

Recurrent embolisms despite adequate anticoagulant therapy in a patient with prosthetic heart valves and atrial fibrillation: a case report

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Background

Antithrombotic management in patients with atrial fibrillation (AF) that have undergone heart valve surgery may be challenging, especially in the context of thromboembolic events during follow-up. The combination of pharmacological therapies with modern transcatheter interventions allows these more complex cases to be overcome.

Case summary

We present the case of a 66-year-old female with a history of AF and mechanical aortic and mitral valve replacement, which was admitted to the hospital complaining of dizziness and unsteady gait. A computerized tomography scan of the brain confirmed the diagnosis of embolic stroke. Two years later, the patient complained of sudden onset of chest pain, accompanied by electrocardiographic abnormalities and elevated high-sensitivity troponin T. Emergency cardiac catheterization revealed embolic myocardial infarction with distal occlusion of the obtuse marginal artery. Again, 2 years later, the patient suffered a new cerebral embolic event. Given the adequate anticoagulation therapy throughout almost the entire clinical course, percutaneous left atrial appendage closure was proposed as an adjunct to vitamin K antagonist treatment. Notably, intraprocedural transoesophageal echocardiography revealed the presence of a previously undetected left atrial appendage thrombus, thus an embolic protection device was used during the procedure, which was successfully carried out without complications.

Discussion

This case report demonstrates the complexity of the antithrombotic management in patients with AF and prosthetic heart valves, and highlights the importance of an individualized approach, integrating new therapeutic strategies to achieve success, in patients that present thromboembolic events despite adequate anticoagulation therapy.

Keywords

Anticoagulant therapy • Embolic stroke • Embolic myocardial infarction • Case report • Left atrial appendage closure

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Learning points

- Coronary embolism is a frequently under-diagnosed mechanism of acute coronary syndrome and can account for 4–13% of cases.
- Society guidelines on antithrombotic therapy in the setting of mechanical heart valves show some disparities regarding the management of thromboembolic events.
- Left atrial appendage closure can be effective as an adjunctive option for patients with recurring cardioembolic events despite optimal anticoagulant therapy.

Introduction

Antithrombotic therapy is a cornerstone of the management of patients after mechanical heart valve replacement and vitamin K antagonist (VKA) drugs are the only anticoagulant agents available for long-term oral anticoagulation in these patients.¹ Currently, available society guidelines offer general guidance on the approach to antithrombotic therapy in these patients. However, in complex clinical scenarios, such as recurrent thromboembolic events, antithrombotic treatment remains challenging. We present the case of a patient with atrial fibrillation (AF), as well as mechanical aortic and mitral prostheses, which presented multiple recurrent thromboembolic events, despite adequate anticoagulation therapy.

Timeline

1992	Mechanical aortic and mitral valve implantation (Bjork-Shiley Monostrut 21 mm and 25 mm, respectively) for rheumatic heart disease
2015	Acute ischaemic embolic stroke in the left superior cerebellar artery territory
February 2017	Non-ST-elevating myocardial infarction due to embolism with distal occlusion of the obtuse marginal artery
March 2017	Aortic heart valve replacement (St. Jude Medical Trifecta, 21 mm) due to pannus formation
February 2019	Acute ischaemic embolic stroke in right corona radiata
July 2020	Left atrial appendage (LAA) thrombus in pre-procedural transoesophageal echocardiography for percutaneous left atrial appendage closure (LAAC)
August 2020	Percutaneous LAAC, supported by cerebral protection system, given the persistence of LAA thrombus

Case presentation

Our patient is a 66-year-old female, who underwent mechanical aortic and mitral valve replacement (Bjork-Shiley Monostrut 21 mm and 25 mm, respectively) for rheumatic heart disease in 1992. In addition, the patient had a history of permanent AF and was on anticoagulant therapy with acenocoumarol. The patient was first admitted to our hospital in 2015 complaining of dizziness and gait instability. She presented with a blood pressure (BP) of 150/80 mmHg, a pulse rate of 81 b.p.m., and a blood oxygen saturation of 99% (ambient air). On physical examination, the patient showed a severe ataxia. Blood analysis showed an international normalized ratio (INR) of 2.4. A computerized tomography (CT) scan of the brain revealed an acute ischaemic area in the superior left cerebellar hemisphere, suggesting embolic stroke in the left superior cerebellar artery territory ([Figure 1A](#)). The patient was discharged after 2 weeks in a good general condition and recovered completely. Anticoagulant therapy was maintained with acenocoumarol, maintaining a target INR of 3.0.

The patient was later admitted to our emergency department in February 2017, complaining of sudden onset of chest pain. Her BP was 160/94, the pulse rate was 65 b.p.m., and blood oxygen saturation was 96% (ambient air). The electrocardiogram showed AF with new ST-segment depression in V4–V6 and a negative T-wave in inferior and lateral leads. Biochemical blood analysis revealed a high-sensitivity Troponin T of 14 ng/L, elevating to 68 ng/L after 2 h (99th percentile upper reference limit of 14 ng/L). The INR at admission was 3.4. Bedside echocardiography showed regional akinesia of the inferior wall, as well as elevated peak and mean pressure gradients of the aortic valve (89 mmHg and 53 mmHg, respectively). Emergency cardiac catheterization was performed, revealing a distal occlusion of the obtuse marginal artery, with angiographic features typical of an embolic aetiology ([Video 1, Figure 2](#)).

In addition, transoesophageal echocardiography (TOE) was performed to assess the elevated pressure gradients of the aortic valve ([Video 2](#)). The TOE assessment revealed an echodense thickening of the aortic annulus, not restricting the leaflet opening, thus suggesting pannus formation. Of note, discs mobility was also preserved in cine-angiography. The patient was discharged with low molecular weight heparin and acetylsalicylic acid (ASA) was added to her treatment. She was referred to cardiac surgery for elective aortic valve replacement (implanting a St. Jude Medical Trifecta, 21 mm), which was performed in March 2017 without complications. Pannus formation was confirmed during surgery. Anticoagulant therapy was continued with Acenocoumarol, increasing the target INR values to 3.5, while ASA was withdrawn on 30 March 2017.

In February 2019, the patient was admitted to Neurology in an outpatient setting due to transient left hemiparesis and dysarthria. A CT of the brain revealed a hypodense area in the right corona radiata, therefore confirming ischaemic stroke ([Figure 1B](#)). The INR at admission was 3.4. Given the recurrent embolic ischaemic events despite adequate VKA therapy, the patient was presented for percutaneous left atrial appendage closure (LAAC) as adjunctive therapy to anticoagulation.

Preprocedural TOE showed a left atrial appendage (LAA) thrombus not identified in previous studies ([Figure 3](#)), thus the procedure

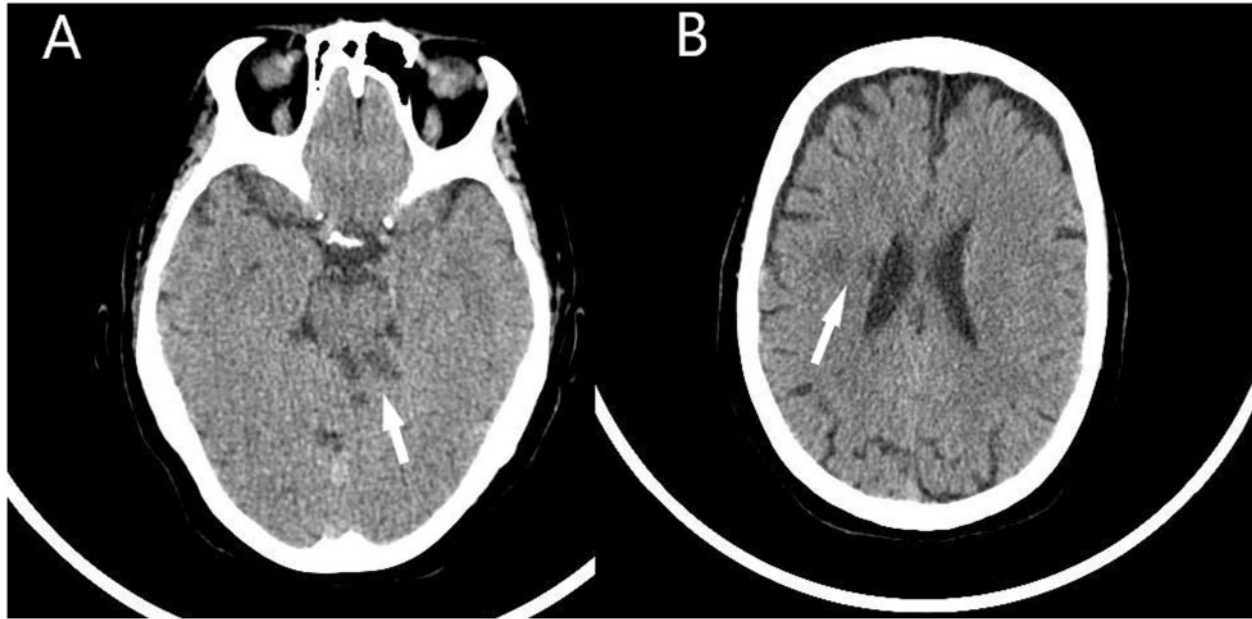


Figure 1 Cerebral computerized tomography scans. (A) December 2015, acute ischaemic area in the superior left cerebellar hemisphere, suggesting embolic stroke in the left superior cerebellar artery territory. (B) February 2019, hypodense area in the right corona radiata, confirming ischaemic stroke; lesions are marked with white arrows.



Video 1 Emergency cardiac catheterization revealed a distal occlusion of the obtuse marginal artery, suggesting embolic myocardial infarction.

was scheduled under embolic protection (*Figure 4, Video 3*). LAAC (Watchman FLX™, Boston Scientific, MA, USA) was performed in August 2020, supported by a double filter cerebral protection system (CPS, SENTINEL™, Boston Scientific, MA, USA). The procedure was carried out without complications and the patient was

discharged the next day. Anticoagulant therapy was continued with acenocumarol and a target INR of 3.5. Until the present date, the patient has not presented new thromboembolic events.

Discussion

We present the rare case of a patient with AF and mechanical heart valves experiencing recurrent thromboembolic events despite optimal anticoagulant treatment during almost the entire clinical course, and describe the therapeutic value of adjuvant LAAC in these challenging scenarios.

Since the use of novel oral anticoagulants (NOACs) increased rates of thromboembolic events and bleeding complications in patients with mechanical heart valves, NOACs are currently not recommended for these patients.^{1,2} Thus, anticoagulation with an VKA agent was the only alternative for our patient. Society guidelines offer general guidance on the approach to antithrombotic therapy in the setting of mechanical heart valves; however, they show some disparities on optimum INR, the addition of low-dose ASA and the management of thromboembolic events (*Table 1*).

The European Society of Cardiology (ESC) guidelines for the management of valvular heart disease recommend a median INR value, rather than a range in order to avoid considering extreme values in the target range as a valid target INR.¹ The initial INR target values recommended by the American Heart Association (AHA) guideline for the management of patients with valvular heart disease and the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines range from 2.5 to 3.0 and are generally lower, when compared with those of the ESC guidelines for the

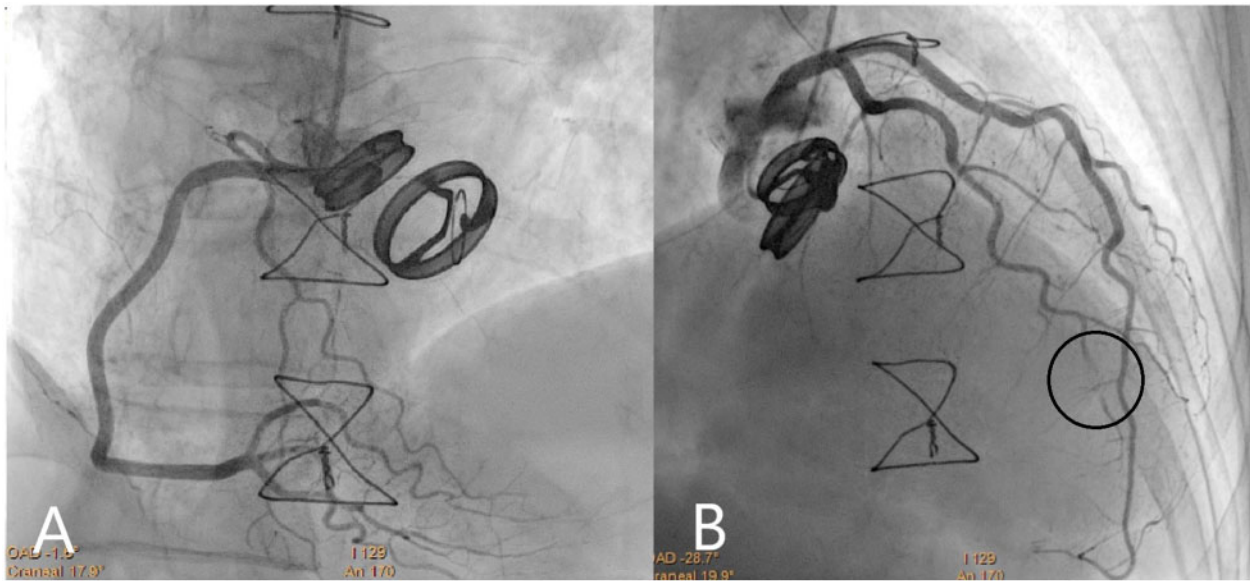
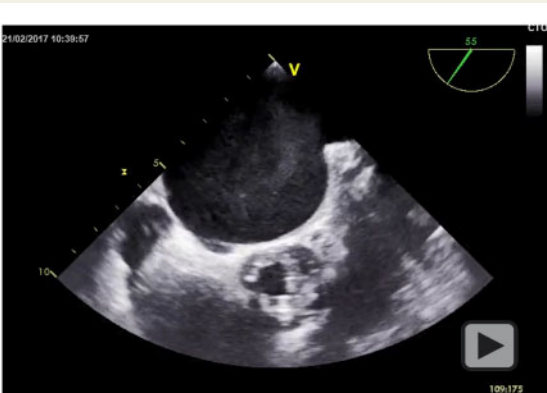


Figure 2 Coronary angiography. (A) Right coronary artery. (B) Distal occlusion of the obtuse marginal artery (circle) with typical features of embolic aetiology (distal, abrupt, absence of atherosclerosis in other arteries).



Video 2 Transoesophageal echocardiography assessment revealed an echodense thickening of the aortic annulus, not restricting the leaflet opening, thus suggesting pannus formation.

management of valvular heart disease, which may reach 4.0 according to the patients' risk factors and valve thrombogenicity.^{1,3,4} Interestingly, in a retrospective analysis of the German Experience With Low-Intensity Anticoagulation Study (GELIA), in patients following St. Jude Medical mechanical valve replacement in the group treated to an INR of 2.0 to 3.0, the risk of thromboembolic events was similar to, however, the risk of bleeding lower than, those of the group treated to an INR of 3.0–4.5.⁵

Management of thromboembolism in such patients should include the treatment of risk factors and the optimization of anticoagulation control.¹ Furthermore, the ESC guidelines indicate the addition of low-dose ASA with a Class 2a recommendation and a level of

evidence C. Likewise, the AHA guidelines recommend either intensification of VKA therapy or the addition of low-dose ASA. Currently, there are no comparative trials from which to assess the relative utility of intensified VKA therapy as compared to the addition of low-dose ASA in these patients. Therefore, whether to increase INR values or to add low-dose aspirin is a shared decision-making that should evaluate several factors, such as bleeding risk.³ A 2013 Cochrane Systematic Review showed that although the addition of an antiplatelet agent reduced the risk of thromboembolic events, this comes with an increased and offsetting risk of major bleeding.⁶

Considering the previous mentioned recommendations, we established an initial target median INR at 3.0.^{1,3,4} Given the recurrence of thromboembolic events, we adjusted the target INR during follow-up, in conjunction with close hospital controls in our centre's haematology outpatient clinic. This strategy achieved INR values in the range of 3.5–4.5 throughout almost the entire clinical course, with only exceptionally values slightly below 3.0. Since this regimen was already considered an intensified VKA treatment, long-term aspirin was not added in order to avoid bleeding complications. Considering the close monitoring at our institution as well as patient preferences, INR self-monitoring was not considered to be an appropriate option that would achieve a substantial benefit in this case.⁷ Given the recurrence of thromboembolic events, the patient was presented to the multidisciplinary thrombosis committee, including cardiologists, neurologists, and haematologists, and it was decided to perform a percutaneous LAAC. LAAC has shown to be safe and effective for stroke prevention in patients with non-valvular AF and contraindication to oral anticoagulation. Although the most common indication for closure are recurrent or intracranial bleedings, interestingly, this technique has also proved to be effective as an adjunctive option for patients with recurring cardioembolic events despite optimal

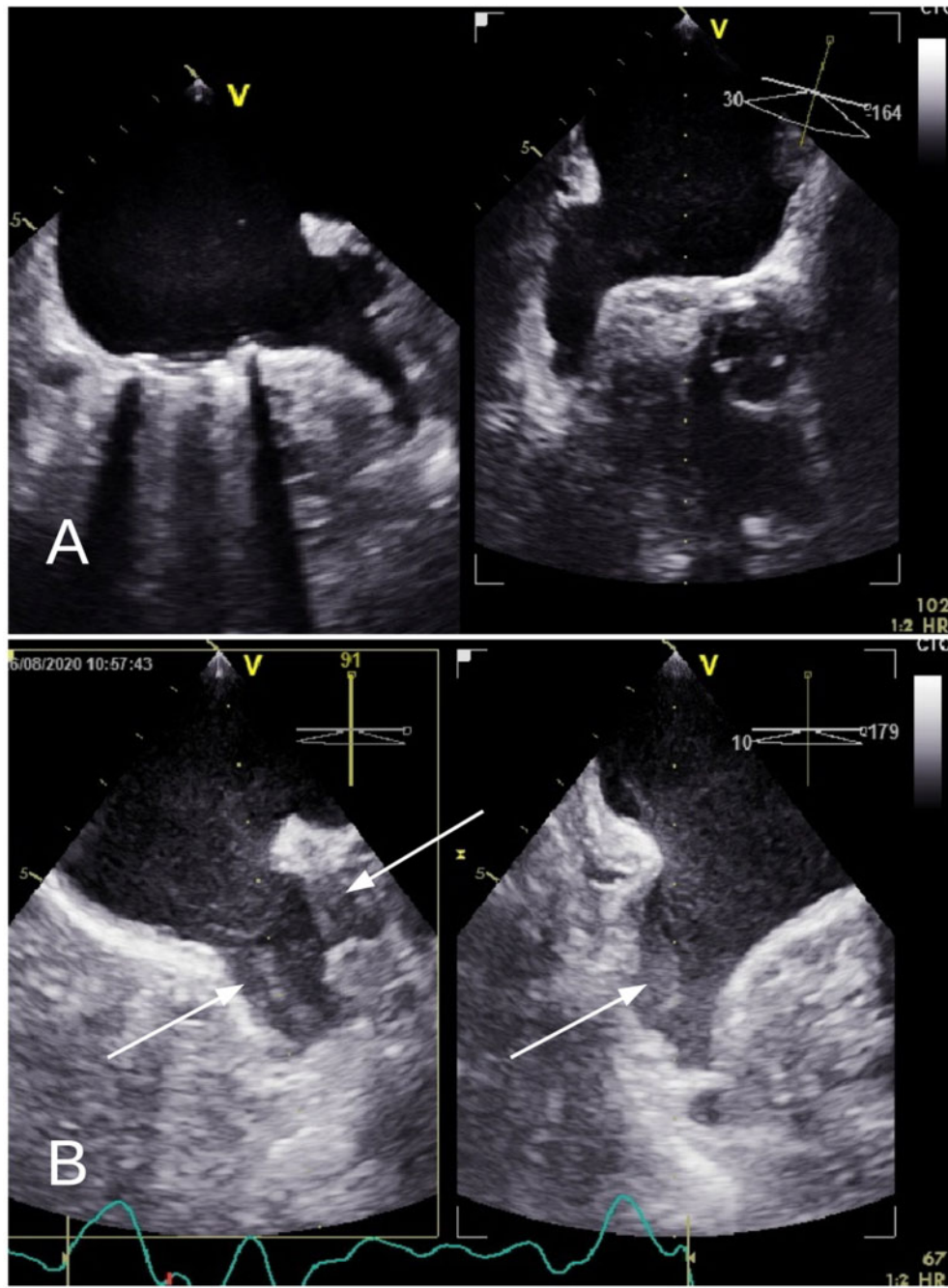


Figure 3 Multiplane transoesophageal echocardiography. (A) December 2019, transoesophageal echocardiography at 74° (left) and 164° (right) showing patent left atrial appendage with no internal thrombus. (B) July 2020, transoesophageal echocardiography at 91° (left) and 179° (right) showing organized left atrial appendage thrombus (white arrows) and spontaneous echo contrast.

anticoagulant therapy.^{8,9} This strategy has shown to be effective even in patients with mechanical prostheses, which can represent up to 22% of recurrent strokes cases.⁸ As an additional interesting feature of our case, the presence of thrombus in the lumen of the LAA could have been considered an absolute contraindication for the procedure due to the risk of intraprocedural embolism.¹⁰ Since LAA thrombus persisted after four additional weeks of adequate anticoagulation

therapy, our group decision was to carry out the LAAC procedure supported by CPS. CPS techniques have been originally proposed and developed in the setting of carotid interventions, and more recently with the development and improvement of transcatheter aortic valve interventions. Encouraged by this background, there is initial evidence that CPS supported LAAC is a feasible option for patients with LAA thrombus.¹¹

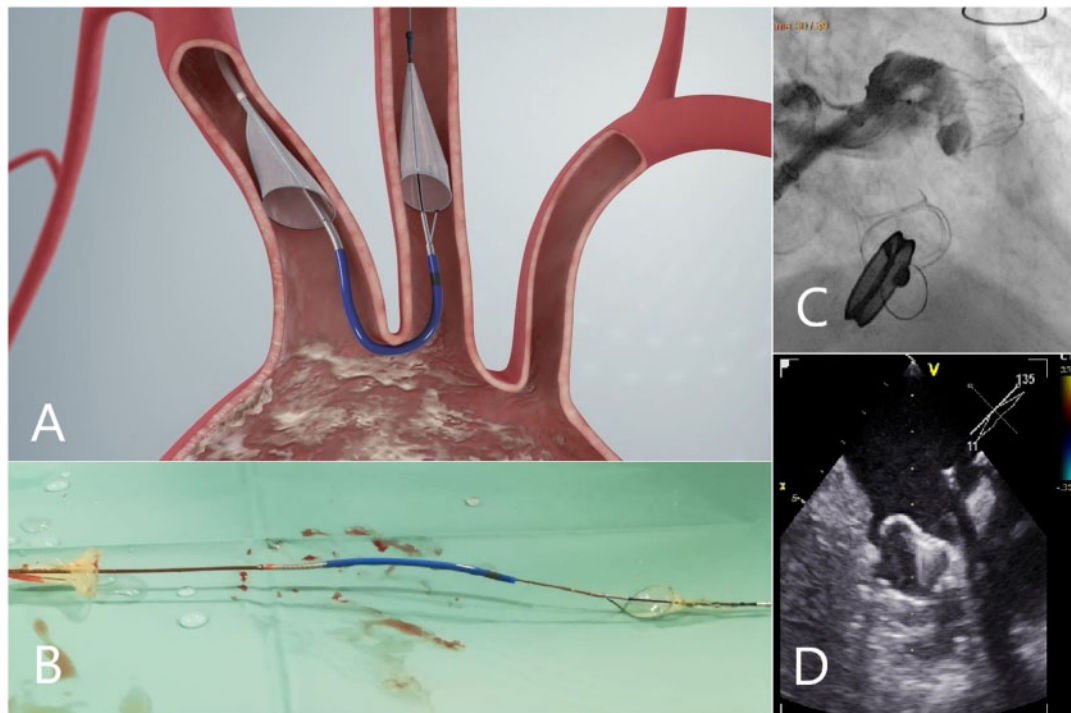
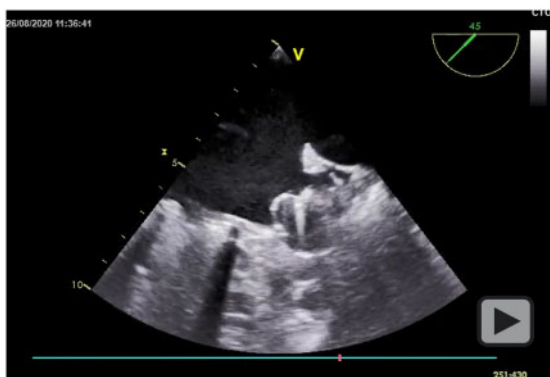


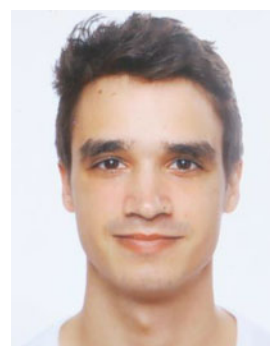
Figure 4 Percutaneous left atrial appendage occlusion using a cerebral protection system. (A) Schematic diagram of the cerebral protection system (SENTINEL™, Boston Scientific, MA, USA) completely expanded, with intraluminal filters placed in brachiocephalic trunk and left common carotid artery. Image courtesy of Boston Scientific. (B) Cerebral protection system device used during the procedure. (C) Angiographic view (right anterior oblique caudal) prior to release of the left atrial appendage closure device (Watchman FLX™ Boston Scientific, MA, USA), shows adequate positioning in main lobe, good sealing and compression. (D) Transoesophageal echocardiographic view (at 135°) of the final result, after release of the left atrial appendage closure device, demonstrating adequate anchoring and compression, with no residual leak, and coverage of the thrombus location area.



Video 3 Percutaneous left atrial appendage occlusion. Intraoperative transoesophageal echocardiography.

This case report demonstrates the complexity of the antithrombotic management in patients with AF and mechanical heart valves, and highlights the importance of an individualized approach, integrating new therapeutic strategies to patients that present thromboembolic events despite adequate anticoagulation therapy.

Lead author biography



Alexander Marschall, MD studied Medicine at the Medical University Graz (Austria). Since 2018, he is a Cardiology resident at the Central Defense Hospital, Madrid, Spain.

Supplementary material

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

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

Table 1 Differences between ESC, AHA, and ACCP guidelines regarding the anti-thrombotic management of patients with mechanical valves

	ESC ^a	AHA ^b	ACCP ^c
Anticoagulation therapy	Oral anticoagulation is recommended lifelong for all patients with mechanical prosthesis (I, LOE B)	Lifelong VKA therapy for all patients with mechanical heart valves (1, LOE A)	VKA therapy is recommended for long-term management (1, LOE B)
Use of direct oral anti-coagulant (DOACs)	Not recommended for patients with mechanical heart valves (III, LOE B)	Not recommended for patients with mechanical heart valves [3, LOE: B (Dabigatran), C (anti-Xa)]	—
Target INR	Low thrombogenicity: 2.5 (3.0 ^d) Medium thrombogenicity: 3.0 (3.5 ^d) High thrombogenicity: 3.5 (4.0 ^d)	With no risk factors ^e : 2.5 With any risk factor ^e : 3.0 Mitral valve: 3.0	AVR: 2.5 MVR: 3.0 Double mechanical valve: 3.0
Antiplatelet agents (APA)	Addition of low-dose aspirin in (IIa, LOE C): • concomitant atherosclerotic disease • thromboembolism despite adequate INR	Addition of low-dose aspirin in (2a, LOE C): • thromboembolism despite adequate INR	Addition of low-dose aspirin in (1, LOE B): • patients at low risk of bleeding
Management of thromboembolism	Treatment of risk factors Optimization of anticoagulation control Addition of low-dose aspirin after careful analysis of risk-benefit ratio (IIa, LOE C)	AVR: increase INR target from 2.5 (2.0–3.0) to 3.0 (2.5–3.5) or add low-dose APA (2a, LOE: C) MVR: increase INR target from 3.0 (2.5–3.5) to 4.0 (3.5–4.0) or add low-dose APA (2a, LOE: C)	—

Low thrombogenicity: Carbomedics, Medtronic Hall, ATS, Medtronic Open-Pivot, St. Jude medical, ON-X, Sorin Bicarbon; Medium thrombogenicity: other bileaflet valves; High thrombogenicity: Lillehei-Kaster, Omniscience, Starr-Edwards, Bjork-Shilley, other tilting-disc valves.

AVR, aortic valve replacement; LOE, level of evidence; MVR, mitral valve replacement.

^a2017 ESC/EACTS Guidelines for the management of valvular heart disease.

^b2020 ACC/AHA Guideline for the management of patients with valvular heart disease.

^cAntithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

^dPatient-related risk factors: mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis of any degree, and LVEF <35%.

^eThromboembolic risk factors: older-generation valve, atrial fibrillation, previous thromboembolism, hypercoagulable state, and LV dysfunction.

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

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