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CASE REPORT
Heart failure

COVID-19 in a patient implanted with a total artificial heart: a case report

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Background The coronavirus disease 2019 (COVID-19) was first identified in December 2019 and is currently still a public health issue affecting millions of people worldwide. Heart failure patients are known to be at higher risk of morbidity and mortality in this case. Yet, few data exist concerning COVID-19 among patients with a left ventricular assistance device, and even less among those with a total artificial heart (TAH).

Case summary A 27-year-old man with Marfan syndrome underwent prophylactic ascending aorta replacement. Shortly after surgery completion, he developed refractory cardiogenic shock with biventricular dysfunction leading to veno-arterial extracorporeal membrane oxygenation (VA-ECMO) implantation. In the context of no appropriate eligible donor during the following 10 days while waiting on the heart transplantation list, the patient was scheduled for a TAH as a bridge to transplantation. Meanwhile, he developed an acute respiratory distress syndrome secondary to SARS-CoV-2. The patient was successfully treated with corticosteroids, prone positioning and mechanical ventilation, and heart transplantation occurred 5 weeks after COVID-19 onset.

Discussion Here, we report the first case of a patient presenting with COVID-19 infection following TAH implantation in a bridge to transplantation. We highlight that (i) cardiogenic shock patients simultaneously infected by COVID-19 should be treated instantly with all-time available technology to ensure best outcomes, including TAH and prone positioning, (ii) heart transplantation safety 5 weeks after COVID-19 onset.

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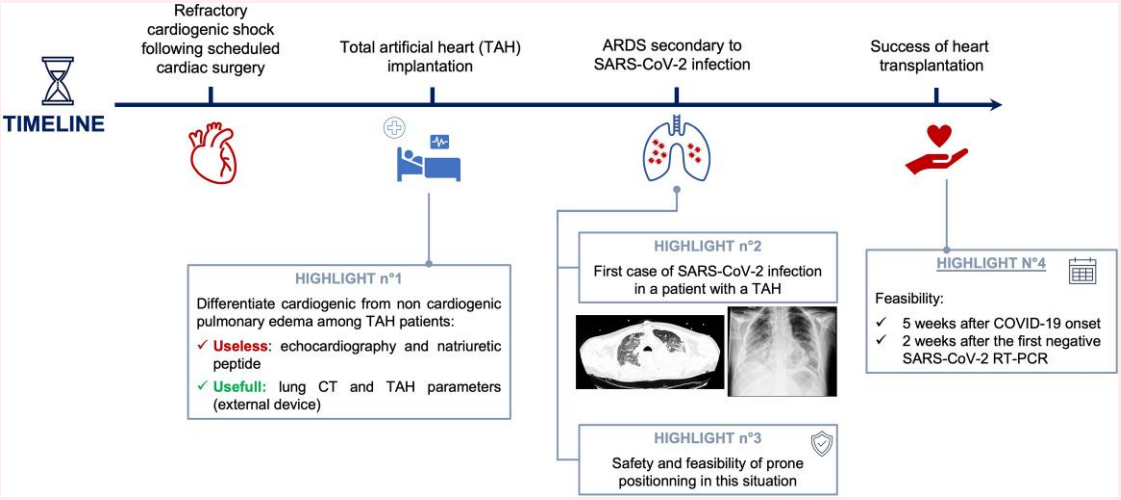
Graphical Abstract



COVID-19 in a patient implanted with a total artificial heart: a case report. This figure represents a schematic timeline of the case report from the refractory cardiogenic shock to the success of heart transplantation. Four learning points are depicted in the 'highlight' boxes. TAH, total artificial heart, CT, computed tomography, ARDS, Acute Respiratory Distress Syndrome, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2, COVID-19, Coronavirus Disease 2019, RT-PCR, reverse transcription polymerase chain reaction.

Keywords Total artificial heart • Coronavirus disease 2019 • Acute respiratory distress syndrome • Heart transplantation • Case report

ESC curriculum 6.1 Symptoms and signs of heart failure • 6.2 Heart failure with reduced ejection fraction • 6.4 Acute heart failure • 7.3 Critically ill cardiac patient • 7.5 Cardiac surgery

Learning points

- To report the first case of SARS-CoV-2 infection in a patient receiving a total artificial heart.
- To differentiate pulmonary cardiogenic oedema from non-cardiogenic causes, i.e., infectious disease.
- To suggest the safety of prone positioning for COVID-19 management in a patient receiving a total artificial heart.
- To emphasize that heart transplantation was feasible after SARS-CoV-2 earlier than recommended.

Introduction

The coronavirus disease 2019 (SARS-COV-2) pandemic has spread worldwide since December 2019. Symptoms range from asymptomatic to acute respiratory distress syndrome (ARDS) requiring intensive management. Both acute and chronic heart failure increase the risk of morbimortality during SARS-COV-2 infection.[1] However, data are limited among patients implanted with a left ventricular assistance device, and even more rare among those with a total artificial heart (TAH).

Timeline

Time	Event
Scheduled surgery	Prophylactic ascending aorta replacement for critical aortic dilatation in a Marfan syndrome patient.

Continued

Continued

Time	Event
Hours	Biventricular dysfunction secondary to post-cardiotomy syndrome, leading to veno-arterial extracorporeal membrane oxygenation implantation.
Day 10	No recovery and no heart donor yielding to total artificial heart implantation.
2 months	Redo surgery for suspected mediastinitis in the context of fever and positive blood cultures with methicillin-sensitive *Staphylococcus Aureus*.
2 months and 10 days	Persistent fever, associated with typical infectious acute respiratory failure syndrome. RT-PCR assay was positive for COVID-19.
2 months and 17 days	Intensive care management including mechanical ventilation support, oxygen supply, prone positioning and corticosteroid therapy.
4 months and 10 days	Successful heart transplantation (five weeks after COVID-19 onset).
6 months	The patient was discharged from hospital.

Case presentation

A 27-year-old white male patient with Marfan syndrome was admitted to Rouen University Hospital to undergo a scheduled ascending aorta replacement due to a 46 mm aneurysm in the context of family history of aortic dissection (*Figure 1*).[2] The patient did not have any other past medical history or baseline medications. Early after extracorporeal circulation weaning, the patient developed refractory cardiogenic shock with biventricular systolic dysfunction, requiring veno-arterial extracorporeal membrane oxygenation implantation. Post-surgery coronary angiogram was normal, and the most likely diagnosis was post-cardiotomy severe biventricular dysfunction due to suboptimal heart protection.

After 24 h, there was no cardiac or haemodynamic improvement despite intensive care, including intravenous Levosimendan. Therefore, the patient was put on the emergent heart transplant waiting list. After 10 days without an appropriate eligible donor, a SynCardia temporary TAH (SynCardia, Tucson, AZ, USA) was implanted as a bridge to transplantation.[3]

Two months after TAH implantation, the patient presented with a high-grade fever, with leucocytes and C-reactive protein elevation (23 G/L and 412 mg/L, respectively). Blood cultures were positive for methicillin-sensitive *Staphylococcus Aureus,* and the patient was put on intravenous Daptomycin and Gentamicin. After 48 h, both fever and biological inflammation were persistent while the sternotomy lower part demonstrated skin reopening and leakage. Redo surgery was performed for mediastinitis suspicion.

After 10 days of effective antibiotic therapy, fever persisted while repeated blood cultures were still negative. Moreover, it was associated with acute respiratory failure syndrome. Further physical examination revealed no further abnormalities.

The differential diagnoses were cardiogenic pulmonary oedema, ventilator-associated pneumonia, pulmonary embolism, acute respiratory distress syndrome (ARDS) secondary to bacterial or viral infection including severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

Chest X-ray showed a diffuse alveolo-interstitial syndrome (*Figure 2*) and blood gas showed severe hypoxaemia (PaO_2 47 mmHg, pH:7.48, $PaCO_2$ 35 mmHg). Computed tomography (CT) pulmonary angiogram showed diffused peripheral opacities (frosted glass infiltrate and 'crazy paving'), pulmonary condensation with atelectasis, pleural effusion without pulmonary embolism, which was compatible either with the diagnosis of coronavirus disease 2019 or any another infectious pneumonia (*Figure 3*). Since echocardiography was not feasible and brain natriuretic peptide level not interpretable with the TAH, the TAH external device was interrogated and did not demonstrate low cardiac output or high filling pressure. Thus, the diagnosis of cardiogenic pulmonary oedema was ruled-out.

Blood cultures, bronchial sampling and pneumococcal and legionella antigenuria were negative. Finally, reverse transcription polymerase chain reaction (RT-PCR) assay was positive for SARS-CoV-2 and a SARS-CoV-2 ARDS diagnosis was retained, also probably favoured by recent mediastinitis.

High-flow oxygen therapy was initiated in addition to intravenous corticosteroids (7 mg once daily for 10 days).[4] While the clinical response was initially favourable, the patient deteriorated 7 days after disease onset occurred and the patient was intubated (PaO_2/FiO_2 ratio 39). After 48 h of follow-up, PaO_2/FiO_2 ratio dramatically decreased from 235 to 110, and the patient was placed in the prone position. After two prone position sessions without deteriorating TAH function or global haemodynamic, the PaO_2/FiO_2 ratio reached 262 followed by progressive ventilatory parameter improvement (*Figure 4*). Four months after TAH implantation and 5 weeks after SARS-COV-2 onset, the patient received a successful heart transplantation.

Two months after the heart transplantation, the patient has been discharged, and he is currently at home with a normal 27-year-old man quality of life. Patient's therapy and vital parameters at discharge are provided in *Table 1*.

Discussion

SARS-COV-2 was only reported in two patients with a left ventricular assistance device (LVAD). Here, we report the first case of SARS-CoV-2 in a patient implanted with a TAH as a bridge to transplantation. Our case report highlights a few critical issues.

First, differentiating pulmonary oedema from cardiogenic vs. non-cardiogenic causes, is challenging among patients with TAH. About 30% of hospitalized SARS-CoV-2 patients have a history of chronic heart failure which tends to worsen,[5] and many clinical signs and symptoms overlap between both. While biomarkers such as

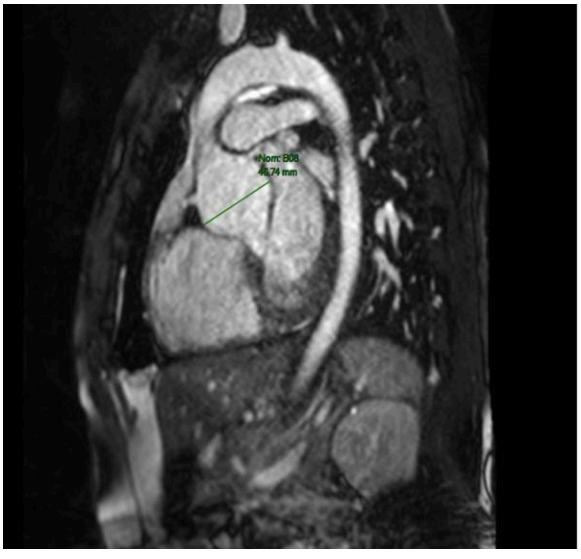


Figure 1 Angio-magnetic resonance imaging. Forty-six millimetres aneurysm.

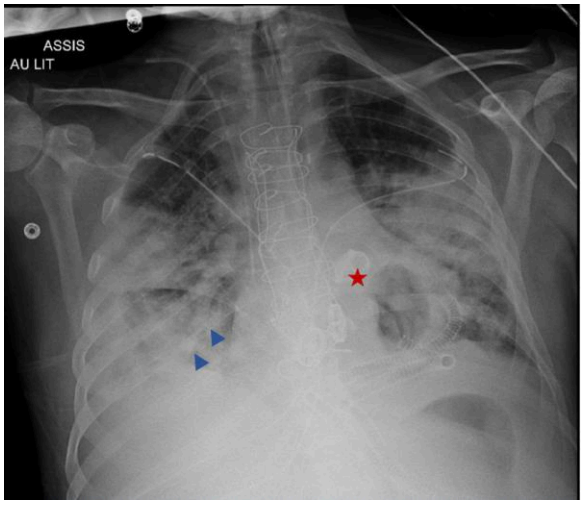


Figure 2 Chest X-ray. Chest X-ray with diffuse alveolo-interstitial syndrome (arrow head) in our patients implanted with a total artificial heart (star).

natriuretic peptides are helpful to diagnose isolated acute heart failure, they are not interpretable because they are often elevated in COVID-19 context and not synthetized within TAH patients. Besides, echocardiography is inappropriate in TAH patients and does not rule out isolated COVID-19 myocarditis.[6] Finally, the diagnosis of non-cardiogenic pulmonary oedema was possible in this patient with the combination of normal external TAH haemodynamic parameters and typical imaging of SARS-CoV-2 infection, including those reported in this clinical case.

Second, we demonstrated the safety of prone positioning in a patient infected by SARS-COV-2 and equipped with a TAH. In two SARS-COV-2 patients with LVAD,[7,8] the authors did not recommend the prone positioning since it has not been evaluated in this population and worried about the risk of outflow graft, driveline, and right ventricular compression.[9] On the contrary, TAH replaces both ventricles and the risk of right ventricle compression was unlikely while the risk of driveline compression was limited by: (i) the gentle rotation of the patient with an experienced team, (ii) the requirement of a team of five caregivers plus two people dedicated to the driveline, (iii) the close haemodynamic monitoring that followed. The time of prone positioning was not reduced, and no unexpected complications have been reported in this case. A former case series reported a remarkable improvement of oxygenation with early mechanical ventilation support weaning in a patient with TAH but without COVID-19.[10] Thus, prone positioning seems to be feasible in TAH patients in experienced teams.

Third, beside traditional management of ARDS, anticoagulation remains an issue among SARS-COV-2 patients. They have an increased likelihood to develop venous thromboembolic events with life-threatening pulmonary embolism.[11] In our patient, anticoagulation was initiated and the CT pulmonary angiogram ruled-out a pulmonary embolism. However, several cases of LVAD thrombosis were recently reported among SARS-CoV-2 patients.[12,13] Therefore, although not standardized in patients receiving TAH or LVAD, the international normalized ratio (INR) should probably by higher in this context. In this case, Warfarin was used for anticoagulation therapy with an INR target of 2.5, however without evidence-based recommendations.

Fourth, despite numerous temporary contraindications including mediastinitis and SARS-CoV-2, our patient was successfully transplanted 5 weeks after infectious onset and 2 weeks after the first negative RT-PCR. It is normally recommended to wait 7 weeks between any surgery and COVID-19.[14] Our strategy was different and we suggest that five weeks was acceptable particularly when elective emergent surgery is needed such as heart transplantation. Afterwards, he was vaccinated twice with the Pfizer Comirnaty vaccine and showed persistent seroconversion. Later, while receiving immunosuppressive therapy, he did not develop a new SARS-CoV-2 infection. He was finally discharged 2 months later and has a normal quality of life today.

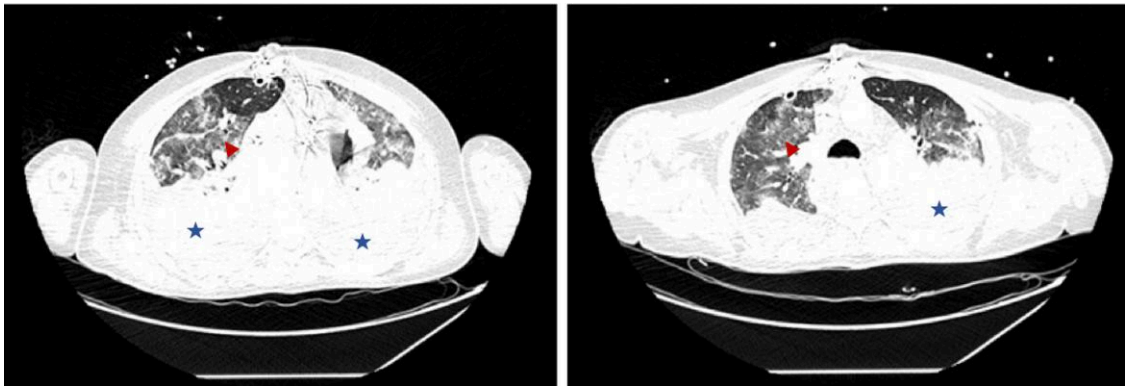


Figure 3 CT pulmonary angiogram. CT pulmonary angiogram showing diffuse frosted glass infiltrate and 'crazy paving' (arrow head) and pulmonary condensation with atelectasis and pleural effusion (stars).

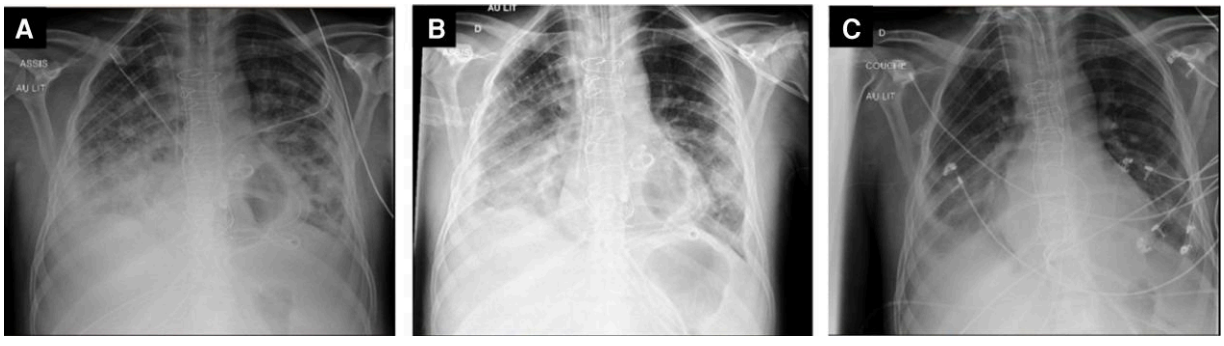


Figure 4 Chest X-ray evolution. Progressive decrease in pulmonary infiltration at (*A*) 7 days, (*B*) 30 days and (*C*) 60 days after the SARS-CoV-2 RT-PCR positivity.

Table 1 Patient's discharge therapy and vital parameters

Specific therapy at discharge	
Mycophenolate mofetil	500 mg twice per day
Tacrolimus	1.5 mg twice per day
Everolimus	0.75 mg twice per day
Prednisolone	30 mg once per day
Acetylsalicylic acid	75 mg once per day
Bisoprolol	3.75 mg once per day
Furosemide	40 mg once a day
Pravastatin	40 mg once a day
Cotrimoxazole	400/80 mg 3 days a week
Vital parameters and biomarkers at discharge	
Systolic/diastolic blood pressure	124/89 mmHg
Heart rate	100 bpm
NTproBNP	889 ng/mL
Temperature	36.2°C

NTproBNP, N-terminal pro-brain natriuretic peptide.

Conclusions

This report is the first published SARS-CoV-2 case in a patient implanted with a TAH, as a bridge to heart transplantation. We suggest the efficiency and safety of the prone position among TAH patients, as well as the possibility of heart transplantation following several weeks after SARS-COV-2 resolution.

Lead author biography

Juliette Lutun is graduated from the University of Reims in 2018. She is currently a cardiology resident at Rouen University Hospital, France. These cardiology interests are heart failure and cardiovascular imaging.

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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 patient was informed and has signed the patient consent form in accordance with COPE guidelines.

Conflict of interest: C.F. reports grants from Pfizer and consulting fees from Jonhson and Jonhson, outside the submitted work. F.B. reports personal fees from Actelion, Johnson and Johnson, Astra Zeneca, Boehringer Ingelheim, and Vifor, Bayer; grants from Pfizer; outside the submitted work. The other authors have no conflicts of interest to declare.

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