Case report: Mechanical mitral prosthetic valve thrombosis in the context of COVID-19 despite effective anticoagulation

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Background
The SARS-CoV2 virus has been an emerging virus since December 2019 and is the cause of a global pandemic whose clinical manifestations extend far beyond respiratory disease.

Case summary
A patient with severe coronavirus disease 2019 respiratory infection, carrying a mechanical mitral valve and under anticoagulation, was admitted to our cardiology department because of a new atrial fibrillation, which turned out to be related to thrombosis of the mitral mechanical valve.

Conclusion
The pro-coagulant effect of the SARS-CoV2 virus does not spare patients at risk of thrombosis, even under effective anticoagulation. In patients with mechanical valves under vitamin K antagonist treatment, there is a high risk of thrombus formation. The treatment is based on thrombolysis by therapeutic anticoagulation, fibrinolysis, or surgery depending on the size, composition of thrombus, and clinical manifestation.

Keywords
Coronavirus • Mechanical mitral valve thrombosis • Thrombolysis anticoagulation • Case report

ESC Curriculum
4.10 Prosthetic valves • 5.3 Atrial fibrillation

Learning points
• The incidence of thrombo-embolic events may increase during the coronavirus disease 2019 (COVID-19) pandemic, due to the procoagulant state induced by severe acute respiratory syndrome coronavirus 2 infection.
• Carriers of mechanical heart valves are at risk of valve thrombosis in the clinical setting of COVID-19 infection.
• Standardized prophylactic anticoagulation protocols for inpatient and outpatient settings are needed due to the high risk of thromboembolic events in COVID-19 patients.

Introduction
Since the beginning of the SARS-CoV-2 pandemic, which began at the end of 2019, numerous studies have reported a wide range of different clinical manifestations of this pathology, including a hypercoagulable state. This complication can affect up to a third of intensive care patients. This observation raises the question of anticoagulation, in both, patients without prior anticoagulation and
particularly previously anticoagulated patients, whose data and recommendations in this context are very limited.

The following clinical case report describes a patient with a mechanical mitral valve on adequate acenocoumarol treatment with severe SARS-CoV-2 infection. We report the discussion regarding the diagnostic and therapeutic management of a heart valve thrombus in the setting of SARS-CoV-2 infection and the need or not for change in anticoagulation therapy in this context.

**Timeline**

| Time                  | Events                                                                 |
|-----------------------|------------------------------------------------------------------------|
| 6 days before admission | The patient, implanted with a Medical Medtronic ATS 27 mm mechanical mitral valve for severe mitral stenosis and under acenocoumarol treatment, had received 10 mg of oral vitamin K following an international normalized ratio (INR) of 7.7 |
| 2 days before admission | The patient is tested coronavirus disease 2019 positive, and the first symptoms appear |
| Day 0                 | Admission to the emergency department of secondary care hospital for respiratory distress and palpitations. When given a D-dimer elevation of 6893 µg/L, a chest computed tomography is done which excludes pulmonary embolism but shows dilation of the left atrium (LA) and signs of pulmonary hypertension. |
| Day 0                 | Transfer to the intensive care department of tertiary referral hospital for severe hypoxaemia due to SARS-CoV2 pneumonia and rapid-ventricular response atrial fibrillation. Upon admission, INR was at 2.7. Discontinuation of vitamin K antagonist treatment in the benefit of enoxaparin 80 mg 2 × day SQ because of the critical patient’s condition. |
| Day 1                 | Because of the patient’s stability from a respiratory perspective, she is transferred to the cardiology department to explore the new onset atrial fibrillation. The first transthoracic echography (TTE) shows a dilated LA, a mean transprosthetic gradient (TPG) at 12 mmHg. Cinefluorography shows hypo-mobility of one of the leaflets of the mitral mechanical valve and complete immobility of the second. The diagnosis of mechanical mitral valve thrombosis is made. Enoxaparin is stopped and therapeutic heparin anticoagulation at 14 000 U/L intravenous is started. |
| Day 5                 | Transoesophageal ultrasound confirms the presence of a thrombus straddling the two leaflets of the mechanical mitral valve, predominantly on the anterior leaflet. |
| Day 11                | 2nd cinefluorography confirmed the presence of thrombus on the leaflets of the mechanical valve. |
| Day 12                | Start of thrombolysis by alteplase. Heparin anticoagulation is paused while lyse was in progress. |
| Day 13                | TTE post-lysis control shows a reduction of the TPG to 4 mmHg, a decrease of the volume of LA and pulmonary arterial pressures. A cinefluorography shows the complete recovery of the mobility of one of the leaflets and persistence of the immobility of the second leaflet |
| Day 14                | Phenprocoumon anticoagulation is started simultaneously with intravenous heparin until a stable therapeutic INR is achieved. |
| Day 22                | The patient goes home with a stable INR under phenprocoumon alone treatment |

**Case presentation**

A 58-year-old female was admitted to the intensive care unit with severe hypoxaemic respiratory failure caused by the SARS-CoV-2 infection. She had been implanted 6 years ago with a Medical Medtronic ATS 27 mm mechanical mitral valve for severe mitral stenosis and was treated with acenocoumarol. International normalized ratio (INR) over the past 3 months was mostly in the therapeutic range of 2.5–3.5. Upon admission, she presented new-onset atrial fibrillation (AF). Laboratory results showed electrolytes in normal range, normal renal and liver function. Troponin T hs was 16 ng/L (n < 14 ng/L), N-terminal prohormone of brain natriuretic peptide 3146 ng/L (n < 300 ng/L), D-dimers 6893 mcg/L (n < 350 mcg/L), INR 2.7. The thoracic CT-scan (Figure 1) showed typical alveolar coronavirus disease 2019 (COVID 19) lesions, indirect signs of pulmonary hypertension (dilated pulmonary artery) without pulmonary embolism, and a massively dilated left atrium (LA). Because of the critical patient’s condition, initial treatment upon admission included mechanical ventilation, discontinuation of vitamin K antagonist (VKA) treatment for the benefit of enoxaparin (80 mg 2 × day SQ).

The respiratory state quickly improved allowing the patient to be transferred to the cardiology department for further investigation regarding the new-onset AF.
Upon arrival in the cardiology department, clinical findings included: heart rate (HR) 125 b.p.m., blood pressure (BP) 103/65 mmHg, pulse oximetry 95% with 2 L/min nasal oxygen therapy, irregular heartbeats, normal mechanical valve clicks, and a diastolic murmur and bilateral pulmonary crackles. The neurological status was normal. A transthoracic echocardiography (Figure 2) showed reduced mobility of the two leaflets of the mechanical mitral prosthesis with an image suggestive of thrombus. Transprothetic mitral Doppler peak velocity was elevated (254 cm/s), pressure half time was prolonged (213 ms). The mean transprosthetic gradient (TPG) was 16 mmHg. The LA was severely dilated (90 mL–59 mL/m²).

The LA was severe enough to cause both arterial and venous thrombosis. Several publications have reported pulmonary embolism, deep venous thrombosis, or acute coronary syndromes in SARS-CoV-2 patients. This case is, to our knowledge, the first report of mitral mechanical valve thrombosis in a SARS-CoV-2 patient.

This case addresses the problem of abnormal mechanical valve function in a SARS-CoV-2 patient despite therapeutic anticoagulation. The presence of an elevated TPG and a hypoechogenic mass attached to the leaflets on the TTE was compatible with valve thrombosis, infectious endocarditis, or pannus (peri-annular fibrous outgrowth) (less likely). Since no biological or imaging testing is pathognomonic of any of these three hypotheses, a careful rule-out strategy should be performed.

Peri-annular fibrous outgrowth, or pannus, is a chronic slowly progressive disease and seemed unlikely to account for an acute valve dysfunction. Furthermore, obstructive pannus is a more common complication of aortic valve prosthesis than mitral. Its typical echocardiographic aspect is hyperechogenic, which differs from our echographic findings in this case. Regarding the possibility of infectious endocarditis, in the presence of repeated negative blood cultures and resolution of clinical and biological signs of infection after SARS-CoV2, we ruled out this differential diagnosis. Therefore, mechanical valve thrombosis seemed to be the most likely diagnosis.

The most frequent cause of mechanical valve thrombosis is non-optimal anticoagulation in 45% of cases according to a cohort study from the Montreal Institute.

Therapeutic anticoagulation with VKA is defined by an INR within the therapeutic more than 70% of time, according to European Society of Cardiology guidelines for atrial fibrillation, otherwise no specific time in therapeutic range (TTR) exists for patients with a mechanical valve. The evolution of INR in our patient and the subsequent interventions are summarized in Figure 5. We detected no lack of compliance to VKA treatment. The patient had received 10 mg of oral vitamin K on 13.11 following an INR of 7.7. Upon admission, INR was in the therapeutic range (2.7). However, the impact of synthetic vitamin K on mechanical valve thrombosis is not precisely described in the literature. Furthermore, subtherapeutic INR values may not increase the thrombotic risk in mechanical heart valve carriers with previously sufficient TTR. We cannot exclude that the few days spent in the subtherapeutic range of the anticoagulation (Figure 5)
may have been a cause for this thrombotic event. However, the chance of thrombotic events over such a short period of time without therapeutic anticoagulation remains very low according to the literature. Therefore, this clinical case raises the question of the role of SARS-CoV-2 infection in the prothrombogenic effect and highlights the issue of the management of anticoagulation during SARS-CoV-2 infection, or other similar viral infections.

After taking into account all the previous considerations, we found valve thrombosis in this patient to be unlikely related to a lack of anticoagulation (or at least not alone). Therefore, we investigated the potential role of the SARS-CoV-2 infection in this matter.

In SARS-CoV-2 patients, the British Nation Institute of Health recommends heparin-mediated prophylactic anticoagulation if hospitalized in the internal medicine department and therapeutic

Figure 2 Pre-lysis transthoracic echocardiography (left) and at Day 1 of lysis (right). Decreased blood flow turbulence and left atrium–left ventricle gradient. Image size: 1800 px × 910 px.

Figure 3 Opening of the mechanical mitral valve in diastole at the patient admission (left) and on D+1 post thrombolysis (right). Original movement of one leaflet is recovered while the immobilization of the second leaflet is persisting. Image size 669 px × 228 px.
No recommendations for modification or increase in anticoagulation have been made regarding cardiac prosthetic valve holders. In addition, there are no studies suggesting that SARS-CoV-2 interacts with VKA. This clinical case raises the question of a possible SARS-CoV-2 related risk of valve thrombosis due to a pro-thrombotic state or VKA resistance. In SARS-CoV-2 patients, only one case of bioprosthetic mitral valve thrombosis and one case of aortic mechanical valve thrombosis have been published.

Surgery is the therapeutic option of choice in case of non-obstructive mechanical prosthetic valve thrombosis (PVT) and if the thrombus is more than 10 mm, complicated by emboli or refractory to anticoagulation. If the operative risk is too high, thrombolysis is the preferred therapy. Since the thrombosis was obstructive but well tolerated, a conservative treatment was chosen, considering the patient’s fragility and preference. Thrombolysis was incompletely successful (according to the decreased gradient on transoesophageal echocardiography, and improved, but not complete, mobility of leaflets), suggesting a mixed component obstruction (pannus and thrombus) whose acute deterioration would be due to a thrombus.

Mechanical valve thrombosis, regardless of its severity is associated with poor short- and long-term outcome. Therefore, should anticoagulation treatment be reinforced in SARS-CoV-2 patients to prevent valve thrombosis?

Would an increase in the usual doses be sufficient, or would a change of the molecule be necessary? Should aspirin be added to VKA? Further studies will be necessary to answer these questions.

### Conclusion

Patients implanted with mechanical valve prosthesis should benefit from therapeutic anticoagulation with VKA for life, with close INR monitoring in order to avoid thrombosis of the prosthesis. This article reports a case of mechanical mitral PVT, despite therapeutic INR, in a critically ill SARS-CoV-2 patient. The PVT was successfully treated by intravenous thrombolysis with rTPA. We suspect an implication of the SARS-CoV-2 virus in the PVT, although the mechanisms are unclear. The SARS-CoV-2 pro-inflammatory and pro-coagulant states may have played a part in the PVT. Further observations will be needed to confirm the suspected increase of PVT risk during SARS-CoV-2 infection, as well as the best preventive and curative strategies.

### Lead author biography

Clarisse Jeckelmann, 26, is a 6th year medical student, studying in University of Lausanne, Switzerland, intending to pursue a career in cardiology.

### Supplementary material

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

**Slide sets:** An edited slide set detailing this case and suitable for presentation is available as supplementary data.

**Consent:** The authors confirm that witnessed verbal consent for submission and publication of this case report including images and associated text has been obtained from the patient detailed in this case report. This has been discussed with the editors.
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