

EUROPEANS DIED WAITING FOR ORGAN TRANSPLANTS DURING LOCKDOWN AS OPERATIONS DROPPED BY AT LEAST 65%

MORRERAM EUROPEUS À ESPERA POR TRANSPLANTES DE ÓRGÃOS DURANTE O BLOQUEIO, DEVIDO À QUEDA DE PELO MENOS 65% DE OPERAÇÕES

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The number of lifesaving organ transplants carried out during lockdown fell by 65%. Some of the patients on the waiting list died due to the lack of services.

Figures from NHS Blood and Transplant show that this year there were a total of 265 transplant operations from April 1st until 31st May compared to 702 for the same period last year. Some centres closed completely, others ran a skeleton emergency service, and many patients were told they had been temporarily suspended from the waiting list. All living donations were cancelled due to the potential risk of infecting the donor while deceased organ transplants continued at reduced levels.

The number of lung transplants fell from 40 at the same time last year down to five, liver transplants dropped from 149 to 73 and the number of heart transplants dropped from 22 to 20. Kidney transplants dropped from 361 last year to 165 this year.

Experts say the NHS staff and equipment being given over to focus on treating coronavirus, together with the added risk of carrying out transplant operations on patients where infection control could not be guaranteed partly explain the fall in transplant operations.

There was also an unexplained drop in donors. The news has raised concerns about the collateral impact of the pandemic on other NHS patients, many of whom needed lifesaving interventions.

Debasish Banerjee et al¹ Reported the first 7 cases of COVID-19 in kidney transplant recipients in south London hospitals.

In this report they discuss their first 7 cases of COVID-19 infection in kidney transplant recipients from south London. Median age of transplant recipients was 54 years (range, 45–69 years) comprising 4 men, 3 women. Of 7 patients, 2 were managed on an outpatient basis and stayed at home, with the remaining 5 (71%) requiring hospital admission. Four among the latter required ITU admission, and 1 was being managed in the renal ward. Of 4 patients sent to ITU, 2 needed intubation and ventilation; the other 2 were managed with oxygen through mask and non-invasive ventilation only. There was 1 death in this small series of 7 patients (mortality rate of 14%). All 3 patients with severe disease were female and also had diabetes. Two patients presented within 3 months of kidney transplantation (1 within 2 weeks) while kidney transplant vintage was 12 months or more in the remaining 5 cases. The patients were managed in



3 centres and the total number of prevalent transplant patients in these centres was 2082, with 32 patients transplanted from December 15, 2019, to March 15, 2020, during the developing pandemic.

Managing immunosuppression in these patients is challenging and should take into account age, severity of COVID-19 infection, associated comorbidities, and time post-transplant.

One of their 7 patients died, which is a mortality rate of 14%, although it is too soon to comment on likely mortality rates in this group of patients. Two of their patients presented within 3 months after transplantation and 1 presented within 2 weeks.

They suggested suspending kidney transplantation during the COVID-19 pandemic particularly for high-risk older recipients with comorbidities. Rigorous adherence to hand hygiene, recommended isolation procedures, and regular assessment, virtually and/or telephonically, of transplant patients will help reduce the incidence and facilitate management of mild-to-moderate cases in the community as they did in 2 of their 7 patients described.

The COVID-19 UK register has been set up by the UK transplant registry held by Organ Donation and Transplantation to record all cases of renal transplant patients presenting with COVID-19 infection and analysis of registry data will help clinicians make informed decisions about management of these complex patients in these uncertain and rapidly evolving times.

Stepan M. Esagian et al² from Greece reported that additional dilemmas arise regarding the potential discontinuation of immunosuppression regimens to improve their immune response to the infection, which must be weighed against the potential adverse event of transplant rejection. Nevertheless, immunosuppression regimens were fully maintained in many of the reported kidney transplant recipient cases. In all these cases, the authors hypothesized that the immunosuppression regimens may have prevented the overt immune response, manifesting as a “cytokine storm,” that is believed to be responsible for many of the severe manifestations of the disease,

such as acute respiratory distress syndrome and multi-organ failure as reported by Mehta P et al³.

In contrast to other infectious diseases where only the transplant recipient is at risk, SARS-CoV-2 could rapidly spread amongst medical personnel, resulting in serious consequences to the community. As a result, it becomes imperative that both patients and medical professionals strictly adhere to all appropriate safety measures geared toward minimizing transmission, in order to ensure that transplant programs can continue to operate uninterrupted for as long as possible, without placing the patients or the community at risk.

Roberta Angelico et al⁴ from Italy has been one of the first countries dealing with the outbreak of COVID-19, and severe measures have been adopted to limit viral transmission. The spread of COVID-19 may have several implications in organ transplant activity that physicians should be aware of. The initial experience gained during the COVID-19 outbreak shows that around 10% of infected patients in Italy need intensive care management to overcome the acute respiratory distress syndrome. Due to the exponential rise of infected patients we are now facing an actual risk of saturation of intensive care unit (ITU) beds. A restriction in the number of ITU beds available for both donors and transplant recipients may unfavourably influence the overall donation activity, and eventually lead to a reduced number of transplants. Preliminary Italian data show that a 25% reduction of procured organs has already occurred during the first 4 weeks of COVID-19 outbreak. This underlines the need to closely monitor what will be further happening in ITUs due to the COVID-19 spread in the attempt to preserve transplant activity, especially in Western countries where deceased donors represent the major organ resource.

Francesca Martino et al⁵, also from Italy considered that there was insufficient evidence available to consider kidney transplantation as a safe procedure in COVID-19 pandemic areas. In emergency situations—eg, in cases of no vascular access, unfeasible dialysis, or a hyperimmune state—the benefits might outweigh



the risks of a kidney transplant. Therefore, decisions should be made on a case-by-case basis, with concerns shared among the transplant team and patient after careful assessment of the risks and benefits. A pressing need exists to evaluate possible solutions to reduce the risk of kidney transplantation procedures during the COVID-19 pandemic, and for research to address the sensitivity issues of diagnostic tests for COVID-19. In the meantime, each case should be carefully discussed and scrutinised by the entire transplant team, and a dedicated consent form would help patients to make well informed decisions.

A.P.J. de Vries et al⁶ reported the first documented case of COVID-19 in the Netherlands, which counts 17.2 million inhabitants, was on February 27, 2020. In less than 60 days, despite increasingly stringent measures of the Dutch government to halt the spread of the infection, 28,153 individuals have tested positive for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), 9127 patients have been admitted to hospitals across the country (of which 2508 in the Intensive Care Units (ITU)

The total amount of all organ transplants markedly decreased from 100 to 150 to 40 transplants per month in the first COVID-19 month, a decrease of 67%. This is in contrast to the COVID-19 outbreak in Italy, where the activity remained stable for each type of solid organ. However, here the first 4 weeks of the outbreak was taken into account, while they have taken the period 27th of February till the 15th of April. Pancreas transplants decreased to 0 and renal transplants from 80 to 100 to 20 per month. The number of liver and lung transplants markedly declined from a mean of 16 to 8 per month and from 18 to 7 per month, respectively, a decrease of approximately 50%. There was no paediatric transplant activity in the first COVID-19 month

Mario Fernández-Ruiz et al⁷ from Spain reported their preliminary experience with 18 solid organ transplant (kidney [44.4%], liver [33.3%], and heart [22.2%]) recipients diagnosed with COVID-19 by March 23, 2020 at a tertiary-care centre at Madrid. Median age at diagnosis was 71.0 ± 12.8 years, and the

median interval since transplantation was 9.3 years. Fever (83.3%) and radiographic abnormalities in form of unilateral or bilateral/multifocal consolidations (72.2%) were the most common presentations. Lopinavir/ritonavir (usually associated with hydroxychloroquine) was used in 50.0% of patients and had to be prematurely discontinued in 2 of them. Other antiviral regimens included hydroxychloroquine monotherapy (27.8%) and interferon- β (16.7%). As of April 4, the case-fatality rate was 27.8% (5/18). After a median follow-up of 18 days from symptom onset, 30.8% (4/13) of survivors developed progressive respiratory failure, 7.7% (1/13) showed stable clinical condition or improvement, and 61.5% (8/13) had been discharged home. C-reactive protein levels at various points were significantly higher among recipients who experienced unfavourable outcome. This frontline report suggests that SARS-CoV-2 infection has a severe course in SOT recipients.

Mihai Oltean et al⁸ from Gotenberg Sweden reported 12 case series totalling 204 kidney transplant recipients with COVID-19 were identified. Most patients (74%) were men. The most frequent symptoms were fever (76%), cough (64%) and dyspnoea (43%). At admission, over 70% of the patients had abnormal radiological findings. Leukocyte counts were in the lower normal range. C-reactive protein, ferritin, and D-dimer were consistently increased. Treatments included lowering immunosuppression, hydroxychloroquine, antivirals, tocilizumab and intravenous immunoglobulins. Thirty-one percent of the patients were admitted to intensive care units (ICUs), and 16% required intubation. The overall mortality was 21.2%. Patients who died were significantly older than those who survived (61 ± 12 vs. 51 ± 15 , $p < .01$). Logistic regression revealed that the odds for death increased by 4.3% for each additional year of age (odds ratio [OR] 1.043, 95% confidence interval [CI] 1.005–1.083, p value = .0265). They concluded that no substantial conclusions could be drawn on the efficacy of any particular treatment. More rigorous patient stratification is needed when analysing and reporting data to facilitate future meta-analyses.



In conclusion, I believe that ideally patients should have been offered the choice to have a transplant if they could have had one knowing all the risks. Patients will have died as a result of this. Hospitals shut down because of the pandemic and these patients are part of the collateral damage. Transplant waiting list patients have been disadvantaged by the Covid pandemic and some may never receive a transplant as a result.

This has been a vital learning experience and we need to plan for the future, for example, how to run hospitals more flexibly so that patients in higher Covid risk areas could be treated in lower Covid risk areas.

We now need to adapt as quickly as possible to the changing circumstances, because for every transplant that does not go ahead, a patient suffers or even dies as a result.

Every service operates on a knife edge and close to the limits in care and it doesn't take much to expose its fragilities as this pandemic has done. The key is rigorous and robust infection control.

The COVID-19 pandemic is posing an unprecedented threat to EU/EEA countries and

the UK, which have been experiencing widespread transmission of the virus in the community for several weeks. In addition, there has been an increasing number of reports of COVID-19 outbreaks in long-term care homes across Europe with high associated mortality, highlighting the extreme vulnerability of the elderly in this setting.

The absence of an effective treatment or a vaccine combined with an exponential growth in infections from late February, led many countries to implement non-pharmaceutical interventions such as 'stay-at-home' policies (recommended or enforced) alongside other community and physical distancing measures such as the cancellation of mass gatherings, closure of educational institutions and public spaces. This approach has collectively reduced transmission and the 14-day incidence in the EU/EEA and the UK overall has declined by 18% since 8 April. In 20 EU/EEA countries, it appears that the initial wave of transmission has passed its peak, with a decline in the number of newly reported cases. I sincerely hope we can resume our transplant activities very soon.

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