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Kidney transplantation and COVID-19 renal and patient prognosis

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ABSTRACT

Coronavirus disease 2019 (COVD-19) emerged as a pandemic in December 2019. Infection has spread quickly and renal transplant recipients receiving chronic immunosuppression have been considered a population at high risk of infection, complications and infection-related death. During this year a large amount of information from nationwide registries, multicentre and single-centre studies have been reported. The number of renal transplant patients diagnosed with COVID-19 was higher than in the general population, but the lower threshold for testing may have contributed to its better identification. Major complications such as acute kidney injury and acute respiratory distress syndrome were very frequent in renal transplant patients, with a high comorbidity burden, but further studies are needed to support that organ transplant recipients receiving chronic immunosuppression are more prone to develop these complications than the general population. Kidney transplant recipients experience a high mortality rate compared with the general population, especially during the very early post-transplant period. Despite the fact that some studies report more favourable outcomes in patients with a kidney transplant than in patients on the kidney waiting list, the higher mortality described in the very early post-transplant period would advise against performing a kidney transplant in areas where the spread of infection is high, especially in recipients >60 years of age. Management of transplant recipients has been challenging for clinicians and strategies such as less use of lymphocyte-depleting agents for new transplants or anti-metabolite withdrawal and calcineurin inhibitor reduction for transplant patients with COVID-19 are not based on high-quality evidence.

Keywords: acute kidney injury, acute respiratory distress syndrome, COVID-19, mortality, renal transplantation, SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the single-strand RNA virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has become a worldwide threat. The first human case of COVID-19 was reported in Wuhan, China, in December 2019, and within a few weeks the infection spread around the world, becoming a pandemic [1]. A total of >62 million people have been diagnosed and 1.45 million died (https://coronavirus.jhu.edu/map.html; accessed 28 November 2020). There was an initial wave during March and April 2020 until a lockdown was ordered by many national governments. After progressive lifting of the lockdowns, a second wave is evolving, with the USA, India, Brazil, Russia, France and Spain having the highest rates of infection. Fever, fatigue and dry cough are the most common symptoms and patients may also experience shortness of breath, myalgia, sore throat and

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gastrointestinal (GI) symptoms [2]. Reverse transcription polymerase chain reaction (RT-PCR) is the gold standard for diagnosis. Treatment is based on oxygen supply and a combination of drugs that have evolved during the pandemic. Initially drugs with potential antiviral activity (e.g. lopinavir/ritonavir, hydroxychloroquine) were widely used, but later, randomized prospective trials demonstrated their lack of efficacy [3] and only remdesivir has been approved by regulatory agencies to treat COVID-19 [4]. Now the agents being studied to mitigate the clinical impact of this infection and decrease its severity are focused on immune mediators, stem cells and agents intended specifically to improve or support lung function (https://www.wcgclinical.com/covid-19/covid-19-trial-insights).

Renal transplant patients have been one of the populations most vulnerable to COVID-19 and many reports have been published. In this setting, immunomodulation has emerged as a promising option for patients with COVID-19-related cytokine storm, but the supporting evidence is scarce and of low quality [5]. Moreover, COVID-19 has had a big impact on wait-listed patients, highlighting the need to properly balance the risks and benefits of transplantation in the setting of an ongoing pandemic [6].

The aim of this article is to review the available literature published until now regarding renal and patient prognosis in renal transplant patients with COVID-19.

EPIDEMIOLOGY OF COVID-19 IN RENAL TRANSPLANT PATIENTS ACROSS THE WORLD

Since the outbreak, a lot of information has been available from nationwide registries and multicentre and local studies. A European study conducted by the ERA-EDTA from the French and Spanish registry yielded an average infection rate of 14/1000 transplants at risk [7]. The Spanish registry [8], with a longer period of observation, showed an incidence of 17.7/1000 transplants, while the French registry [9], with a shorter observation period, showed an incidence of 9.5/1000 transplants. The kidney registry of the Dutch-speaking Belgian Society of Nephrology reports a similar incidence of 14.0/1000 transplants [10]. Similar incidences were reported from multicentre studies including patients from the USA, Italy and Spain [11, 12]. Importantly, the incidence during the observation periods was 2–5 times higher in renal transplants than in the general population. Even in small countries like Scotland with a lower COVID-19 incidence, with only 24 transplant patients diagnosed with COVID-19, the incidence was 3 times that of the general population [13]. However, single-centre analysis conducted in areas with a high rate of infection revealed higher incidences [14–16]. A summary of the larger studies conducted is shown in Table 1. During the initial wave there were no studies providing information about asymptomatic patients since they were not generally screened. During the first wave, the hospitalization rate of symptomatic patients with COVID-19 was >80% in the nationwide registries and multicentre studies (Table 1). Likewise, in a cohort of 44 patients with mild symptoms, 34 needed to be referred to the emergency department and managed as inpatients while only 9 patients with suspected COVID-19 (never tested due to limitations) were managed as outpatients, and the only patient with confirmed COVID-19 was never hospitalized [17]. Finally, in a cohort of 41 patients, the hospitalization rate was 55% for those patients with confirmed COVID-19 while it was 5% for suspected but never tested patients [18].

Tests to detect antibodies against SARS-CoV-2 were incorporated into clinical practice later and they allow characterizing the proportion of asymptomatic or pauci-symptomatic patients not screened by RT-PCR. In a large study conducted in the Bronx borough of New York City, the combination of RT-PCR and antibodies characterized an incidence as high as 234/1000 transplant patients, with 41% diagnosed only by the presence of antibodies against SARS-CoV-2 [19]. For symptomatic patients (PCR positive), the hospitalization rate was high (84.1%), while for the overall cohort it was lower (48.5%).

Thus, although the number of renal transplant patients diagnosed with COVID-19 was higher than in the general population, the lower threshold for testing may have contributed to its better identification while many oligosymptomatic individuals in the general population were not tested and do not appear in the official statistics [10].

The mean age of renal transplant patients with COVID-19 was ∼60 years and the proportion of males (two-thirds) and comorbidities (arterial hypertension >80%, diabetes >25%) correlates with the characteristics of transplanted patients. Clinical presentation is characterized by fever, cough and shortness of breath in >60% of patients, while GI symptoms were described in about one-third of patients [20].

AKI IN RENAL TRANSPLANT PATIENTS WITH COVID-19

Acute kidney injury (AKI) is a common complication in patients with COVID-19 and is associated with increased intensive care unit (ICU) admission and mortality [21, 22]. AKI incidence is higher in patients admitted to the ICU due to COVID-19 than in patients admitted for other reasons [23]. In a large retrospective study (9657 patients), 39.9% developed AKI, of which 6.6% required renal replacement therapy (RRT) [24]. Approximately one-third of patients with AKI do not fully recover renal function [25]. The main risk factors associated with AKI are advanced age, male gender, severity of respiratory impairment, mechanical ventilation, pre-existing chronic renal failure, co-infection with other organisms and systemic inflammatory response [22–24]. Noticeably, AKI was increased in the subgroups with diabetes compared with subgroups without this condition [26]. A group to highlight is patients of African descent, in whom a greater risk of COVID-19 infection has been described [22, 27, 28]. In this population, the *APOL1* genotype is closely related to the development of nephropathy and evidence suggests that the SARS-CoV-2 infection could act as a 'second blow' that leads to podocyte dysregulation [29].

Considering that kidney transplant patients have a single functional kidney, receive a tacrolimus-based regimen that has nephrotoxic effects [30], have a high prevalence of hypertension and diabetes [31] and that Black race increases the risk of AKI in kidney recipients [32, 33], a higher incidence and severity of AKI in these settings would be expected. However, few studies have attempted to compare AKI in kidney transplant patients with the general population. Aziz *et al.* [34] reviewed 19 articles reporting AKI incidence in kidney transplant and non-transplanted patients. Despite the fact that AKI incidence was higher in kidney transplant patients (27.5% versus 13.3%), as well as RRT (15.4% versus 3.3%), the mortality rate was similar between groups. In a systemic review conducted by Marinaki *et al.* [35] including 420 patients, 44% of hospitalized kidney transplant patients developed AKI and 23% required RRT. In a multicentre study including 104 hospitalized kidney transplant

Table 1. Incidence of COVID-19 in nationwide registries and multicentre or single-centre studies

Reference	Registry	Time frame (2020)	RT with COVID-19	Incidence of RT/1.000 (95% CI)	Incidence of GP/1.000	Relative risk (95% CI)	Hospital admission (%)
Jager *et al.* [7]	ERA-EDTA[a]	1 February–30 April	1013	14 (13–16)	2.7	5.23 (4.92–5.56)	–
Coll *et al.* [8]	Spain	20 February–13 July	621	17.7 (16.4–19.2)	5.5	3.22 (2.98–3.45)	90.1
Caillard *et al.* [9]	France	1 March–21 April	426	9.5 (8.6–10.4)	1.7	5.67 (5.16–6.23)	87.1
De Meester *et al.* [10]	Belgium (Flandes)	2 March–25 May	46	14.0 (10.5–18.6)	6.4	2.20 (1.65–2.93)	82.6
Bell *et al.* [13]	Scotland	1 March–31 May	24	8.3 (5.9–11.8)	2.8	2.98 (2.11–4.21)	–
Cravedi *et al.* [11]	TANGO Consortium[b]	2 March–15 May	144	14.7 (12.2–17.2)	–		100
Fava *et al.* [12]	Catalonia Albacete[c]	4 March–17 April	112	15.8 (13.1–19.0)	–	–	97.3
Bossini *et al.* [15]	Brescia (Italy)	1 March–16 April	53	44.2 (33.9–57.3)	–	–	84.9
Elias *et al.* [14]	Paris[d]	1 March–30 April	66	54.3 (42.9–68.5)	–	–	90.9
Crespo *et al.* [16]	Barcelone[e]	12 March–4 April	16	49.4 (30.6–78.7)	–	–	100
Mehta *et al.* [17]	New York-Bronx[f]	16 March–2 June	228	234 (209–262)	–	–	84.1

RT with COVID-19: number of renal transplant patients diagnosed with COVID-19; Incidence RT: incidence of COVID-19 in renal transplant patients per 1000 patients at risk provided by national registries; Incidence in GP: incidence of COVID-19 in the general population provided by the national registries. The relative risk of renal transplants versus general population was calculated by standard formulas.

[a]The ERA-EDTA registry only includes renal transplants from Spain and France in this report.

[b]TANGO consortium: 12 centres from the USA ($n = 6$), Italy ($n = 4$) and Spain ($n = 2$).

[c]Renal transplants managed in four hospitals from Catalonia and Albacete (Spain).

[d]Prospective study in renal transplant patients managed at Hospital Saint Louis and Hospital Bichat from Paris (France).

[e]Renal transplant patients >65 years of age managed by Hospital del Mar from Barcelona (Spain).

[f]Symptomatic patients diagnosed by RT-PCR ($n = 132$) and by serology ($n = 96$). Hospitalization rate for the overall cohort was 48.5% (111 of 228 patients).

Table 2. Incidence of AKI and need for RRT in hospitalized kidney transplant patients and in the general population with COVID-19 infection

	No. of patients	% AKI	% RRT
Kidney transplantation			
Marinaki *et al.* [33]	345	44.0	9.9
Favá *et al.* [12]	104	45.0	Not reported
Cravedi *et al.* [11]	144	52.0	Not reported
Elias *et al.* [14]	66	42.0	11.0
Weighted average	659	45.7	10.1
General population			
Chan *et al.* [25]	3993	46.0	8.7
Fisher *et al.* [23]	3345	56.9	4.9
Richardson *et al.* [26]	2351	22.2	3.2
Ng *et al.* [24]	9657	39.9	6.6
Weighted average	19 346	41.9	6.3

Incidence of AKI in studies including >1000 patients from the general population and studies including >50 kidney transplant patients. The incidence of AKI and the need for RRT was summarized as the weighted average.

patients, AKI was observed in 47% of patients and, interestingly, it was observed that tacrolimus trough levels were higher in patients with Stage 3 AKI. However, AKI or Stage 3 AKI were not associated with mortality [12]. Table 2 describes the incidence of AKI and the proportion of patients requiring RRT in kidney transplant and non-transplanted patients hospitalized due to COVID-19 infection.

If we consider the incidence of AKI in the general population and in kidney transplant patients, available data do not clearly support a higher incidence of AKI in transplanted patients. However, this statement should be taken with caution since more information is needed, especially, in kidney transplant patients.

AKI AND HISTOLOGY

Acute tubular necrosis is the main finding in patients with AKI [36, 37]. However, a high proportion of patients display proteinuria (44–66%) and microhaematuria (27–42%), suggesting that, in addition to classical factors leading to AKI, a direct cytopathic effect of the virus may contribute to renal damage [21, 38]. Angiotensin-converting enzyme 2 receptor is highly expressed in kidney podocytes and tubular cells, and viral particles have been observed in electron microscopy studies [36, 38, 39]. In the vast majority of patients, haematuria and proteinuria rapidly disappeared; however, in patients with severe proteinuria, collapsing glomerulopathy [40–45], minimal change disease, thrombotic microangiopathy [46, 47] and pauci-immune crescentic glomerulonephritis [48] have been described.

In kidney transplant patients there is scarce information on histological findings. In patients with AKI, apart from acute tubular injury, minimal change disease [49], cortical necrosis [50] and

collapsing glomerulopathy [51–53] have also been described. In addition, very few cases of T cell– or antibody-mediated rejection have been described, raising the question of whether COVID-19 infection may enhance the alloimmune response [46, 50].

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN RENAL TRANSPLANT PATIENTS WITH COVID-19

In the general population, the spectrum of COVID-19 varies widely, from asymptomatic to pneumonia and life-threatening complications, including ARDS, multisystem organ failure and ultimately death. ARDS occurs because of an acute systemic inflammatory response that can be caused by insults to the lung, either direct or indirect. The reported incidence of ARDS in the general population is 12–31%, being severe in 56–79% of cases [26, 54–60]. Age and the presence of comorbidities are the main risk factors for developing ARDS [61].

Kidney transplant recipients may be at high risk of developing severe COVID-19 disease due to chronic immunosuppression, comorbidities and frequent contact with the healthcare system. Indeed, they may be more likely to be diagnosed when they have symptoms due to closer follow-up at the transplant centre [8, 62–64]. However, there are few studies comparing ARDS in kidney transplant patients and the general population. In a study conducted at our centre [63], 46 solid organ transplant (SOT) recipients (30 renal transplants) admitted due to COVID-19 were matched by age, sex and age-adjusted Charlson comorbidity index to 166 controls. As expected, hypertension and chronic kidney disease were more frequent in transplant recipients. A total of 27 (58.7%) transplant recipients and 71 (42.8%) controls suffered progressive respiratory failure. In a similar study conducted in Michigan, 41 SOT recipients (67% were Black; 16 single and 5 combined kidney transplants) were matched by age, race and admission status to 121 controls [32]. Severe disease-adjusted risk of death was similar in both groups and the severity of COVID-19 and number of intubations were also similar, but the incidence of AKI requiring RRT was higher in transplant patients (29.3% versus 5.8%).

Data from multicentre studies yielded similar results; Cravedi *et al.* [11] identified 144 hospitalized adult kidney transplant recipients and 29% required orotracheal intubation. A Spanish multicentre kidney transplant study with 104 hospitalized patients reported that 54.8% developed ARDS and that it was associated with obesity [odds ratio (OR) 2.63; $P = 0.04$] [12]. No significant age difference was found between patients who developed or did not develop ARDS; however, the elderly may have a higher risk of death. Bossini *et al.* [15] found that in 45 patients admitted to the hospital due to severe symptoms, 60% developed ARDS. A trend for an increased risk of ARDS was recorded in patients on tacrolimus {OR 2.77 [95% confidence interval (CI) 0.91–8.9]}, whereas a protective trend towards the risk of ARDS was a transplant vintage >10 years [OR 0.37 [95% CI 0.12–1.1]) and the presence of GI symptoms at disease onset [OR 0.21 (95% CI 0.04–1.1)]. Similarly, Akalin *et al.* [65] reported an initial series of 36 patients with COVID-19; 28 were admitted to the hospital and 27 (96%) had radiographic findings that were consistent with viral pneumonia. Eleven of 27 (39%) required mechanical ventilation and 7 of them (64%) died. Table 3 describes the incidence of ARDS and its severity in kidney transplant patients and in the general population hospitalized for COVID-19 infection.

Table 3. Incidence of ARDS in hospitalized kidney transplant recipients and the general population with COVID-19 infection

References	No. of patients	% ARDS	% Severe
Kidney transplantation			
Coll *et al.* [8]	375	35.7	Not reported
Cravedi *et al.* [11]	144	29.0	Not reported
Favà *et al.* [12]	104	54.8	16.3
Bossini *et al.* [15]	45	60.0	Not reported
Elias *et al.* [14]	66	68.0	Not reported
Cavalcanti *et al.* [66]	36	39.0	Not reported
Weighted average	770	41.4	16.3
General population			
Petrilli *et al.* [58]	1099	16.7	72.9
Richardson *et al.* [26]	2634	12.2	Not reported
Berengue *et al.* [59]	2741	23.6	60.4
Cummings *et al.* [60]	3979	31.5	67.4
Wu *et al.* [61]	1150	22.0	79.0
Weighted average	11 603	21.2	55.6

Incidence of ARDS in studies including >1000 patients from the general population and studies including >30 kidney transplant patients. The incidence of ARDS and its severity was summarized as the weighted average.

Despite the high incidence of ARDS in the transplanted population and its deleterious consequences, more detailed studies are neeeded to support that organ transplant recipients receiving chronic immunosuppression are more prone to develop ARDS than the general population.

During the first wave of the pandemic, the most widely used agents with presumed antiviral activity were hydroxychloroquine, antibiotics (azithromycin) and protease inhibitors, showing no benefit for prevention or treatment in both the general [54, 66–68] and SOT populations [8, 9, 11, 12, 14, 15], and increasing the risk of interactions with other drugs [63, 69]. In the general population, remdesivir has been shown to decrease the in-hospital stay, but with no effect on the mortality rate. Importantly, its use is contraindicated in patients with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 and there are no studies on the use of remdesivir in the transplanted population [70].

It has been shown that besides viral evasion to immune response, cytokine storm plays an important role in COVID-19 disease progression. Thus efforts have been made to mitigate the immune response with immunomodulators and large reviews exist on the potential role, efficacy and safety of these agents in the management of severe COVID-19 [71, 72]. Non-randomized studies have shown that treatment with tocilizumab in critically ill patients may offer some benefit in both the general [73] and kidney transplant population [74]. However, prospective randomized studies in hospitalized patients with COVID-19 pneumonia showed that although tocilizumab may reduce the likelihood of progression to mechanical ventilation, it did not improve survival [75, 76]. Importantly, the large RECOVERY trial showed that dexamethasone decreases 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone, but not among those receiving no respiratory support [77]. Thus research efforts should focus not only on the most relevant immunomodulatory strategies, but also the optimal timing of such immunomodulatory interventions to maximize the therapeutic effect [71].

In kidney transplantation, the most widely used interventions were the modification of immunosuppression, reducing or suspending the antimetabolite or inhibitors of the mammalian

target of rapamycin, while the calcineurin inhibitor was suspended in patients at risk for interaction with protease inhibitors [8, 11, 12, 66, 78]. Recently, the *in vitro* efficacy of cyclosporine A and FK506 to inhibit the replication of SARS-CoV-1 and other human coronaviruses has been reported [79]; however, there is no clinical evidence for a protective effect to reduce the likelihood of severe COVID-19 or to treat the cytokine storm. Also, there is no evidence on what the management of immunosuppression should be. An approach like that of other serious viral infections (mycophenolate withdrawal and calcineurin inhibitor reduction) seems a safe option since this change in immunosuppression has been associated with very low incidences of acute rejection.

PATIENT MORTALITY AND RISK FACTORS FOR DEATH IN RECIPIENTS WITH COVID-19

A British population-based study showed that SOT patients had one of the highest in-hospital risks of death (HR 4.23) due to COVID-19 [80]. In a large multicentre US study (423 SOT patients, including 318 kidney or kidney–pancreas recipients), the overall mortality rate by Day 28 was 20.5% among the hospitalized patients and 18.5% among the overall cohort [62]. Risk factors for mortality included age >65 years, chronic heart failure, chronic lung disease and obesity. Also, the presence of pneumonia and lymphopaenia at diagnosis were independently associated with mortality. Of interest, none of the multiple surrogates for immunosuppression that were explored showed any association with mortality.

Focusing on renal transplants, a recent systematic review based on 20 studies from different countries revealed a patient mortality higher than in general population, ranging between 18% and 43% [81]. Risk factors associated with mortality (Table 4) included older age [13, 15, 74, 82–84], plasma viral load [82] and the presence of higher inflammatory biomarkers such as C-reactive protein, interleukin-6 (IL-6), D-dimer or serum lactate dehydrogenase [8, 12, 74, 82]. Interestingly, in a Turkish cohort of 40 renal recipients, the use of previous antirejection treatment was an independent predictor for mortality and the use of cyclosporine as a maintenance immunosuppressant was associated with better survival [85]. Likewise, in a study that included 29 renal transplant patients, patients on cyclosporine-based immunosuppression experienced less mortality compared with immunosuppression minimization [86].

The Spanish registry included 423 kidney transplants with a mortality rate of 28% [8]. Interestingly, the mortality rate declined to 15.8% after adjusting for age and gender, implying that baseline characteristics rather than the immunosuppressive state or the transplant itself has a remarkable effect on survival. Overall, the risk of death increased with age (>60 years) and mortality was higher among recipients who developed ARDS and in those with nosocomial COVID-19. No differences were found regarding baseline immunosuppression between survivors and non-survivors, but in patients with ARDS in whom the antimetabolite agent was discontinued, the mortality was lower [8]. A French registry–based study that included 279 renal transplant patients reported a mortality rate of 22.8% and independent risk factors for mortality included age >60 years, cardiovascular disease and dyspnoea [9].

In the TANGO multicentre study (144 hospitalized kidney transplants), the mortality rate was 32% and older age, lower lymphocyte counts, higher lactate dehydrogenase, procalcitonin and IL-6 levels and lower eGFR were associated with mortality [11]. Moreover, the presence of dyspnoea at onset (61% versus 83%) was associated with mortality while the presence of diarrhoea was more frequent in survivors (45% versus 24%). Other factors such as the type of transplantation (living versus deceased donor), time post-transplantation (<1 versus >1 year), comorbidities or type of immunosuppression were not associated with mortality. None of the treatment strategies with

Table 4. Risk factors independently associated with mortality in renal transplant recipients with SARS-CoV-2 infection

Variable	References	Reference group	Relative risk	95% CI
Age	Craig-Shapiro *et al.* [6]	>60 years	4.0	1.4–11.2
	Coll *et al.* [8]	>60 years	3.7	2.5–5.5
	Caillard *et al.* [9]	>60 years	3.8	1.6–9.3
	Cravedi *et al.* [11]	>60 years	2.6	1.3–5.8
	Benotmane *et al.* [82]	>60 years	4.3	1.9–10.2
	Favà *et al.* [12]	Per year	1.10	1.05–1.16
	Ravanan *et al.* [83]	Per year	1.07	1.04–1.09
Gender	Craig-Shapiro *et al.* [6]	Male	5.7	1.5–21.7
Immunosuppression	Williamson *et al.* [80]	Rejection treatment	9.7	1.2–77.7
		Cyclosporine	0.08	0.02–0.32
Nosocomial COVID-19	Coll *et al.* [8]	Yes	3.0	1.9–4.9
Dyspnoea at onset	Cravedi *et al.* [11]	Yes	3.1	1.3–1.7
	Fava *et al.* [12]		4.2	1.6–11.2
	Caillard *et al.* [9]		2.3	1.2–4.5
Diarrhoea at onset	Cravedi *et al.* [11]	Yes	0.4	0.2–0.9
Acute respiratory	Coll *et al.* [8]	Yes	28.9	17.6–47.4
distress syndrome	Fava *et al.* [12]	Yes	2.1	1.03–8.23
Lactate dehydrogenase	Cravedi *et al.* [11]	>325 U/L	3.5	1.6–7.8
	Fava *et al.* [12]	UI/L	1.003	1–1.005
C-reactive protein	Fava *et al.* [12]	mg/L	1.003	1.002–1.005
Pro-calcitonin	Cravedi *et al.* [11]	>0.5 ng/mL	3.0	1.4–6.9
eGFR	Cravedi *et al.* [11]	mL/min	0.97	1.07–3.9
Cardiovascular disease	Caillard *et al.* [9]	Yes	2.04	1.07 3.9
Diabetes	Craig-Shapiro *et al.* [6]	Yes	2.97	1.03–8.57

antivirals used to treat COVID-19 had any impact on survival. Again, patients with nosocomial SARS-CoV-2 infection had the highest mortality rate (77.8%) [11].

In a multicentre study from Spain that included 104 kidney recipients, the mortality rate was 28% and older age, higher serum lactate dehydrogenase and having ARDS at admission were independently associated with a higher risk of death [12].

A Belgium registry–based study that included 46 kidney transplant recipients with COVID-19 showed a mortality similar to that reported in the general population (14% versus 15.3%), but much lower than in patients on dialysis (14% versus 29%) [10].

In another study that involved several European countries (ERACODA), 305 renal transplant patients were included, with a 28-day mortality rate of 21.3% as compared with 25% in patients on dialysis, and older age was the predominant risk factor for mortality in renal recipients [87].

Most of the available data on survival involves long-term stable recipients, and there is scarce information regarding early transplant recipients. In studies in which the subgroup of early transplant recipients was analysed for <6 months [12] or <1 year [12, 88], mortality was not different between groups, although in some of them there was a trend towards a higher mortality for the early group [12]. A recent report that included 24 recipients with COVID-19 diagnosed within 60 days after transplantation revealed a significant impact on patient survival with a mortality rate of 46% [89]. Recipients who died were older (61 versus 70 years), received high-dose steroids less frequently (25% versus 82%) and usually needed ventilation support (15% versus 78%). In another study that included 237 patients in the first-year post-transplant, of whom 16 had a COVID-19 diagnosis, the mortality rate was 37% [90].

In this pandemic era, management of induction and maintenance immunosuppression has been challenging to clinicians treating kidney transplant patients. Regarding the use of induction therapy with lymphocyte-depleting agents (anti-thymocyte globulins, alemtuzumab and rituximab), a large study conducted in the USA showed that their use decreased during the first several weeks of the pandemic compared with the three previous years, while the use of basiliximab or no induction increased. Importantly, during the pandemic, lymphocyte-depleting agents were associated with a lower risk of acute rejection, but without significant differences in mortality. These results question whether this shift in induction immunosuppression was a safe and effective approach to address the novel infectious risk [91]. Additionally, small studies conducted in single centres show that renal transplant patients treated with thymoglobulin who acquired the COVID-19 infection early after transplantation had a modest risk for severe disease [92], especially using low doses [93]. However, it seems prudent to monitor absolute lymphocyte count following lymphocyte-depleting induction and consider temporary an antimetabolite dose reduction in patients with severe lymphopaenia [92]. Conversely, management of steroids was not modified in the USA during the pandemic and the practice of steroid avoidance/withdrawal has not been modified and its use did not modify the graft failure or mortality rates [91].

OUTCOMES IN KIDNEY RECIPIENTS VERSUS PATIENTS ON THE WAITING LIST

Since the beginning of the pandemic, all transplant programmes have dramatically reduced their activity [94, 95]. In the early outbreak period, general recommendations from the different societies in areas in which the virus was widespread implied avoiding living-donor transplantation and reserving deceased-donor transplantation for life-threatening conditions or for hypersensitized patients with a suitable donor [96–98]. In this pandemic scenario, there are several studies that aimed to address whether it would be safer to undergo a renal transplantation or remain on the waiting list. In a single-centre study in which the outcomes of 56 patients included on the waiting list were compared with the outcomes of 80 kidney transplant recipients, wait-listed patients with COVID-19 were not only more likely to require more hospitalization (82% versus 65%), but also had an increased risk of death (25% versus 16%), with comparable baseline demographics and comorbidities between groups [6]. In this cohort, risk factors independently associated with mortality were wait list status, male sex, age and diabetes. On the same note, in a registry-based study from France in which renal transplant recipients and patients included on the waiting list were compared in different time periods, an increase in deaths was detected in both populations between March and June 2020 as compared with the same period in the two previous years [99]. This was explained by COVID-19, which caused the deaths of 44% of recipients and 42% of wait-listed patients. Interestingly, the increase in risk of death in both populations was similar in high-risk geographic areas, but in low-risk areas the risk of death in wait-listed patients 4-fold higher, but there was no additional risk for renal transplant recipients, suggesting that transplant programmes should not be suspended in geographic areas with a low spread of infection. In a multicentre study in London, an area with a high prevalence of COVID-19 [100], outcomes after SARS-CoV-2 infection in kidney transplant recipients ($n = 121$) were compared with patients on the waiting list ($n = 51$). Although no differences in mortality were found (30% versus 27%), the only risk factor independently associated with mortality was being >60 years of age in the kidney transplant group [OR 4.3 (95% CI 1.8–10.2)] [88]. Finally, in contrast with the previous data, there is a single-centre study performed in London in which the overall survival on a population level between wait-listed and kidney transplant patients was not different, but the mortality rate following SARS-CoV-2 infection was higher in the renal transplant group (37% versus 11%) [90]. Few studies exist in the paediatric population, but the available data support that since chronic immunosuppression is not associated with an increased risk of COVID-19 in young kidney transplant patients, transplant activity should be maintained even in areas with a high incidence of SARS-CoV-2 infection [101].

CONCLUSIONS

The COVID-19 pandemic has been challenging for kidney transplantation programmes around the world, with a big impact on transplant policies and in the management of infected and uninfected patients. The rate of infected transplants was high in geographic areas with widespread infection and patient outcomes were compromised due to high rates of complications and COVID-19-related deaths. In managing infected patients during the pandemic, only the use of steroids and remdesivir has been demonstrated to be useful after performing randomized controlled clinical trials. Since chronic immunosuppression may influence a patient's outcome, different changes based on art and theory were applied. Thus, in the absence of trial-based evidence, we should include transplant patients in prospective studies and registries to help guide optimal care [102].

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts interest.

REFERENCES

1. Zhu N, Zhang D, Wang W *et al.* A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382: 727–733
2. Burke RM, Killerby ME, Newton S *et al.* Symptom profiles of a convenience sample of patients with COVID-19 – United States. *MMWR Morb Mortal Wkly Rep* 2020; 69: 904–908
3. Siemieniuk RA, Bartoszko JJ, Ge L *et al.* Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ* 2020; 370: m2980
4. U.S. Food and Drug Administration. FDA's approval of Veklury (remdesivir) for the treatment of COVID-19—The Science of Safety and Effectiveness. https://www.fda.gov/drugs/drug-safety-and-availability/fdas-approval-veklury-remdesivir-treatment-covid-19-science-safety-and-effectiveness (1 December 2020, date last accessed)
5. Fernández-Ruiz M, Aguado JM. Immunomodulatory therapies for COVID-19 in solid organ transplant recipients. *Curr Transplant Rep* 2020. doi: 10.1007/s40472-020-00306-x
6. Craig-Schapiro R, Salinas T, Lubetzky M *et al.* COVID-19 outcomes in patients waitlisted for kidney transplantation and kidney transplant recipients. *Am J Transplant* 2020; doi: 10.1111/ajt.16351
7. Jager KJ, Kramer A, Chesnaye NC *et al.* Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. *Kidney Int* 2020; 98: 1540–1548
8. Coll E, Fernández-Ruiz M, Sánchez-Álvarez JE *et al.* COVID-19 in transplant recipients: the Spanish experience. *Am J Transplant*; doi: 10.1111/ajt.16369
9. Caillard S, Anglicheau D, Matignon M *et al.* An initial report from the French SOT COVID registry suggests high mortality due to Covid-19 in recipients of kidney transplants. *Kidney Int* 2020; 98: 1549–1558
10. De Meester J, De Bacquer D, Naesens M *et al.* Incidence, characteristics, and outcome of COVID-19 in adults on kidney replacement therapy: a regionwide registry study. *J Am Soc Nephrol* 2020; 32: 385–396
11. Cravedi P, Suraj SM, Azzi Y *et al.* COVID-19 and kidney transplantation: results from the TANGO international transplant consortium. *Am J Transplant* 2020; 20: 3140–3148
12. Favà A, Cucchiari D, Montero N *et al.* Clinical characteristics and risk factors for severe COVID-19 in hospitalized kidney transplant recipients: a multicentric cohort study. *Am J Transplant* 2020; 20: 3030–3041
13. Bell S, Campbell J, McDonald J et al. COVID-19 in patients undergoing chronic kidney replacement therapy and kidney transplant recipients in Scotland: findings and experience from the Scottish renal registry. *BMC Nephrol* 2020; 21: 419
14. Elias M, Pievani D, Randoux C *et al.* COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. *J Am Soc Nephrol* 2020; 31: 2413–2423
15. Bossini N, Alberici F, Delbarba E *et al.* Kidney transplant patients with SARS-CoV-2 infection: the Brescia Renal COVID task force experience. *Am J Transplant* 2020; 20: 3019–3029
16. Crespo M, Pérez-Sáez MJ, Redondo-Pachón D *et al.* COVID-19 in elderly kidney transplant recipients. *Am J Transplant* 2020; 20: 2883–2889
17. Mehta SA, Leonard J, Labella P *et al.* Outpatient management of kidney transplant recipients with suspected COVID-19—single-center experience during the New York City surge. *Transplant Infect Dis* 2020; 22: e13383
18. Husain SA, Dube G, Morris H *et al.* Early outcomes of outpatient management of kidney transplant recipients with coronavirus disease 2019. *Clin J Am Soc Nephrol* 2020; 15: 1174–1178
19. Azzi Y, Parides M, Alani O *et al.* COVID-19 infection in kidney transplant recipients at the epicenter of pandemics. *Kidney Int* 2020; 98: 1559–1567
20. Crespo M, Mazuecos A, Rodrigo E *et al.* Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. *Transplantation* 2020; 104: 2225–2233
21. Pei G, Zhang Z, Peng J *et al.* Renal involvement and early prognosis in patients with COVID-19 pneumonia. *J Am Soc Nephrol* 2020; 31: 1157–1165
22. Hirsch JS, Ng JH, Ross DW *et al.* Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int* 2020; 98: 209–218
23. Fisher M, Neugarten J, Bellin E *et al.* AKI in hospitalized patients with and without COVID-19: a comparison study. *J Am Soc Nephrol* 2020; 31: 2145–2157
24. Ng JH, Hirsch JS, Hazzan A *et al.* Outcomes among patients hospitalized with COVID-19 and acute kidney injury. *Am J Kidney Dis* 2020; 77: 204-215.e1
25. Chan L, Chaudhary K, Saha A *et al.* AKI in hospitalized patients with COVID-19. *J Am Soc Nephrol* 2020; 32: 151–160
26. Richardson S, Hirsch JS, Narasimhan M *et al.*Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. *JAMA* 2020; 323: 2052–2059
27. Price-Haywood EG, Burton J, Fort D *et al.* Hospitalization and mortality among black patients and white patients with Covid-19. *N Engl J Med* 2020; 382: 2534–2543
28. Aldridge RW, Lewer D, Katikireddi SV *et al.* Black, Asian and minority ethnic groups in England are at increased risk of death from COVID-19: indirect standardisation of NHS mortality data. *Wellcome Open Res* 2020; 5: 88
29. Nasr SH, Kopp JB. COVID-19–associated collapsing glomerulopathy: an emerging entity. *Kidney Int Rep* 2020; 5: 759–761
30. Shimizu T, Tanabe K, Tokumoto T *et al.* Clinical and histological analysis of acute tacrolimus (TAC) nephrotoxicity in renal allografts. *Clin Transplant* 1999; 13(Suppl 1): 48–53
31. Azancot MA, Ramos N, Moreso FJ *et al.* Hypertension in chronic kidney disease: the influence of renal transplantation. *Transplantation* 2014; 98: 537–542
32. Sharma P, Chen V, Fung CM *et al.* COVID-19 outcomes among solid organ transplant recipients: a case-control study. *Transplantation* 2020; 105: 128–137
33. Shrivastava P, Prashar R, Khoury N *et al.* Acute kidney injury in a predominantly African American cohort of kidney

transplant recipients with COVID-19 infection. *Transplantation* 2020; 105: 201–205
34. Aziz F, Mandelbrot D, Singh T *et al.* Early report on published outcomes in kidney transplant recipients compared to nontransplant patients infected with coronavirus disease 2019. *Transplant Proc* 2020; 52: 2659–2662
35. Marinaki S, Tsiakas S, Korogiannou M *et al.* A systematic review of COVID-19 infection in kidney transplant recipients: a universal effort to preserve patients' lives and allografts. *J Clin Med* 2020; 9: 2986
36. Su H, Yang M, Wan C *et al.* Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int* 2020; 98: 219–227
37. Xia P, Wen Y, Duan Y *et al.* Clinicopathological features and outcomes of acute kidney injury in critically Ill COVID-19 with prolonged disease course: a retrospective cohort. *J Am Soc Nephrol* 2020; 31: 2205–2221
38. Farkash EA, Wilson AM, Jentzen JM. Ultrastructural evidence for direct renal infection with SARS-CoV-2. *J Am Soc Nephrol* 2020; 31: 1683–1687
39. Diao B, Wang C, Wang R *et al.* Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. *medRxiv* 2020; doi: 10.1101/2020.03.04.20031120
40. Deshmukh S, Zhou XJ, Hiser W. Collapsing glomerulopathy in a patient of Indian descent in the setting of COVID-19. *Renal Fail* 2020; 42: 877–880
41. Gupta RK, Bhargava R, Shaukat A-A *et al.* Spectrum of podocytopathies in new-onset nephrotic syndrome following COVID-19 disease: a report of 2 cases. *BMC Nephrol* 2020; 21: 326
42. Kissling S, Rotman S, Gerber C *et al.* Collapsing glomerulopathy in a COVID-19 patient. *Kidney Int* 2020; 98: 228–231
43. Malhotra V, Magoon S, Troyer DA *et al.* Collapsing focal segmental glomerulosclerosis and acute oxalate nephropathy in a patient with COVID-19: a double whammy. *J Invest Med High Impact Case Rep* 2020; 8: 232470962096363
44. Nlandu YM, Makulo JRR, Pakasa NM *et al.* First case of COVID-19-associated collapsing glomerulopathy in sub-Saharan Africa. *Case Rep Nephrol* 2020; 2020: 8820713
45. Sharma Y, Nasr SH, Larsen CP *et al.* COVID-19–associated collapsing focal segmental glomerulosclerosis: a report of 2 cases. *Kidney Med* 2020; 2: 493–497
46. Akilesh S, Nast CC, Yamashita M *et al.* Multicenter clinicopathologic correlation of kidney biopsies performed in COVID-19 patients presenting with acute kidney injury or proteinuria. *Am J Kidney Dis* 2020; 77: 82–93.e1
47. Jhaveri KD, Meir LR, Flores Chang BS *et al.* Thrombotic microangiopathy in a patient with COVID-19. *Kidney Int* 2020; 98: 509–512
48. Sharma P, Uppal NN, Wanchoo R *et al.* COVID-19–associated kidney injury: a case series of kidney biopsy findings. *J Am Soc Nephrol* 2020; 31: 1948–1958
49. Yamada M, Rastogi P, Ince D *et al.* Minimal change disease with nephrotic syndrome associated with coronavirus disease 2019 after apolipoprotein L1 risk variant kidney transplant: a case report. *Transplant Proc* 2020; 52: 2693–2697
50. Kudose S, Batal I, Santoriello D *et al.* Kidney biopsy findings in patients with COVID-19. *J Am Soc Nephrol* 2020; 31: 1959–1968
51. Doevelaar AAN, Hölzer B, Seibert FS *et al.* Lessons for the clinical nephrologist: recurrence of nephrotic syndrome induced by SARS-CoV-2. *J Nephrol* 2020; 33: 1369–1372
52. Noble R, Tan MY, McCulloch T *et al.* Collapsing glomerulopathy affecting native and transplant kidneys in individuals with COVID-19. *Nephron* 2020; 144: 589–594
53. Lazareth H, Péré H, Binois Y *et al.* COVID-19–related collapsing glomerulopathy in a kidney transplant recipient. *Am J Kidney Dis* 2020; 76: 590–594
54. Chen N, Zhou M, Dong X *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395: 507–513
55. Huang C, Wang Y, Li X *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497–506
56. Wang D, Hu B, Hu C *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323: 1061–1069
57. Guan WJ, Ni ZY, Hu Y *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708–1720
58. Petrilli CM, Jones SA, Yang J *et al.* Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* 2020; 369: m1966
59. Berenguer J, Ryan P, Rodríguez-Baño J *et al.* Characteristics and predictors of death among 4035 consecutively hospitalized patients with COVID-19 in Spain. *Clin Microbiol Infect* 2020; 26: 1525–1536
60. Cummings MJ, Baldwin MR, Abrams D *et al.* Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 2020; 395: 1763–1770
61. Wu C, Chen X, Cai Y *et al.* Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020; 180: 934–943
62. Kates OS, Haydel BM, Florman SS *et al.* COVID-19 in solid organ transplant: a multi-center cohort study. *Clin Infect Dis* 2020; doi: 10.1093/cid/ciaa1097
63. Miarons M, Larrosa-García M, García-García S *et al.*COVID-19 in solid organ transplantation: a matched retrospective cohort study and evaluation of immunosuppression management. *Transplantation* 2021; 105: 138–150
64. Alberici F, Delbarba E, Manenti C *et al.* A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. *Kidney Int* 2020; 97: 1083–1088
65. Akalin E, Azzi Y, Bartash R *et al.* Covid-19 and kidney transplantation. *N Engl J Med* 2020; 382: 2475–2477
66. Cavalcanti AB, Zampieri FG, Rosa RG et al. Hydroxychloroquine with or without azithromycin in mild-to-moderate Covid-19. *N Engl J Med* 2020; 383: 2041–2052
67. Mitjà O, Corbacho-Monné M, Ubals M *et al.* A cluster-randomized trial of hydroxychloroquine for prevention of Covid-19. *N Engl J Med* 2021; 384: 417–427
68. RECOVERY Collaborative Group. Lopinavir-ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet* 2020; 396: 1345–1352
69. Elens L, Langman LJ, Hesselink DA *et al.* Pharmacologic treatment of transplant recipients infected with SARS-CoV-2: considerations regarding therapeutic drug monitoring and drug-drug interactions. *Ther Drug Monit* 2020; 42: 360–368

70. Rochwerg B, Agarwal A, Zeng L *et al*. Remdesivir for severe covid-19: a clinical practice guideline. *BMJ* 2020; 370: m2924
71. Rizk JG, Kalantar-Zadeh K, Mehra MR *et al*. Pharmaco-Immunomodulatory therapy in COVID-19. *Drugs* 2020; 80: 1267–1292
72. Kim MS, An MH, Kim WJ *et al*. Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: a systematic review and network meta-analysis. *PLoS Med* 2020; 17: e1003501
73. Fernández-Ruiz M, López-Medrano F, Pérez-Jacoiste AMA *et al*. Tocilizumab for the treatment of adult patients with severe COVID-19 pneumonia: a single-center cohort study. *J Med Virol* 2021; 93: 831–842
74. Pérez-Sáez MJ, Blasco M, Redondo-Pachón D *et al*. Use of tocilizumab in kidney transplant recipients with COVID-19. *Am J Transplant* 2020; 20: 3182–3190
75. Stone JH, Frigault MJ, Serling-Boyd NJ *et al*. Efficacy of tocilizumab in patients hospitalized with covid-19. *N Engl J Med* 2020; 383: 2333–2344
76. Salama C, Han J, Yau L *et al*. Tocilizumab in patients hospitalized with Covid-19 pneumonia. *N Engl J Med* 2021; 384: 20–30
77. RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 – preliminary report. *N Engl J Med* 2020; doi: 10.1056/NEJMoa2021436
78. Chaudhry ZS, Williams JD, Vahia A *et al*. Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: a case-control study. *Am J Transplant* 2020; 20: 3051–3060
79. Carbajo-Lozoya J, Müller MA, Kallies S *et al*. Replication of human coronaviruses SARS-CoV, HCoV-NL63 and HCoV-229E is inhibited by the drug FK506. *Virus Res* 2012; 165: 112–117
80. Williamson E, Walker AJ, Bhaskaran K *et al*. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. medRxiv 2020; doi: 10.1101/2020.05.06.20092999
81. Mahalingasivam V, Craik A, Tomlinson LA *et al*. COVID-19 and kidney transplantation: a systematic review. *Kidney Int Rep* 2020; 6: 24–45
82. Benotmane I, Gautier-Vargas G, Wendling MJ *et al*. In-depth virological assessment of kidney transplant recipients with COVID-19. *Am J Transplant* 2020; 20: 3162–3172
83. Ravanan R, Callaghan CJ, Mumford L *et al*. SARS-CoV-2 infection and early mortality of wait-listed and solid organ transplant recipients in England: a national cohort study. *Am J Transplant* 2020; 20: 3008–3018
84. Sánchez-Álvarez JE, Pérez FM, Jiménez MC *et al*. SARS-CoV-2 infection in patients on renal replacement therapy. Report of the COVID-19 Registry of the Spanish Society of Nephrology (SEN). *Nefrologia* 2020; 40: 272–278
85. Demir E, Uyar M, Parmaksiz E *et al*. COVID-19 in kidney transplant recipients: a multicenter experience in Istanbul. *Transpl Infect Dis* 2020; 22: e13371
86. Rodriguez-Cubillo B, de la Higuera MAM, Lucena R *et al*. Should cyclosporine be useful in renal transplant recipients affected by SARS-CoV-2? *Am J Transplant* 2020; 20: 3173–3181
87. Hilbrands LB, Duivenvoorden R, Vart P *et al*. COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. *Nephrol Dial Transplant* 2020; 35: 1973–1983
88. Mamode N, Ahmed Z, Jones G *et al*. Mortality rates in transplant recipients and transplantation candidates in a high prevalence COVID-19 environment. *Transplantation* 2020; 105: 212–215
89. Pascual J, Melilli E, Jiménez-Martín C *et al*. COVID-19-related mortality during the first 60 days after kidney transplantation. *Eur Urol* 2020; 78: 641–643
90. Clarke C, Lucisano G, Prendecki M *et al*. Informing the risk of kidney transplantation versus remaining on the wait list in the COVID-19 era. *Kidney Int Rep* 2020; 6: 46–55
91. Bae S, McAdams-DeMarco MA, Massie AB *et al*. Early changes in kidney transplant immunosuppression regimens during the COVID-19 pandemic. *Transplantation* 2021; 105: 170–176
92. Santeusanio AD, Zendel A, Fenig Y *et al*. Kidney transplantation using lymphocyte depleting induction and standard maintenance immunosuppression at the height of the SARS-CoV-2 pandemic in New York City: a single-center experience. *Clin Transplant* 2020; 34: e14055
93. Shingare A, Bahadur MM, Raina S. COVID-19 in recent kidney transplant recipients. *Am J Transplant* 2020; 20: 3206–3209
94. Boyarsky BJ, Po-Yu CT, Werbel WA *et al*. Early impact of COVID-19 on transplant center practices and policies in the United States. *Am J Transplant* 2020; 20: 1809–1818
95. Loupy A, Reese, AO Bastien, PPO *et al*. C. Organ procurement and transplantation during the COVID-19 pandemic. *Lancet* 2020; 23: e95–e96
96. Ahn C, Amer H, Anglicheau D *et al*. Global transplantation COVID report March 2020. *Transplantation* 2020; 104: 1974–1983
97. Zidan A, Alabbad S, Ali T *et al*. Position statement of transplant activity in the Middle East in era of COVID-19 pandemic. *Transplantation* 2020; 104: 2205–2207
98. Cravedi P, Schold JD, Safa K *et al*. The COVID-19 pandemic: a community approach. *Clin Transplant* 2020; 34: e14059
99. Thaunat O, Legeai C, Anglicheau D *et al*. IMPact of the COVID-19 epidemic on the moRTAlity of kidney transplant recipients and candidates in a French Nationwide registry sTudy (IMPORTANT). *Kidney Int* 2020; 98: 1568–1577
100. Office of National Statistics. Deaths registered weekly in England and Wales, provisional: week ending 13 November 2020. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregisteredweeklyinenglandandwalesprovisional/weekending13november2020
101. Angeletti A, Trivelli A, Magnasco A *et al*. Risk of COVID-19 in young kidney transplant recipients. Results from a single-center observational study. *Clin Transplant* 2020; 34: e13889
102. Lentine KL, Mannon RB, Josephson MA. Practicing with uncertainty: kidney transplantation during the COVID-19 pandemic. *Am J Kidney Dis* 2012; doi: 10.1053/j.ajkd.2020.12.003