated with atrial fibrillation, larger left atrial size, and reduced appendage function.

Discussion

In developing nations, rheumatic mitral stenosis continues to be a substantial cause of cardiovascular morbidity. Its correlation with atrial fibrillation and left atrial appendage thrombus increases the risk of systemic thromboembolism. The current study used serial echocardiographic evaluation in a real-world tertiary care setting to investigate the impact of oral anticoagulation on LAA thrombus clearance in patients with rheumatic mitral stenosis. The results of this investigation shed light on the clinical and echocardiographic variables affecting thrombus clearance in this high-risk group as well as the efficacy of vitamin K antagonist-based anticoagulation.

The study population's demographic profile emphasizes how rheumatic mitral stenosis can cause major difficulties at a young age. The age group of 21 to 30 years old accounted for more than half of the cases, with a definite female predominance. This finding is in line with earlier research conducted in India and around the world, which found that young adults and women, especially those from socioeconomically deprived backgrounds, had a greater frequency of rheumatic heart disease [16,17]. The study's large percentage of patients from lower socioeconomic backgrounds supports the documented connection between rheumatic heart disease and insufficient primary and secondary prevention, poverty, and limited access to healthcare.

Nearly three-fourths of the patients in our group had atrial fibrillation, highlighting its crucial role in the pathophysiology of left atrial appendage thrombus in rheumatic mitral stenosis. A substrate for atrial fibrillation and blood stasis within the left atrial appendage is created by chronic pressure overload of the left atrium, which causes atrial dilatation, fibrosis, and electrical remodeling. Atrial fibrillation is the most significant clinical predictor of thrombus development in rheumatic mitral stenosis, according to several previous investigations [18, 19]. Patients with persistent AF had a much higher prevalence of

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thrombus than those in sinus rhythm. These observations are consistent with the current study's findings.

All patients had severe mitral stenosis, with significantly decreased mitral valve area and increased transmitral gradients, according to echocardiographic evaluation. All patients had left atrial enlargement and increased left atrial volume, which were indicative of severe illness and chronic pressure overload. Significantly, low emptying velocities and a lower LAA ejection fraction on baseline transesophageal echocardiography indicated compromised left atrial appendage function. Previous investigations have consistently linked these parameters to an elevated risk of thrombus development and embolic events [20,21]. The extreme degree of atrial blood stasis is further highlighted by the nearly universal occurrence of spontaneous echo contrast at baseline in this sample.

This study's main finding is that oral anticoagulation with acenocoumarol significantly reduced the size of the left atrial appendage thrombus. The mean thrombus size significantly decreased over a period of continuous therapeutic anticoagulation; some patients showed total resolution, while others showed partial clearance. These results demonstrate that vitamin K antagonist medication is beneficial in both preventing thromboembolic events and promoting the clearance of pre-existing thrombi. Previous observational studies have reported similar resolution rates, with 60–75% of patients achieving complete thrombus clearance following 4–8 weeks of therapeutic anticoagulation [22, 23].

Numerous factors seem to have an impact on the variation in thrombus resolution seen among the patients in this study. Full or almost full thrombus clearance was more common in patients with sinus rhythm, smaller left atrial dimensions, greater LAA emptying velocities, and sustained therapeutic INR levels. On the other hand, patients with atrial fibrillation, bigger atrial size, and significantly reduced appendage function were more likely to experience persistent thrombus. These results are consistent with earlier studies that found rhythm status, left atrial size, and LAA flow velocity to be significant predictors of thrombus persistence [24, 25]. Additionally, it has been consistently demonstrated that poor INR control limits thrombus resolution and raises embolic risk, underscoring the significance of routine monitoring and dose modification [26].

The decrease in left atrial spontaneous echo contrast intensity after anticoagulant medication was a significant supplementary finding in this investigation. SEC is a low-flow, prothrombotic state in the atrium, but it is not a thrombus in and of itself. A decrease in red blood cell aggregation and an improvement in atrial blood flow dynamics are reflected in a reduction in SEC, which may be a factor in both thrombus regression and decreased embolic potential. Even in the absence of apparent thrombus, previous research has shown that dense SEC is independently linked to thrombus development and stroke risk [27]. Thus, the physiological effect of long-term therapeutic anticoagulation in rheumatic mitral stenosis is further supported by the reported improvement in SEC after anticoagulation.

The current study's conclusions have significant clinical ramifications. First, they support existing guidelines that advocate vitamin K antagonists as the preferred anticoagulant for individuals with atrial fibrillation and rheumatic mitral stenosis [28]. Secondly, they emphasize the need for imaging-guided follow-up with transesophageal echocardiography before electrical cardioversion or percutaneous transvenous mitral commissurotomy. Without confirming imaging, relying only on the length of anticoagulation may put patients at unnecessary risk for emboli. Third, clinicians may be able to tailor the length of anticoagulation and the timing of intervention by identifying predictors of thrombus clearance.

The results of the study must be understood in light of several limitations, notwithstanding its merits. The study was carried out at a single location and had a rather small sample size, which may restrict generalizability. Long-term consequences were not evaluated, such as thrombus recurrence, stroke, or bleeding issues after the follow-up period. Furthermore, as direct oral anticoagulants are currently contraindicated in this population, the trial only examined vitamin K antagonist therapy, making it unable to assess comparative efficacy. However, the study offers useful prospective data from a cohort of Indians, a group that is still underrepresented in major clinical studies.

In summary, the current study shows that individuals with rheumatic mitral stenosis can significantly reduce and, in many cases, completely resolve left atrial appendage thrombus with oral anticoagulation with acenocoumarol. Treatment response is mostly dependent on good echocardiographic characteristics, rhythm condition, and adequate INR management. These results highlight the significance of repeated echocardiographic examination and standardized anticoagulation procedures for improving clinical outcomes and procedural safety in this high-risk population.

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Generalizability

Although this study was conducted at a single tertiary care center, the findings apply to similar populations in low- and middle-income countries where rheumatic heart disease remains prevalent and access to advanced interventions is limited.

Conclusion

The current study shows that in patients with rheumatic mitral stenosis, oral anticoagulation with a vitamin K antagonist is beneficial in achieving a considerable reduction and, in a significant proportion of patients, complete clearance of left atrial appendage thrombus. Thrombus regression is largely dependent on the sustained maintenance of therapeutic INR levels, underscoring the significance of routine monitoring and dose modification in clinical practice.

Favorable thrombus resolution was more common in patients with sinus rhythm, smaller left atrial size, improved left atrial appendage functional characteristics, and less advanced atrial remodeling. On the other hand, inadequate or delayed thrombus clearance was linked to persistent atrial fibrillation, significant left atrial enlargement, and significantly reduced appendage emptying, underscoring the necessity of customized anticoagulation methods and prolonged therapy in certain individuals.

The physiological advantage of treatment in enhancing atrial blood flow dynamics and lowering thromboembolic potential is further supported by the reported decrease in left atrial spontaneous echo contrast after anticoagulation. These results support the use of transesophageal echocardiography as a crucial diagnostic technique for left atrial appendage thrombus as well as for directing treatment choices and establishing procedural eligibility.

For the treatment of left atrial appendage thrombus in rheumatic mitral stenosis, structured oral anticoagulation combined with imaging-guided follow-up is an efficient and useful strategy. The study's findings confirm current guidelines that prefer vitamin K antagonists in this high-risk population and contribute to the scant prospective data from the Indian subcontinent. To better identify the ideal duration of anticoagulation, long-term results, and thrombus recurrence predictors, larger multicenter trials with longer follow-up are necessary.

Limitations

This study was limited by its single-center design and relatively small sample size, which may restrict generalizability. Long-term outcomes such as thrombus recurrence and bleeding events were not assessed.

Recommendations

Routine use of vitamin K antagonists with strict INR monitoring and repeat transesophageal echocardiography should be adopted before considering cardioversion or PTMC in patients with rheumatic mitral stenosis and left atrial appendage thrombus.

Abbreviations:

AF – Atrial fibrillation
LAA – Left atrial appendage
MS – Mitral stenosis
PTMC – Percutaneous transvenous mitral commissurotomy
TEE – Transesophageal echocardiography
INR – International normalized ratio

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Conflict of Interest:

The authors declare no conflict of interest.

Data Availability:

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author contributions

PK: Concept, data collection, analysis, manuscript drafting.
RVP: Study supervision, critical revision, and final approval of manuscript.

Author biography

Praveen Kumar is a DM Resident in Cardiology at IGIMS, Patna, with research interests in rheumatic heart disease and echocardiography.

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