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GRAND ROUND
Valvular heart disease

The first reported case of embolic protection device implantation in a patient with prosthetic valve thrombosis treated with thrombolytic therapy: a case report

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Background Prosthetic valve thrombosis (PVT) is a rare but one of the most dreaded complications of implanted mechanical valves. Although surgery is the first-line treatment modality particularly in symptomatic obstructive mechanical valve thrombosis, it is associated with high rates of morbidity and mortality. Thrombolytic therapy has also been used as an alternative to surgical treatment. The risk for cerebral thromboembolism associated with thrombolytic therapy seems to be the main limitation for its use in left-sided mechanical valve thrombosis. To the best of our knowledge, this is the first case of implantation of embolic protection devices during thrombolytic therapy of PVT.

Case summary Our report describes management of patient with obstructive PVT of the aortic valve. Fluoroscopy showed an immobile anterior disc of the aortic prosthesis. Transoesophageal echocardiography (TOE) detected the severely restricted prosthetic valve motions and a huge mass at the supravalvular site. A patient had very high surgical risks. Although, thrombolytic treatment was not without risk due to the large thrombus (>10 mm) increasing the risk of thromboembolism. We implanted embolic protection devices into both internal carotid arteries followed by the administration of a thrombolytic therapy with 50 mg Alteplase. After the procedure an embolized thrombus was detected at the apex at the left-sided placed device. There were no signs of transient ischaemic attack nor stroke, and the procedure was ended uneventful. The TOE performed on the next day confirmed successful resolution of the thrombus.

Discussion Mechanical left-sided prosthetic valve obstruction is a serious complication with high mortality and morbidity and requires urgent therapy. The choice between surgery, thrombolysis, and escalation of anticoagulation is considered on an individual basis. In patients with high surgical risk and high risk of embolization, an embolic protection device may be used in conjunction with thrombolytic therapy to decrease the risk of embolic cerebral events.

Keywords Prosthetic valve thrombosis • Thrombolytic therapy • Embolic protection device • Fluoroscopy • Case report

ESC Curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 4.2 Aortic stenosis • 6.1 Symptoms and signs of heart failure • 7.4 Percutaneous cardiovascular post-procedure

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Learning points

- The management of prosthetic valve thrombosis is high risk, whatever the option taken.
- Bilateral internal carotid artery embolic protection device may be considered in patients with left-sided prosthetic valve thrombosis with large (>0.8 cm^2 or >10 mm) and mobile thrombus during thrombolytic treatment.
- The protection devices may theoretically reduce morbidity related to stroke following thrombolytic therapy and might improve quality of life.

Primary specialties involved other than cardiology

Cardiac surgery, anaesthesiology, and neurology.

Introduction

Prosthetic valve thrombosis (PVT) is a potentially life-threatening complication of heart valve replacement. Early diagnosis is crucial for the prevention of significantly morbid and lethal complications. Surgery is the preferred therapy for patients in NYHA Class III/IV and with a large thrombus (≥0.8 cm^2).[1] Although, a previous history of cerebrovascular event and a thrombus size >0.8 cm^2 or >10 mm are the major risk factors for systemic embolic complications of thrombolytic therapy,[2] recent studies show that thrombolytic therapy is non-inferior to surgery in terms of efficacy and safety.[3] Our report describes management of a patient with obstructive PVT of the aortic valve. Intravenous systemic thrombolysis was given after the implantation of embolic protection devices into both internal carotid arteries.

Timeline

Time point	Event
2010 (first operation)	Patient underwent an aortic valve replacement with a mechanical prosthesis (St. Jude Medical 23 mm), due to rheumatic aortic stenosis.
17 May 2022 (symptom onset)	Patient experiences difficulty in breathing during exertion, dyspnoea and ankle swelling
29 May 2022 (presentation and clinical assessment)	*Presentation* Patient reports dyspnoea even in rest. *Clinical assessment* BP 145/80 mmHg, HR 85 b.p.m., respiratory rate 19/min, signs of heart failure.
29 May 2022 (investigation)	TTE revealed a markedly elevated transaortic peak and mean pressure gradients of 87 and 65 mmHg, respectively, with impaired movement of prosthesis discs. Left ventricular EF was 28%. Fluoroscopy showed an immobile anterior disc of the aortic prosthesis. TOE detected severely restricted prosthetic valve motions, and a huge thrombus at the supravalvular site with the size of 2 cm^2 and 17 mm.
1 June 2022 (intervention)	Bilateral implantation of embolic protection devices into the internal carotid arteries and thrombolytic therapy with a tissue plasminogen activator.
2 June 2022 (control investigation)	Patient reported complete resolution of symptoms. The TOE confirmed successful resolution of the thrombus. Also, peak and mean pressure gradients had returned to appropriate values (17 and 10 mmHg, respectively).
6 June 2022 (discharge from the hospital)	INR elevated up to 2.1, patient walked 450 m in 6 min without any complaint.
30 June 2022 (follow-up)	INR level 2.4. Patient reported no symptoms.

Case presentation

A 66-year-old man presented to the emergency department with dyspnoea started within the last 2 weeks. He was hemodynamically stable (blood pressure 145/80 mmHg, heart rate 85/min, respiratory rate 19/min) with signs of heart failure. The body mass index (BMI) was 32. The physical examination revealed mild bilateral ankle oedema with bilateral basal crackles and a systolic murmur at the right second intercostal space. He underwent an aortic valve replacement with a mechanical prosthesis (St. Jude Medical 23 mm, St. Jude Medical Inc., Minnesota, MN) 12 years ago, due to rheumatic aortic stenosis. His electrocardiogram and chest X-ray were unremarkable. Laboratory analysis showed normal sedimentation rate and C-reactive protein level. Serum creatinine was 0.85 mg/dL, and troponin test was negative.

On his medical reports, the last follow-up data were obtained 6 months ago before the symptom onset. Previous echocardiography showed peak transvalvular gradient of 24 mmHg with EF of 55%. At that time, he had no complaints and INR was (2.1). His current pharmacological therapy on admission was warfarin 2.5 mg o.d. Despite being on oral anticoagulation therapy his INR was below his target range (1.3).

The emergency transthoracic echocardiography (TTE) revealed a markedly elevated transvalvular peak and mean pressure gradients of 87 and 65 mmHg, respectively, with impaired movement of prosthesis discs (*Figure 1A*). Left ventricular systolic function was impaired with the ejection fraction of 28% and no mass was visualized in conjunction with the prosthesis. Fluoroscopy showed an immobile anterior disc of the

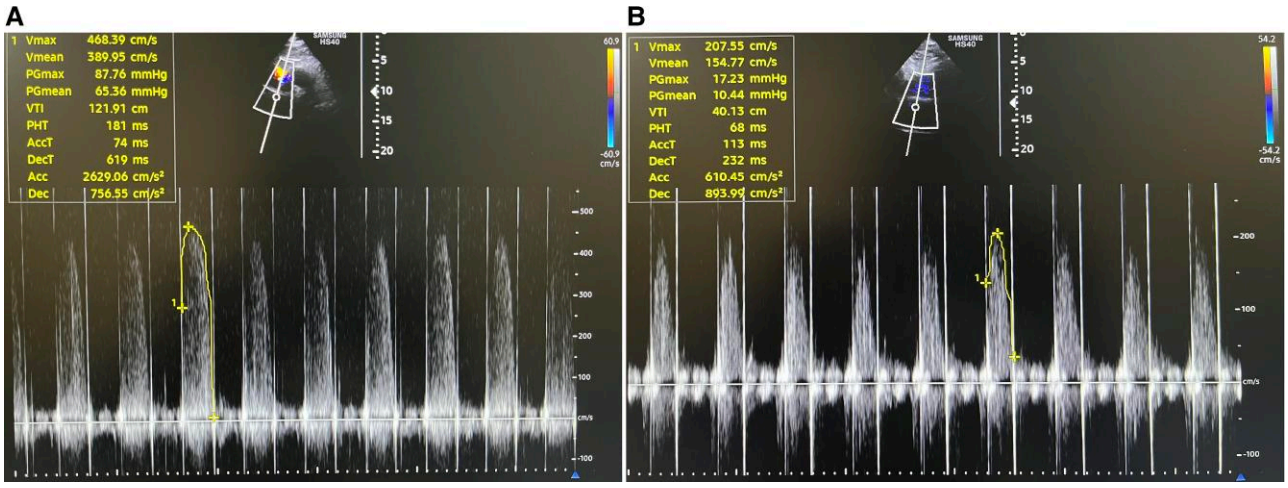

Figure 1 The right parasternal TTE view was required for accurate evaluation of prosthetic aortic valve stenosis severity. There were markedly elevated transvalvular peak (87 mmHg) and mean (65 mmHg) pressure gradients (*A*). Prosthetic valve peak and mean pressure gradients had decreased to 17 and 10 mmHg, respectively, after the thrombolytic treatment (*B*).

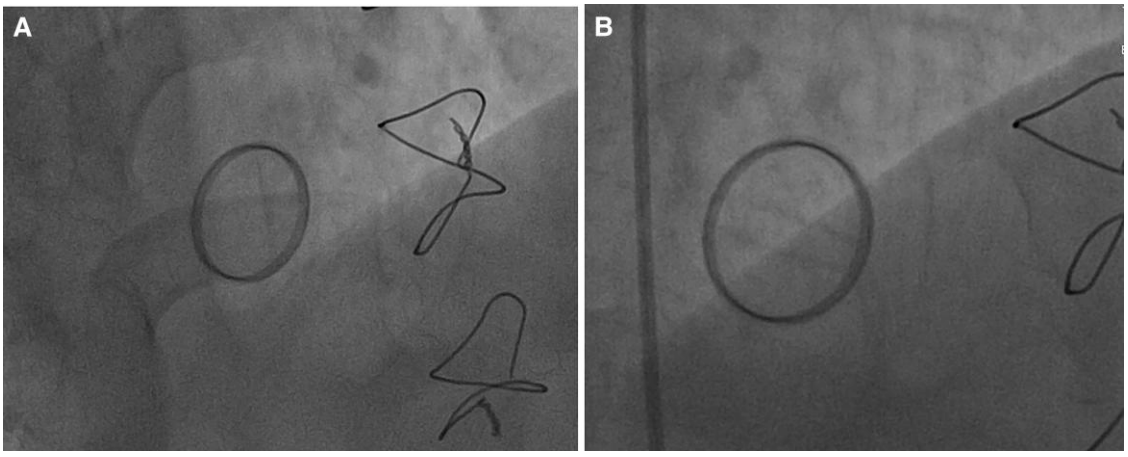

Figure 2 Fluoroscopy revealed stucked leaflet of one of the prosthesis disc and only one of the leaflets is visible (*A*). Ninety minutes after the starting of administration of a t-PA the fluoroscopy revealed full opening of both of the leaflets of prosthetic valve (*B*).

aortic prosthesis (*Figure 2A*). Transoesophageal echocardiography (TOE) confirmed severely restricted valve motions by a huge and partially mobile mass, compatible with thrombus, at the supravalvular site of 2 cm^2 in size with maximal diameter of 17 mm (Supplementary material online, *Videos S1 and S2*).

Based on the medical history with acute onset of symptoms, inadequate anticoagulation, and restricted leaflet motion we diagnosed a PVT and referred the patient to a cardiac surgeon. A patient was declined for surgery due to low EF, high BMI, risks of resternotomy, and embolization of thrombus. To address the complex medical issue at hand, a collaborative effort involving cardiologists, cardiac surgeons, anaesthesiologists, and neurologists was necessary. A decision to undergo thrombolytic treatment following bilateral carotid embolic device protection implantation was made. We performed a 'half-dose' fibrinolytic therapy with 50 mg Alteplase; a tissue plasminogen activator (t-PA), without a bolus and with an infusion period of 2 h. We decided for this treatment because we administered a t-PA in the catheter laboratory after implanting embolic protection devices (ev3 SpiderFX, Medtronic Inc., Minneapolis, MN) into both internal carotid arteries (*Figure 3*). The right radial artery was punctured to implant an embolic protection device into the right internal carotid artery. The right common femoral artery below 2 cm of the inguinal ligament was punctured for the implantation of protection device into the left internal carotid artery. 6F sheaths were used for both arterial access. During the procedure, sites of the arterial access were continuously monitored for bleeding and haematoma, to prevent their progression by immediate manual compression. Fortunately, no haematoma nor bleeding occurred during the procedure and there was no need for compression. Also we planned to check the prosthetic valve mobility by performing serial fluoroscopy during the treatment period. After 75 min we

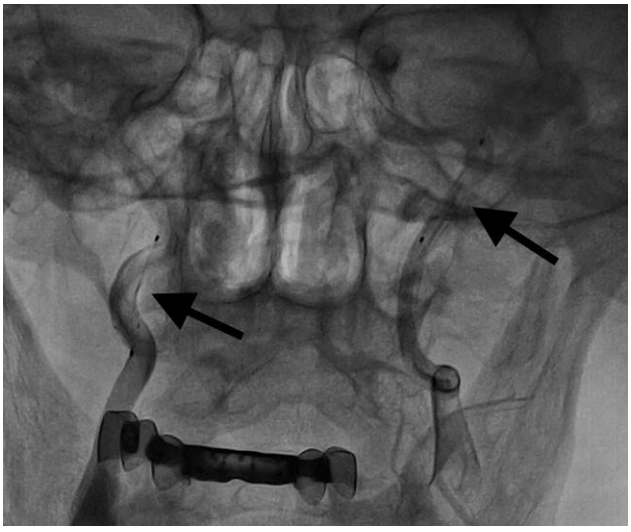

Figure 3 Embolic protection devices located in both of the internal carotid arteries. Arrows indicating embolic protection devices.

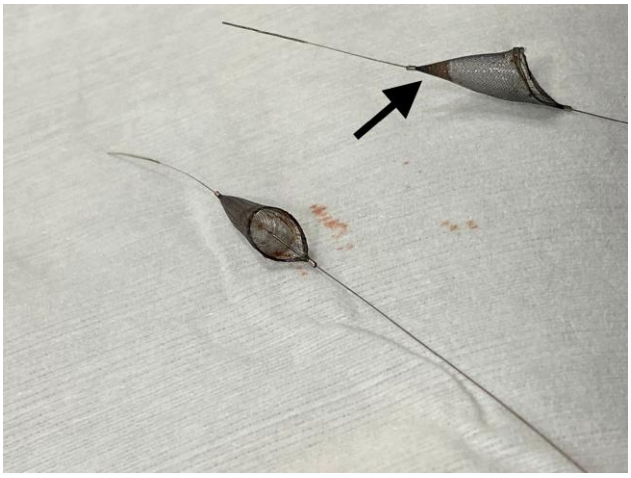

Figure 4 An embolized thrombus (arrow) at the apex of the device that was placed in the left carotid artery was detected.

detected partial movement of stucked leaflet of prosthetic valve. Ninety minutes after the starting of administration of a t-PA the fluoroscopy showed full mobilization of both of the leaflets of prosthetic valve (*Figure 2B*). The protection devices have been removed 15 min after the end of the administration of a t-PA. An embolized thrombus at the apex of the device that was placed in the left carotid artery was detected (*Figure 4*). The size of thrombus at the apex of embolic protection device was 2.8 mm. We did not confirm a thrombus by the histology because of the clear mechanism. There was no sign of transient ischaemic attack (TIA) nor stroke and the procedure was ended uneventful. However, there was no sign of emboli in other arterial beds we did not perform CT or MRI to prove the absence of embolization. The TOE performed on the next day confirmed successful resolution of the thrombus as well as the motion of the prosthesis discs were normal (Supplementary material online, *Videos S3 and S4*). Prosthetic valve pressure gradients had returned to appropriate values (*Figure 1B*). An unfractionated heparin was started 2 h (5000 units i.v. injection four times a day) after the end of thrombolysis. A warfarin 5 mg o.d. was started the next day. When we reached INR level ≥2.0 heparin therapy was discontinued.

After discharge, the patient has been regularly seen in our outpatient clinic. He has been doing well and has no cardiac symptoms. The last echocardiography was performed 4 weeks after discharge showing a normal function of the aortic valve prosthesis with improved LV systolic function (EF 50%) and dimensions. The range of an INR keeps 2.2–2.8 with Warfarin 5 mg o.d.

Discussion

Our report describes management of a patient with obstructive PVT of the aortic valve. The patient's condition necessitated a comprehensive approach involving the expertise of a multidisciplinary team.

Thrombolytic therapy following emboli protection of both internal carotid arteries was done.

Prosthetic heart valve obstruction is mainly due to prosthetic thrombosis and is always a serious complication associated with a high mortality rate particularly in obstructive cases. Optimal management of these situations remains controversial despite surgery is usually favoured. Published guidelines differ over the best line of therapy for PVT; the 2021 ESC/EACTS guidelines for the management of valvular heart disease recommend surgery as a Class I treatment for obstructive PVT in critically ill patients or for non-obstructive thrombosis with thrombus >10 mm or embolic phenomena (Class IIa) and to consider standard-dose thrombolytic therapy when surgery is not available or deemed very high risk (Class IIa recommendation), while the 2020 ACC/AHA guidelines recommend urgent initial treatment with either slow-infusion low-dose fibrinolysis, or emergency surgery (Class I recommendation) for obstructive PVT.[4,5]

Redo surgery for mechanical valve thrombosis has a high mortality rate, especially for symptomatic patients. There is a wide spectrum of presentation from the asymptomatic patient to those with embolic complications or cardiogenic shock. Mortality rates following surgery mainly depend on the NYHA class of the patient; those patients in Classes I–III have a mortality rate of 4.7%, whereas 60% of patients in Class IV die during the intra- or post-operative period.[6]

Roudaut *et al*. reported their single-centre study on prosthetic valve obstruction in 210 patients (263 episodes).[7] The study results showed that the two treatment arms had similar mortality rates (surgery 10% vs. fibrinolysis 11%), and the authors favoured surgical therapy over fibrinolysis as the embolic and major bleeding complications in the fibrinolytic group were higher than in those patients treated surgically (15–0.7% and 4.7–0.7%, respectively).

When making decisions about the role of thrombolytic therapy in PVT, clinicians must be knowledgeable about the associated risks of thrombolytic therapy and individually evaluate patient risk factors prior to determining appropriate candidacy for thrombolytic therapy. Thrombolytic treatment is not without risk and patients with a high operative risk also tend to be the ones with the highest haemorrhagic risk (e.g. elderly patients, anaemia, chronic kidney disease, other comorbidities). In an international multicentre registry (PRO-TEE study), patients with PVT underwent thrombolysis, and all of them had undergone TOE before therapy.[2] This study found a previous history of cerebrovascular event and a thrombus size >0.8 cm^2 as one of the major risk factors for systemic embolic complications of thrombolytic therapy. The favourable clinical outcomes with recently introduced slow or ultra-slow infusions of Alteplase,[3] when compared with relatively poor surgical results, have rendered thrombolytic therapy the first-line treatment option in most eligible patients with PVT.

There is nothing known of embolic protection devices in the medical treatment of thrombi (thrombolytic treatment and/or anticoagulation). The protection devices may theoretically reduce morbidity related to stroke following thrombolytic therapy, particularly in patients in whom embolization risk is particularly high as in our patient with large thrombus (>10 mm according to the 2021 ESC/EACTS guidelines and >0.8 cm^2 according to the 2020 ACC/AHA guideline[4,5]). However, arterial access site bleeding and/or haematoma should be kept in mind as the potential complications.

As a clinician our mission is treating without harm, and maintaining independence should always be as important as preventing death. Coylemwright *et al*. showed that patients may regard stroke as a worse health state than death.[8] To decrease the risk of TIA or ischaemic stroke we decided to protect both internal carotid arteries. Fortunately, the embolic protection device catched an embolized thrombus from the thrombosed prosthetic valve and the procedure ended successfully without any sign of embolization or bleeding.

Aortic stenosis represents an increased afterload state for the left ventricle. The LVEF reduction in patients with aortic stenosis may be initially due to afterload/contractility mismatch.[9] In a patient, we reported the inflammatory markers and troponin were negative at presentation. Although we did not perform a coronary angiography avoiding risk of embolization, the thrombosis of prosthetic aortic valve causing acute and severe stenosis might be the main cause of decreased LVEF in our patient. A real-time pressure–volume loop analysis during transcatheter aortic valve implantation has shown an acute increase in LVEF after valve replacement and LV unloading.[10] We suggested that the early improvement of LVEF of this case, after the resolution of prosthetic aortic valve obstruction by thrombolysis, is due to elimination of afterload/contractility mismatch.

In conclusion, we present the first report in the world on the implantation of embolic protection devices during thrombolytic therapy of PVT. It may decrease TIA or ischaemic stroke in this patient population, especially if thrombus is large and mobile. Patients with obstructive PVT could be evaluated by performing serial cinefluoroscopy, for the treatment success, during the thrombolytic therapy. Also, we highlight TOE utility in evaluating prosthetic valve before and after thrombolytic therapy.

Lead author biography

Damirbek Osmonov, MD, is a graduate of Hacettepe University, School of Medicine in 2005, Ankara, Turkey. He has completed his Cardiology residency in Siyami Ersek cardiovascular surgery centre in 2011, Istanbul, Turkey. His field of interests are interventional cardiology, echocardiography, and invasive arrhythmology.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case including images and associated text has been obtained from patient in line with COPE guidance.

Conflict of interest: All authors have no conflicts of interest to disclose.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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