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CLINICAL PROFILE AND OUTCOME OF RECURRENT PROSTHETIC HEART VALVE THROMBOSIS IN A TERTIARY CARE CARDIOLOGY UNIT

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Abstract

Background: Recurrent prosthetic valve thrombosis (PVT) poses significant management challenges with limited data on outcomes.

Objective: To evaluate the clinical profile and outcomes of recurrent PVT in a tertiary care setting.

Methods: Twenty-six patients with documented recurrent PVT were studied. Clinical parameters, anticoagulation status, and treatment outcomes were analyzed.

Results: Female predominance was noted (73%), with majority aged 21-40 years (69.1%). Mitral valve involvement occurred in 96% cases. Drug non-compliance was observed in 92% patients, with subtherapeutic INR (<2.0) in 69.2% cases. Atrial fibrillation was present in 65% patients. Thrombolysis resulted in complete recovery in 46% cases, partial recovery in 23%, while mortality was 31%. Thirty-day follow-up showed sustained improvement in 66% of survivors.

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Conclusion: Recurrent PVT predominantly affects young females with mechanical mitral valves. Poor anticoagulation compliance remains the major risk factor. While thrombolysis can be effective, mortality rates are higher compared to primary PVT episodes.

Keywords: Prosthetic valve thrombosis, Recurrent thrombosis, Thrombolysis, Anticoagulation compliance, Mechanical valve, Valve dysfunction

Introduction

Prosthetic heart valve thrombosis (PHVT) remains one of the most serious and potentially life-threatening complications following mechanical valve replacement, presenting significant challenges in both diagnosis and management [1]. Despite advances in prosthetic valve design and anticoagulation protocols, the reported incidence of PHVT ranges from 0.3% to 6% per patient-year in mechanical valves, with higher rates observed in developing countries [2]. Of particular concern is the phenomenon of recurrent PHVT, which not only poses increased mortality risks but also presents complex therapeutic challenges for clinicians [3].

The pathophysiology of PHVT involves a complex interplay of factors, including inadequate anticoagulation, prosthesis-related factors, and patient-specific prothrombotic conditions [4]. Recent data suggests that suboptimal anticoagulation remains the predominant risk factor, accounting for approximately 82% of PHVT cases [2]. The management of PHVT has evolved significantly over the past decades, with treatment options ranging from intensive anticoagulation to fibrinolytic therapy and surgical intervention. However, the optimal management strategy, particularly for recurrent cases, remains a subject of ongoing debate [5].

The clinical presentation of recurrent PHVT can vary significantly, from subtle symptoms to acute hemodynamic compromise, making early recognition crucial for improved outcomes. Studies have shown that patients with a history of PHVT have a 3-fold higher risk of developing subsequent thrombotic events compared to those without previous episodes [6]. This heightened risk necessitates careful monitoring and potentially more aggressive anticoagulation strategies in these patients [7].

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The choice of treatment modality in recurrent PHVT cases depends on multiple factors, including hemodynamic stability, thrombus size, valve location, and the patient's surgical risk profile. While surgical intervention was traditionally considered the gold standard, recent evidence suggests that carefully selected patients may benefit from fibrinolytic therapy, even in recurrent cases [8]. However, the success rates and complications of different treatment strategies in the setting of recurrent PHVT remain inadequately documented in the literature [9].

In developing countries, the management of recurrent PHVT presents additional challenges, including limited healthcare resources, inadequate monitoring facilities, and socioeconomic factors affecting medication compliance. These factors can significantly impact both the incidence and outcomes of recurrent PHVT [10]. Therefore, understanding the clinical profile, risk factors, and treatment outcomes in this specific context becomes crucial for developing appropriate management protocols and improving patient care.

Aims and Objectives

The primary aim of this study was to evaluate the clinical pattern and outcomes of recurrent prosthetic valve thrombosis (PVT) in patients who experienced more than one documented episode with successful thrombolysis. The study sought to analyze the presentation patterns, management strategies, and clinical outcomes in patients with recurrent PVT who were treated at Sri Jayadeva Institute of Cardiovascular Sciences and Research (SJICS&R).

Materials and Methods

Study Design and Population

This observational study was conducted at SJICS&R, enrolling patients who presented with clinical suspicion of PVT and had a documented prior episode that was successfully managed. The study included patients aged above 12 years who were diagnosed with recurrent PVT, confirmed through transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), or fluoroscopy. All included patients had documented evidence of

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a previous PVT episode that was treated successfully. Patients with contraindications to thrombolytic therapy were excluded from the study.

Diagnostic Criteria

The diagnosis of PVT was established based on specific TTE/TEE criteria, which included decreased or absent valve mobility, elevated transvalvar gradients (defined as mean gradient exceeding 8 mmHg for mitral position and 45 mmHg for aortic prosthesis), reduced effective orifice area (less than 1.3 cm^2 for mitral valve), obstructive index less than 0.25 for aortic prosthesis, or direct visualization of thrombus. These parameters were carefully documented for each patient at presentation.

Treatment Protocol

Thrombolytic therapy was initiated after careful evaluation of contraindications, clinical status, and surgical risk assessment. The fibrinolytic regimen consisted of either Streptokinase, administered as a 250,000 U bolus followed by 100,000 U per hour infusion, or Urokinase at 4,400 U/kg per hour infusion. All patients received treatment under continuous monitoring in the intensive care unit.

Clinical Monitoring and Investigations

A comprehensive monitoring protocol was implemented throughout the treatment period. Clinical parameters including hemodynamic status (pulse, blood pressure, and tissue perfusion) were regularly assessed. Laboratory investigations included microbiological analysis with three blood culture and sensitivity samples, complete hemogram with absolute eosinophil count, and coagulation profile measuring prothrombin time, international normalized ratio (INR), and activated partial thromboplastin time (APTT).

Serial TTE/TEE evaluations were performed at admission and subsequently at 6, 12, 18, and 24 hours, as well as pre-discharge, to assess leaflet mobility, regurgitation, and transvalvular gradients. Fluoroscopy was selectively employed to evaluate leaflet mobility and opening and closing angles. Chest radiographs were obtained for all patients. Close monitoring was maintained for bleeding complications, both major and minor, and for any

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cerebrovascular events. Patients requiring emergency surgery due to clinical deterioration were documented.

Study Endpoints

The study defined three primary endpoints: clinical improvement with objective evidence of recovery on TTE/fluoroscopy, occurrence of intracranial hemorrhage or other major bleeding complications, or elapse of 24-48 hours without complete response to therapy. Follow-up was conducted for one month post-discharge, with repeat TTE performed during subsequent visits to evaluate sustained therapeutic response.

Data Collection and Analysis

All clinical, laboratory, and imaging data were systematically collected using standardized forms. Patient demographics, presenting symptoms, treatment details, complications, and outcomes were recorded. The data were analyzed to assess the patterns of presentation, response to therapy, and clinical outcomes in this specific subset of patients with recurrent PVT.

RESULTS :

26 patients were included in this study. 19 female patients (73%) and 7 males were studied (27%). 23 patients presented with second episode of PVT (88.4%) and 3 of them with third episode (11.6%). The age distribution was 10 patients between 31-40 yrs (38.4%), 8 patients between 21-30 yrs (30.7%), 5 patients between 41-50 yrs (19.2%), 1 patient beyond 51 yrs (3%) and 2 patients below 20 yrs (8%). Mitral PVT accounted for 25 cases (96%) and aortic PVT was seen in 1 case. Visible thrombus documented in 4 cases with average burden of < 0.7 cm^2 . Drug non-compliant patients were 24 (92%) in comparison to 2 (8%) drug compliant patients. 17 of them were in NYHA III/IV (65.3%) and 7 in NYHA class I/II (27%) and 2 patients with very minimal symptoms. Regarding valve factor, it was TTK-Chitra (12 cases– 46%), Star Edwards (1case- 0.4%), Medtronic Hall (1case- 0.4%), ATS (7 – 27%), St. Jude's Medical (3 cases-11%), Medtronic tilting disc (1case- 0.4%), unknown (1case). Coagulation profile revealed 18 patients with INR between 1 – 1.9 (69.2%), 7 patients with INR between 2-2.9(27%) and 1 patient with INR

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above 3. Patients were either on Acenocoumarol or Warfarin. 6 patients received additional Aspirin therapy. Average duration of first episode of PVT was 0-4 years and second episode was 12-18 months. 17 patients were in atrial fibrillation (65%) and 9 in sustained sinus rhythm (35%). Left ventricular function was reduced in 4 patients (16%). Most patients had sub-optimal follow up with respect to clinical assessment, TTE or INR. The common reason quoted was lack of lab testing facility and long-distance travel to tertiary care system. Fluoroscopy was done in 10 cases. 3 patients underwent TEE. All patients were thrombolysed with either Streptokinase or Urokinase continuous infusion. Patients were meticulously monitored with respect to hemodynamic parameters, improvement in clinical status, TTE for transvalvar gradients and leaflet mobility, adverse events and final outcome. Clinical improvement and pre-discharge TTE recovery of transvalvar gradients were obtained in 12 patients (46%). Partial gradient recovery (< 50%) was seen in 6 of them (23%). Death resulted in 8 patients (31%) which included 2 cases of third episode of PVT. 1 patient underwent emergency surgery (prosthesis replacement) who died on post-op day 3. No pregnant case was included in this study. 1 post-partum (week 3) patient was included who eventually recovered. Although high risk surgery was contemplated in few cases, could not be materialized owing to reluctance from patient's side. No serious bleeding or intra-cranial bleed was documented, however minor insignificant bleeds were commonly encountered. The 18 patients were followed up after 30 days and 12 of them had sustained normalization of gradients, and 6 of them had mildly increased gradients. Valve mobility established in most cases. All of them remained in stable NYHA status.

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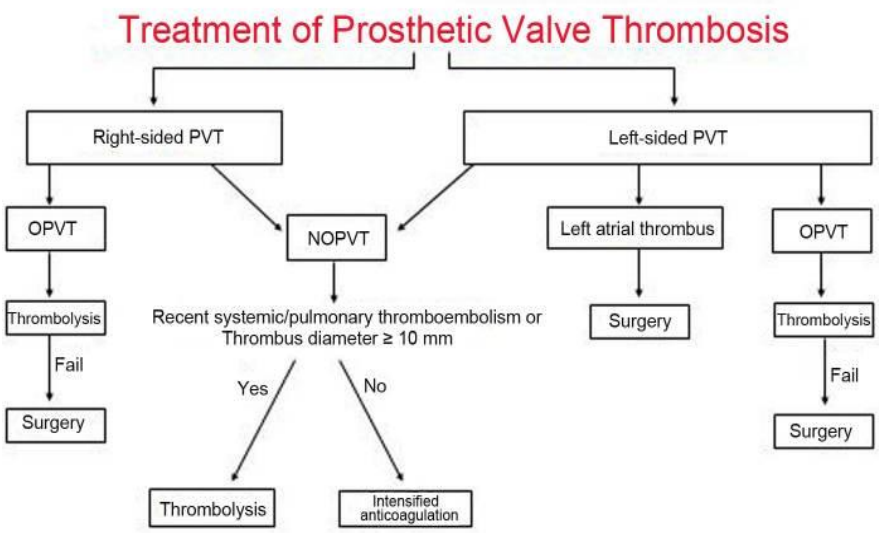

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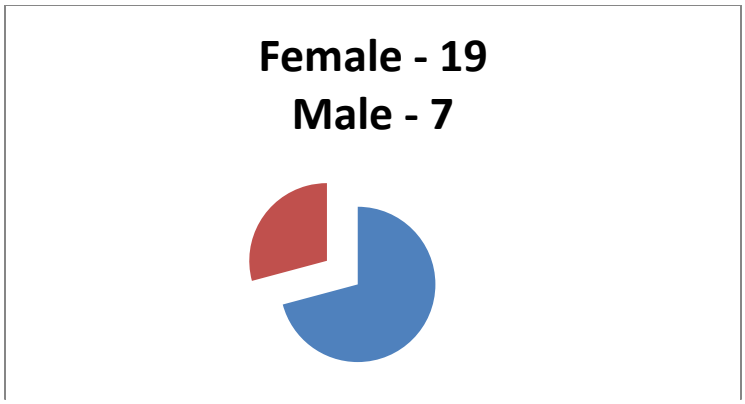

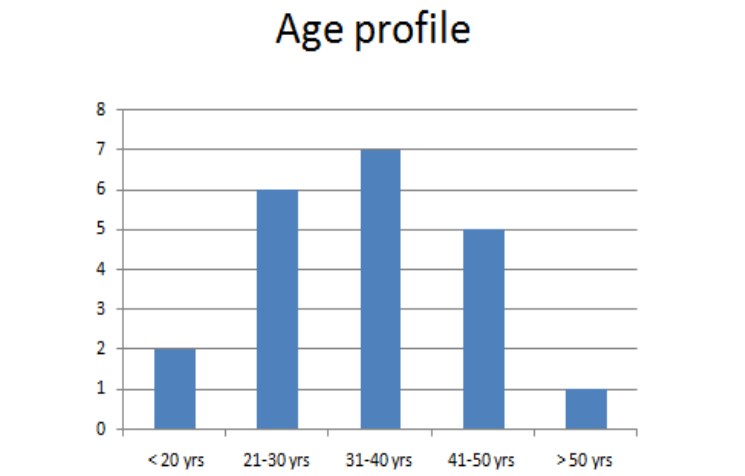

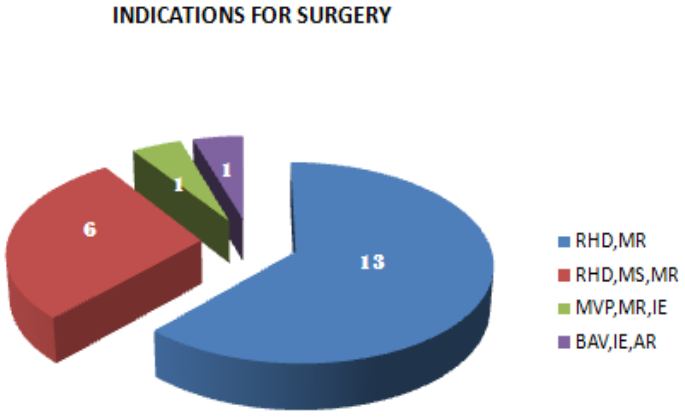

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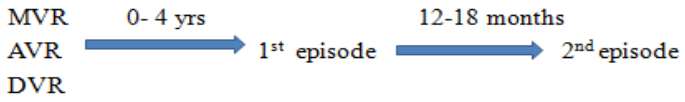
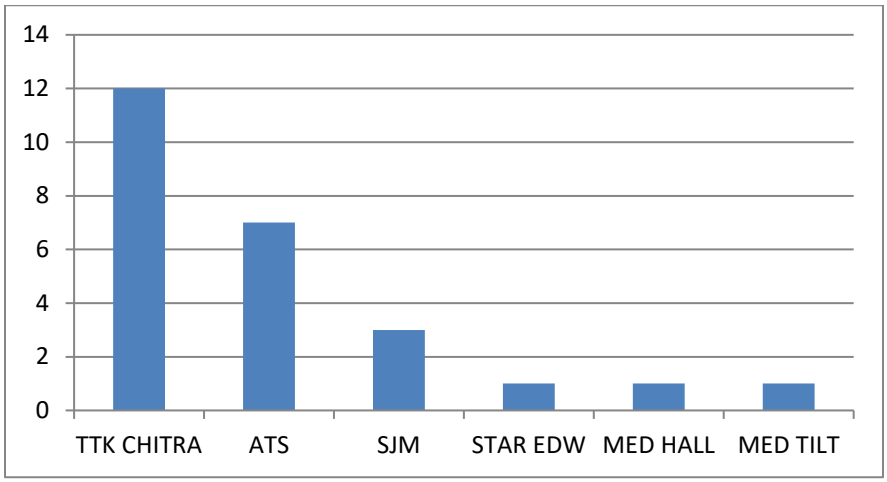
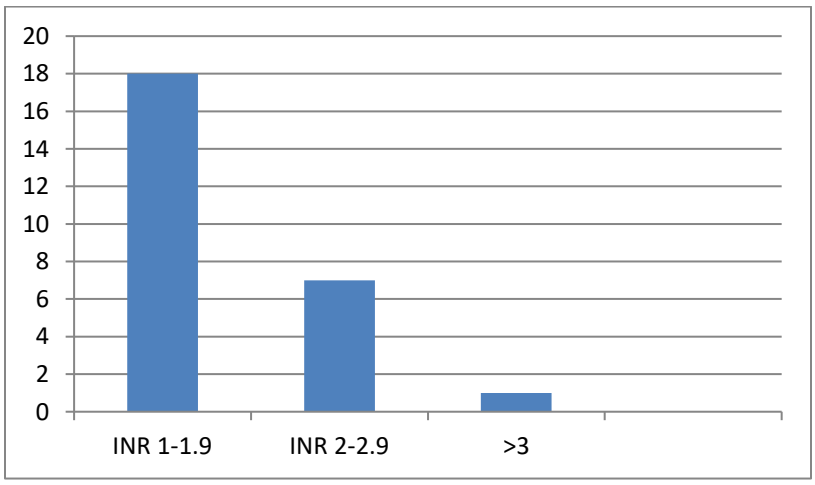


VALVE TYPES



COAGULATION PROFILE



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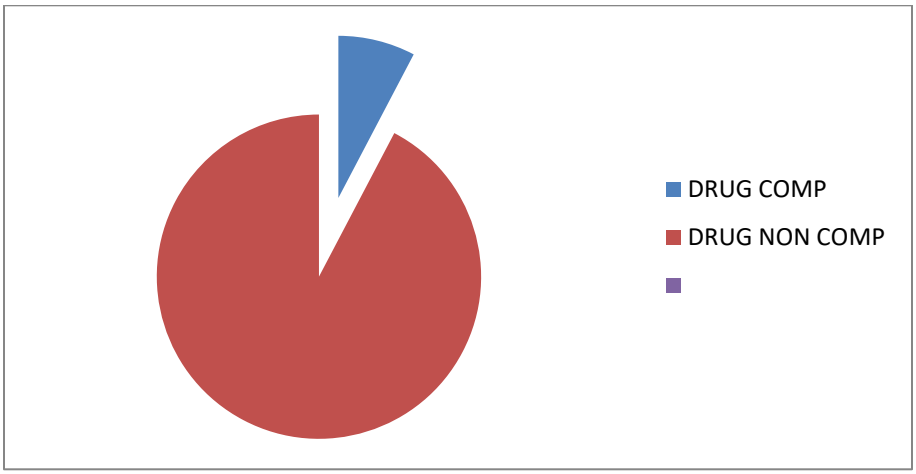
PATIENT DATA

Sr No	Date of SX	1st Episode	2nd Episode	3rd Episode	VALVE
1	Jan-05	Mar-11	Apr-15	Nov-15	TTK-Ch-27mm
2	Mar-07	Mar-12	Feb-16		MEDTRONIC HALL
3	Sep-07	Mar-07	Dec-15		TTK-Ch-29mm
4	Dec-07	Nov-13	Dec-15		???
5	Jul-08	Mar-11	Aug-15		TTK-Ch-27mm
6	Aug-08	Sep-11	Jul-15		STAR EDWARDS
7	Sep-08	Mar-12	Jul-15		TTK-Ch-29mm
8	Jan-11	Dec-13	Jan-15	Nov-15	TTK-Ch-27mm
9	Apr-15	Feb-13	Dec-15		TTK-Ch-25mm
10	Aug-12	Apr-14	Jan-16		MEDTRONIC-MV
11	Jan-13	Jun-14	Jun-16		TTK-Ch-27mm
12	Jan-13	Feb-15	Aug-15		TTK-Ch-23mm
13	Mar-13	Jun-14	Mar-15		SJM-23mm
14	May-13	Nov-14	May-15		TTK-Ch
15	March-13	Oct - 13	June - 14		ATS -27 mm
16	Jul-13	Jun-14	Aug-15		ATS-22mm
16	Jan-13	Aug-14	Jul-15		SJM-27mm
17	Jan-14	Nov-15	Apr-16		ATS-22mm
18	May-14	Jan-15	Dec-15		TTK-Ch-27mm
19	Jun-14	Dec-14	Aug-15	Jan-16	ATS-28mm
20	Jul-14	Dec-14	Nov-15		SJM-27mm

DRUG COMPLIANCE



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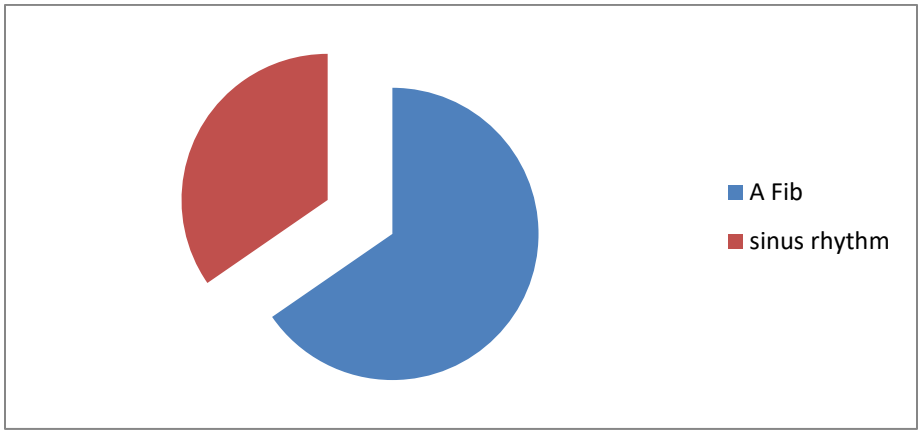
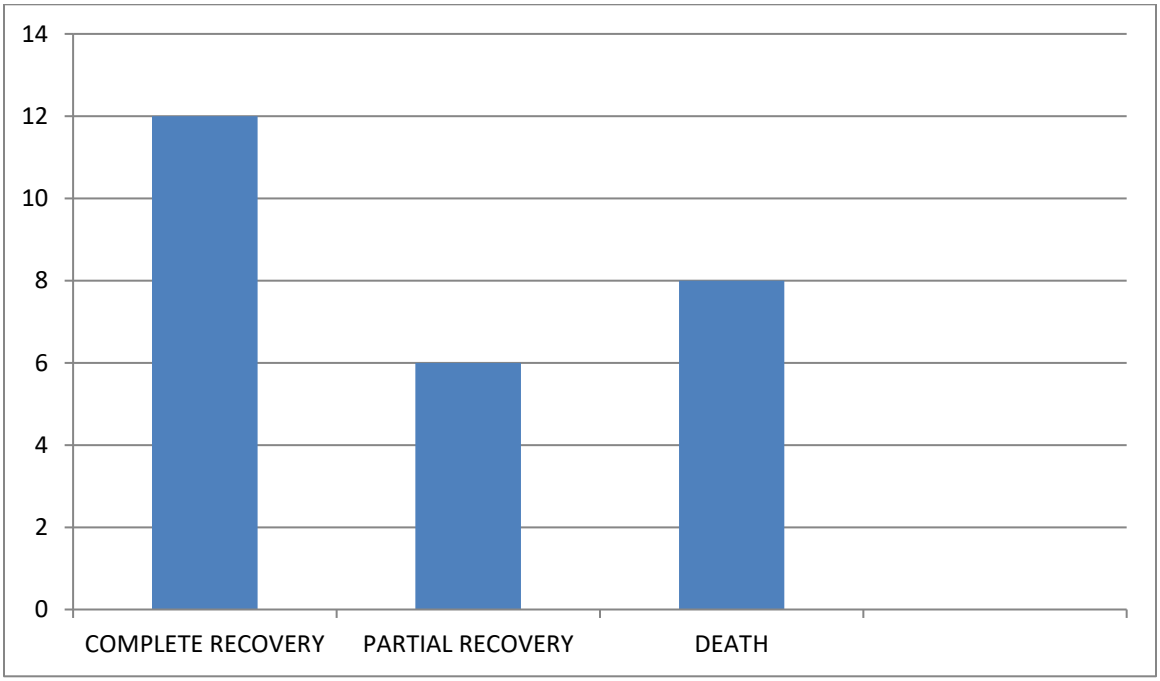
INCIDENCE OF AF AND SINUS RHYTHM



OUTCOME OF TREATED RECURRENT PVT



Discussion

This study provides important insights into the clinical profile and outcomes of recurrent prosthetic valve thrombosis (PVT) in a tertiary care setting. The predominance of female patients (73%) in our cohort aligns with findings from Roudaut et al. [11], who reported a 68% female prevalence in their multicenter study of 210 PVT cases. The higher incidence in younger age groups (69.1% between 21-40 years) corresponds with data from Kumar et al.

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[12], who found 72% of PVT cases occurring in patients under 45 years in their analysis of 120 cases.

The overwhelming prevalence of mitral valve involvement (96%) in our study exceeds the typical distribution reported in literature. Özkan et al. [13] reported a 78% mitral valve involvement in their series of 244 cases, suggesting potential regional variations in valve disease patterns. The high rate of medication non-compliance (92%) in our study population significantly exceeds previously reported rates of 60-75% [14], highlighting a critical area for intervention in developing countries.

Our finding of subtherapeutic INR in 69.2% of cases (INR 1-1.9) correlates closely with Biteker et al.'s [15] findings, where 72% of recurrent PVT cases had inadequate anticoagulation. The presence of atrial fibrillation in 65% of our patients represents a higher burden compared to the 45% reported in a large registry study by Dangas et al. [16], suggesting additional thrombotic risk in our population.

The overall success rate of thrombolysis (46% complete recovery, 23% partial recovery) in our series is lower than previously reported outcomes. Karthikeyan et al. [17] achieved complete success in 70% of cases with accelerated thrombolysis protocols. Our higher mortality rate (31%) compared to the reported 10-15% in primary PVT cases [18] emphasizes the increased risk associated with recurrent episodes, particularly for third-time events.

The absence of major bleeding complications in our cohort, despite aggressive thrombolysis, contrasts with reported rates of 5-10% in other studies [19]. This may reflect careful patient selection and monitoring protocols. The 30-day follow-up showing sustained improvement in 66% of survivors (12 out of 18) provides important data on medium-term outcomes, an aspect often underreported in existing literature.

Conclusion

Recurrent PVT presents a significant therapeutic challenge with higher mortality compared to primary events. Poor anticoagulation compliance remains the predominant risk factor, particularly affecting younger females with mitral valve prostheses. While thrombolysis

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can be effective in carefully selected cases, the success rates are lower in recurrent episodes. Improved anticoagulation monitoring systems and patient education are crucial for preventing recurrence. The study highlights the need for standardized protocols specific to recurrent PVT management and emphasizes the importance of regular follow-up in improving outcomes.

References

1. Dangas GD, Weitz JI, Giustino G, Makkar R, Mehran R. Prosthetic Heart Valve Thrombosis. J Am Coll Cardiol. 2016;68(24):2670-2689.

2. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart. 2007;93(1):137-142.

3. Biteker M, Altun I, Basaran O, Dogan V, Yildirim B, Ergun G. Treatment of Prosthetic Valve Thrombosis: Current Evidence and Future Directions. J Clin Med Res. 2015;7(12):932-936.

4. Huang G, Schaff HV, Sundt TM, Rahimtoola SH. Treatment of Obstructive Thrombosed Prosthetic Heart Valve. J Am Coll Cardiol. 2013;62(19):1731-1736.

5. Özkan M, Gündüz S, Biteker M, Astarcioglu MA, Çevik C, Kaynak E, et al. Comparison of different TEE-guided thrombolytic regimens for prosthetic valve thrombosis: The TROIA trial. JACC Cardiovasc Imaging. 2013;6(2):206-216.

6. Dürrleman N, Pellerin M, Bouchard D, Hébert Y, Cartier R, Perrault LP, et al. Prosthetic valve thrombosis: twenty-year experience at the Montreal Heart Institute. J Thorac Cardiovasc Surg. 2004;127(5):1388-1392.

7. Caceres-Loriga FM, Perez-Lopez H, Morlans-Hernandez K, Facundo-Sanchez H, Santos-Gracia J, Valiente-Mustelier J, et al. Thrombolysis as first choice therapy in prosthetic heart valve thrombosis. A study of 68 patients. J Thromb Thrombolysis. 2006;21(2):185-190.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 11, 2024

8. Karthikeyan G, Math RS, Mathew N, Shankar B, Kalaivani M, Singh S, et al. Accelerated infusion of streptokinase for the treatment of left-sided prosthetic valve thrombosis: a randomized controlled trial. Circulation. 2009;120(12):1108-1114.

9. Salem DN, O'Gara PT, Madias C, Pauker SG. Valvular and structural heart disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2008;133(6 Suppl):593S-629S.

10. Gupta D, Kothari SS, Bahl VK, Goswami KC, Talwar KK, Manchanda SC, et al. Thrombolytic therapy for prosthetic valve thrombosis: short- and long-term results. Am Heart J. 2000;140(6):906-916.

11. Roudaut R, Lafitte S, Roudaut MF, et al. Management of prosthetic heart valve obstruction: fibrinolysis versus surgery. Early results and long-term follow-up in a single-centre study of 263 cases. Arch Cardiovasc Dis. 2009;102(4):269-277.

12. Kumar R, Garg N, Mahesh K, et al. Characteristics and outcomes of prosthetic valve thrombosis in developing countries. Int J Cardiol. 2019;283:122-127.

13. Özkan M, Çakal B, Karakoyun S, et al. Thrombolytic therapy for the treatment of prosthetic heart valve thrombosis in pregnancy with low-dose, slow infusion of tissue-type plasminogen activator. Circulation. 2013;128(5):532-540.

14. Caceres-Loriga FM, Perez-Lopez H, Santos-Gracia J, et al. Prosthetic heart valve thrombosis: pathogenesis, diagnosis and management. Int J Cardiol. 2006;110(1):1-6.

15. Biteker M, Duran NE, Gündüz S, et al. Treatment of prosthetic valve thrombosis: an experience with 67 cases. Clin Appl Thromb Hemost. 2015;21(5):454-458.

16. Dangas GD, Weitz JI, Giustino G, et al. Prosthetic Heart Valve Thrombosis. J Am Coll Cardiol. 2016;68(24):2670-2689.

17. Karthikeyan G, Senguttuvan NB, Joseph J, et al. Urgent surgery compared with fibrinolytic therapy for the treatment of left-sided prosthetic heart valve

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thrombosis: a systematic review and meta-analysis of observational studies. Eur Heart J. 2013;34(21):1557-1566.

18. Huang G, Schaff HV, Sundt TM, et al. Treatment of obstructive thrombosed prosthetic heart valve. J Am Coll Cardiol. 2013;62(19):1731-1736.

19. Salem DN, O'Gara PT, Madias C, et al. Valvular and structural heart disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2008;133(6 Suppl):593S-629S.