# Effectiveness of alteplase infusion for the management of prosthetic mitral valve thrombosis in pediatric age group and proposed algorithm

Mohamed H Mashali (1,2) , Zaheer Ahmad (1), Mohammed Omar Galal (1) and Amjad Al-Kouatli (1)

1 Pediatric Cardiology Department, King Faisal Specialist Hospital and Research center, Jeddah, Saudi Arabia and

2 Department of Pediatrics, Faculty of medicine, Cairo University, Cairo, Egypt

## Introduction

Prosthetic valve thrombosis leading to valvular obstruction could potentially be a life-threatening complication whose treatment remains controversial (1).

Early diagnosis followed by treatment is of paramount importance as any delay can lead to significant morbidity and mortality (2). There is a lack of definite guidelines for the treatment of prosthetic valve thrombosis not only in the pediatric population but also in the adult population as well. Treatment options vary from anticoagulation, thrombolytic therapy, or in extreme cases might need urgent prosthetic valve replacement (3).

Though **thrombolysis** has been used in the pediatric population for a long time for different indications, especially in patients with central venous catheter thrombosis, and after arterial access problems, there is still limited data on its risks and benefits in this population (4).

Out of all the thrombolytic agents, **alteplase** has shown to have a high affinity for fibrin (5). Given this fact, alteplase is the most recommended thrombolytic agent. One other potential advantage which alteplase has over other thrombolytics is its short half-life (6).

There is growing literature of its efficacy and safety in prosthetic valve thrombolysis in the adult population (7). However, its role in pediatric prosthetic valve thrombosis is still not clearly established. Moreover, there is no clear dosing regimen as well (8)

## Objectives

The aim of this study is to present our experience regarding the effectiveness of **low dose alteplase** for pediatric prosthetic mitral valve thrombosis. **The primary outcome** was successful thrombolysis without major bleeding complications. Moreover, we would like to suggest an algorithm for the management of prosthetic valve thrombosis in the pediatric population.

## Materials and Methods

This **retrospective chart review** included patients who underwent thrombolysis (alteplase) for prosthetic mitral valve thrombosis from June 2011 to June 2021. We identified 10 patients with 20 attempts of alteplase infusion (three patients received alteplase infusion more than once).

**Dose: Thrombolysis** was done using **alteplase** with a dose of 0.1 – 0.5 mg/kg/hour.

**Successful thrombolysis** was defined as a drop of the mean gradient to baseline level and complete normalization of valve function (normal leaflet motion either by echocardiography or fluoroscopy).

**Partial response** was defined as > 50% reduction in gradients but with restricted leaflet motion.

**Failure of thrombolysis** was declared if there was <50% reduction of gradient along with restricted leaflet motion.

**Major bleeding** was defined as gastrointestinal bleeding, intra- cranial bleeding, or any bleeding requiring blood transfusion.

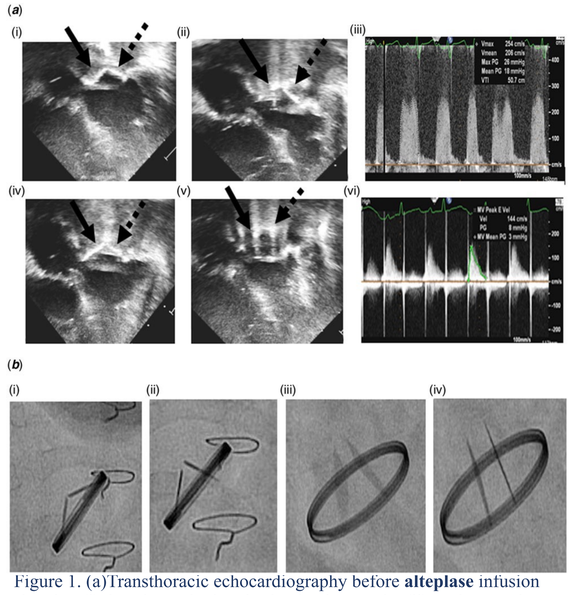



Figure 1. (a)Transthoracic echocardiography before **alteplase** infusion showing (i)closed prosthetic mitral valve in systole, (ii)stuck posterior mitral valve leaflet in diastole and (iii) increased mean gradient across the valve. Post-**alteplase** infusion echocardiography reveals (iv) closed prosthetic mitral valve in systole, (v) both leaflets opening normally in diastole, and (vi) return of mean gradient across prosthetic mitral valve back to baseline. Anterior leaflet is shown in bold arrow and posterior leaflet in dotted arrow. (b) Fluoroscopy of prosthetic mitral valve showing closed mechanical valve during systole (i), stuck mitral valve leaflet (ii), partial opening of mitral valve leaflets (iii), and normal opening of mitral valve leaflets (iv).

## Results

A total of 10 patients with 20 trials of alteplase infusion from June 2011 to June 2021 were included.

Demographic data and outcome of patients are shown in Table 1.

**Table 1.** Demographic data and outcome of patients

| Patient | Age | Weight in kg | Diagnosis | Valve type and size in mm | Type of presentation | Access | Dose in mg/kg/hour | Duration of alteplase in hours | Echo mean gradient on presentation in mmHg | Echo mean gradient on stopping alteplase in mmHg | Outcome of alteplase treatment | Complications of alteplase | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 12.5 years | 29 | AVSD | St Jude (21) | Heart failure | Peripheral | 0.3 | 48 | 22 | 8 | Success | Mild bleeding gum | Stable |
| 2 | 6 months | 5.6 | Congenital MR | St Jude (19) | Acute renal failure | Central | 0.1 | 72 | 10 | 2 | Success | None | Death MOF |
| 3 | 15.5 years | 26.5 | AVSD | Carbomedics (21) | Heart failure | Central | 0.3 | 14 | 23 | 12 | Success | Mild haemoptysis | Elective redo MVR |
| 4 | 9 months | 7 | TOF – congenital MR | Epic (21) | Routine follow-up | Central | 0.1 | 12 | 9 | 8 | Success | None | Elective redo MVR |
| | 11 months | 7.5 | | | Gastroenteritis | Central | 0.1 | 24 | 14 | 5 | Success | None | |
| | 12 months | 8 | | | Routine follow-up | Central | 0.1 | 10 | 8 | 4 | Success | None | |
| | 13 months | 8 | | | Gastroenteritis | Central | 0.1 | 16 | 15 | 12 | Success | None | |
| | 13 months | 8 | | | Routine follow-up | Central | 0.1 | 8 | 12 | 6 | Success | None | |
| 5 | 24.5 years | 25 | Congenital MR | St Jude (23) | Heart failure | Peripheral | 50 mg bolus 0.14 | 6 | 20 | 7 | Success | Non | Stable |
| 6 | 4.5 years | 15 | AVSD. | Carbomedics (18) | Routine follow-up | Central | 0.05 | 36 | 20 | 14 | Partial response | Haematoma around central line | Emergency redo MVR |
| 7 | 9 years | 18 | Single ventricle | St Jude (25) | Routine follow-up | Central | 0.1 | 15 | 18 | 8 | Success | None | Elective redo MVR |
| | 9.5 years | 19 | | | Routine follow-up | Central | 0.1 | 72 | 17 | 6 | Success | None | |
| 8 | 8 months | 6.4 | Shone's complex | St Jude (19) | Routine follow-up | Central | 0.1 | 6 | 20 | 5 | Success | None | Elective redo MVR |
| | 8.5 months | 6.6 | | | Routine follow-up | Peripheral | 0.1 | 6 | 24 | 4 | Success | None | |
| | 9 months | 6.6 | | | Heart failure | Central | 0.3 | 9 | 20 | 7 | Success | Haematoma around central line | |
| | 13 months | 7.8 | | St Jude (21) | Heart failure | Peripheral | 0.1 | 24 | 11 | 3 | Success | None | Stable |
| | 13.5 months | 7.8 | | | Heart failure | Peripheral | 0.1 | 12 | 20 | 3 | Success | None | |
| | 14.5 months | 8 | | | Heart failure | Peripheral | 0.1 | 24 | 14 | 3 | Success | None | |
| 9 | 15 years | 32 | Congenital MR | St Jude (19) | Heart failure | Peripheral | 0.1 | 6 | 22 | 7 | Success | None | Stable |
| 10 | 10 years | 32 | Congenital MR | St Jude (25) | Routine follow-up | Peripheral | 0.1 | 16 | 24 | 5 | Success | None | Stable |

Abbreviations: AVSD = atrioventricular septal defect; MOF = multiorgan system failure; MR = mitral regurgitation; MVR = mitral valve replacement; TOF = tetralogy of Fallot.

## Discussion

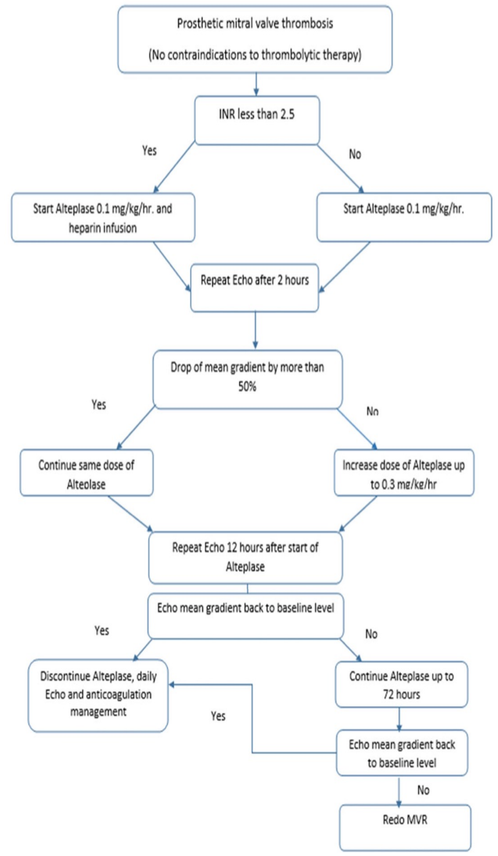
In this study, we have shown that **alteplase** infusion is highly effective in the management of prosthetic valve thrombosis in the pediatric population. Moreover, the risk of fatal complications is negligible. The overall success rate was more than 95%. Low-dose regimen appears to be as effective as high dose. Additionally, we demonstrated that alteplase can be administered safely and effectively via peripheral line.

Based on our experience regarding **alteplase** infusion, in the majority of our patients, we used slow infusion of **0.1–0.3 mg/kg/hour** rate with the aim of reducing embolic and bleeding complications while keeping the success rate as high as possible. We did not come across any major complications . We also looked at the risk factors which could have precipitated prosthetic valve thrombosis, but all of the patients seem to be well anticoagulated at the time of presentation. Another possible explanation could be some sort of mechanical issue which renders the valve liable for thrombogenicity.

In the pediatric population, we do not have any standard guidelines to treat prosthetic valve thrombosis. The decision of starting thrombolysis needs to be made on a case-by-case basis comparing the risks and benefits (11). We suggest an algorithm for the management of this condition in the pediatric population.

The first step in the algorithm is the diagnosis of prosthetic mitral valve thrombosis by echocardiography and confirmation by fluoroscopy in doubtful cases. Alteplase is started if there is no contraindication for thrombolysis.

### Algorithm for management of prosthetic mitral valve thrombosis: Figure 2




*Mashali MH, et al. 2022 Effectiveness of alteplase infusion for the management of prosthetic mitral valve thrombosis in paediatric age group and proposed algorithm. Cardiology in the Young*

## Conclusions

**Alteplase** infusion as preferred fibrinolytic therapy in the paediatric population appears to be a safe option in cases of acute prosthetic valve thrombosis. We recommend using it as a low-dose infusion through the peripheral line rather than a loading or high-dose regimen. There should be a low threshold to start this to prevent long-term complications of prosthetic valve thrombosis.

## References

1. Biteker M, Altun I, Basaran O, Dogan V, Yildirim B, Ergun G. Treatment of prosthetic valve thrombosis: current evidence and future directions. J Clin Med Res 2015; 7: 932–936.

2. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diag- nosis and therapeutic considerations. Heart 2007; 93: 137–142.

3. HuangF,LanY,ChengZ,ZhangZ,RenF.Thrombolytictreatmentofpros-thetic valve thrombosis: a study using Urokinase. J Cardiothorac Surg 2020; 15: 286.

4. Silber H, Khan SS, Matloff JM, Chaux A, DeRobertis M, Gray R. The St. Jude valve: thrombolysis as the first line of therapy for cardiac valve throm- bosis. Circulation 1993; 87: 30–37.

5. VitaleN,RenzulliA,CerasuoloFetal.Prostheticvalveobstruction:throm-bolysis versus operation. Ann Thorac Surg 1994; 57: 365–370.

6. El-SegaierM, KhanM, KhanZ, MomenahT, GalalMO. recombinanttissue plasminogen activator in the treatment of neonates with intracardiac and great vessels thrombosis. Pediatr Cardiol 2015; 36: 1582–1587.

7. Dillon GM, Stevens S, Dusenbury WL, Massaro L, Toy F, Purdon B. Choosing the Correct "-ase" in acute ischemic stroke: alteplase, tenecte-plase, and reteplase. Adv Emerg Nurs J 2019; 41: 271–278.

8. Bivard A, Lin L, Parsonsb MW. Review of stroke thrombolytics. J Stroke 2013; 15: 90–98.

9. Dangas G, Weitz J, Giustino G, Makkar R, Mehran R. Prosthetic heart valve thrombosis. JACC. 2016; 68: 2670–2689.

10. Ootaki Y, Yamaguchi M, Yoshimura N, et al. A successful thrombolytic therapy for thrombosed ATS valve in the mitral position in a child; report of a case. Kyobugeka. Japanese J Thorac Surg. 2003; 56: 790–792.

11. Tarango C and Manco-Johnson MJ. Pediatric Thrombolysis: A Practical Approach. Front Pediatr 2017; 5: 260.