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.

with more severe COVID-19, or with evidence of IL-1-mediated hyperinflammation.

As the field of IL-1 inhibition in COVID-19 moves forward, key questions still need addressing. The main challenge is to identify patients who might most benefit from treatment, either through correct timing of administration or through molecular taxonomy of individual inflammatory responses. Because IL-1α and IL-β are notoriously hard to measure in circulation, clinically useful biomarkers for patient selection include C-reactive protein, IL-6, ferritin (all proxies for IL-1 bioactivity),[3] and the soluble urokinase plasminogen activator receptor.[8] Also, since corticosteroids became the standard of care for severe COVID-19, future studies of IL-1 inhibitors will have to prove incremental benefit over corticosteroid treatment. Of related and notable interest is IL-1 inhibition in patients with COVID-19 and with type 2 diabetes: insulin use is associated with increased mortality for COVID-19,[9] and since use of corticosteroids typically results in increased insulin demands, IL-1 inhibition might be a preferable alternative anti-inflammatory strategy for such populations.

Overall, the impression stands that IL-1 inhibition has therapeutic rationale in COVID-19. Besides anakinra, available strategies to inhibit IL-1 include the monoclonal antibody canakinumab and the soluble IL-1 trap rilonacept. Orally available drugs inhibiting IL-1 also hold promise, such as novel and potent inhibitors of the NLR family pyrin domain containing 3 inflammasome.[10] Clinical trials assessing these agents for treatment in patients with severe disease will ultimately determine the right place for IL-1 inhibition in COVID-19.

GC declares consultation honoraria from Sobi, Novartis, Roche, Sanofi, Cerecor. GC is supported by AIRC under MFAG 2018 (ID 22136 project); Italian Ministry of Health (GR-2018-12366385); and Foundation for Research in Rheumatology (Career Award 2020). LD declares consultation honoraria from Sobi, Novartis, Roche, Sanofi.

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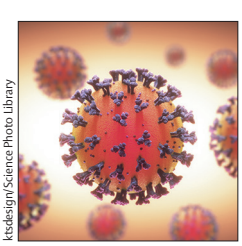
Risks of lung transplantation in the SARS-CoV-2 era



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Published **Online** December 1, 2020 https://doi.org/10.1016/S2213-2600(20)30561-0

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As the COVID-19 pandemic has swept the world, the provision of health care for conditions that are unrelated to COVID-19 has been extensively disrupted. This is especially the case for patients in need of solid organ transplantation, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have complicated the approach that transplant centres must take to ensure that recipients are not placed at risk of potentially fatal outcomes or severe allograft dysfunction should they become infected with SARS-CoV-2.

Many DNA and RNA viruses pose both immediate and delayed-onset, potentially serious risks for lung transplant recipients,[1] and disruption of host–virus relationships after solid organ transplantation can lead to both reactivation of latent viruses residing in donor tissues and new infections. Additionally, lung transplant recipients who have had successful transplantations are at risk of developing community-acquired respiratory virus infections, which have been linked to both acute and chronic lung allograft dysfunction.[2]

Infection with the novel SARS-CoV-2 is associated with substantial morbidity and mortality, and many survivors of COVID-19 have long-term or permanent detrimental health effects.[3] Airborne transmission is

the predominant route of disease spread[4] and it has become clear that virus-containing aerosols can linger in ambient air for hours before settling out via gravity. Asymptomatic infected individuals can be important vectors of virus spread, and should solid organ transplant recipients become infected with SARS-CoV-2, they might be at increased risk of severe disease and a fatal outcome compared with the general population.[5] However, community-acquired SARS-CoV-2 infections in lung transplant recipients can have a benign clinical course.[6]

SARS-CoV-2 rapidly replicates once it gains access to respiratory epithelium.[3,4] It can then spread via the circulation as it infects endothelial cells, not only causing respiratory dysfunction—organising pneumonia, diffuse alveolar damage, intravascular clotting, and acute respiratory distress syndrome (ARDS)—but potentially causing severe dysfunction of other organs, including heart, brain, gastrointestinal tract, and kidneys.[7] Viral loads can be very large and virus shedding can persist for many weeks.[8]

Transplanting lungs from a SARS-CoV-2-positive donor into a SARS-CoV-2-naive recipient or transplanting donor lungs into a patient whose irreversible respiratory failure has occurred as a consequence of severe ARDS with pulmonary fibrosis associated with COVID-19 are two potential scenarios in which a SARS-CoV-2 primary infection or SARS-CoV-2 reactivation could cause life-threatening complications and a poor outcome for lung transplant recipients.

In *The Lancet Respiratory Medicine*, Laurens Ceulemans and colleagues[9] report a successful double-lung transplantation using lungs from a SARS-CoV-2 IgG antibody-positive donor who had recovered from a presumed case of symptomatic COVID-19 3 months before transplantation. The SARS-CoV-2-naive recipient had a typical post-transplantation course, and although a lung biopsy done at the time of implantation showed the presence of SARS-CoV-2 RNA by PCR testing, post-transplantation nasopharyngeal swab testing, repeated PCR tests of bronchoalveolar lavage specimens, viral culture of bronchoalveolar lavage and donor lung tissue to detect viral replication, and serum anti-SARS-CoV-2 antibodies were negative. The good transplantation outcome and absence of virus activation despite the intense immunosuppression regimen given to the recipient suggest that transplanting organs harvested from a donor whose SARS-CoV-2 infection has resolved can be safely performed.

Although many patients succumb to respiratory failure with acute COVID-19 pneumonia, a substantial number of survivors with refractory ARDS develop severe, non-resolving pulmonary fibrosis that leaves them persistently ventilator-dependent and unlikely to survive without a lung transplant. Lang and colleagues[10] reported using lung transplantation as a salvage therapy for a patient with severe, treatment-refractory COVID-19-induced ARDS requiring prolonged extracorporeal membrane oxygenation support. Repeated nasopharyngeal swabs and bronchoalveolar lavage specimens before transplantation were PCR positive, but Vero cell cultures did not show viable virus. Although post-transplant PCR on multiple sequential nasopharyngeal swab and bronchoalveolar lavage specimens remained positive before turning negative after day 10, Vero cell cultures were negative, suggesting that infective virus was no longer present, and the recipient had a good transplantation outcome.

What lessons do these case reports provide? As new cases of COVID-19 are exponentially on the rise in the general population in many countries, it is increasingly likely that donors might have a history of previous infection, either resolved or still active, when assessed for transplantation suitability. Potential donors must be thoroughly screened for active SARS-CoV-2 infection, but transplanting lungs from a donor whose infection has resolved and whose respiratory function is not compromised can be safe, possibly even if SARS-CoV-2 RNA persists in lung tissue. Additionally, when lung transplantation is considered in patients with end-stage ARDS or fibrosis caused by COVID-19, although PCR from respiratory tract specimens might be persistently positive up to and shortly after transplantation, active infection with shedding of viable virus is not necessarily observed, as shown by Lang and colleagues,[10] and lung transplantation can be safely performed. Experienced transplant teams need to adequately screen donor lungs for active SARS-CoV-2 infection, and transplant candidates whose transplant indication is refractory COVID-19 ARDS must be carefully selected. Because there is still much to learn concerning the effect of the SARS-CoV-2 virus on lung transplantation outcomes, a careful approach with attention to short-term and long-term follow-up after transplantation is essential.

Although effective vaccines might soon be available and vaccination combined with other strategies will hopefully curb and eventually stop the COVID-19 pandemic, infections will probably continue to affect world populations for months to years. Evolving experience in the era of SARS-CoV-2 at lung transplantation centres around the world will provide guidance for developing best practices to deal with the threat that this novel virus poses to successful solid organ transplantation.

I report grants from the US National Institutes of Health, Genentech/Roche, Galapagos, Parion, Biogen, and Promedior, outside of the submitted work.

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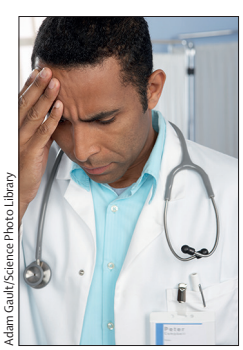
COVID-19: a heavy toll on health-care workers



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Published **Online**
February 5, 2021
https://doi.org/10.1016/S2213-2600(21)00068-0

The COVID-19 pandemic has challenged and, in many cases, exceeded the capacity of hospitals and intensive care units (ICUs) worldwide. Health-care workers have continued to provide care for patients despite exhaustion, personal risk of infection, fear of transmission to family members, illness or death of friends and colleagues, and the loss of many patients. Sadly, health-care workers have also faced many additional—often avoidable—sources of stress and anxiety, and long shifts combined with unprecedented population restrictions, including personal isolation, have affected individuals' ability to cope.

As the pandemic unfolded, many health-care workers travelled to new places of work to provide patient care in overwhelmed facilities; those who volunteered in unfamiliar clinical areas were often launched into the pandemic ICU setting with insufficient skills and training. The burden of training and supervising these volunteers fell on already stressed clinicians. Hospital-based health professionals worked long hours wearing cumbersome and uncomfortable personal protective equipment (PPE), after initial shortages of PPE had been addressed. They strived to keep up with emerging knowledge, institutional and regional procedures, and changing PPE recommendations, while trying to distinguish accurate information from misinformation. Health-care workers had to adopt new technologies to fulfil patient care and educational responsibilities, including the provision of telemedicine.

Insufficient resources and the absence of specific treatments for COVID-19 added to the challenges of managing severely ill patients. Health-care workers had to care for colleagues who were ill, offer comfort to dying patients who were isolated from their loved ones, and inform and console patients' family members remotely. Some health-care workers were burdened with emotionally and ethically fraught decisions about resource rationing and withholding resuscitation or ICU admission. They shared the pain of patients without COVID-19 who had their surgery or other essential treatments cancelled or postponed.

The fear of transmitting COVID-19 led many health professionals to isolate from their families for months. Working remotely and being shunned by community members further contributed to loneliness. Many health-care workers experienced lost earnings because of cancellations in outpatient visits and elective procedures. The training of health-care workers (eg, medical students, residents, and allied health learners) was also interrupted, leading to loss of tuition fees, missed learning opportunities, missed exams, and