

Clinical profile and management of prosthetic valve thrombosis in Tertiary cardiac Centre of Nepal, a prospective study.

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Abstract

Background and Aims: Prosthetic valve thrombosis is a life-threatening complication of post-valve replacement surgeries. A number of patients present with thrombotic complications mainly due to poor anticoagulation status with irregular INR checkup especially from remote areas of Nepal. Our aim was to study the clinical profile and management of prosthetic valve thrombosis in our center.

Methods: A prospective observational study of 45 patients (July 2017 – Jun 2019) admitted at Shahid Gangalal National Heart Centre, with the diagnosis of prosthetic valve thrombosis were studied. The demographic profile, clinical parameters and in hospital and 1 year outcome were analyzed.

Results: Out of 45 patients, majority were female (60%) with the age 11-67 years with mean age of 34.9 ± 6.7 . Twenty nine patients (64.4%) presented with sub-therapeutic INR value at admission. 46.7% patient had atrial fibrillation at the time of presentation. 88% patients presented within one week of onset of symptoms with shortness of breath being primary complaint, present in 95.6% of the patients. Forty two (86.9%) were thrombolysed with streptokinase while 3 patients underwent surgery. Valve thrombosis was most common at the mitral position 39(87%) patients. In hospital mortality was 13.3% and there were no major bleeding events or new stroke noted.

Conclusion: Majority of patients with prosthetic valve thrombosis presented with a sub-therapeutic INR value and poor patients' compliance. Thrombolysis is a useful option in the management of prosthetic valve thrombosis patients especially in countries like Nepal.

Keywords: Prosthetic valve thrombosis, Sub-therapeutic, Thrombolysis

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Introduction

Prosthetic valve (PV) thrombosis is a pathological entity characterized by thrombus formation on the prosthetic structures, with subsequent prosthetic valve dysfunction with or without thromboembolism.¹ Prosthetic valve thrombosis is a life-threatening complication of heart valve surgery, ranging from 0.5% to 15% and is associated with substantial morbidity and mortality.² In developing countries, the mortality rate is even higher.³ Most PV thrombosis may occur within months or even years after the valve replacement.

Risk of developing thromboembolic event and prevalence of PV thrombosis were higher with Mechanical Heart Valves than Biological one, more frequent in the mitral position than the aortic position, and higher in right-sided than left-sided PVs.⁴

Prosthetic valve implantation is still on the rise since rheumatic heart disease is still prevalent especially in context of Nepal. Many patients present with both late and early complications of valve

replacement mainly bleeding and PV thrombosis. Although there have been numerous reports worldwide on the clinical manifestations and treatment options and methods for patients with PV thrombosis, the best treatment is still controversial. Treatment options depend on many factors, such as the presence of valve obstruction, the patient's clinical condition, the size of the thrombus, the local medical and economic level, the experience with reoperation and most importantly, in context of our situation, patient's choice.^{5,6}

In a setup like Nepal where the burden of cardiovascular disease including rheumatic heart disease is still high, managing patient with Rheumatic heart disease (RHD), post valve replacement is more challenging mainly due limited infrastructure for monitoring regular PT/INR profile secondary to geographic and financial limitations. Patients often presents with various complications such as bleeding or thrombotic events especially PV thrombosis. Thrombolytic therapy has been and still remains the mainstay for

management of PV thrombosis in our context mainly due to financial reasons. Main objective of this study is to study the clinical profile, management trends and short-term outcome of patients presenting with PV thrombosis.

Methods

It was a prospective observational study with all cases of prosthetic valve thrombosis admitted in Shahid Gangalal National Heart Centre, from July 2017 to June 2019, were enrolled. The study was conducted after approval from the hospital ethical review committee. Informed consent were taken for inclusion in the study and for the treatment as well.

Details about the clinical profile, echocardiography reports and the mode of management, during the hospital stay and complications if present were recorded. All the patients were followed up for 1 year and telephone visit were performed. Statistical analysis was done using SPSS version 20 and data were presented in the form of tables and diagrams. Appropriate statistical tests were carried out to compare the data, and a level of significance of 0.05 was used. Continuous variables were expressed as mean, standard deviation, while categorical variables were presented as numbers and percentage.

For patients undergoing thrombolysis, complete success was considered to have normal or near-normal cross-valve gradients restored without any serious complications. Partial success means that the cross-valve gradient was reduced by more than 50% or the hemodynamic was significantly improved without any serious complications. The failure of TT was considered to be no significant improvement in valve activity and the cross-valve gradient after treatment or serious complications during thrombolysis.

Results

During the study period, forty five patients were admitted with the confirmed diagnosis of PV thrombosis. All the patients were analyzed clinically and echocardiogram was performed and was further confirmed by fluoroscopy. The age group presenting with PV thrombosis ranged from (11 -67 years) with median age of 35 years. Majority of patients were female (N=27, 60%), as shown in Table 1.

Table 1: Demographic Characteristic

Total Patients	45
Gender	
Male	18(40%)
Female	27(60%)
Age	
Maximum	67 years
Minimum	11 years
Mean	34.9 ±6. 7

Most of the patients (38, 88.4%) presented within a week of onset of symptoms. There was a wide range of time duration from the time of valve surgery to the symptoms presentation. The median time duration to presentation was 60 months with the earliest case presented at 2 months and the latest one at 144months from the time of valve surgery. Most patients (43, 95.6%) presented with the complaint of shortness of breath while two patients presented with chest pain. Most of the patients (73.3%) presented in NYHA class III, followed by class IV (22.2%).Six patients (13.3%) had previous history

such as thromboembolic event in past. Twenty nine patients (64.44%) had sub-therapeutic INR value, while fourteen patients (31.1%) had a baseline INR in the therapeutic range at presentation whereas two patients had supra- therapeutic INR value. Details are shown in table 2.

Table 2: Clinical Characteristic

Characteristics	No. (%)
Symptoms	
Shortness of breath	43(95.6)
Chest Pain	2(2.2)
NYHA Class	
Class II	2(4.4)
Class III	33(73.3)
Class IV	10(22.2)
Time from onset of symptoms	
Less than seven days	38(88.4)
Seven days or more	7(11.6)
ECG(rhythm)	
Sinus	23(51.1)
Atrial Fibrillation	21(46.7)
Pacing	1(2.2)
Past history of Embolic events	6(13.3)
Hypertension	2(2.2)
Physical examination	
DMC	34(75.6)
DMC with crepitations	11(24.4)
INR Value	
Sub-therapeutic	29(64.4)
Optimal	14(31.1)
Supra-therapeutic	2(4.4)
Complications	
Serum sickness	8.9(8.9)
Cardiogenic shock	2(4.4)
Non fatal Bleeding	2(4.4)
Mortality	6(13.3)

Mechanical prosthetic St. Jude Bileaflet valve was used in all the patients. Thrombolysis was the most commonly used initial mode of treatment, used in forty two patients (92.3%) while three patients directly underwent surgery. Among the patients undergoing thrombolysis, thirty five patients achieved complete success while six patients had partial success; however one patient had treatment failure that later underwent surgery in the same setting. Streptokinase was used as thrombolysing agent in all 42 patients who underwent thrombolysis. Prosthetic mitral valve thrombosis were seen in 39(86.7%) patients while isolated aortic valve thrombosis were seen in 6 (13.3%) patients.

The mean gradient across stuck prosthetic mitral valve during admission ranged from 14 to 31 mmHg with mean value of 21.8 ± 5.2 mm Hg. The mean gradient across stuck aortic valve ranged from 42 to 76 mmHg with the mean of 58.67 ± 9.87 mmHg (Table 3). For

patients who underwent thrombolysis, mean value of post-thrombolysis mean gradient across mitral valve was 8.8 ± 3.2 mmHg; while across aortic prosthetic valve was 21.5 ± 5.3 mmHg.

In hospital mortality was seen in 6 (13.3%) patients, all of them had undergone thrombolysis as mode of treatment. Among the expired patients, 4 patients had complete success while 2 patients had partial success. Most common cause of death was refractory heart failure followed by cardiogenic shock. Details are listed in Table 4 and 5 and Figure 1.

Figure 1: Types of valve involved

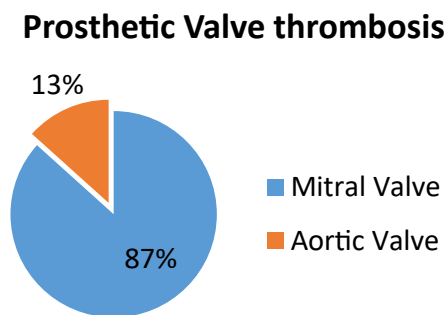


Table 3: Gradient across prosthetic valve with PVT

Valve	Maximum	Minimum	Mean
Mitral			
Peak gradient(mmHg)	43.3	21.3	
Mean gradient(mm Hg)	31.2	14.4	21.8 ± 5.2
Aortic			
Peak gradient (mm Hg)	99.1	52.3	
Mean gradient(mm Hg)	76.1	42.6	58.67 ± 9.87

Table 4 Treatment Characteristics

	No.(%)
Mode of Treatment	
Thrombolysis	42(93.3)
Surgery	3(6.7)
Thrombolysis Result	
Total	42
Complete Success	35(83.3)
Partial Success	6((14.3)
Failure	1(2.3)

Table 5 Mortality (cause)

Cause	No.
Refractory Heart failure	3
Cardiogenic Shock	2
Septic shock	1
Total	6

All patients discharged from the hospital were followed up for one year and telephone follow-up was done after 1 year duration. All the patients discharged were prescribed warfarin, whereas, Aspirin was prescribed in about half of the patients discharged. Medication at the time of discharge and 1 year follow-up details are listed in Table 6 and 7 respectively.

Table 6: Discharge Medications

Medications at discharge	No.(%)
Aspirin	21(53.8)
Warfarin (Mean Dose 4.7 ± 3.3)	39(100)
Diuretics	39(100)
ACEI/ARB	31(79.4)
Betablockers	8(20.5)

Table 7: One-year Follow-up

Description	
Lost contact	10
Under regular medication n followup	29
Recent hospital admission	6
Heart failure	4
Supra-therapeutic INR	2
Total	39

We compared the mortality rate among the different groups in the study populations. Mortality rate was relatively higher in Male patients, those younger than 40 years, patients undergoing thrombolysis as mode of treatment, patients with partial success of thrombolysis and MV replacement patients as compared to their counterpart. However none of these were statistically significant. Mortality rate was significantly higher in patients who presented in NYHA class IV and INR value more than 10, which was also proven statistically (details in table 8).

Table 8: Comparing Mortality among different groups

Group	Total (N)	Mortality (%)	p value
Gender			0.16
Male	18	4(22.2)	
Female	27	2 (7.4)	
Age			0.15
Less than 40 years	25	5(20)	
40 years or more	20	1(5)	
Mode of treatment			0.71
Thrombolysis	42	6(14.2)	
Surgery	3	0	
Symptoms (NYHA class)			0.016
Class I-III	35	2(5.7)	
Class IV	10	4(40)	

Valve			0.41
Mitral	39	6(15.3)	
Aortic	6	0	
Thrombolysis result			0.47
Complete success	39	4(10.2)	
Partial success	6	2(33.3)	
Failed	1	0	
INR			0.006
Sub optimal	29	2(6.8)	
Optimal	14	2(14.2)	
Supra therapeutic	2	2(100)	

Discussion

In our study, 45 patients were admitted with PVT with median age of 35 years, predominantly female comprising of 60%. A retrospective study done few years back in our center by Hirachan et. al. also showed similar female predominance and mean age of 35 years.⁷ However, some of the international studies have reported a higher mean age, above 50 years, but findings of women being more predisposed to PV thrombosis were similar to our study.⁸⁻¹⁰ In some studies from India, there was slightly higher frequency among men as compared to women and mean age were under 40 years.^{3,11} Several studies have confirmed that mitral PV thrombosis is 2–3 times more frequent than thrombosis of an aortic prosthesis which was also reflected in our study as most common valve involved with obstruction was mitral 39(87%) patients followed by aortic valve 6 (13%) patients which was similar to study by Gupta et al, with 87.3% of the PVT episodes occurring in the mitral position.^{3,7-10}

Successful thrombolysis or complete success was achieved in 35(83.3%) patients, this finding was similar to some other studies done in past where streptokinase was used as thrombolytic agent,^{12,13} however in one of the study by Feng et. al. where urokinase was used as the thrombolytic agent, complete success rate was slightly lower at 69.6%.¹⁴

Overall mortality of our study was 13.3%, all of whom had undergone TT, which is around 15.4% of the total TT group. This mortality rate is lower than previous study done in same center⁷ however this rate was slightly higher than that in some international studies, where the mortality rate was around 6%.^{12,15} However some of the recent studies,^{14,16} have shown similar mortality rate ranging from 13-16% in TT group.

Most of the patients in our study had poor drug compliance which was reflected by lower baseline INR value at the time of presentation as majority of patients (64.4%), had sub-therapeutic INR. This type scenario is mostly common in developing countries like Nepal, where poor socioeconomic condition of the patients also plays a big role. Poor drug compliance and suboptimal anticoagulation with sub-therapeutic INR have been the main culprit for PV thrombosis worldwide as shown by many studies.^{7,17-19} There was a very wide difference when comes to time from surgery to PV thrombosis in different studies done worldwide,^{20,21} in our study, it ranged from 2 months to 144 months with the median duration of 60 months. Along with inadequate anticoagulation, presence of atrial fibrillation (AF) may have a role in development of PV thrombosis.

In our study, 46.7% had AF previously, which was similar to some studies,^{20,22} however in some other international studies AF prevalence in PV Thrombosis was much higher.^{23,24}

In a study by Karthikeyan, there were no significant difference in major outcomes (improvement in transvalvular pressure gradient and serious complications) between surgery and thrombolysis. However, they suggested that an emergency surgical intervention in an experienced centre is preferable to thrombolysis.²¹ Another study by Sabahattin et. al., showed that the mortality rate for surgery was as high as 69%, while the reported mortality rate for TT was as high as 16%, depending on the NYHA grade and the urgency of the surgery.²⁵ Limited availability and high surgical costs and most importantly reluctance for re-do surgery in some cases, have made TT optimal treatment besides surgery for PV thrombosis in hospitals especially in underdeveloped areas.

The major limitation of the study is that it is only a single center study with small sample size which may represent just a small proportion of the whole community. Another limitation of the study may be shorter follow-up period which was one year by telephone. A large scale study with long term follow-up and regular echocardiography may provide clearer picture.

Conclusion

Mechanical prosthetic valve thrombosis is a clinical emergency which is associated with high rates of morbidity and mortality. Low socioeconomic and education status of most of the patients results in poor compliance of oral anticoagulation therapy and regular follow-up. Even after PV thrombosis, many patients still had poor achievement of optimal INR level which was reflected in our study as well, as more than one fourth of the patients were out of contact during one year follow-up. There have been many studies in PV thrombosis and treatment guidelines are being regularly updated for its management, but in the context of our country, the focus should be more on the prevention of such events. For that, proper patient education for better drug compliance and regular follow-up should be implemented.

References

- Dangas GD, Weitz JI, Giustino G, Makkar R, Mehran R. Prosthetic Heart Valve Thrombosis. *J Am Coll Cardiol*. 2016;68(24):2670-2689. doi:10.1016/j.jacc.2016.09.958
- Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: Diagnosis and therapeutic considerations. *Heart*. 2007;93(1):137-142. doi:10.1136/hrt.2005.071183
- Karthikeyan G, Math RS, Mathew N, et al. Accelerated Infusion of Streptokinase for the Treatment of Left-Sided Prosthetic Valve Thrombosis A Randomized Controlled Trial. 2009. doi:10.1161/CIRCULATIONAHA.109.876706
- Prosthetic Heart Valve Thrombosis | Elsevier Enhanced Reader. <https://reader.elsevier.com/reader/sd/pii/S0735109716366001?token=AE7194881F63680D87DA5FB559DE5A32300182C302DEC4065C056434A6FB0F5EC519F44107E1AE0C67E803139FFA0478&originRegion=eu-west-1&originCreation=20220204105840>. Accessed February 4, 2022.

5. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the Management of Valvular Heart Disease. Vol 38.; 2017. doi:10.1093/eurheartj/ehx391
6. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.; 2021. doi:10.1161/CIR.0000000000000923
7. Hirachan A, Roka M, Prajapati D, et al. Prosthetic valve thrombosis in a tertiary cardiac centre. Nepal Hear J. 2017;14(1):9-11. doi:10.3126/njh.v14i1.17188
8. N E, H A, H A, M B, S B, AT S. Comparison of fibrinolytic versus surgical therapy in the treatment of obstructive prosthetic valve thrombosis: a single-center experience. Heart Surg Forum. 2011;14(2). doi:10.1532/HSF98.20101062
9. Lengyel M VL. The role of thrombolysis in the management of left-sided prosthetic valve thrombosis: a study of 85 cases diagnosed by transesophageal echocardiography - PubMed. J Hear Valve Dis. 2001. <https://pubmed.ncbi.nlm.nih.gov/11603604/>. Accessed July 24, 2021.
10. R R, S L, MF R, 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. doi:10.1016/J.ACVD.2009.01.007
11. Kathirvel D, Justin Paul G, Prathap kumar G, et al. Tenecteplase versus streptokinase thrombolytic therapy in patients with mitral prosthetic valve thrombosis. Indian Heart J. 2018;70(4):506-510. doi:10.1016/J.IHJ.2017.10.014
12. M L, V F, M K, et al. Guidelines for management of left-sided prosthetic valve thrombosis: a role for thrombolytic therapy. Consensus Conference on Prosthetic Valve Thrombosis. J Am Coll Cardiol. 1997;30(6):1521-1526. doi:10.1016/S0735-1097(97)00345-8
13. FM C-L, H P-L, K M-H, 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. doi:10.1007/S11239-006-4969-Y
14. Huang F, Lan Y, Cheng Z, Zhang Z, Ren F. Thrombolytic treatment of prosthetic valve thrombosis: A study using Urokinase. J Cardiothorac Surg. 2020;15(1):1-6. doi:10.1186/s13019-020-01324-7
15. Castilho FM, De Sousa MR, Mendonça ALP, Ribeiro ALP, Cáceres-Lóriga FM. Thrombolytic therapy or surgery for valve prosthesis thrombosis: Systematic review and meta-analysis. J Thromb Haemost. 2014;12(8):1218-1228. doi:10.1111/JTH.12577
16. S G, MK, MOG, AG, M Ö. Diagnosis, treatment & management of prosthetic valve thrombosis: the key considerations. Expert Rev Med Devices. 2020;17(3):209-221. doi:10.1080/17434440.2020.1733972
17. Krishnan. Prosthetic heart valve thrombosis: Diagnosis and newer thrombolytic regimes. J Pract Cardiovasc Sci. 2016;2(1):7. doi:10.4103/2395-5414.182993
18. Khan HS, Ijaz Z, Ali M, et al. Clinical Outcomes of Mechanical Prosthetic Valve Thrombosis. Cureus. 2020;12(6). doi:10.7759/CUREUS.8760
19. Chitturi KR, Castro MA, Salazar E, et al. MINI-FOCUS ISSUE ON VALVULAR HEART DISEASE CASE REPORT: CLINICAL CASE Mechanical Mitral Valve Thrombosis in a Patient With Prior Nonbacterial Thrombotic Endocarditis. 2020. doi:10.1016/j.jaccas.2020.01.029
20. Thrombolysis is an effective and safe therapy in stuck bileaflet mitral valves in the absence of high-risk thrombi | Elsevier Enhanced Reader. <https://reader.elsevier.com/reader/sd/pii/S0735109700006409?token=CD53A29E8B6853394E38C2FA4AB4AEEBD2F68EDCD79A4C6AB6BBA95778C82C8E6FF319B05DE16DBB1320520FD6F506A&originRegion=us-east-1&originCreation=20210727104306>. Accessed July 27, 2021.
21. Karthikeyan G, Senguttuvan NB, Joseph J, Devasenapathy N, Bahl VK, Airan B. 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):1557-1566. doi:10.1093/eurheartj/ehs486
22. N D, M P, D B, et al. Prosthetic valve thrombosis: twenty-year experience at the Montreal Heart Institute. J Thorac Cardiovasc Surg. 2004;127(5):1388-1392. doi:10.1016/J.JTCVS.2003.12.013
23. S K, P H, MC H, et al. Comparison of thrombolysis versus surgery as a first line therapy for prosthetic heart valve thrombosis. Am J Cardiol. 2011;107(2):275-279. doi:10.1016/J.AMJCARD.2010.09.013
24. N E, H A, H A, M B, S B, AT S. Comparison of fibrinolytic versus surgical therapy in the treatment of obstructive prosthetic valve thrombosis: a single-center experience. Heart Surg Forum. 2011;14(2). doi:10.1532/HSF98.20101062
25. Gündüz S, Kalçık M, Gürsoy MO, Güner A, Özkan M. Diagnosis, treatment & management of prosthetic valve thrombosis: the key considerations. <https://doi.org/101080/1743444020201733972>. 2020;17(3):209-221. doi:10.1080/17434440.2020.1733972