

Original article:

Effect of thrombolysis on stuck metallic valve prosthesis using Alteplase And Reteplase

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Abstract:

Background: Prosthetic valve thrombosis (PVT) is a severe complication of heart valve replacement, often necessitating prompt treatment. Options include thrombolysis, surgery, and anticoagulation therapy, with outcomes varying by patient condition and local resources.

Methods: This retrospective study, conducted between December 2020 and February 2023, involved 25 patients with PVT who received thrombolysis using alteplase and reteplase. Contraindications excluded eight patients from thrombolysis. Patients were monitored for complications and outcomes. Treatment involved subcutaneous low molecular weight heparin, alteplase, or reteplase, followed by bed rest. Warfarin or niocumerol was initiated alongside thrombolysis.

Results: Thrombolysis successfully treated 76% of patients, with a partial success rate of 32%. Hemorrhagic complications were observed in 16% of patients, and two patients experienced fatal cerebral hemorrhages. There were no thromboembolic complications. The overall mortality rate was 8%, with no clear correlation between complications and cardiac function.

Conclusion: Thrombolysis with bolus doses of alteplase and reteplase demonstrated efficacy in treating PVT, especially when emergency surgery was not feasible. Education on PVT prevention is crucial. Thrombolysis should be considered in resource-constrained settings or when surgery carries significant risks.

Keywords: Prosthetic valve thrombosis, thrombolysis, alteplase, reteplase, complications.

Introduction:

We tried to analyse the effectiveness of thrombolysis of stuck prosthetic valves in mitral and aortic valves in our center and complications caused by thrombolysis . A total of 25 patients underwent thrombolysis using alteplase and reteplase in our institute in which alteplase at the dose of single bolus dose of 50 mg and reteplase divided dose of 9 mg each given half an hr a part were given to patients with a prior dosage of low molecular weight heparin 0.4ml sub cutaneous 2 hrs prior to thrombolysis and bd dose next 5 days with warfarin or acitrom ie niocumerol and supportive care .patient is closely monitored for complications and results of thrombolysis and discharged after stabilizing of the patient or patient prepared for redo surgery . Stuck prosthetic valve or prosthetic valve thrombosis (PVT) is characterized by formation of thrombus on the prosthetic valve causing valve dysfunction with or without thromboembolism

The incidence of PVT is about 0.3 % to 1.3 %in developed world and quite a high 6.1 in developing nations within 6 months of surgery (1) Intravenous TT has been used as an alternative treatment to surgery in PVT patients [2]. Compared with that of TT, the mortality rate of emergency surgery in PVT patients is higher.so thrombolysis is still the treatment to go to in PVT as the other modes like aggressive anticoagulation(under treatment) and surgery(though effective) carries significant morbidity and mortality. Here we report our centers retrospective study of thrombolysis with alteplase and reteplase and its results .

Methodology:

Between december 2020 and feb 2023 at our institute(GIPMER) a total of 38 patients had presented with pvt in emergency of which 25 patients chose thrombolysis as a treatment option owing to financial constraints and risks involved in surgery and 8 patients were not offered thrombolysis due to one of the following contraindications. 1. Uncontrolled hypertension with blood pressure above 180/110 mmHg; 2. Ischaemic stroke or cerebral haemorrhage within half a year; 3. Intracranial tumour; 4. Active internal bleeding in the last 4 weeks; 5. Suspected aortic dissection; 6. History of major surgical operations in the last 3 weeks; 7. Large vessel puncture at an uncompressible site was performed within 2 weeks; 8. Pregnancy; 9. Active stomach ulcers; and 10. Allergy to thrombolytic drugs. There were 13 females and 12 males . the average age was 38 years (25 to 54) and the time frame between onset of symptoms from time of surgery ranged from 6 months to 5 years there were 25 cases of mitral valve and one patient had increased gradient on aortic position the valves that were stuck included 6 ttk chitra (single leaflet) 6 sjm ,4 carbomedioics ,8ATS ,1 .SORIN all bileaflet valves. All the patients had nyha iii / iiii The main clinical symptoms of PVT are thromboembolism, dyspnoea, and limited activity. Eight patients with acute pulmonary edema (APE) caused by large area occlusion of the prosthesis were classified as New York Heart Association class IV (NYHA IV). . All patients were confirmed by clinical symptoms, blood examination, electrocardiogram, and xray fluoroscopy Additional investigation of all patients confirmed the clinical suspicion of PVT. TEE was used only if was necessary as most patients were very sick to tolerate tee to diagnose the dysfunction of artificial heart valves.

Thrombolytic therapy

All cases were treated with fibrinolysis, regardless of the operation team. All the patients were given low molecular weight heparin 0.4 ml sub cutaneous followed by, if alteplase 50 mg single dose and complete bed rest next 4 hrs and reteplase 9 mg two doses half an hour apart and bed rest for next 4 hrs .and we needed to repeat the dose only in 2 patients .and low molecular weight heparin continued twice daily 12 hrs apart 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 hemodynamics were significantly improved without any serious complications. Transthoracic echocardiography (TTE) was used every 12 h to monitor whether the thrombus was reduced and whether there was hemodynamic improvement and transvalvular gradient decreased by at least 50 %.warfarin or niocumerol started from day one of thrombolysis . The failure of TT was considered to be no significant improvement in valve activity and everyday Routine blood tests, the prothrombin time (PT), international normalized ratio (INR) and complications were observed every day.the cross-valve gradient after treatment or serious complications during thrombolysis.

Results

Efficacy of Fibrinolytic treatment

Of the twenty-five patients, nineteen (76%) were successfully treated with thrombolytic therapy: 1/1(100%) aortic valves (Fig. 3) and 19/21 (66.7%) mitral valves (Fig. 4). The partial success rate of this study was 8 (2/25), and these patients received 1 cycle of either alteplase or reteplase treatment. However, even after 2 cycles, four patients did not show any improvement in haemodynamics. Except for two patient who died of cerebral haemorrhage, the other 2 were taken up for surgery

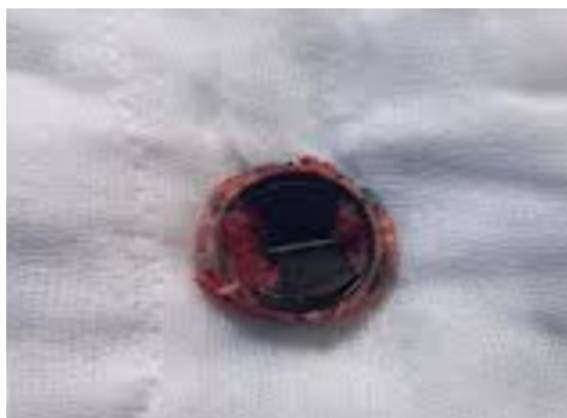


FIG 1 Post surgery valve prosthesis with pannus

Dosage of alteplase and reteplase

The dosage of alteplase in patients with successful thrombolysis was 50 mg single dose and reteplase was 9 mg two doses iv half an hr apart . most patients with successful thrombolysis

The dosage of alteplase and reteplase was same as previous dose only one extra dose in other patients where thrombolysis was not successful.



FIG 2 Pre thrombolysis TTE of mitral valve prosthesis

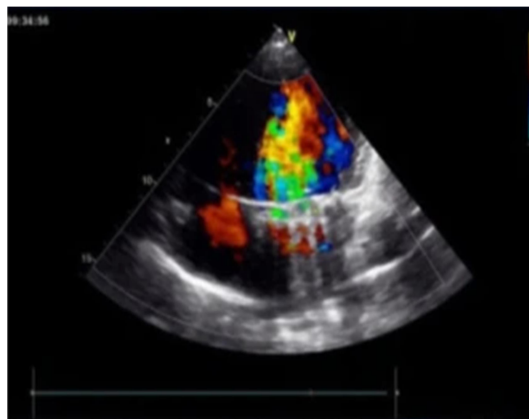


FIG 3 Post thrombolysis TTE of mitral valve prosthesis

Complications of Fibrinolytic therapy

Haemorrhagic complications: 4 patients had slight haematuria. two patients died of severe cerebral haemorrhage and shock. Embolic episodes: No thromboembolic complications occurred in any of the patients. The overall mortality was 8% (2/25), including two patients who died after subsequent surgery. There was no obvious relationship between cardiac function classification and complications. However, all patients who died were classified as NYHA functional grade IV.

Discussion

The treatment for PVT includes intensive anticoagulation therapy, TT and emergency surgery. The effectiveness of PVT anticoagulant therapy has been examined in only a few publications [3,4,5]. It has been reported that the treatment of small asymptomatic thrombi (length < 10 mm) by optimizing anticoagulant therapy has a good prognosis [6]. These patients had a high mortality rate during TT and surgery.

In the past few decades, thrombolytic therapy has been increasingly used in PVT. Although there have been numerous reports worldwide on the clinical manifestations in and treatment options and methods for patients with artificial valve 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, and the experience with reoperation. Karthikeyan analysed 690 cases in seven PVT thrombolysis studies and found no significant difference in major outcomes (improvement in transvalvular pressure gradient and serious complications) between surgery and thrombolysis [7]. However, they suggested that an emergency surgical intervention in an experienced centre is preferable to TT. Compared to this meta-analysis, previous data 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 [8]. Therefore, surgical treatment is not suitable for all patients. Limited availability and high surgical costs have made TT the optimal treatment for PVT in hospitals that do not have reoperation experience or are located in economically underdeveloped areas.

Several fibrinolytic medicines commonly used in previous studies, such as urokinase, streptokinase, tenecteplase and recombinant plasminogen activator, have different therapeutic effects and different levels of safety in PVT. Recombinant plasminogen activator and tenecteplase thrombolytic therapy for PVT has been widely used in many studies, but no one has reported it in China. alteplase and reteplase are commonly used antithrombolytic agents .all our patients received either rt-pa or alteplase depending on the availability of the total 25 patients 21 had a successful thrombolysis 2 of them died of cerebral hemorrhage which occurred within half an hr of injecting the agents .4 patients had slight hematuria and 2 of them were taken up for surgery which and died after the surgery. because the patients were very sick with NYHA III symptoms our study has near about same success ratio as ultraslow promete trial which was observational single center study where 114 patients with 120 episodes of PVT were lysed with low dose rt-pa 25 mg given over 25 hrs avoiding a bolus dose and concomitant anti coagulants (12) they reported overall success rate of 90% and complication rate of 6.7 %. Similar to our study Ari et al . reported 100% clinical success in a small series of eight patients with 25 mg slow infusion of rt-PA over 6 hrs(13)which was more successful than ours and Krishnan et al . showed that low dose rt-PA had lowest complication rate 10.5 percent similar to ours .

When thrombolysis was compared with surgery in a meta analysis by Karthikeyan et al . asurgery resulted in complete success with significantly lesser complications(14) which is similar to my institute experience and another metaanalysis revealed lower mortality with thrombolysis . however there is a need for adequate INR values to prevent thrombosis of prosthetic valves, emphasizing the need for close supervision of INR values coupled with regular echo cardiographic flow up . cardiac ct is considered better imaging modality in evaluating prosthetic valve dysfunction and to differentiate between pannus and thrombus .which is not performed in our cases due to multiple constraints and also is a limitation of our study so is transesophageal echocardiography owing to sickness and symptoms of the patients .

Conclusion:

Conclusions prosthetic valve dysfunction is dreadful complications for treating surgeons or cardiologists .early diagnosis and prompt treatment lead to better outcomes with shorter hospital stays and lesser complications alteplase and reteplase in bolus doses have shown good results similar to slow infusion and lesser bleeding complications .patient education is the key to prevent PVT and thrombolysis should be considered whenever emergency surgery is not feasible .

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