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ORIGINAL ARTICLE

Prosthetic valve thrombosis—should thrombolysis be considered as first line of management?

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Abstract
Background Traditionally prosthetic valve thrombosis has been managed with emergency surgery. However, there is growing evidence that thrombolysis is a suitable alternative. In this study, we aim to examine the safety and efficacy of thrombolysis in the management of prosthetic valve thrombosis (PVT).
Material and methods This retrospective study was carried out at a single center between June 2010 and June 2014. All patients presenting with PVT were included in the study. All patients were treated with thrombolysis using our institutional protocol.
Results Nineteen patients presented with 24 episodes of PVT. Overall, 73.6 % (14/19) of the patients were successfully treated with thrombolysis leading to clinical as well as haemodynamic improvement. Four (21 %) patients were taken directly for an operative intervention. The remaining 15 patients had a trial of thrombolysis which was successful in all cases. However, four of these patients had a recurrence within 2 weeks and were offered a second trial of thrombolysis. Three of these patients had a satisfactory outcome, and one patient was taken for surgery. Overall, 73.6 % (14/19) of the patients were successfully treated with thrombolysis. There was one incidence of intracerebral bleed leading to death. Mitral valve was the commonest valve involved in our study.
Conclusions Thrombolysis is safe and may be considered as primary treatment strategy for first episode of prosthetic valve thrombosis. In recurrent thrombosis as well, a trial of thrombolysis can be given.

Keywords Prosthetic valve thrombosis · Thrombolysis · Mitral valve

Introduction

Prosthetic valve thrombosis is an uncommon complication with an incidence rate of 0.03–4.3 % patient-years [1]. Despite its low incidence when it occurs, the implications can be severe, even fatal. Thrombolysis for prosthetic cardiac valve thrombosis has generally been recommended for critically ill patients when surgery is not immediately available, in right-sided prosthetic valve thrombosis (PVT) or during pregnancy [2].

Although for the right-sided PVT, thrombolytic therapy has long been proven to be the mainstay of treatment options [1], there is no specific consensus for the management of left-sided PVT. While operative intervention, due to the emergent nature and concomitant hemodynamic compromise, carries a high mortality [3] and significant morbidity, the critics of thrombolysis cite the risk of clot fragmentation and embolism to the brain as a potential complication. Risk of hemorrhagic stroke during thrombolysis remains another concern.

The aim of this study was therefore to assess the effectiveness of thrombolysis for first time left-sided prosthetic valve thrombosis and to assess if it can be used as a first-line treatment option in prosthetic valve thrombosis. We also sought to examine if thrombolysis was safe in these situations.

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Table 1 Different procedures prior to presenting with prosthetic valve thrombosis

Initial operation prior to presentation with prosthetic valve thrombosis	Total numbers
Aortic valve replacements	3
Aortic+mitral valve replacements	3
Aortic+mitral valve replacement+tricuspid repair	1
Mitral valve replacement±tricuspid repair	9
Re-operative mitral valve replacement	1
Ventricular septal defect+aortic valve replacement	1
LA myxoma+mitral valve replacement	1

Material and methods

This retrospective single-center study was carried out between June 2010 and June 2014, and all patients presenting with a prosthetic valve thrombosis were included in the study. Ethical approval was obtained for the study. A diagnosis was established on clinical history including auscultation for murmur and transthoracic echocardiography (TTE). If there was any doubt, transesophageal echocardiography or fluoroscopy was performed. Thrombolysis if indicated was performed using our institutional protocol. The thrombolytic agent of choice in our study was streptokinase and was started in all first time prosthetic valve thrombosis patients. In recurrent cases of prosthetic valve thrombosis, where streptokinase was used before, tissue plasminogen activator (t-PA) or urokinase was used. Streptokinase infusion was given for a maximum of 72 h. The dosage regime was injection streptokinase 2,00,000 IU over 30 min followed by 1,00,000 IU/h for 6 h and 50,000 IU/h for 48–72 h. TTE was done every 12 h to assess the status of the valve and coagulation profile studied. A satisfactory outcome was one where there was hemodynamic improvement along with adequate valve leaflet excursion. Failure was defined as no clinical improvement with or without improvement in valve leaflet excursion. Failure of the thrombolytic therapy was treated with surgical intervention. Following thrombolysis or surgical intervention, these patients are seen at 1 week, 6 weeks, and then 3 months post discharge. In the absence of any further complications, they are seen every 6 months thereafter. Once a stable target international normalized ratio (INR) was achieved, the patient was discharged with a booklet on INR management designed specifically for valve patients in their native language. They were given an INR testing regime and were encouraged to call for advice after the test.

Results

During the study period, a total of 1131 valves were implanted of which 19 (1.67 %) patients developed PVT. During this period, 1 out of 69 monoleaflet valves implanted had PVT. This was in the mitral position. Two hundred and twenty-seven patients had double valve replacement of which two (0.88 %) patients had PVT, both in the mitral position. Isolated bileaflet mitral valve replacement was performed in 518 patients of which 12 (2.31 %) had PVT. Of the 317 isolated aortic valve replacements, four (1.26 %) patients had PVT. In total, these 19 patients presented with 23 episodes of PVT. The different procedure the patients underwent prior to presenting with prosthetic valve thrombosis is mentioned in

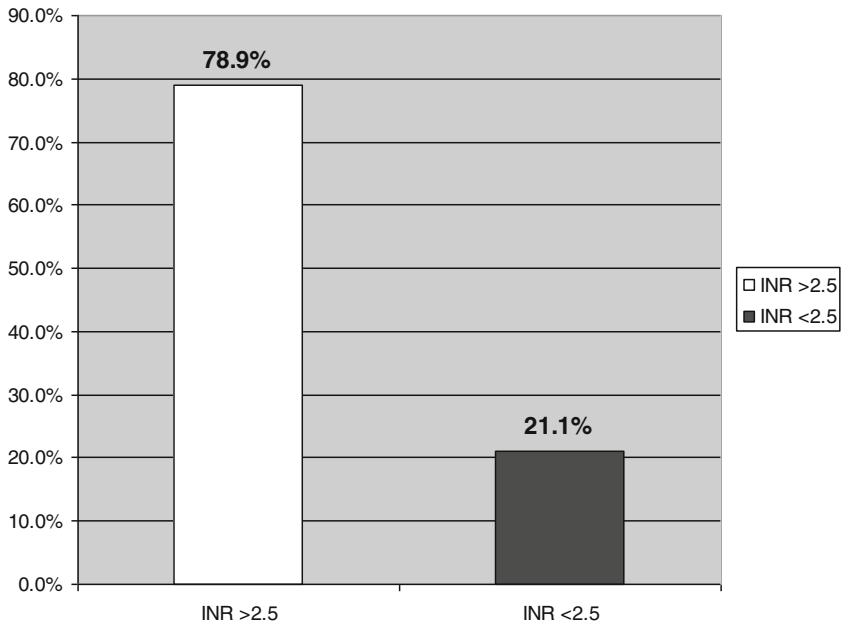

Fig. 1 Comparison of patients with INR >2.5 and INR <2.5

Table 1. The valves implanted at the primary procedure were bileaflet in all cases except one where a single leaflet valve was used. The mean duration between primary operative procedure and presentation with a prosthetic valve thrombosis was 449 days (range 54 to 1884 days). Four patients were taken for surgery due to contraindication to thrombolysis (n=2), severe hemodynamic compromise (n=1), and concomitant clot in the left atrium (n=1). The remaining 15 patients had a trial of thrombolysis according to our institutional protocol. Thrombolysis was successful in all the cases. However, four of these patients had a recurrence within 2 weeks and were offered a second trial of thrombolysis tissue plasminogen activator (t-PA). Three of these patients had a satisfactory outcome, and one patient was taken for surgery. Overall, 73.6 % (14/19) patients were successfully treated with thrombolysis.

The mitral valve was involved in 78.9 % cases (15/19) and the aortic valve in four cases (21.05 %), but this association was not significant [odds ratio 1.30 (95 % CI 0.34–4.95)]. At the time of presentation, 78.9 % of the patients had an INR >2.5 with a mean±SD of 3.60±1.71 (Fig. 1). There were no documented thrombo-embolic episodes before or after the treatment in our study.

However, of the 19 episodes of thrombolysis, there was one (5.26 %) incidence of intracerebral bleed and it was fatal. There were no other complications of thrombolysis in our study.

Operative intervention was undertaken in five patients in total. Two of these patients were found to have pannus formation on the ventricular side of the prosthetic valve. The prosthetic valve was replaced in all cases. There were no deaths in the surgical group.

Discussion

The main finding of our study was that thrombolysis was safe and effective in treating first episodes of prosthetic valve thrombosis involving the left side. In recurrent thrombosis as well, thrombolysis was successful in majority of the procedures and perhaps justifies a trial thrombolysis to resolve the problem.

Comparison between surgery and fibrinolysis in managing left-sided prosthetic valve thrombosis has not confirmed the superiority of surgery. It has been shown in a systematic review and meta-analysis of observational studies that urgent surgery is not superior to thrombolytic therapy in managing left-sided PVT [4]. In fact, thrombolysis was shown to be superior to surgery in obstructive PVT, especially in NYHA (New York Heart Association) class IV patients with severe complications of thrombolysis noted only in the critically ill patients [5].

With regard to concern about thrombolysis-induced cerebral bleeds or embolic phenomenon, studies carried out in high-risk groups in left-sided PVT have shown satisfactory safety outcomes as most of the thromboembolic events did not cause any serious consequences [6, 7]. This is in keeping with our study where the neurological event rate was low, 5.26 % (1 out of 19).

In our study, the strategy of thrombolysis was applied to all patients presenting with left-sided PVT irrespective of NYHA class or other risk factors and was found to be effective in majority of the patients with a very low complication rate. Other studies have shown similar results with success of thrombolysis previously been shown to be independent of the thrombolytic agent used and the position or the type of valve and is also independent of New York Heart Association functional class, suboptimal international normalized ratio on admission, or previous aspirin use [8, 9].

As thrombolysis appears to be effective with a safety margin that is acceptable and compares favorably with operative re-intervention [10], the obvious question therefore is why we should subject the patients to a repeat surgery which carries higher mortality and morbidity risks. Moreover, in the Indian setup, where majority of the surgical procedures still come at a significant cost to the patients; the additional issue of finances further makes a compelling case for using thrombolysis as a first-line management strategy for prosthetic valve thrombosis. In our study, even though four of the patients had a recurrence due to incomplete clot resolution, three of them responded to repeat thrombolysis. Based on our findings and evidence from existing literature, we would like to conclude that thrombolysis may be considered as first-line treatment for management of first episode of prosthetic valve thrombosis. In recurrent episodes of prosthetic valve thrombosis, thrombolysis may be attempted but a decision based on the index patients may be more appropriate.

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