ORIGINAL ARTICLE

Prosthetic Valve Thrombosis: Fibrinolysis, Surgery, or Percutaneous Manipulation?

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Abstract

A total number of 20 cases of prosthetic valve thrombosis (PVT) involving left-sided bileaflet St Jude's prosthesis (16), Medtronic Hall (3), and pulmonary prosthesis (1) are reported. Streptokinase (STK) fibrinolysis provided excellent results in 66.6% of cases with thrombosed St Jude's mitral prosthesis and remains the preferred option for this subset. Percutaneous manipulation of the mitral disk proved a useful adjuvant. Reteplase produced gratifying results in pulmonary mechanical prosthesis. However, thrombosed aortic prosthesis responded unfavorably to fibrinolysis.

About six patients who failed to respond to thrombolysis had excellent results with valve replacement surgery. Two patients (10%) succumbed due to extremely high-risk clinical characteristics.

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Introduction

Rheumatic heart disease (RHD) continues to be a common cause of multivalvular involvement requiring valve replacement at a young age.[1,2] Prosthetic valve thrombosis (PVT) is a rare but serious complication of valve replacement, mostly observed with mechanical prosthesis. The incidence of PVT for mechanical valves varies between 0.3 and 1.3% patient-years.[3] The outcome of PVT is determined by clinical status, degree of valvular obstruction, and valve location (left- or right-sided).

Obstructive left-sided PVT is generally considered an indication for surgery but is limited by excessive mortality and morbidity in patients with New York Heart Association (NYHA) class III or IV or cardiogenic shock.[4] The excessive cost of reoperation is also relevant in resource-constrained patients. Alternative therapeutic modalities include heparin and fibrinolysis. Interventional techniques have been utilized for hemodynamic stabilization in unstable patients.[5]

The present communication, a retrospective study, reports experience from a tertiary care unit in treating 20 cases involving mechanical PVT. The results of fibrinolysis, surgery, and interventional techniques are discussed.

Materials and Methods

The material for this retrospective study was obtained from records of 20 cases of PVT diagnosed and treated during January 2021 to 2023 in a tertiary care referral teaching institution.

Diagnosis of PVT was based on clinical features, fluoroscopic, and transthoracic echocardiography (TTE) findings. Clinical criteria for PVT included progressive dyspnea, heart failure (HF), low output state, or systemic embolization. Muffling or disappearance of click sounds and appearance of new regurgitation or obstructive murmur were additionally recorded. Cinefluoroscopy findings in multiple views provided information about the type of valve (single or bileaflet) and its leaflet mobility.

Transthoracic echocardiography data, including color Doppler and pulse Doppler, were available in standard parasternal long-axis, short-axis, and four-chamber views. The following data were specifically analyzed:

- Transvalvular gradients across the prosthetic valve. For mitral prosthesis, a mean gradient >8 mm Hg and for aortic prosthesis, a mean gradient >45 mm Hg supported the diagnosis when PVT is suspected.[4]
- Prosthetic valve visualization for reduced mobility, valve thrombosis, or pannus. Thrombus was diagnosed as a soft, mobile mass or homogeneous echo located on the valve leaflet, whereas pannus was visualized as a fixed, calcific, bright echo density on the valve ring.[6]
- Pulmonary artery (PA) pressures and left ventricular (LV) function.

Thrombolysis Protocol

The choice of the thrombolytic agent was decided by financial considerations and availability of the agent. One of the following thrombolytic regimens was used:

- Streptokinase (STK): 2,50,000 units intravenous (IV) for 30 minutes, followed by slow IV infusion at 1,00,000 units per hour for 48–72 hours.
- Tenecteplase (TNK): 0.5 mg/kg bodyweight as a bolus.
- Reteplase: 10 unit IV bolus over 2 minutes followed by 10 units IV after 30 minutes.

Fluoroscopy and TTE was performed at 24, 48, and 72 hours.

Depending on the response to thrombolysis, patients were categorized as responders and nonresponders. Responders were those individuals who had clinical improvement, accompanied by a reduction in transvalvular gradients by 70% and restoration of disk mobility on fluoroscopy.

Nonresponders had little or no clinical improvement, and transvalvular gradients were reduced by <50% from basal values, with sluggish or only single-leaflet mobility on fluoroscopy.

The complications of thrombolysis were classified as major or minor. Major complications included intracranial bleed, ischemic stroke, need for blood transfusion, anaphylactic shock, or inhospital mortality. Minor complications included hematoma, petechiae, access site bleeding, hematuria, hematemesis, or allergic reactions.

The nonresponders were subsequently treated either by interventional procedure or by surgical valve replacement. Two patients (case 11, 15) with mitral PVT underwent transcatheter manipulation of the prosthetic valve disk after transvenous transseptal cauterization using the protocol as described earlier.[5,7] A 6 F Judkins right (JR) coronary guiding catheter was manipulated thrice across the prosthetic valve disk under fluoroscopic guidance. Fragmentation of the thrombus was also attempted using a

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1.5 × 10 mm noncompliant (NC) balloon at 10 atm. Disk mobility changes were recorded on fluoroscopy, and gradients were recorded on TTE.[7]

Mitral valve replacement (MVR) and aortic valve replacement (AVR) were performed in six cases using conventional open-heart surgery.

Results

The duration between PVT and valve replacement was 6.3 years for the mitral position and 16.6 years for the aortic position. The results of this study were analyzed depending on the response to thrombolytic therapy and percutaneous intervention and are shown in Tables 1 and 2 and Figures 1 and 2.

Table 1 (case number 1–9) shows data of responders, who all had St Jude's mitral prosthesis and were treated with STK. About 66% (6) were males, and the age range was 30–70 (m = 43.5 years). The clinical picture was dominated by dyspnea NYHA class II and III [5 (55.6%)], HF [3 (33.3%)], and atrial fibrillation (AF) [9 (100%)]. Subtherapeutic international normalized ratio (INR) was observed in the majority [8 (88.8%)] and ranged between 1.34 and 2.17 (mean: 1.68). Following thrombolysis, all nine patients with mitral PVT had rapid clinical and hemodynamic stabilization. Mitral gradients reduced as follows:

	Average mitral gradients (mm Hg)		
	Peak	*Mean*	*%Reduction*
Prethrombolysis	32.5	15.3	–
Postthrombolysis	10.4	5.2	68%

Cinefluoroscopy showed remarkable improvement in leaflet mobility (Fig. 1, panels C and D).

A 30-year-old female (case 10) with primary intracardiac repair for tetralogy of Fallot (TOF) underwent pulmonary valve replacement (PVR) in 2009 and 2021 using Bicor and St Jude's prosthesis, 21 mm respectively, for recurrent pulmonary regurgitation (PR). She presented with pulmonary PVT and responded to reteplase bolus after developing an allergic reaction to STK. Transpulmonary gradients reduced significantly (Table 1).

Table 2 summarizes data of the nonresponders. About six (60%) were females, and the age range was 33–74 years (mean 47.9). AF was observed in the majority, 7 (70%), and 1 (10%) patient had complete heart block (CHB). The clinical picture was dominated by NYHA class II and III dyspnea 6 (60%), 2 (20%) HF, and one patient had cardioembolic stroke, angina, and low output. Both St Jude's and Medtronic Hall prosthetic valves were involved irrespective of the location of PVT. Thrombolytic failure was seen both with STK and TNK. In the nonresponder with mitral PVT, gradients were:

	Average mitral gradients (mm Hg)		
	Peak	*Mean*	*%Reduction*
Prethrombolysis	33	16	–
Postthrombolysis	17.4	8.5	47%

Fluoroscopy showed one or both leaflets remaining stuck. Three cases (Sr. No. 12, 13, 14) underwent MVR. Figure 2 shows the thrombosed prosthesis with underlying pannus at surgery.

Two patients (Sr. No. 11, 15) were reluctant for a third surgery, and a transcatheter procedure was performed with reduction in Doppler gradients and complete or partial improvement in disk mobility on fluoroscopy (Table 2).

Aortic PVT (St Jude and Medtronic Hall) patients responded poorly to thrombolysis. Aortic gradients were as follows:

	Average aortic gradients (mm Hg)		
	Peak	*Mean*	*%Reduction*
Prethrombolysis	85.3	46	–
Postthrombolysis	58	31.6	30%

Case no. 17, 18, and 20 underwent successful AVR. One patient, Sr. No. 16, presented with cardioembolic stroke, CHB, and complex aortic root anatomy. Surgery was refused by the family, and the patient succumbed after a few days of conservative therapy, including heparin.

No major complications were observed. Minor bleeding complications were seen in four patients after thrombolysis, and one had an allergic reaction to STK. Two patients (16 and 19) had fatal outcomes due to progressive shock and extremely high-risk for surgery. All patients were discharged in stable condition with advice on INR monitoring during follow-up.

Discussion

The present communication deals with 20 cases of PVT treated in a tertiary care center. PVT remains a serious condition with high mortality and morbidity. A rapid diagnosis is essential and can be promptly made by clinical history, cinefluoroscopy, and echo-Doppler techniques. This study includes 19 cases who had thrombosis of left-sided mechanical prosthesis and a case of pulmonary prosthesis. About 80% of patients with PVT had St Jude's bileaflet prosthesis, 15% Medtronic Hall, and one had bio-prosthesis. Obstructive PVT was common in young females with

Table 1: Clinical and investigative profile of responders

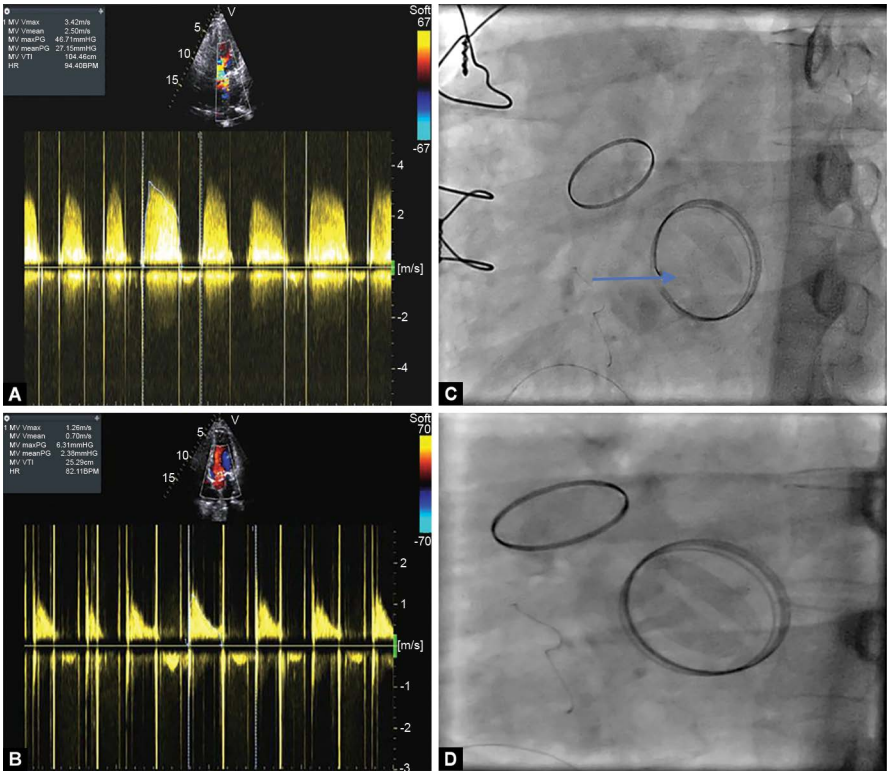
Sr. No.#	*Age*	*Sex*	*Clinical presentation*	*INR (ratio)*	*Interval (months)**	*Thrombolytic agent*	*TTE gradient*	
							Peak	*Mean*
1	39	M	HF, low output, AF	2.03	6	STK	49 (6)	21 (3)
2	41	F	NYHA III, AF	1.9	96	STK	44 (13)	20 (8)
3	54	F	NYHA III, AF	2.17	108	STK	32 (14)	15 (5)
4	51	M	NYHA III, ANGINA, AF	2.0	108	STK	25 (6)	8 (3)
5	28	M	NYHA II, ANGINA, AF	1.3	12	STK	39 (17)	20 (10)
6	31	F	NYHA III, AF	1.85	12	STK	25 (12)	12 (6)
7	49	M	HF, AF	1.34	108	STK	33 (8)	20 (3)
8	70	M	HF, low output, AF	1.26	132	STK	20 (12)	12 (6)
9	30	M	NYHA III, AF	1.5	180	STK	25 (6)	10 (3)
10[#]	30	F	NYHA II, palpitation	2.0	18	Reteplase	72 (31)	40 (19)

[#]Mitral valve PVT in all expect case 10 who has pulmonary valve involvement; *Interval between valve replacement and presentation with PVT; Gradients in () indicate values postthrombolysis; F, female; M, male; others as in text

Table 2: Clinical and investigative profile of nonresponders to thrombolysis

Sr. No.	*Age*	*Sex*	*Clinical presentation*	*Valve (location, type)*	*Thrombolytic agent*	*TTE gradients*		*Intervention*	*Outcome*
						Pre (P/M)	*Post (mm Hg)*		
11	42	M	NYHA III, SR	Mitral, ST Jude	STK	35/20	19/10	Transcath	Gradients reduced*
12	45	F	Angina, AF	Mitral, Med Hall	STK	17/10	12/6	MVR	Asymp
13	57	F	NYHA III, AF	Mitral, ST Jude	STK	47/27	11/6	MVR	NYHA I
14	29	M	NYHA III, AF,	Mitral, Med Hall	STK	44/15	30/12	MVR	NYHA I
15	53	F	NYHA II, AF	Mitral, ST Jude	STK	22/8	15/8	Transcath	Success#
16	74	M	CVA, NYHAIII, CHB	Aortic, ST Jude	Heparin	94/65	–	No	Expired
17	33	F	NYHA III, AF	Aortic, ST Jude	STK	86/40	54/20	AVR	NYHA I
18	33	F	HF, NYHA III, AF	Aortic, ST Jude	TNK	90/50	60/40	AVR	NYHA I
19	63	M	Low output, HF SR	Aortic, Med Hall	STK	90/45	60/35	No	Expired
20	50	F	NYHA III, AF	Aortic, ST Jude	STK	80/48	60/35	AVR	NHYA I

*TTE gradients reduced to 14/8 mm Hg and one leaflet briskly moving; #TTE gradients reduced to 12/6 mm Hg and both leaflets mobile; Asymp, asymptomatic; CVA, cerebrovascular accident; Med Hall, Medtronic Hall; MG, mean gradient; PG, peak gradient; SR, sinus rhythm; Transcath, transcatheter; Other abbreviations as in text

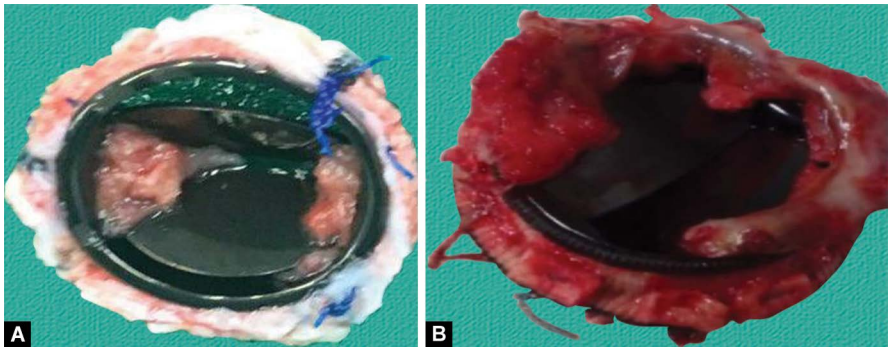


Figs 1A to D: Pre- and postthrombolysis echocardiographic continuous-wave Doppler and cinefluoroscopic views in a patient with mitral PVT: (A) Prethrombolysis peak gradient of 46 mm Hg and mean gradient of 27 mm Hg; (B) Postthrombolysis peak gradient of 6 mm Hg and mean gradient of 2 mm Hg; (C) Prethrombolysis left anterior oblique caudal views showing bileaflet tilting-disk valve in mitral position with one leaflet stuck (indicated by arrow); and (D) Postthrombolysis left anterior oblique caudal views showing bileaflet tilting-disk valve in mitral position with both leaflets mobile

AF and subtherapeutic INR, similar to the precipitating factors reported earlier.[8] It is noteworthy to note that despite widespread availability of pathological laboratories, subtherapeutic INR remains the underlying factor for PVT and was observed in 80% of patients. The Global Rheumatic Heart Disease Registry (the REMEDY study) reported no INR monitoring in 12.1%, limited monitoring in 34.1%, subtherapeutic values in 32.7%, and therapeutic values in only 28.3%.[1] About 60% of participants were unaware of the therapeutic range of INR values. It is worth emphasizing that current American College of Cardiology (ACC) and European Society of Cardiology (ESC) guidelines recommend an INR range of 2–3 for aortic and 2.5–3.5 for mitral prosthesis to prevent thromboembolism.[9–11]

Obstruction of a mechanical prosthesis requires aggressive management. Surgery is the preferred therapy for left-sided PVT but can be associated with high-risk in sick patients.[4,12,13] Fibrinolytic therapy is an attractive alternative to surgery and was used in 95% of patients in this study. The response to this therapy depends on valve position, size, and characteristics of thrombus, type of the agent, and the comorbidities. There are reports in Indian literature using STK or TNK with varying success.[13–18] STK was preferred in this study due to its easy availability and low cost. STK produced gratifying results in patients with thrombosed St Jude's bileaflet prosthesis in the mitral position (Table 1). The overall success with STK was 66.6% in mitral PVT and 55.5% in the entire series. There was a low incidence of complications, and none had an embolic episode. It is possible that there was accumulation of small amounts of thrombus at the disk pivot points, which dissolved with thrombolysis. From the current study and previous data, it can be concluded that fibrinolytic therapy using STK can be used as a first-line therapy in thrombosed St Jude's mitral prosthesis.

On the contrary, STK administration failed to achieve thrombus dissolution in Medtronic Hall and St Jude's bileaflet valve in aortic position, resulting in fatal outcome or need for surgery. The aortic bileaflet mechanical St Jude's prosthesis has a low



Figs 2A and B: (A) Thrombosed bileaflet tilting-disk (ST Jude's valve) in mitral position, and (B) stuck bileaflet tilting-disk (ST Jude's valve) in mitral position

complication rate, with a thrombosis rate of 0.03% per patient year.[19] The valve design, which provides laminar flow, a low-pressure gradient, and a large orifice area, seems responsible for reduced risk of thrombus formation. The exact cause of aortic PVT and poor response to thrombolysis remain unclear but seems related to large valve area, longer period after valve replacement (16.6 years in this study), and subtherapeutic INR. Pulmonary prosthesis thrombosis is a serious and rare complication with high mortality in patients with operated TOF. Subtherapeutic INR and complex heart surgery with two previous PVR provided the nidus for thrombosis. Third-generation thrombolytic, reteplase, provided excellent symptomatic relief and dramatic reduction in echo gradients. A previous case report also describes successful results with reteplase.[20]

Percutaneous manipulation of a valve disk using a percutaneously placed cardiac catheter has been utilized to stabilize patients with mitral and aortic PVT.[5,7] We utilized this modality effectively in two patients with mitral PVT who did not respond to thrombolysis and were considered very high-risk for surgery. The conventional wisdom and teaching have been to avoid crossing of the prosthetic valve by guide wire or catheter due to potential complications like embolization or wire entrapment. The procedure proved safe and effective in both patients with all necessary precautions; however, large data are needed to support the use of this technique.

Surgery was performed in six patients with fibrinolytic therapy failure. Three patients each had MVR and AVR, with prompt restoration of valve function and hemodynamics. Excellent results could be obtained with improved surgical techniques and skills. High surgical success with excellent short- and long-term results has been reported.[4,21]

Conclusion

Prosthetic valve thrombosis is common in females with AF, low output, and subtherapeutic INR. STK-based fibrinolysis can be therapy of first choice, with gratifying results in thrombosed St Jude's mitral prosthesis. Percutaneous transcatheter manipulation of the prosthetic disk is an alternative modality in high surgical risk patients. Valve replacement surgery was safe and lifesaving in individuals with thrombolysis failure.

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