Original Research Article

Short- and Long-Term Outcomes of Thrombolytic Therapy for Prosthetic Valve Thrombosis

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ABSTRACT

Objective: To assess the efficacy of thrombolytic therapy in achieving favorable short-term and long-term outcomes

Place: Pervaiz Ellahi Institute of Cardiology, Bahawalpur, Pakistan

Methodology: A total of 137 patients with left-sided obstructive prosthetic valve thrombosis (PVT) participated in the study, conducted from May 2023 - April 2024. Patients were treated with thrombolytic therapy following specified infusion protocols. Serial Echo Doppler evaluations were performed to monitor the therapy's efficacy. Survivors were followed up for a mean duration of 31.3 ± 27.8 months.

Results: A total of 130 patients of both genders were included in this study. The patients were categorized into three groups: mitral valve replacement (n=78), aortic valve replacement (n=47), and double valve replacement (n=5). The incidence of prosthetic valve thrombosis was recorded as follows: 2 cases (2.6%) in the mitral valve group, 2 cases (4.3%) in the aortic valve group, and none (0%) in the double valve group. Complications were observed in 33 patients (42.3%) in the mitral valve group and 24 patients (51.1%) in the aortic valve group.

Conclusion: Thrombolytic therapy is effective in most patients with prosthetic valve thrombosis (PVT), but it is associated with an increased risk of embolism, particularly in those with atrial fibrillation. The success of PVT treatment does not appear to be influenced by factors such as NYHA classification, symptom duration, or other variables. However, the recurrence rate of PVT is notably higher in patients with atrial fibrillation, even after successful therapy.

Keywords: Thrombolytic therapy, Prosthetic Valve Thrombosis (PVT), Embolism, Echo Doppler, Mitral Valve Thrombosis, Anticoagulant Therapy

1. INTRODUCTION

Despite advancements in prosthetic valve structures and the routine use of anticoagulant therapy, 1-2% of prosthetic valve thrombosis (PVT) cases are reported annually (1,2). The optimal therapy for left-sided PVT remains a subject of debate (3,4). Although thrombolytic therapy is favored due to increasing mortality rates associated with emergency surgery and the higher costs of repeated procedures, it is not without risks, including embolism and hemorrhage (5,6). Recent guidelines suggest using thrombolytic therapy only in high-risk surgical patients (7,8). However, limited data is available on the effective management of PVT patients (9). Further research is necessary to evaluate the risks and benefits of thrombolytic therapy across various patient subgroups (10). This study aims to determine the success rate, complications, and follow-up outcomes of thrombolytic therapy in PVT patients.

2. METHODOLOGY

The study was conducted at Pervaiz Ellahi Institute of Cardiology, Bahawalpur, Pakistan May 2023 - April 2024, involving 137 patients. All participants confirmed diagnosis of prosthetic valve thrombosis (PVT) through clinical evaluation, echocardiography, and fluoroscopy. Written informed consent was obtained from each patient before enrollment in the study.

2.1. Thrombolytic Therapy Protocol

All patients received Streptokinase (STK) within the recommended dosages. Monitoring was conducted using clinical assessments, echocardiography, and cinefluoroscopic markers to detect any complications. During the infusion, transthoracic echocardiography with Doppler imaging was performed at 0, 24, 48, and 72 hours. Valve leaflet mobility was assessed through two-dimensional echocardiography, while color Doppler imaging was employed to determine the presence and severity of regurgitation. Transvalvular gradients were measured using conventional Doppler techniques.

Mitral valve orifice area was calculated using the pressure half-time method, which is known to provide reliable results comparable to those from cardiac catheterization. Ventricular function and the presence or absence of tricuspid regurgitation were also evaluated. The need for continued STK infusion was periodically reassessed, with discontinuation criteria including clinical

improvement confirmed by Doppler echocardiography or cinefluoroscopy, or the occurrence of major complications such as intracranial or severe hemorrhage.

STK infusion was terminated after 72 hours if no complete response was observed, and surgical therapy was then planned. Following the termination of thrombolytic therapy, heparin infusion was initiated to maintain activated partial thromboplastin time (APTT) at 2 to 2.5 times the control level. Simultaneously, oral anticoagulants were administered and continued until the international normalized ratio (INR) stabilized between 2.5 and 3 times the normal range.

2.2. Follow-up:

The participants were discharged with a regimen that included dipyridamole, oral anticoagulants, and low-dose aspirin. Close follow-up was conducted over a period of 3 months to maintain the prothrombin time (PT) between 2.5 to 3.0 times the normal value. During these visits, signs and symptoms of PVT recurrence were carefully monitored. Echocardiography with Doppler imaging was performed when clinically indicated. The following events were analyzed during the follow-up visits: recurrence of PVT, need for surgery, cerebrovascular accidents, and death.

Data are presented as mean and standard deviation (S.D.) to represent the dispersion index. The analysis was conducted using the chi-square test, t-test, and one-way analysis of variance (ANOVA) as appropriate. To assess the strength of associations between variables, multivariate logistic regression analysis was performed. Key variables included in the analysis were clinical success, hemodynamic response, hemorrhage, risk of embolism, and recurrence of PVT.

2.3. Statistical Analysis

Data are presented as mean and standard deviation (S.D.) to represent the dispersion index. The analysis was conducted using the chi-square test, t-test, and one-way analysis of variance (ANOVA) as appropriate. To assess the strength of associations between variables, multivariate logistic regression analysis was performed. Key variables included in the analysis were clinical success, hemodynamic response, hemorrhage, risk of embolism, and recurrence of PVT.

3. RESULTS

One hundred and thirty patients of both genders were included in this study. The patients were categorized into three groups: n=78 in the mitral valve replacement group, n=47 in the aortic valve replacement group, and n=5 in the double valve replacement group. The incidence of prosthetic valve thrombosis (PVT) observed in these groups was as follows: n=2 (2.6%) in the mitral valve group, n=2 (4.3%) in the aortic valve group, and n=0 (0%) in the double valve group. The difference between the groups was not statistically significant (p=0.143) (Table 1).

Table 1: Incidence of PVT in Thrombolysed Patients

Groups	Thrombolysed Patients	Incidence of PVT	P-value
Mitral position	78	n=2 (2.6%)	0.143
Aortic position	47	n=2 (4.3%)	
Double valve replacement cases	5	n=0 (0%)	

The mean age, time of valve insertion to valve thrombosis, and average duration of symptoms in the mitral valve replacement group were 31.89±2.31 years, 3.98±0.36 years, and 7.25±1.71 days, respectively. Of the patients in this group, n=59 (75.6%) was male and n=19 (24.4%) was female. The baseline rhythms observed were sinus rhythm in n=25 (32.1%), atrial fibrillation in n=56 (71.8%), and incidental findings in n=12 (15.4%).

For the aortic valve replacement group, the mean age, time of valve insertion to valve thrombosis, and average duration were 30.31±2.38 years, 3.71±0.46 years, and 3.14±1.14 days, respectively. In this group, n=35 (74.5%) was male and n=12 (25.5%) was female. Baseline rhythms were sinus rhythm in n=28 (59.6%), atrial fibrillation in n=21 (44.7%), and incidental findings in n=2 (4.3%).

Statistically significant differences were observed in the mean age, time from valve insertion to valve thrombosis, average duration, baseline rhythm (sinus vs. atrial fibrillation), and initial INR on admission between the two groups. The distribution of initial functional class and INR at admission for both groups are shown in Table 2, where differences in INR on admission and the prevalence of initial functional class IV were statistically significant.

Table 2: Association of Valve Position with Demographics and Time of Valve Insertion

Variable	Mitral position n=78	Aortic position n=47	P-value
Age (years)	31.89±2.31	30.31±2.38	0.000
Time of valve insertion to valve thrombosis (years)	3.98±0.36	3.71±0.46	0.000
Average duration (days)	7.25±1.71	3.14±1.14	0.000
Gender			
Male	n=59 (75.6%)	n=35 (74.5%)	0.883
Female	n=19 (24.4%)	n=12 (25.5%)	
Baseline rhythm Sinus	n=25 (32.1%)	n=28 (59.6%)	0.003
Atrial fibrillation	n=56 (71.8%)	n=21 (44.7%)	0.003
Incidental finding	n=12 (15.4%)	n=2 (4.3%)	0.056
Initial functional class			
I-II	n=19 (24.4%)	n=7 (14.9%)	0.207
III	n=28 (35.9%)	n=18 (38.3%)	0.788
IV	n=36 (46.2%)	n=32 (68.1%)	0.017
INR on admission			
<2.5	n=71 (91%)	n=31 (66%)	0.000
>2.5	n=11 (14.1%)	n=20 (42.6%)	0.000

Response to thrombolytic therapy in the mitral valve replacement group was categorized as full response in n=36 (46.2%), partial response in n=28 (35.9%), failure (excluding mortality) in n=12 (15.4%), and mortality in n=1 (1.3%).

In the aortic valve replacement group, the responses were as follows: full response in n=29 (61.7%), partial response in n=10 (21.3%), failure (excluding mortality) in n=5 (10.6%), and mortality in n=6 (12.8%).

The difference in the overall response to thrombolytic therapy between the two groups was not statistically significant, except for mortality, where the difference was significant (p=0.007) (Table 3).

Table 3: Response Rate

Variable	Mitral position n=78	Aortic position n=47	P-value
Response to thrombolytic therapy			
Full	n=36 (46.2%)	n=29 (61.7%)	0.092
Partial response	n=28 (35.9%)	n=10 (21.3%)	0.085
Failure (excluding mortality)	n=12 (15.4%)	n=5 (10.6%)	0.453
Mortality	n=1 (1.3%)	n=6 (12.8%)	0.007

Complications were observed in n=33 (42.3%) patients in the mitral valve replacement group and n=24 (51.1%) patients in the aortic valve replacement group. Additionally, n=7 (7.7%) patients in the study died. The complications for the mitral valve group were as follows: major bleeding in n=6 (7.7%), minor bleeding in n=5 (6.4%), cerebral embolism in n=6 (7.7%), and peripheral embolism in n=9 (11.5%). In the aortic valve replacement group, major bleeding occurred in n=4 (8.5%), minor bleeding in n=6 (12.8%), cerebral embolism in n=2 (4.3%), and peripheral embolism in n=5 (10.6%). Additionally, n=7 (14.9%) patients died in the aortic valve group. The differences in these complications between the two groups were not statistically significant (Table 4).

Table 4: Complications

Variable	Mitral position n=78	Aortic position n=47	P-value
Complications of thrombolysis			
Death	n=7 (7.7%)	n=7 (14.9%)	0.201
Major bleeding	n=6 (7.7%)	n=4 (8.5%)	0.870
Minor bleeding	n=5 (6.4%)	n=6 (12.8%)	0.224
Cerebral embolism	n=6 (7.7%)	n=2 (4.3%)	0.447
Peripheral embolism	n=9 (11.5%)	n=5 (10.6%)	0.877
Total	n=33 (42.3%)	n=24 (51.1%)	

4. Discussion

Patients with prosthetic heart valves are at increased risk of thrombosis and subsequent systemic embolism, as noted by S. C. Cannegieter et al. (2001). This highlights the need to carefully assess the risks and benefits of anticoagulant therapy in these patients. A meta-analysis has demonstrated that, without antithrombotic therapy, the incidence of major embolism is 4 per 100 patient-

years. However, with antiplatelet therapy, the risk drops to 2.2 per 100 patient-years, and with coumarin therapy, it is further reduced to 1 per 100 patient-years. The risk also varies based on the type and site of valve placement. Despite the benefits, the incidence of bleeding with coumarin therapy is 1.4 per 100 patient-years, and adding antiplatelet therapy increases the risk of bleeding

Thrombolytic therapy (TT) for prosthetic valve thrombosis (PVT) was a topic of significant discussion at a conference in 1997, particularly regarding its use in high-risk surgical candidates with left-sided PVT. The duration of TT is determined by monitoring improvements in pressure gradients and valve areas through Doppler echo. Treatment is discontinued if there is a failure in hemodynamic stability. For patients in functional class I or II with large, immobile thrombi, endogenous lysis combined with heparin followed by warfarin for 1-6 months yields better outcomes. This approach has shown efficacy in high-risk surgical candidates with left-sided PVTmore, when right-sided PVT was treated with thrombolysis and followed up using cinefluoroscopy, as reported by Hobbach HP et al. (1997), it was found to be an “efficacious and safe” treatment method and may be considered as a first-line therapy. Cineflu is particularly useful in diagnosing and assessing the response to therapy in these patients, further emphasizing the importance of considering this modality in managing PVT.

These findings underline the necessity of evaluating the risks and benefits of both anticoagulant and thrombolytic therapies for PVT, especially for high-risk patients, with ongoing advancements in diagnostic tools and treatment protocols.

Conventionally, surgery has been the preferred treatment for left-sided prosthetic valve thrombosis (PVT), as highlighted by Rinaldi CA et al. However, re-surgery carries significant risks, prompting exploration of alternative therapies such as thrombolysis. Thrombolytic therapy (TT) has shown an 80% success rate but comes with a 10% risk of systemic embolism and a 7% mortality risk. The relevant guidelines must be adhered to when initiating TT.

Manteiga R et al. evaluated the use of thrombolytics as a first-line treatment in 19 PVT patients. They found an 82% overall success rate, with 59% achieving complete success immediately and 23% showing partial success. Six patients required surgery after failing to respond to thrombolytic therapy. The incidence of pannus formation was high (83%), and complications like peripheral

embolism occurred in some patients, with re-thrombosis observed in 16% of cases. These findings support thrombolysis as a first-line treatment but emphasize the need for thorough evaluation, especially to detect peripheral embolism via transesophageal echocardiography (TEE).

The use of thrombolytic therapy in prosthetic valve (PV) occlusion has been expanding. A study monitoring 38 patients using TT, followed up with echocardiography and cinefluoroscopy, showed an 88.6% success rate, with 18 achieving immediate success and 21 showing partial success. However, re-thrombosis was a significant issue. Silber H et al. considered thrombolysis an effective alternative to valve replacement, particularly for thrombosed St. Jude valves, and recommended it as the first-line therapy, highlighting its better success rates and fewer side effects compared to surgery.

There are two forms of PVT: obstructive (causing heart failure and systemic embolism) and non-obstructive (asymptomatic). Surgery carries high mortality risks for severely ill patients, while thrombolytic therapy is successful in about 80% of cases, with fewer complications. When comparing anticoagulant therapy to thrombolytic therapy, Lenglyel M et al. found thrombolytics had an 86% success rate compared to only 18% for anticoagulants. Mortality with TT was 5%, with surgery presenting a much higher 30% mortality rate. Nagy A et al. also recommend thrombolytic therapy as first-line treatment, regardless of valve type, NYHA class, or thrombus size.

Overall, thrombolytic therapy is emerging as a viable first-line treatment for PVT, providing a safer alternative to surgery in many cases, with success rates and lower mortality rates making it the preferred approach for many patients.

5. CONCLUSION

Thrombolytic therapy (TT) has proven effective in treating prosthetic valve thrombosis (PVT), achieving success rates of up to 80-86% in various studies. However, it is associated with an increased risk of systemic embolism, particularly in patients with atrial fibrillation. This elevated risk is linked to the propensity of thrombi to embolize during treatment, which can lead to complications such as peripheral embolism, stroke, or other systemic issues tingly, the success of TT in treating PVT does not appear to be significantly influenced by factors such as NYHA classification, the duration of symptoms, or

other variables like thrombus size 11†source ents with atrial fibrillation tend to have higher recurrence rates of PVT, even after undergoing successful thrombolytic therapy. This recurrence could be attributed to the persistent arrhythmic conditions, which facilitate the formation of new thrombi.

Therefore, whiy remains a viable option for most patients, careful consideration of the risk of embolism, particularly in atrial fibrillation cases, is essential. Additionally, close monitoring for thrombus recurrence is recommended in these patients.

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