

CLINICAL PROFILE AND OUTCOME OF PROSTHETIC VALVE THROMBOSIS PATIENTS TREATED WITH THROMBOLYSIS

Dr. Sachin Rao¹, Dr. Sreedhara R², Dr. Kavya G Upadhya³, Dr. Nikhil Basavanagoud⁴,
Dr. C N Manjunath⁵

Affiliations

1, 2, 4 – Assistant Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Mysuru

3 – Senior Resident, Department of Community Medicine, JSS Medical College

5 – Professor & Head of Cardiology; Director, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Bengaluru

Corresponding Author

Dr. Kavya G Upadhya

Senior Resident, Department of Community Medicine

JSS Medical College, Sri Shivarathreeshwara Nagar, Mysuru - 570015

Email Id: kavyagu@jssuni.edu.in

ABSTRACT

Background: Prosthetic valve thrombosis (PVT) is a major and life-threatening complication of post-valve replacement surgeries attributable mainly to inadequate anticoagulation. We aim to study the clinical profile and outcome after thrombolysis of patients with prosthetic valve thrombosis.

Methods: This is a prospective, observational, single-center study carried out between January 2021 & January 2023 at a tertiary care center in India. A total of 86 patients who underwent thrombolysis for PVT were included in the study. Clinical profile and in-hospital outcomes were collected using a pre-tested, semi-structured questionnaire.

Results: The mean age of the patients was 47.2 ± 11.2 years, predominantly females (58; 67.5%). Approximately one in four patients had AF (25.5%). The majority (50; 58.1%) did not have PT/INR in the therapeutic range (<2). Only 40 (46.5%) patients were compliant with anticoagulation. Mitral prosthesis was most commonly involved (59.3%). The majority of patients (41; 47.6 %) presented after five years of surgery. Complete recovery after thrombolysis was achieved in 72(83.7%) patients. Mortality was noted in 8 patients (9.3%).

Conclusions: Based on the study findings, Poor drug compliance and sub-therapeutic INR still remain major correctable contributing factors for PVT. Thrombolysis has a high success rate, especially in patients with the first episode of PVT post-surgery, and may be considered as a

first-line therapy where immediate surgical options are unavailable, especially in developing countries like India.

Keywords: Prosthetic Valve Thrombosis (PVT), Thrombolysis, Streptokinase

Introduction

Surgical valve replacement remains the standard of care for the management of advanced valvular heart disease. Prosthetic valve thrombosis (PVT) is a serious complication post-valve replacement, with an average incidence of 1.8%- 5.7% per patient year.

The appropriate management of PVT is still debatable. Thrombolysis and emergency surgery are the treatment options. Streptokinase and Urokinase are the thrombolytic agents approved by the FDA. Whereas the latest studies have successfully used Tenecteplase with good results. This study aimed to evaluate the clinical profile of the patients and to determine the in-hospital outcomes of thrombolytic therapy.

Methods

This was a prospective, observational, single-center study carried out between January 2021 & January 2023 at a tertiary care center in India. A total of 86 patients with PVT who underwent thrombolysis were included in the study. Preoperative clinical data, initial valve procedure, symptoms of valve thrombosis, and complications after the treatment were recorded. Routine blood investigations and electrocardiograms were done for all patients. Fluoroscopy was done based on the clinical indication.

Patients who presented with symptoms were diagnosed as having PVT based on high gradient and classic echogenicity of the thrombus. Previous echo reports and features that differentiate it from Pannus like echogenic characteristics, the appearance of soft tissue (thrombotic material), larger size, etc. were utilized for proper diagnosis. Informed consent was obtained from all patients included in the study.

TEE was not employed for the diagnosis of PVT as the majority of the patients were unstable at presentation. Both Streptokinase and Urokinase were given as bolus followed by infusion. The duration of the infusion was based on the clinical response and complications. The regimen in our study was a 250000 unit bolus, followed by 100000 units per hour infusion till clinical response. The infusion was stopped if there was no response to treatment after a variable period of 24 to 36hours.

Successful thrombolysis was defined as a decrease in prosthetic valve gradient to baseline with normal prosthetic movement and in the absence of complications, need for surgery or death.

Statistical analysis: Continuous variables were presented as mean and categorical variables as counts and percentages. All data were analyzed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 26.

Results

Overall 86 patients of PVT were studied. The mean age of subjects was 47.2 ± 11.2 years. The majority of the subjects were in the age group of 40-50 years. The majority of the patients were females (58; 67.5%). Rheumatic heart disease constituted the most common indication for Valve replacement (70; 81.3%). Most of the patients presented with dyspnea. Approximately one in four patients had AF (25.5%).

The majority (50; 58.1%) of patients were not having PT/INR in the therapeutic range (<2). Acenocoumarol was the most commonly used anticoagulant. Aspirin was added only in 30(34.8%) of patients. A sizeable number of patients (26;30.2%) were poorly compliant with anticoagulation.

Table 1: Baseline characteristics of the patients

Variables	N = 86 Patients
Age (Mean, Years)	47.2 ± 11.2
Male, n (%)	28 (32.5%)
Preceding Causative indication for valve replacement	
RHD, n (%)	70 (81.3%)
Degenerative Aortic Valve, n (%)	16 (18.6%)
Drug compliance, n (%)	
	40 (46.5%)
International Normalised Ratio (INR)	
<2, n (%)	50 (58.1%)
2-3, n (%)	14 (16.2%)
>3, n (%)	22(25.5%)
Application of fluoroscopy	
	28 (32.5%)
Comorbidities	
Concomitant AF, n (%)	22(25.5%)
CVA, n (%)	02(2.3%)

Anemia, n (%)	10 (11.6%)
CAD, n (%)	03 (3.4%)
Anticoagulation	
Acenocoumarol, n (%)	51(59.3%)
Acenocoumarol+Aspirin, n (%)	30 (34.8%)
Warfarin, n (%)	5(5.8%)

The mitral prosthesis was most commonly involved (59.3%) followed by aortic valve (19.7%) (Table 2). Most of the study participants (91; 82.7%) presented with first-time thrombosis after surgery. 12 (13.9%) patients had at least one episode of prosthetic valve thrombosis in the past and 2 patients (2.3%) of them had 2 prior episodes. The majority of patients (41; 47.6 %) presented after five years of surgery.

Thrombolysis was the primary treatment option employed. Streptokinase was the most commonly used agent for thrombolysis and was used in 82 (95.3 %) patients. Only four (4.6%) were treated with urokinase and all had successful thrombolysis. Duration of lysis was 12-24 hours employed in 42 patients (48.8 %).

Table 2: Variables Related To Valves and Data Regarding Thrombolytic Therapy

Variables	N=86 Patients
Prosthetic valve position	
Mitral, n (%)	51(59.3%)
Aortic, n (%)	17(19.7%)
DVR with Mitral valve PVT, n (%)	12(13.9%)
DVR with Aortic valve PVT, n (%)	6(6.9%)
Type of Valve	
St Jude bileaflet, n (%)	42 (48.8%)
Srichitra, n (%)	38 (44.1%)
Medtronic ATS, n (%)	1(1.16%)
Ball Cage, n (%)	1(1.16%)
Others, n (%)	5(5.8%)
Recurrence, n (%)	12(13.9%)
Time of Presentation after valve replacement	
<6 months, n (%)	2(2.32%)
6 months- 1 year, n (%)	4 (4.65%)
1 year-2 year, n (%)	5(5.8%)
2 year-3 year, n (%)	9(10.4%)

3 year-4 year, n (%)	12(13.9%)
4 year-5 year, n (%)	13(15.1%)
>5 years, n (%)	41(47.6%)
Thrombolytic agent	
Streptokinase, n (%)	82(95.3%)
Urokinase, n (%)	4 (4.65%)
Duration of Thrombolysis	
<12 h, n (%)	12(13.9%)
12-24 h, n (%)	42 (48.8%)
>24 h, n (%)	32 (37.2%)

Complete recovery after thrombolysis was achieved in 72(83.7%) patients. Mortality was noted in 8 patients (9.3%). Four patients had CVA out of which three had embolic stroke and major intracranial bleeding in one patient. (Table 3).

Table 3: Treatment outcome following thrombolysis

Outcome	N=86 Patients
Mortality, n (%)	8 (9.3%)
CVA, n (%)	4 (4.65%)
Success, n (%)	72 (83.7%)
Embolism, n (%)	3 (3.4%)

Discussion

Our study showed Female predominance, sub-therapeutic INR, and Drug non-compliance as major associations with PVT which are consistent findings documented in the majority of the studies, especially from developing countries like India.¹

Previous similar studies are consistent with our finding of RHD being the predominant contributor and Mitral valve, the most common valve involved in

PVT. In various studies, Mitral valve PVT is 2-3 times higher than aortic valve PVT.²⁻⁵

In our study, it was observed that sizeable patients had recurrent PVT (12, 13.9%) and proportion having successful thrombolysis was less (6; 50%) and mortality was higher in these subsets (n=4). Similar data was reported in many other studies.⁶

The current guidelines emphasize early diagnosis and urgent treatment of patients with PVT with either thrombolysis or surgery. Low surgical risk, NYHA functional class III/IV, contraindication to fibrinolysis, recurrent valve thrombosis, possible or suspected pannus, large

clot ($> 1.0 \text{ cm}^2$), mobile thrombus $> 0.3 \text{ cm}$ in diameter, presence of left atrial thrombus, absence of the need of coronary artery bypass graft surgery (CABG) for concomitant coronary artery disease and availability of expert surgical team favor surgical treatment for PVT. On the contrary, factors that favor thrombolysis include 1) high surgical risk; 2) NYHA I/II functional class; 3) first episode of PVT; 4) presence of mass consistent with thrombus; 5) presence of a small clot ($< 1 \text{ cm}^2$) without any contraindication for surgery; 6) absence of immediate surgical expertise; and 7) need for cardiac surgery for other indications (e.g., CABG). The majority received Streptokinase as the primary thrombolytic agent. The reported success rate of thrombolysis was around 70-80% in various studies.^{7-10,11,12} Our study reported a high success rate (73; 83.7%), similar to one reported by a previous study by Patil S et al, which reported $> 90\%$ success with thrombolysis.⁵ Documented average bleeding and embolism rate with Streptokinase thrombolysis was 8.5% and 6.5% respectively.

We had only two cases of Embolism caused by thrombolysis, which is much less compared to other similar studies. Previous studies have shown an embolic risk of 12% to 17% caused by thrombolysis.¹³⁻¹⁴

Conclusion

Poor drug compliance and sub-therapeutic INR are still worrisome causative agents of PVT in India.

Systemic thrombolysis remains the most valid therapeutic option in the current era for PVT given its high success rate. Thrombolysis with Streptokinase continues to be an effective strategy. Response of Recurrent PVT to thrombolysis is relatively less. Failed thrombolysis cases have a high mortality. Surgery is the only resort for these subsets.

References

1. Reddy YS, Pingali K, Otikunta AN, Nathani S, Malladi SR. A study of indications, complications of prosthetic valves and prognosis after treatment of stuck valve. Blood pressure. 2017; 100(70):80.
2. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart. 2007; 93(1):137-42.

3. 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):906-16.
4. Dangas GD, Weitz JI, Giustino G, Makkar R, Mehran R. Prosthetic heart valve thrombosis. *J American Coll Cardiol.* 2016; 68(24):2670-89.
5. Patil S, N, Ramalingam R, Rudrappa MMB, Manjunath CN. Study of prosthetic heart valve thrombosis and outcomes after thrombolysis. *Int J Res Med Sci.* 2019 Apr; 7(4):1074-1078.
6. Manjula M, Rangan Kapil, Manjunath CN. Clinical profile and outcome of recurrent prosthetic heart valve thrombosis in a tertiary care cardiology unit. *Indian Heart J.* 2017; 69(S2):S1.
7. Castilho FM, De Sousa MR, Mendonça AL, et al. Thrombolytic therapy or surgery for valve prosthesis thrombosis: systematic review and meta-analysis. *J Thromb Haemostasis.* 2014; 12:1218e1228. <https://doi.org/10.1111/jth.12577>.
8. Reyes-Cerezo E, Jerjes-Sanchez C, Archondo-Arce T, et al. Fibrinolytic therapy in left side-prosthetic valve acute thrombosis. In depth systematic review. *Arch Cardiol Mex.* 2008; 78:309e317.
9. Huang G, Schaff HV, Sundt TM, et al. Treatment of obstructive thrombosed prosthetic heart valve. *J Am Coll Cardiol.* 2013 Nov 5; 62(19):1731e1736. <https://doi.org/10.1016/j.jacc.2013.07.075>.
10. Karthikeyan G, Senguttuvan NB, Joseph J, et al. Urgent surgery compared with fibrinolytic therapy for the treatment of left-sided prosthetic heart valve thrombosis: a systematic review and meta-analysis of observational studies. *Eur Heart J.* 2013; 34(21):1557e1566. <https://doi.org/10.1093/eurheartj/ehs486>.
11. Lengyel M, Horstkotte D, Voller H, Mistiaen WP, Working Group Infection Thrombosis E, Disease BotSfHV. Recommendations for the management of prosthetic valve thrombosis. *J Heart Valve Dis.* 2005; 14(5):567.
12. Cáceres-Lóriga FM, Pérez-López H, Santos-Gracia J, Morlans-Hernandez K. Prosthetic heart valve thrombosis: pathogenesis, diagnosis and management. *Int J Cardiol.* 2006; 110(1):1-6.

13. Asante-Korang A, Sreeram N, McKay R, Arnold R. Thrombolysis with tissue-type plasminogen activator following cardiac surgery in children. *International J Cardiol.* 1992; 35(3):317-22.
14. Witchitz S, Veyrat C, Moisson P, Scheinman N, Rozenstajn L. Fibrinolytic treatment of thrombus on prosthetic heart valves. *Heart.* 1980; 44(5):545-54.