

CASE PRESENTATION

Third Re-Do Surgery in a Young Woman with Massive Early Double-Valve Prosthesis and Thromboembolic Stroke

Andreea-Antonia NICA¹, Andrea-Olivia CIOBANU^{1,2}, Roxana-Cristina RIMBAS^{1,2}, Alexandru VASILESCU¹, Vlad VINTILA^{1,2}, Dragos VINERANU^{1,2}

ABSTRACT

Valvular heart disease affects more than 100 million people worldwide. Valvular replacement remains the only definite treatment for most of the patients with severe disease. Careful medical management and periodic follow-up of valve function is mandatory in order to prevent or diagnose prosthesis-related complications. We present a case of extensive mitral and aortic valve thrombosis and possible recurrent endocarditis in a 44-year-old woman non-adherent to anticoagulation therapy, presented with stroke. She also had a history of two mitral and aortic valvular heart replacement surgeries. Comprehensive and repeated imaging was used to evaluate and monitor the patient progression and outcome. Failure of adequate anticoagulation therapy to improve prosthesis function during hospitalization required third re-do surgery for mitral and aortic valve replacement with mechanical prosthesis.

Keywords: mechanical prosthesis, thrombosis, anticoagulant treatment, compliance, re-do.

REZUMAT

Bolile cardiace valvulare afectează peste 100 de milioane de oameni din întreaga lume. Înlocuirea valvulară rămâne singurul tratament eficient pentru majoritatea pacienților cu afectare valvulară severă. Acești pacienți necesită monitorizare atentă și urmărirea periodică pentru a preveni sau diagnostica o complicație legată de proteză. Aducem în atenție un caz de tromboză extensivă de valvă mitrală și aortică și posibil endocardită recurentă la o pacientă de 44 de ani neaderentă la tratamentul anticoagulant, ce s-a prezentat cu accident vascular cerebral. Ea are istoric de două operații de înlocuire valvulară mitrală și aortică. Investigațiile imagistice în dinamică au fost utilizate pentru a evalua și monitoriza progresia sub tratament. Eșecul terapiei anticoagulante adecvate de a îmbunătăți funcția protezei în timpul spitalizării, a dus la necesitatea unei a treia intervenții chirurgicale de înlocuire a valvei aortice și mitrale cu proteză mecanică.

Cuvinte cheie: proteză mecanică, tromboză, tratament anticoagulant, complianța, reoperație.

INTRODUCTION

Valvular heart disease affects more than 100 million people worldwide¹. Valvular replacement remains the only definite treatment for most patients with severe disease.² Careful medical management and periodic follow-up of valve function is mandatory in order to prevent or diagnose prosthesis-related complications: prosthetic valve obstruction (thrombosis and/or pannus formation), thromboembolic or bleeding events, prosthetic valvular or paravalvular regurgitation, infective endocarditis, prosthetic valve-induced hemolysis^{2,3}.

Mechanical heart valves (MHV) are durable and offer good hemodynamic performance. However, MHV are more thrombogenic compared to bioprosthetic valves, requiring lifetime efficient anticoagulation in order to avoid both thrombotic and bleeding complications³.

We report a case of a young woman with a history of two heart valve surgeries, admitted for a recurrent thromboembolic event caused by mechanical mitral and aortic valve thrombosis, as a result of suboptimal oral anticoagulation. Following the lack of prosthesis function improvement with efficient anticoagulation, double-valve replacement with mechanical prosthesis was performed with optimal result.

¹ Department of Cardiology and Cardiovascular Surgery, Emergency University Hospital, Bucharest, Romania

² „Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

► Contact address:

Andrea O. Ciobanu, Department of Cardiology and Cardiovascular Surgery, Emergency University Hospital, Bucharest, Romania.
E-mail: andreaciobanu7@yahoo.com

CASE PRESENTATION

A 44-year-old woman presented at the emergency department with left-sided paresthesia, dizziness and diplopia. Symptoms onset was 12 hours prior to presentation.

Her cardiovascular history proved to be very complex. In 2009, when she was 33-year-old, she underwent double-valve replacement with bioprosthetic mitral valve size 27 St Jude Biocor and aortic size 21 ATS Stentless valve respectively, for severe rheumatic heart valve disease. After a 10-year symptom-free period, she was admitted and treated for blood culture-negative infective endocarditis involving the bioprosthetic aortic valve, complicated with acute right limb ischemia, followed by surgical arterial thrombectomy. By that time, significant bioprosthetic degeneration was also identified. The association with acute endocarditis resulted in significant valvular dysfunction consistent with severe aortic stenosis

and regurgitation, and moderate mitral stenosis and regurgitation, addressed with double mechanical valve replacement during the same index hospitalization. At discharge, mitral size 27 Sorin Carbomedics and aortic size 18 ATS prosthesis functional parameters were in the normal range, with no perioperative complications after the second open-heart surgery. The patient remained asymptomatic during the following months, until June 2020, although she reported stopping anti-coagulation treatment over the last 6 months, without seeking medical advice.

On admission, the patient was afebrile, with dyspnea at minimal activity, tachycardic at rest, with normal blood pressure values. Clinical examination revealed regular cardiac rhythm, with no significant murmur, mechanical aortic and mitral closing click, no signs of pulmonary congestion, but moderate peripheral congestion. Neurological examination revealed left-sided paresthesia, with preserved motor functions and left homonymous hemianopsia.

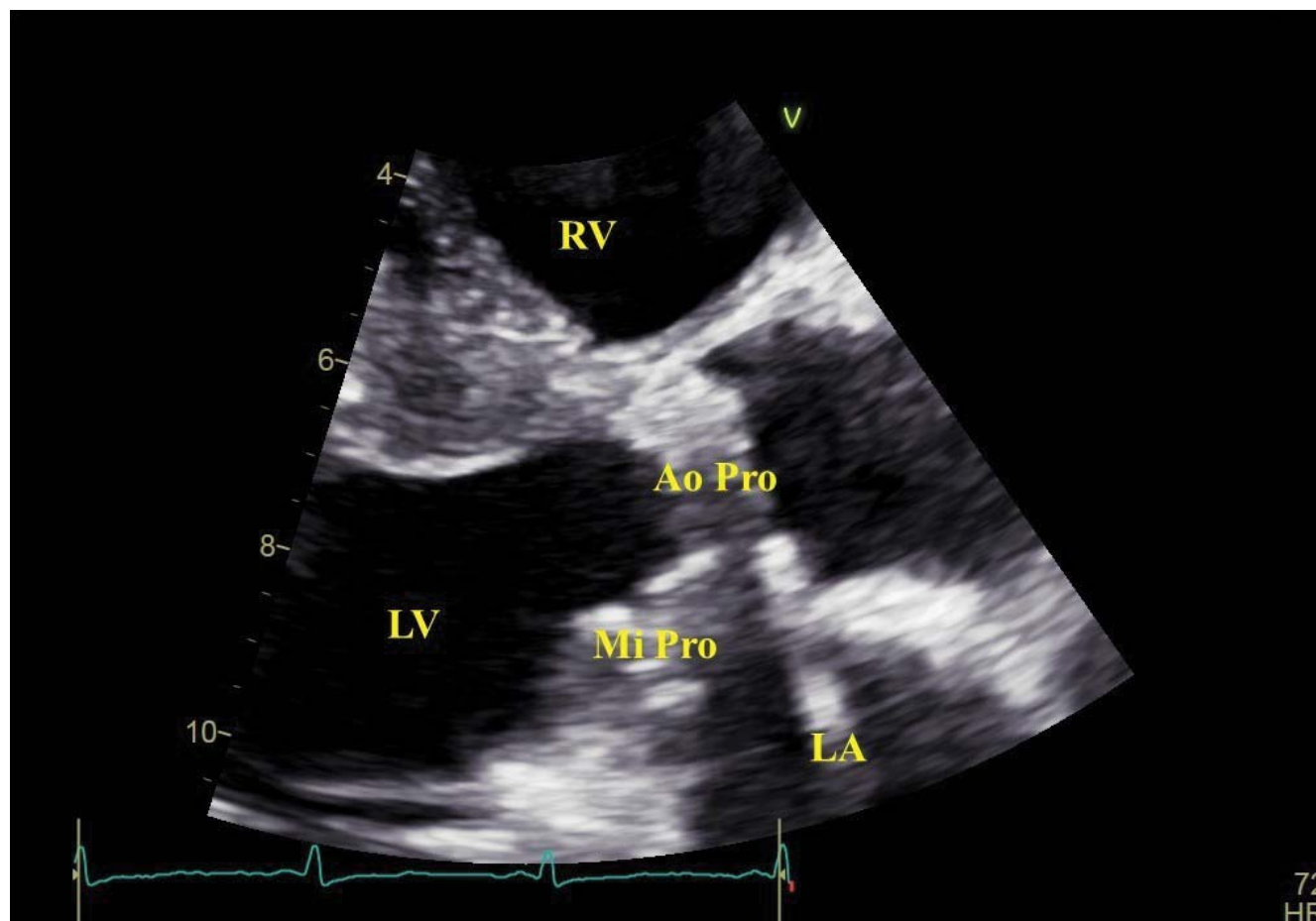


Figure 1. Transthoracic echocardiography, parasternal long axis view, zoom on the aortic and mitral prosthesis. Structural changes of the mitral prosthesis suggestive of possible thrombosis. No significant changes seen on the aortic prosthesis. Ao Pro, aortic prosthesis; LA, left atrium; LV, left ventricle; Mi Pro, mitral prosthesis; RV, right ventricle.

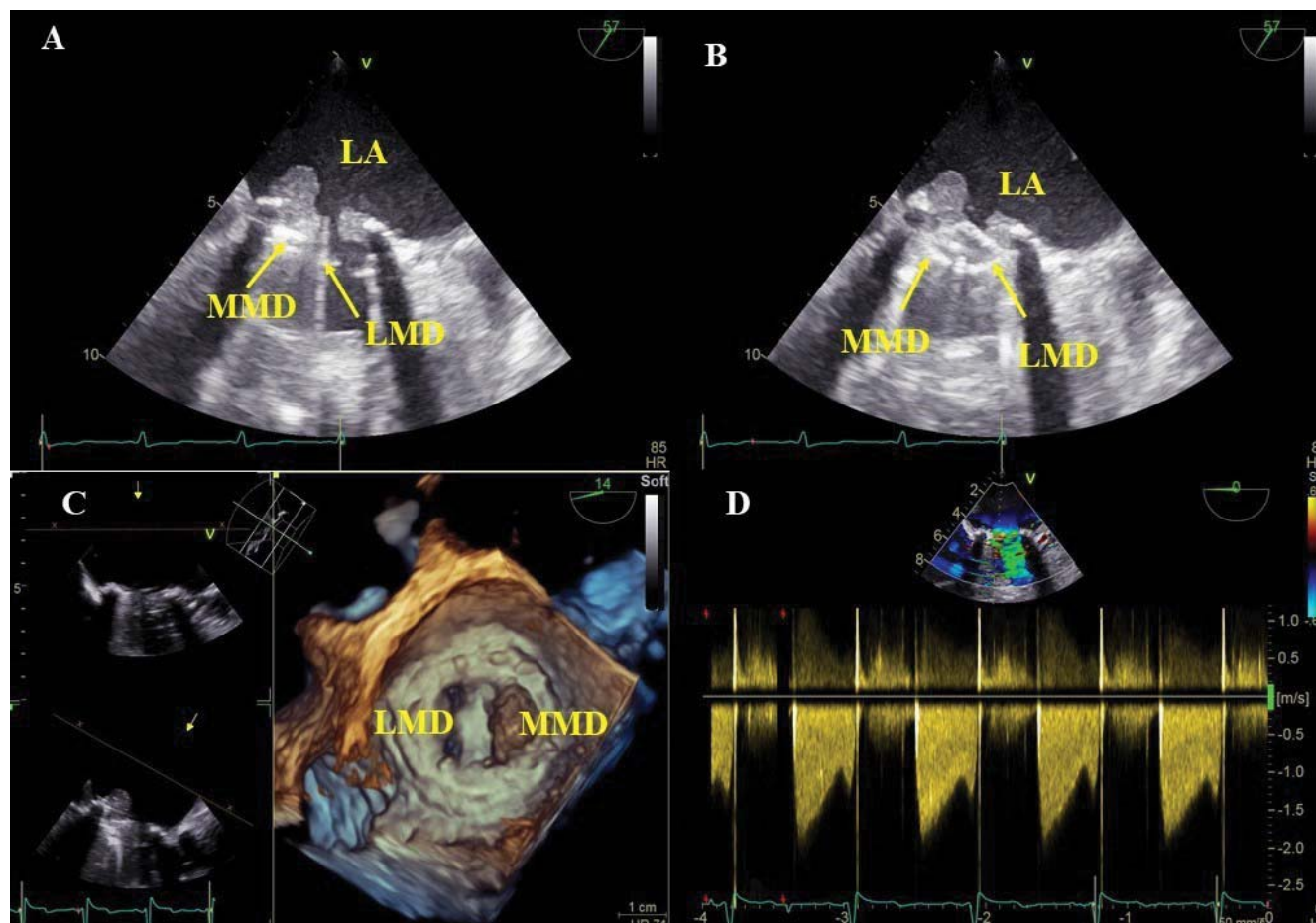


Figure 2. Transesophageal echocardiography evaluation of the mitral prosthesis. Bicommissural views (A- diastole, and B- systole) showing massive mitral prosthesis thrombosis with a blocked medial disc and incomplete closing of the lateral disc due to extensive thrombosis. C. 3D-TEE en-face view of the mitral prosthesis showing medial obstructed disc with an organized thrombus. D. Continuous wave Doppler interrogation of the mitral prosthesis demonstrating elevated transmitral gradients. LA, left atrium; LMD, lateral mitral disc; MMD, medial mitral disc.

Blood tests showed iron deficiency mild anemia, elevated inflammatory markers with high levels of C-reactive protein up to 10 times the upper limit of normal and elevated NT-proBNP. Kidney, liver and thyroid functional were in the normal range. On admission, INR level was 1.7. The urine test was normal, with no signs of infection.

12-lead electrocardiogram showed sinus tachycardia and left ventricular hypertrophy with strain.

Urgent multimodality imaging was performed as part of the evaluation for a possible cardiac source of embolism. Cerebral computed tomography (CT) scan revealed right occipital hypodensity in the para-hippocampal gyrus, suggesting subacute posterior cerebral artery ischemic stroke. Doppler ultrasound imaging of carotid and vertebral arteries showed normal arterial caliber with two small stable left carotid sinus atherosclerotic plaques, with no signs of stenosis and good peak systolic and diastolic velocities. Transthoracic

echocardiography (TTE) revealed hypertrophic and non-dilated left ventricle, with apical dyskinesia and ejection fraction of 50%. Left atrium was severely dilated with dense spontaneous echo-contrast. Prosthetic mitral valve disc mobility was impaired by several echo-dense masses attached to both discs. Continuous wave Doppler interrogation demonstrated elevated mean trans-mitral gradient of 9.5 mmHg. Evaluation of prosthetic aortic valve revealed high velocities and gradients, with a maximum aortic velocity of 3.6 m/s and trans prosthetic mean gradient of 33 mmHg, and an effective orifice area of 0.55 cm². Mild mitral and aortic regurgitations were noted. There was right heart enlargement, without significant RV dysfunction. Tricuspid valve leaflets were thickened and restricted consistent with mild rheumatic tricuspid stenosis and severe regurgitation. Pulmonary artery pressure was 40 mmHg.

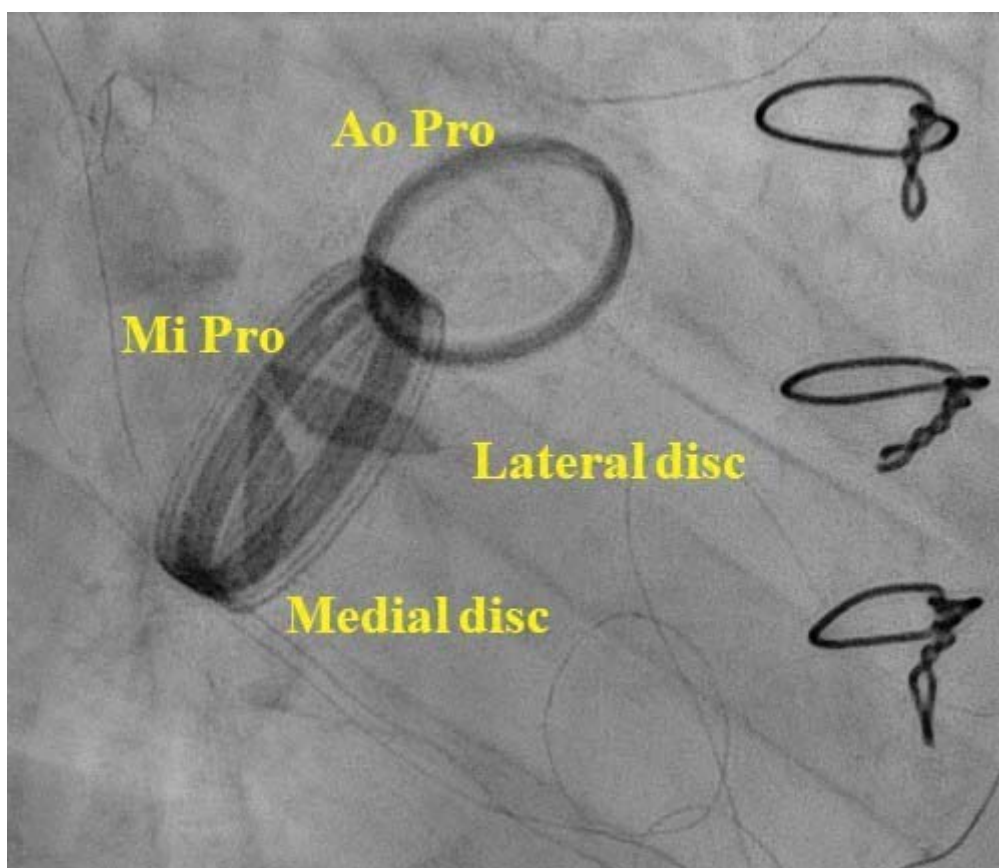


Figure 3. Fluoroscopy showing blocked medial mitral disc. Ao Pro, aortic prosthesis; Mi Pro, mitral prosthesis.

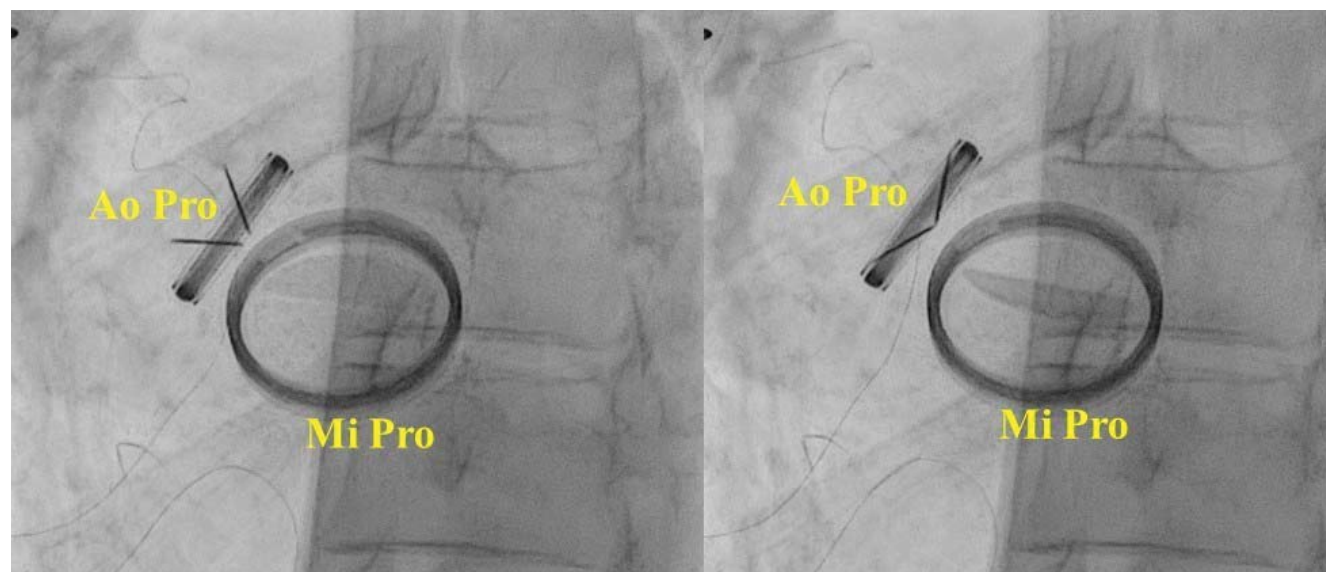


Figure 4. Fluoroscopy showing normal opening (left) and closing (right) of both aortic prosthesis discs. Ao Pro, aortic prosthesis; Mi Pro, mitral prosthesis.

Emergency transesophageal echocardiography (TEE) was performed for a more accurate assessment of prosthesis function and characterization of compli-

cations. Both mitral and aortic prosthesis were severely affected by extensive irregular echogenic structures on the atrial and ventricular site of the pros-

thesis respectively, suggestive of massive thrombosis with possibly coexisting vegetations. Moreover, mitral prosthesis medial disc blockage was identified in 2D-TEE and confirmed with 3D-TEE and fluoroscopy, associated with incomplete lateral disc closing (Figure 2, 3 and 4). Other significant TEE findings included left atrial appendage thrombosis and confirmation of rheumatic tricuspid valve changes noted on 2D-TTE, associated with severe tricuspid regurgitation, as well as dilated tricuspid ring. Aortic prosthesis function was also assessed with fluoroscopy and showed normal discs mobility.

Patient history, biological and imaging data altogether raised the suspicion of associated infective endocarditis. Two sets of blood cultures when afebrile were collected and empirical antimicrobial therapy with vancomycin and gentamicin was started. The decision to continue the antimicrobial therapy with an association of vancomycin, gentamicin and ceftriaxone for at least 4 to 6 weeks was made together with the infectious disease specialist, despite negative blood cultures. Unfractionated heparin (UFH) was also started after careful consideration with the neurologist specialist, to avoid cerebral bleeding complications.

Clinical course was favorable, with no significant heart failure symptoms or fever. Partial remission of paresthesia and dizziness was also attained. Inflammatory markers decreased to normal values. The patient developed transient acute kidney injury due to nephrotoxicity of gentamicin, resolved with proper hydration and stopping the nephrotoxic drugs. Other causes for acute kidney injury such as renal embolism, urinary obstructions, hypotension were excluded. Of note, blood tests for inherited thrombophilia, lupus and rheumatic disease were negative.

Repeat TEE showed no significant changes in prosthesis appearance and function after 11 days of UFH. Hence, VKA treatment with close monitoring of therapeutic INR was restarted.

Following the Heart Team decision, the patient underwent another replacement of the aortic and mitral dysfunctional prosthesis with aortic size 21 Medtronic mechanical prosthesis and mitral size 29 Sorin Caromedics mechanical prosthesis. Tricuspid repair was also performed. Postoperative outcome was uneventful. We achieved and maintained therapeutic INR, and also resumed the antibiotic regimen recommended by the infectious disease specialist, despite no significant intraoperative evidence of infected vegetations associated with prosthesis thrombosis. The patient

was discharged after thorough counseling on the vital importance of lifetime anticoagulation. At 6 months follow-up, the patient remained asymptomatic, with good treatment adherence and therapeutic INR levels.

DISCUSSION

We present a very challenging case of a young woman with a history of rheumatic heart disease and two open-heart surgeries for severe aortic and mitral valve disease, with previous infective endocarditis and embolic limb ischemia, who presented with early massive thrombosis of both prosthesis due to lack of anticoagulation adherence, recurrent embolic event and possibly recurrent endocarditis.

There are several factors associated with prosthetic valve thrombosis such as thrombogenicity of the prosthesis, atrial fibrillation, left atrial geometry, abnormal prosthetic blood flow and suboptimal anticoagulation.⁴ Inadequate anticoagulation is the most important pathogenetic factor in prosthetic valve thrombosis. Reported incidence of symptomatic prosthetic heart valve thrombosis with obstruction is 0.3% to 1.3% per year among patients with therapeutic anticoagulation and 6% per year among patients with inadequate anticoagulation. Mortality rate is very high without treatment, despite emergency surgical intervention⁵.

Some studies showed that mitral mechanical prosthesis thrombosis and embolization might be twice as frequent as aortic mechanical prosthesis thrombosis⁶. One explanation could be a higher thrombogenicity of the mitral valve. However, data is scarce and with limited statistical power to make any definite differentiations between the two sites of prosthesis implantation⁷.

Guidelines recommend chronic anticoagulation treatment with vitamin K antagonist with watchful monitoring of INR. Target INR should be set according to the type and thrombogenicity of the mechanical prosthesis, and individual risk factors^{8,9}. Both American and European guidelines recommend a median INR value rather than a range, in order to avoid INR fluctuations associated with increased complications and mortality in these patients. Patients should be appropriately trained to monitor INR levels and regular check-ups are recommended. There is evidence that INR self-management reduces INR variability and clinical events¹⁰.

The clinical history and subtherapeutic anticoagulation should alert the physician and take into consideration prosthetic valve thrombosis. Patients usually present with recent dyspnea or an embolic event. Comprehensive evaluation by 2D- and 3D transesophageal

echocardiography and fluoroscopy are recommended to confirm the diagnosis,^{8,9} as it was the case with our patient. Association with infective endocarditis must always be taken in consideration, especially in patients with previous episodes of endocarditis, as it is related to worse prognosis. Management of valve thrombosis depends on the size of the thrombus, associated valvular disease or the thromboembolic event and includes anticoagulation, fibrinolysis and surgery^{8,9}. In this case, we opted for unfractionated heparin to optimize the anticoagulation level, associated with empiric antibiotic treatment for a possible blood-culture-negative infective endocarditis. However, there was no significant improvement in thrombus appearance and prosthesis dysfunction, as demonstrated by repeated TEE. The decision to reoperate was made after careful consideration of the Heart Team regarding the perceived benefits and possible complications associated with a third open-heart surgery by the age of 44 years old. After a successful re-do surgery followed by an uneventful recovery, the patient was trained with respect to the crucial importance of strict adherence and close monitoring of the anticoagulation treatment, in order to achieve and maintain lifetime optimal INR.

CONCLUSION

The aim of this challenging clinical case is to raise awareness on the life-threatening complications in patients with mechanical valvular prosthesis, the role of constant counseling to maintain treatment and behavioral adherence, in addition to the real benefit in a third re-do high-risk surgery.

Abbreviations

2D	two-dimensional
3D	three-dimensional
Ao Pro	aortic prosthesis
CT	computed tomography
INR	international normalized ratio
LA	left atrium
LMD	lateral mitral disc
LV	left ventricle
Mi Pro	mitral prosthesis
MMD	medial mitral disc
MHV	mechanical heart valve
RA	right atrium
RV	right ventricle
TEE	transesophageal echocardiography
TTE	transthoracic echocardiography

TV	tricuspid valve
UFH	unfractionated heparin

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

1. Raman K, Mohanraj A, Palanisamy V, Ganesh J, Rawal S, Kurian VM, Sethuramnam R. Thrombolysis and surgery for mitral prosthetic valve thrombosis: 11-year outcomes. *Asian Cardiovasc Thorac Ann* 2019;27: 633-40.
2. Lancellotti P, Pibarot P, Chambers J, Edvardsen T, Delgado V, Dulgheru R, Pepi M, Cosyns B, Dweck MR, Garbi M, Magne J, Nieman K, Rosenhek R, Bernard A, Lowenstein J, Vieira MLC, Rabischoffsky A, Vyhmeister RH, Zhou X, Zhang Y, Zamorano JL, Habib G. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J - Cardiovasc Imaging* 2016;17: 589-90.
3. Vesey JM, Otto CM. Complications of Prosthetic Heart Valves. *Curr Cardio Rep* 2004;6: 106-11.
4. Magarakis M, Macias AE, Ghodsizad A, Salerno TA. Surgical management of cardiovascular thrombotic conditions. In *Cardiovascular Thrombus: From Pathology and Clinical Presentations to Imaging, Pharmacotherapy and Interventions* 2018, Elsevier, p.367-76.
5. Durrleman N, Pellerin M, Bouchard D, Hebert Y, Cartier R, Perrault PL, Basmadjian A, Carrier M. Prosthetic valve thrombosis: twenty-year experience at the Montreal Heart Institute. *J Thorac Cardiovasc Surg* 2004;127: 1388-92.
6. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. *Heart* 2007;93: 137-42.
7. Cannegieter SC, Rosendaal FR, Briet E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. *Circulation* 1994;89: 635-41.
8. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Muñoz R, Rosenhek R, Sjögren J, Mas PT, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal* 2017;38: 2739-91.
9. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A, Toly C. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021;143: e72-e227.
10. Heneghan C, Ward A, Perera R; Self-Monitoring Trialist Collaboration, Bankhead C, Fuller A, Stevens R, Bradford K, Tyndel S, Alonso-Coello P, Ansell J, Beyth R, Bernardo A, Christensen TD, Cromheecke ME, Edson RG, Fitzmaurice D, Gadisseur AP, Garcia-Alamino JM, Gardiner C, Hasenkam JM, Jacobson A, Kaatz S, Kamali F, Khan TI, Knight E, Körtke H, Levi M, Matchar D, Menéndez-Jándula B, Rakovac I, Schaefer C, Siebenhofer A, Souto JC, Sunderji R, Gin K, Shalansky K, Völler H, Wagner O, Zittermann A. Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data. *Lancet* 2012;379:322-34.