Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

subset of patients with PAH may benefit most while minimizing overall risk and resource utilization.[4–6] It will be crucially important to identify those patients with PAH that have a reasonable perspective for recovery. One way to assess this is to determine which patients with PAH have low-to-intermediate calculated 1-year mortality (such as using the Registry to Evaluate Early and Long-Term PAH Disease Management 2.0 score (≤8 is favorable). Perhaps, this small subset of patients with PAH should continue to be considered for mechanical support and/or transplant, irrespective of PAH itself, however noting that this will require ongoing input and assessment from the advanced transplant team, weighing risks/benefits and considering similar parameters in other individuals concurrently listed, to identify those patients with the best chance for a full recovery and least resource utilization (utility).

We must also consider the effects of COVID-19 on the patient with PAH more specifically. It is not entirely clear whether patients with underlying pulmonary disease and PAH do worse with COVID-19.[7] Therefore, it is not likely fair (justice) to impart resource restriction to the patient with PAH listed for transplant during the pandemic on the basis of disease process alone. Reflecting further on PAH, one must consider the unique pathophysiologic consequences inflicted upon the cardiovascular and pulmonary systems in those infected with COVID-19. Indeed, both the disease itself and subsequent treatment (ventilation and positive end-expiratory pressure) have profound adverse effects on the right ventricle, which in many cases is already adversely remodeled in PAH. Thus, it would be anticipated that patients with PAH with COVID-19 would not fare well and that resource allocation might be best utilized for others. Conversely, given that significant endothelial dysfunction and vascular complications are implicated in COVID-19, theoretically, PAH-specific medications may be beneficial as they target endothelial function and offload the right ventricle.[4,5] In addition, several PAH-specific therapies may also impart direct anti-Coronaviridae viral effects.[8,9]

In summary, operational ethical principles applied to the overarching cardiovascular and pulmonary transplant groups should equally extend to those with an underlying diagnosis of pulmonary vascular disease. It is important to maintain accessibility to invasive hemodynamic testing in those patients with new and/or suspected worsening of PAH despite the stage of the current pandemic. Finally, advanced resources such as mechanical circulatory support and organ transplant may be considered in a small subset of patients with PAH identified as having a reasonable perspective of recovery and if overall vetted risk among other recipients remains relatively low.

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COVID-19 leading to acute encephalopathy in a patient with heart transplant

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There is increasing evidence that severe acute respiratory syndrome coronavirus (CoV) 2 (SARS-CoV-2) impacts the neurologic system.[1–3] However, how the immunosuppressed state modifies neurologic involvement and clinical course remains uncertain.[4] We describe a patient with heart transplant who developed prolonged symptoms of encephalopathy late in CoV disease 2019 (COVID-19) illness.

A 67-year-old man was admitted with fever, cough, nasal congestion, sore throat, and diarrhea 20 months after an uneventful heart transplantation. He was not hypoxic. Chest computed tomography (CT) showed bilateral multifocal peripheral ground-glass opacities (GGOs). White blood cell count was 4,720/μl with lymphocyte count of 1,040/μl. Blood cultures and cytomegalovirus polymerase chain reaction (PCR) were unremarkable. C-reactive protein (CRP) was 0.55 mg/dl. Nasopharyngeal PCR for SARS-CoV-2 was positive, consistent with COVID-19 illness. Immunosuppression included 500 mg mycophenolate

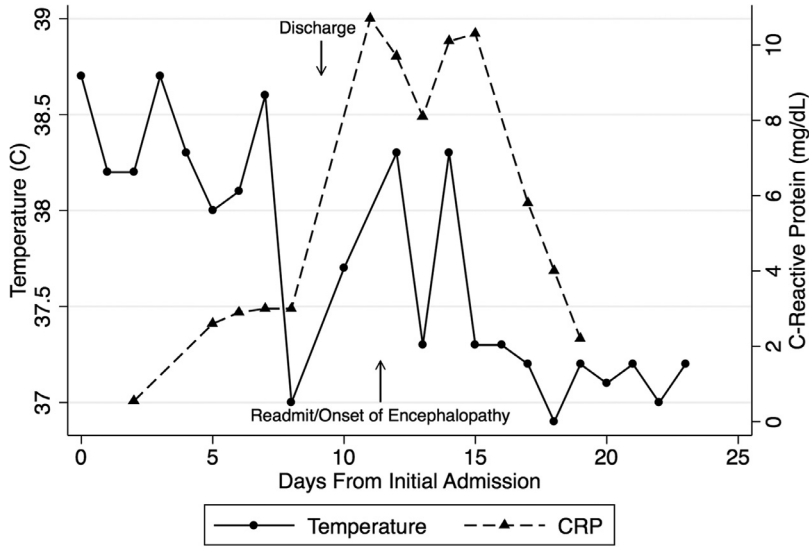

Figure 1 Fever and CRP Trend Following Admission. CRP, C-reactive protein.

twice daily (BID) and tacrolimus with trough level of 7.6 ng/ml at admission. Mycophenolate was discontinued. Tacrolimus was maintained for a goal level of 7−10 ng/ml. He continued to have intermittent fevers (Figure 1) but was never hypoxic. Chest CT on Day 6 showed worsening GGOs. Hydroxychloroquine was started on Day 7 (400 mg BID on the first day, then 200 mg BID for 4 days). He was discharged on Day 9.

He was readmitted after 2 days with confusion, anorexia, and emesis. He was alert, oriented only to person, and febrile. He had no previous history of delirium or encephalopathy and was on stable home dose of venlafaxine for the treatment of a history of depression. Examination was notable for postural and action tremor, without focal neurologic deficits. CRP was increased to 10.7 mg/dl with a mild elevation in aspartate transaminase and alanine transaminase to a maximum of 74 U/liter and 79 U/liter, respectively. Serum ammonia and thyroid-stimulating hormone were normal. Serum sodium was decreased to 133 milliequivalents/liter (normal range 135−145 milliequivalents/liter) but returned to normal by Day 2 of readmission. Blood urea nitrogen and serum creatinine were 42 mg/dl and 1.73 mg/dl, respectively, unchanged from baseline. Trough tacrolimus level at readmission was 11.5 ng/ml and averaged to 10 ± 1.2 ng/ml during the admission. Hydroxychloroquine was discontinued.

CT scan of the head was unremarkable. Chest CT showed minimal progression of GGOs. Brain magnetic resonance imaging showed mild scattered foci of peri-ventricle deep and sub-cortical white matter ischemia. There was no evidence of encephalitis, posterior reversible encephalopathy, or leukoencephalopathy. Repeat magnetic resonance imaging after 1 week was unchanged. Electroencephalogram showed mild non-specific diffuse multifocal cerebral dysfunction with no seizure seen. Lumbar puncture showed 1 lymphocyte, normal protein, and glucose. Cerebrospinal fluid (CSF) was negative for herpes simplex PCR and *Cryptococcus* antigen. PCR of CSF, not validated for the detection of SARS-CoV-2, was negative. By Day 16, CRP began to decline. Mental status slowly improved, and he was discharged 13 days after readmission. Executive function and memory remained poor but gradually returned to normal approximately 45 days after the onset of the encephalopathy.

Whereas we were unable to demonstrate the presence of SARS-CoV-2 virus in the CSF of our patient, no alternative diagnosis for his encephalopathy was found. Sepsis was unlikely to be an explanation because symptoms started after clinical stabilization and he had limited signs or symptoms of organ dysfunction. Hydroxychloroquine has been associated with neurologic changes, but symptoms persisted for more than 2 weeks after discontinuation.[5] The onset of encephalopathy coincided with increased markers of inflammation, most notably CRP. The impact of immunosuppression in patients with COVID-19 remains uncertain, and the severity of illness in case reports has been varied.[6,7] It is possible that immunosuppression may attenuate the severity of disease by limiting the extent of cytokine release, which may be the primary mediator of injury[8]; however, a recent report suggests poor outcomes in hospitalized patients with solid organ transplant.[9] The optimal degree of immunosuppression in patients with heart transplant with COVID-19 remains uncertain.

COVID-19 has been associated with acute hemorrhagic necrotizing and hypoxic encephalopathy, encephalitis, delirium, and anosmia.[1,10−12] Other β-CoVs such as severe acute respiratory syndrome-CoV-1 and Middle East respiratory syndrome-CoV have been shown to be neurotropic and manifest with delirium.[1] The angiotensin-converting enzyme 2 receptor (the primary source of cell entry of the virus) is expressed in both neurons and glia and could serve as a mechanism of direct viral entry into the nervous system. Alternatively, the inflammatory state itself may give rise to encephalopathy,[13] and patients with acute respiratory distress syndrome have been shown to have a high rate of persistent dysexecutive syndrome similar to that of our patient[3]; however, our patient was never hypoxic or

severely ill before the onset of symptoms, and symptoms persisted for many days after normalization of markers of inflammation. Given the novel presentations of COVID-19, we believe it is important for transplant centers to consider the potential for delayed neurologic manifestations.

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Collapsing glomerulopathy associated with COVID-19 infection in a heart transplant recipient

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A 56-year-old African American male with ischemic cardiomyopathy and chronic kidney disease who underwent heart transplantation over 1 year before presentation was admitted to our institution with dry cough, myalgias, and diarrhea concerning for coronavirus disease 2019 (COVID-19) infection. Nasal swab polymerase chain reaction assay was positive for the severe acute respiratory syndrome−coronavirus-2 (SARS-CoV-2) virus. Initial labs revealed acute kidney injury (creatinine, 1.86 mg/dl). Initial ferritin and IL-6 levels were within reference range. D-dimer was elevated at 306 ng/ml and C-reactive protein was elevated at 20.5 mg/liter. Treatment with hydroxychloroquine and nitazoxanide was initiated. Azithromycin was deferred because of a prolonged corrected QT of 517 ms. Immunosuppression with tacrolimus was resumed because of multiple episodes of allograft rejection in the past; however, mycophenolate and prednisone were stopped. Baseline urine studies had revealed mild nephrotic range proteinuria (1,973 mg/dl). Over the course of 7 days, his renal dysfunction rapidly progressed (creatinine peak, 7.78 mg/dl) with marked elevation in urine protein/creatinine ratio to 7,354 mg/dl. Inflammatory markers continued to rise (ferritin 637 ng/ml, IL-6 11 pg/ml, C-reactive protein 61.1 mg/liter, and D-dimer 1,562 ng/ml). Percutaneous needle core kidney biopsy showed acute tubular injury as well as collapsed capillary tufts with overlying visceral epithelial cell hyperplasia and protein droplets within Bowman's space, diagnostic of collapsing glomerulopathy (Figure 1). Electron microscopy revealed coronavirus particles within the tubular epithelial cells (Figure 2). There was no evidence of immune complex−mediated or monoclonal-associated disease. Anti-neutrophil cytoplasmic antibodies, anti−double stranded DNA antibodies, HIV, and hepatitis serologies were negative. Chest radiography showed progressive patchy bilateral infiltrates consistent with atypical pneumonia; however, the patient remained afebrile with adequate oxygen saturation on room air and did not require respiratory support. His inflammatory markers subsequently downtrended, as his renal function improved with supportive care. He did not require dialysis and was eventually discharged home.

Collapsing glomerulopathy has a known association to viral infections, including the first SARS-CoV from the outbreak in 2002.[1] To our knowledge, this is the first case of collapsing glomerulopathy associated with COVID-19 infection reported in a heart transplant recipient. Rare reports of similar cases in non-transplant patients have recently emerged in the literature.[2,3] One case involved a 44-year-old African American female who was homozygous for the G1 risk allele in the *APOL1* gene (a known risk factor for collapsing glomerulopathy).[2] In that report, SARS-CoV-2 RNA was detected in the biopsy specimen, but whether the patient's glomerulopathy was triggered by the virus directly or the resulting cytokine storm is unclear. Our patient had baseline proteinuria before transplantation and feasibly could have had an undiagnosed focal segmental glomerulosclerosis before SARS-CoV-2 infection; however, the rapidly progressive nature of his renal dysfunction and subsequent improvement following resolution of his illness suggests an association.

The incidence of acute kidney injury (AKI) as a complication of COVID-19 has been variably reported. A case