Archivos Peruanos de Cardiología y Cirugía Cardiovascular

Arch Peru Cardiol Cir Cardiovasc. 2021;2(3):196-199.

Case Report

# Prosthetic valve thrombosis and thrombolytic therapy in the modern era: a case report

Oswaldo E. Aguilar-Molina[1], David Prada-Escobar[2], Jairo A. Gándara-Ricardo[1,3], Héctor D. Arroyave- Páramo[2,3], Juan M. Senior-Sánchez[1,3], Edison Muñoz-Ortiz[1,3]

Received: July 26, 2021
Accepted: September 05, 2021

**Authors' Affiliation**

[1] Cardiology Section, Internal Medicine Department, University of Antioquia, Medellin, Colombia.
[2] Anesthesiology and Reanimation Department, University of Antioquia, Medellin, Colombia.
[3] Clinica Cardiobstetrica, Cardiopulmonary and Peripheral Vascular Functional Unit, San Vicente Fundacion University Hospital, Medellin, Colombia.

***Correspondence**
David Prada Escobar
64th street # 51 D – 154, San Vicente Fundación University Hospital, Medellín, Colombia.
Postal Code: 050010

**Email**
david.pradae@udea.edu.co

**Funding**
The authors declare they did not receive any funding or sponsorship for the making of this article.

**Conflict of Interest**
The authors declare they have no conflict to disclose.

**Cite as:**
Aguilar-Molina OE, Prada-Escobar D, Gándara-Ricardo JA, Arroyave-Páramo HD, Senior-Sánchez JM, Muñoz-Ortiz E. Prosthetic Valve Thrombosis and Thrombolytic Therapy in the Modern Era: A Case Report. Arch Peru Cardiol Cir Cardiovasc. 2021;2(3):196-199. doi: 10.47487/apcyccv.v2i3.149.

## ABSTRACT

Prosthetic valve thrombosis is a feared complication with an annual incidence ranging between 0.3 to 1.3%. Diagnostic approach is essential for a better prognosis and ultimately determines the chosen therapeutic strategy. Emergent valvular surgery is usually recommended in hemodinamically unstable patients, large thrombus or recurrent embolic episodes. These high-risk conditions are often not the case. Therefore, in many patients the surgical risk is much greater than that of bleeding associated with thrombolytic administration. Ultra-slow infusions have been reported with similar efficacy and lower rates of bleeding complications. We present a case of mitral prosthetic valve thrombosis considered not feasible to surgical management and subsequently treated with an ultra-slow tissue plasminogen activator infusion.

**Keywords:** Thrombosis; Heart Valve Diseases; Thrombolytic Therapy; Heart Failure; Therapeutics (source: MeSH NLM).

## Introduction

Prosthetic valve thrombosis (PVT) is a medical condition associated with high morbidity and mortality rates [1]. It is uncommon in the developed world, but frequent in underdeveloped countries. A multimodal approach that includes transthoracic and transesophageal echocardiography, fluoroscopy or computed tomography is required for prompt diagnosis. Any therapeutic alternative has a high risk of complication [2,3]. We report a mechanical mitral valve thrombosis case in a female patient who was considered inoperable and was successfully treated with an ultraslow infusion of recombinant tissue plasminogen activator (r-TPA).

## Case report

A 53-year-old woman with rheumatic fever sequels, heart failure with reduced ejection fraction and mitral and aortic mechanical prosthetic valves presented to the emergency department with atypical chest pain that started 10 days prior to admission and dyspnea triggered by lower degrees of exertion than usual. Physical examination revealed tachycardia and a muffled mitral occluder click, but no murmurs or other significant findings. An inappropiately low international normalized ratio (INR of 1.09) was identified at admission despite warfarin therapy.

A transthoracic echocardiography (TTE) showed a left ventricle ejection fraction of 17% due to severe global hypokinesia, severe right and left atrial enlargement, and the following mitral valve doppler parameters: mean gradient of 11 mmHg, maximum velocity of 212 cm/s, pressure half-time of 96 ms and an effective orifice area of 2.29 $cm^2$. It was impossible to assess the leaflets movement due to an inadequate acoustic window. The high suspicion of valve thrombosis led to intensification of the intravenous unfractionated heparin (UFH) treatment. Fluoroscopy demonstrated a mitral bi-leaflet tilting disk with complete restriction of a single leaflet **(Figure 1A).** Anticoagulation was mantained along with beta-blockers and angiotensin-converting enzyme (ACE) inhibitors. A transesophageal echocardiography (TEE) **(Figure 2A)** revealed a 17 x 10 mm thrombus blocking the movement of the medial leaflet.

A medical team consisting of cardiologists, cardiac surgeons and intensive care experts considered the patient to be of prohibitive risk for surgery so thrombolysis was chosen as therapy instead. The thrombolysis protocol was adopted from the successful experience in the PROMETEE trial [4] which used an ultraslow infusion guided by TEE. The patient received a total of 4 cycles, each one consisting of a r-TPA solution (50 mg of Alteplase

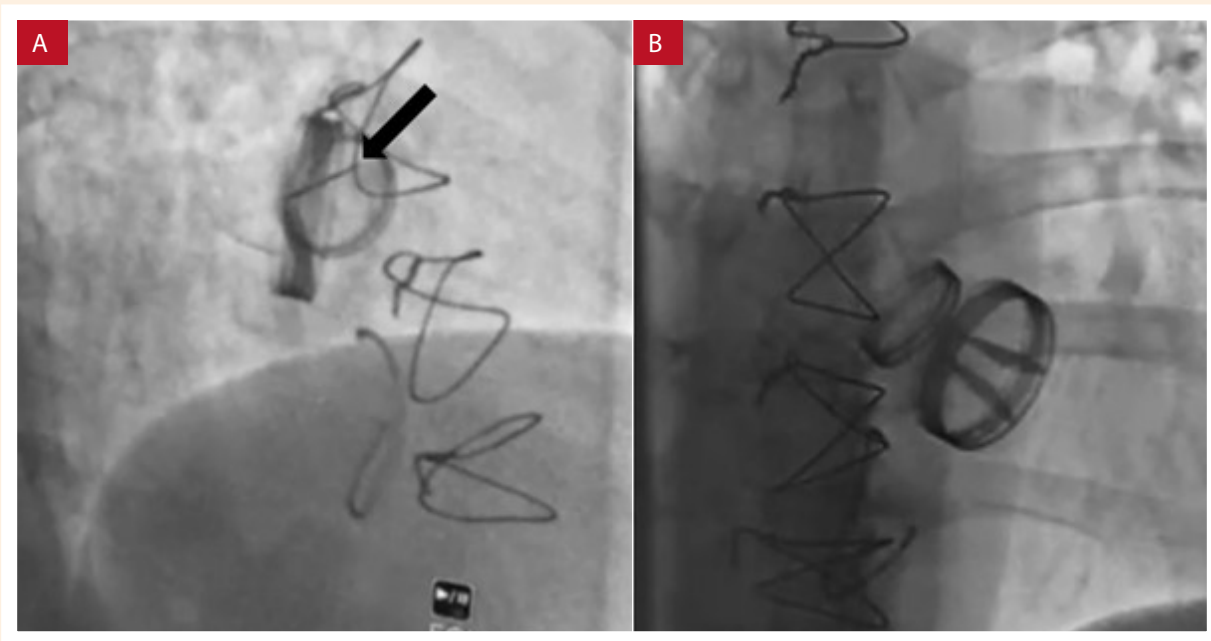


**Figure 1.** Fluoroscopy. **A.** Excursion of a single leaflet of the mitral prosthetic valve (arrow). **B.** Both leaflets open after four ultra slow thrombolysis cycles.

in 1000 mL of 0.9% saline solution) at a 1 mg per hour pace for 25 hours. Anticoagulation with intravenous UFH was withheld during r-TPA infusion and resumed immediately after each cycle for 6 hours. A new TEE was performed before starting a new cycle.

After the fourth cycle of r-TPA, thrombus resolution criteria were met with recovered leaflet mobility **(Figure 1B)**, an over 75% reduction in thrombus area and mitral valve gradient improvement (mean gradient of 6 mmHg and maximum velocity of 180 cm/s) **(Figure 2B)**. The patient stayed in the intensive care unit throughout thrombolysis therapy and did not developed hemorrhagic, cardiovascular or neurological complications. There was an adequate INR prior to discharge. Optimal heart failure medical therapy was established as well. A new echocardiography 30 days after discharge verified a correct mitral prosthetic valve function.

## Discussion

The incidence of obstructive PVT for mechanical valves varies between 0.3–1.3% patient years [5]. Urgent valvular surgery or thrombolysis are associated with high morbidity and mortality rates [6,7]. To date, no randomized clinical trial has compared thrombolysis versus surgery for obstructive PVT. The European Society of Cardiology (ESC) and the American Heart Association (AHA) recommend urgent surgery in patients presenting with hemodynamic instability, large thrombus or recurrent embolism [8,9]. However, when surgical risk exceeds bleeding risk or when surgery is not available or is considered not adequate, thrombolysis represents a valid alternative. The ESC proposes a thrombolysis protocol consisting of a 10 mg r-TPA bolus followed by a 90 mg infusion in 90 minutes [9], which carries a high hemorrhage and stroke risk. In contrast, the American guidelines recommends an ultraslow low dose r-TPA infusion based on observational studies [4,10].

In our case, based on previous successful reports, we opted for an ultraslow r-TPA scheme in order to minimize the complication risk. The 25 mg of r-TPA in 25 hours protocol shows the same efficacy of conventional protocols with a lower hemorrhage risk. Özkan *et al.*, performed an indirect comparison of different regimens of thrombolysis including: fast streptokinase (group I), slow streptokinase (group II), high dose (100 mg) r-TPA (group III), half-dose (50 mg) and slow infusion (6 hours) of r-TPA without bolus (group IV), and a low dose (25 mg) and slow infusion (6 hours) of r-TPA without bolus (group V). The overall success rate in the whole series was 83.2% and it did not differ significantly among groups I through V. However, the complication rate was significantly lower in group V (10.5% vs 37.5%, 24.4%, 33.3%, and 29.6% in groups I through IV) [10].

The UFH infusion, with a target of activated partial thromboplastin time (aPTT) between 1.5 and 2.0 times the control, was started immediately after each cycle and administered for six hours. The r-TPA regime could be repeated until thrombus resolution criteria (over 75% reduction in thrombus area) were met up, to a maximum total dose of 200 mg (8 cycles) [4]. We expect most cases to resolve with 3 or less cycles of r-TPA. In our case, resolution needed 100 mg (4 cycles of 25 mg) during 5 days

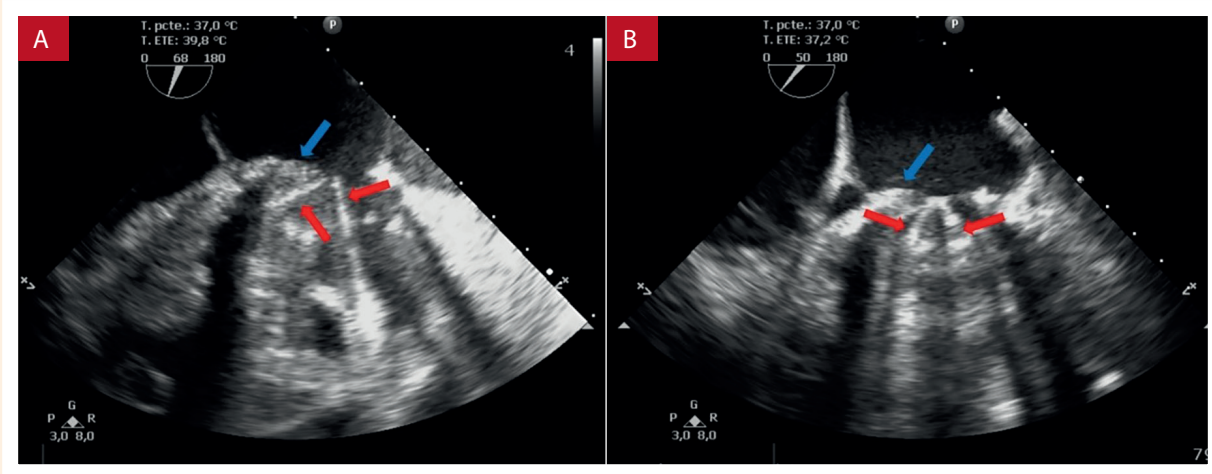


**Figure 2.** Transesophageal echocardiography. **A.** Thrombus (blue arrow) causing restriction of the medial leaflet of the mitral valve (red arrows). **B.** Reduction of the thrombus size (blue arrow) and adequate movement of both leaftlets (red arrows) after the fourth thrombolysis cycle.


Arch Peru Cardiol Cir Cardiovasc. 2021;2(3):196-199. doi: 10.47487/apcyccv.v2i2.149.

of treatment (considering the 6 hours pauses between each cycle). The reported success rate is up to 90% with a non fatal complication rate of 4%. Similar results have been achieved with a 6 hours protocol [10]. Most bleeding risk scores were validated in the myocardial infarction scenario and can not be applied in this case.

Finally, we performed a successful thrombolysis without complications, with improvement of echocardiographic valve parameters and release of the restricted leaflet. We conclude that, if no contraindication is present, systemic fibrinolysis is an acceptable alternative in patients with high or prohibitive risk for surgery, low experienced centers, patients with a small thrombus load (thrombus area below 0.8 $cm^2$), mild heart failure symptoms (NYHA class I or II) and low bleeding risk [11,12].

### Acknowledgements

We thank San Vicente Fundacion University Hospital and University of Antioquia's Faculty of Medicine.

### Author's contribution

All the authors participated in data collection and manuscript redaction.

## References

1. Akins CW, Miller DC, Turina MI, Kouchoukos N, Blackstone E, Grunkemeier G, et al. Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions. Ann Thorac Surg. 2008;85(4):1490-1495. doi:10.1016/j.athoracsur.2007.12.082
2. Laplace G, Lafitte S, Labèque J-N, Perron JM, Baudet E, Deville C, *et al.* Clinical significance of early thrombosis after prosthetic mitral valve replacement. J Am Coll Cardiol. 2004;43(7):1283-1290. doi:10.1016/j.jacc.2003.09.064
3. Ozkokeli M, Sensoz Y, Ates M, Ekinci A, Akcar M, Yekeler I. Surgical Treatment of Left-sided Prosthetic Valve Thrombosis. Int Heart J. 2005;46(1):105-111. doi:10.1536/ihj.46.105
4. Özkan M, Gündüz S, Gürsoy OM, Karakoyun S, Astarcioglu M, Kalçik M, *et al*. Ultraslow thrombolytic therapy: A novel strategy in the management of PROsthetic MEchanical valve Thrombosis and the prEdictors of outcomE: The Ultra-slow PROMETEE trial. Am Heart J. 2015;170(2):409-418.e1. doi:10.1016/j.ahj.2015.04.025
5. 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
6. 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
7. Karthikeyan G, Senguttuvan NB, Joseph J, Devasenapathy N, Bahl V, 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
8. Nishimura RA, Otto CM, Bonow RO, Carabello B, Erwinlll J, Fleisher L, *et al.* 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Vol 135.; 2017. doi:10.1161/CIR.0000000000000503
9. Baumgartner H, Falk V, Bax J, De Bonis M, hamm C, Holm PJ, *et al*. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2018;39(21):1980-1980. doi:10.1093/eurheartj/ehx636
10. Özkan M, Gündüz S, Biteker M, Astarcioglu MA, Çevik C, Kaynak E, *et al*. Comparison of different TEE-guided thrombolytic regimens for prosthetic valve thrombosis: The TROIA trial. JACC Cardiovasc Imaging. 2013;6(2):206-216. doi:10.1016/j.jcmg.2012.10.016
11. Otto CM, Nishimura RA, Bonow RO. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021 Feb 2;143(5):e35-e71. doi: 10.1161/CIR.0000000000000932
12. Kumar BM, Justin Paul G, Swaminathan N, Gnanavelu G, Ravishankar G, Kumar N, *et al*. Assessment of hemodynamic and clinical response in thrombolytic therapy for prosthetic valve thrombosis. Indian Heart J. 2017;69:S6. doi: 10.1016/j.ihj.2017.09.215