A Systematic Review of COVID-19 and Kidney Transplantation

Mahalingasivam, V., Craik, A., Tomlinson, L. A., Ge, L., Hou, L., Wang, Q., Yang, K., Fogarty, D., & Keenan, C. (2020). A Systematic Review of COVID-19 and Kidney Transplantation. Kidney International Reports, 6(1), 24-45. https://doi.org/10.1016/j.ekir.2020.10.023

Published in:
Kidney International Reports

Document Version:
Publisher's PDF, also known as Version of record

Queen's University Belfast - Research Portal:
Link to publication record in Queen's University Belfast Research Portal

Publisher rights
Copyright 2020 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

Download date: 15. Jul. 2021
A Systematic Review of COVID-19 and Kidney Transplantation

Viyaasan Mahalingasivam1, Alison Craik2, Laurie A. Tomlinson2, Long Ge3,4, Liangying Hou3,4, Qi Wang3, Kehu Yang3,5, Damian G. Fogarty6 and Ciara Keenan7,8

1Department of Renal Medicine, Barts Health NHS Trust, London, UK; 2Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK; 3Evidence Based Social Science Research Center, School of Public Health, Lanzhou University, China; 4Department of Social Medicine and Health Management, School of Public Health, Lanzhou University, China; 5Evidence Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, China; 6Department of Nephrology, Belfast Health and Social Care Trust, Belfast, UK; 7Campbell UK & Ireland, Queen’s University Belfast, Belfast, UK; and 8Cochrane Ireland, National University of Ireland Galway, Galway, Ireland

Introduction: Kidney transplant recipients are at increased susceptibility to many viral infections leading to justifiable anxiety about the effects of coronavirus disease 2019 (COVID-19).

Methods: We performed literature searches from multiple resources in April and August 2020 for relevant English and Chinese literature. Abstracts were screened, followed by full-text review with data extraction of reports that included at least 20 kidney transplant recipients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and completed outcomes.

Results: Twenty studies had sufficient data, which we have summarized. Studies were predominantly descriptive and came from France, Italy, Spain, Turkey, United Kingdom, and United States. Quality assessment demonstrated limitations in selection of comparison groups and controlling for additional factors. Mortality rates from published studies were variable. Based on early data early from Spain, 46% of patients who developed COVID-19 within 60 days of transplantation died. Acute kidney injury was common, and mycophenolate was discontinued in most patients.

Conclusion: Given the rapid global spread of COVID-19, reliable evidence is needed to inform public health policies. Hospitalized kidney transplant recipients with COVID-19 are at a high risk of death in early reports but interpretation of these data requires caution, as studies were susceptible to period effects. reassuringly, the quality of observational data is improving. Detailed and comprehensive data collection through linked registries will be necessary to conduct accurate analyses of risk factors for adverse outcomes, not least given the risks of stopping immunosuppression. This report highlights the early mortality excess in transplant recipients but medium- and longer-term outcomes remain uncertain and merit careful investigation.

Kidney Int Rep (2021) 6, 24-45; https://doi.org/10.1016/j.ekir.2020.10.023

KEYWORDS: COVID-19; kidney transplantation; systematic review

Correspondence: Viyaasan Mahalingasivam, Renal Unit, Whipps Cross University Hospital, Barts Health NHS Trust, Whipps Cross Road, London, E11 1NR, UK. E-mail: viyaasan.mahalingasivam@nhs.net

Received 3 July 2020; revised 25 September 2020; accepted 21 October 2020; published online 3 November 2020

On December 31, 2019, the Wuhan Health Commission in China reported an outbreak of atypical pneumonia to the World Health Organization. The causative pathogen was found to be the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) capable of human-to-human transmission through respiratory droplets. The associated disease was named COVID-19, and its spectrum of severity ranges from no symptoms to life-threatening organ dysfunction, the scale of which can place extreme burden on health care resources without control of transmission. After spread across several continents, COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020.

Severe lung injury and other organ-threatening complications in COVID-19 are understood to be the result of a dysregulated systemic inflammatory response in the days after infection, leading to some immunosuppressive therapies being repurposed both inside and out of clinical trial settings in conventional management. Only low-dose dexamethasone has so far demonstrated mortality benefit compared with usual practice. Imunosuppressant drugs used to prevent allograft rejection render kidney transplant recipients at increased susceptibility to many viral infections, and such
infections are an important cause of morbidity and mortality in this population. The immune response to SARS-CoV-2 infection in immunosuppressed kidney transplant recipients, many with other comorbidities, may result in differences in presentation, outcomes, and therapeutic responses compared with the general population.

Given the rapid and global spread of COVID-19, there is a need to gather evidence and disseminate as quickly as possible. Our aim was to conduct a complete systematic review of the early literature to synthesize, analyze, and appraise what has been learned so far to help clinicians and policy makers better understand the risks to kidney transplant recipients, as well as identify gaps for future collaborative research for this global health challenge.

METHODS

Search Strategy
Inclusion and exclusion criteria were formulated to ensure comprehensive searching and screening for articles relevant to COVID-19 in chronic kidney disease, specifically including kidney transplantation. Variables of interest were defined based on the PICOS (patient/population, intervention, comparison, outcomes, study designs) strategy. Our protocol was prospectively published via PROSPERO (CRD42020182134).

Initial searches were conducted on April 28, 2020, including all relevant English- and Chinese-language research up to that date from December 1, 2019; papers not written in these languages were excluded because of a lack of resources to obtain timely translation. Published and nonpublished literature was searched on MEDLINE (Ovid), EMBASE (Ovid), China National Knowledge Infrastructure, the Wanfang database, the Chinese Biomedical Literature Database, clinicaltrials.gov, the Chinese Clinical Trial Register, the World Health Organization database of COVID-19 research, and the Chinese Medical Journal Network. Search terms are listed in Supplementary Material S1. An updated search was deemed necessary due to the rapidly evolving evidence base and was conducted on August 4, 2020, via MEDLINE (Ovid), EMBASE (Ovid), World Health Organization COVID-19 database, and bioRxiv and medRxiv preprint servers. The strategy for the update searches is attached in Supplementary Material S2.

Screening, Data Extraction, and Quality Assessment
Duplicates were removed from the studies generated by both searches and the remaining studies were imported to the SysRev Platform (https://sysrev.com). Screening was undertaken at abstract level by separate teams of 2 independent authors for both English and Chinese; a senior author adjudicated where there was non-concordance. Reference lists were hand-searched for any additional studies that may have been missed. Full-text articles were then further assessed for eligibility, including the exclusion of case reports or studies with populations of interest of fewer than 20 confirmed cases. As all studies were observational, further quality assessment was undertaken using the Newcastle-Ottawa Quality Assessment Scale.9 Where articles did not report all outcomes specifically in kidney transplant populations, we contacted authors to request disaggregated data (Supplementary Material S3).

Data were extracted for each included study, including online publication date, study population, timeframe, total number of cases (including how many patients had completed outcomes, that is, death or recovery to discharge), patient characteristics, clinical presentation, outcomes, baseline immunosuppression adjustment, and COVID-19 therapy. Inpatient mortality for each study was calculated as a proportion of patients with completed outcomes.

RESULTS

Study Identification
The PRISMA flow diagram is shown in Figure 1. A total of 1377 studies were identified through database searching, after which 762 remained after de-duplication; of these, a further 695 were excluded after abstract screening, leaving 65 that met criteria for full-text assessment for eligibility with no additional articles identified after hand-searching reference lists. A further 47 studies were excluded after detailed assessment. To be more comprehensive, we included 2 additional studies published shortly after our search was completed.10,11 In total, 20 studies underwent data extraction.

Quality Assessment
There were no randomized controlled trials or case-control studies. Comparative analysis between different exposure groups was limited. Sánchez-Alavarez et al.12 was a report from a national COVID-19 registry across Spain, whereas Pascual et al.13 and Pérez-Sáez et al.14 reported on subgroups from this registry (those within 60 days of transplantation, and those treated with tocilizumab respectively). Bell et al.15 and Ravanan et al.16 reported from national transplant registries in Scotland and England, respectively, whereas Manganaro et al.16 reported on from a regional registry in Italy. Kates et al.10 reported on data entered to a registry by more than 50 transplant centers, almost all from the United States, whereas Cravedi et al.17 was a report of a consortium registry of 12 transplant centers across the United States, Italy, and
Spain. Boyarsky et al.\textsuperscript{18} and Vistoli et al.\textsuperscript{19} were cross-sectional reports of national surveys from the United States and Italy, respectively. The remaining studies were either single-center or small multicenter case series of either inpatients, or both inpatient and outpatient kidney transplant recipients with COVID-19. Using death as the main outcome of interest, formal quality assessment is shown in Table 1 using the Newcastle-Ottawa Quality Assessment Scale.\textsuperscript{9}

Quality assessment demonstrated consistent weaknesses in selection of control groups (e.g., home dialysis patients on the transplant waiting list) and inadequate control for additional confounding factors. Case series are descriptive and do not make comparisons with a control group, whereas single-center reports may yield biased results when compared with the source population. Kates et al.\textsuperscript{10} was susceptible to selection bias, as participating centers may not have systematically submitted all cases. Some studies did not report how many patients had been discharged, meaning mortality estimates may have been inaccurate due to misclassification of patients who died after the end of follow-up, but more recent reports had longer and more complete follow-up. Although Boyarsky et al.\textsuperscript{18} and Vistoli et al.\textsuperscript{19} had high response rates to their surveys, they may not be completely reliable, as they were not linked to individual patient records.

**Study Populations**

All studies identified by our search are listed in Supplementary Table S4, along with other studies reporting on ≥5 kidney transplant recipients. Our searches of studies with ≥20 recipients with confirmed COVID-19 and completed outcomes identified studies from only 6 countries (France, Italy, Spain, Turkey, United Kingdom, and United States); at least 5 of the 7 studies with patients from United States included cases from New York City. There have been smaller published studies not included in our review from Belgium, China, Iran, Netherlands, Portugal, and Switzerland.

We note that some studies had overlapping cohorts: patients from Mohamed et al.\textsuperscript{20} would be included in Ravanan et al.\textsuperscript{11} whereas patients in Pereira et al.\textsuperscript{21} would have been included in Lubetzky et al.\textsuperscript{22} Some cases from Rodriguez-Cubillo et al.\textsuperscript{23} are
likely to have been included in the registry report by Sánchez-Álvarez et al., whereas Pascual et al. and Pérez-Sáez et al. were reports of subgroup analyses from this registry. Cravedi et al. excluded any patients from studies that had already been published, but these were smaller studies not included in our summary. Kates et al. did not report which centers submitted data to its registry but there were more than 50, of which >98% were from the United States; our review includes 6 other studies with data from the United States that may have overlapped. Some centers from the United States and Italy reported in our review are likely to have contributed to the surveys published by Boyarsky et al. and Vistoli et al.

Data Analysis
Data and results from each study are summarized in Table 2. The 20 studies were published online between April 10 and August 11, 2020; one was a preprint with the remainder in journals. The last day of follow-up for each study ranged from March 17 to May 31, 2020. The studies ranged from 24 to 489 kidney transplant recipients in total.

Patient Characteristics
Of the studies with available patient demographic data, average age ranged from 45 years in Demir et al. to 66 years in Rodriguez-Cubillo et al. The percentage of male patients ranged from 46% in Pascual et al. to 79% in Bossini et al.

Clinical Presentation
Fever was common in studies, ranging from 52% to 95%; cough ranged from 49% to 78%, and dyspnea from 28% to 70%. Gastrointestinal symptoms were also reported, as high as 53% in Chaudhry et al. Four studies reported data on acute kidney injury or graft dysfunction at presentation, ranging from 28% in Mohamed et al. to 77% in Chen et al. No report described asymptomatic infection.

Baseline Immunosuppression Adjustment
A wide range of approaches was taken to adjust immunosuppression both between and within the studies. The dominant practice across other studies was to favor withholding or reducing antiproliferative drugs or mammalian target of rapamycin inhibitor over reduction in calcineurin inhibitor dose.

COVID-19 Therapy
Thirteen studies reported the use of COVID-19 therapies. Hydroxychloroquine was used in 11 studies, either alone or in combination with another therapy, with the proportion of patients receiving the drug ranging from 38% to 100%. Ten studies either started corticosteroid therapy or increased dosage. High-dose corticosteroid was reported in 6 studies for between 4% and 62% of patients. Remdesivir use was reported

Table 1. Description of each study design and quality assessment using the Newcastle-Ottawa Quality Assessment Scale, listed by order of online publication date

| Study               | Study design         | Selection | Comparability | Outcome |
|---------------------|----------------------|-----------|---------------|---------|
| Manganaro et al.    | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Boyarsky et al.     | Cross-sectional national survey | ++**  ++ **  ++ *** |             |         |
| Pereira et al.      | Two-center case series | ++**  ++ **  ++ *** |             |         |
| Sánchez-Álvarez et al. | National registry cohort | ++**  ++ **  ++ *** |             |         |
| Vistoli et al.      | Cross-sectional national survey | ++**  ++ **  ++ *** |             |         |
| Rodriguez-Cubillo et al. | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Pascual et al.      | National registry case series | ++**  ++ **  ++ *** |             |         |
| Chen et al.         | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Mehta et al.        | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Bossini et al.      | Multicenter case series | ++**  ++ **  ++ *** |             |         |
| Cravedi et al.      | Multicenter case series | ++**  ++ **  ++ *** |             |         |
| Chaudhry et al.     | Multicenter case series | ++**  ++ **  ++ *** |             |         |
| Pérez-Sáez et al.   | National registry case series | ++**  ++ **  ++ *** |             |         |
| Demir et al.        | Multicenter case series | ++**  ++ **  ++ *** |             |         |
| Lubetzky et al.     | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Bell et al. (preprint) | National registry case series | ++**  ++ **  ++ *** |             |         |
| Mohamed et al.      | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Kates et al.        | Multicenter case series | ++**  ++ **  ++ *** |             |         |
| Benatmane et al.    | Single-center case series | ++**  ++ **  ++ *** |             |         |
| Ravanan et al.      | National registry cohort | ++**  ++ **  ++ *** |             |         |

From left to right, quality items were starred black if they fulfilled predefined criteria: selection was starred on representativeness of patients with the exposure of interest (kidney transplant), selection of the nonexposed group, ascertainment of exposure, and demonstration that outcome of interest (death) was not present at start of the study; comparability was starred on the study controlling for the exposure of interest, and any additional factor; outcome was starred on how the outcome was assessed, whether follow-up was long enough for the outcome to occur, and whether loss to follow-up was adequate enough to be unlikely to introduce bias.
### Table 2. Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study                  | Online publication date in 2020 | Study population                                                                 | Setting                                                                                      | Timeframe in 2020 | Total number of cases | Patient characteristics                                                                 | Clinical presentation | Outcomes                                                                                   | Baseline IS adjustment | COVID-19 therapy                  |
|------------------------|---------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|-------------------|-----------------------|-------------------------------------------------------------------------------------------|-----------------------|---------------------------------------------------------------------------------------------|------------------------|-----------------------------------|
| Manganaro et al. 16    | 10 April                        | All inpatients and outpatients with COVID-19 confirmed by swab                    | Nephrology and Dialysis Units, Piedmont and Aosta Valley, Italy                            | Up to 27 March    | 26                    | Age median 61 y (range 26–80)                                                            | ICU admission         | 5/26 (21%) (for dialysis patients 9/102 [8%])                                             |                        |                                   |
| Boyarsky et al. 18      | 13 April                        | Patients with COVID-19                                                            | 88/111 centers conducting >100 solid organ transplants/year, United States                | Up to 24 March    | 103                   | Mild illness (no pneumonia) 58/103 (56%)                                                  | 103/103 (18%)         | Moderate illness (pneumonia) 18/103 (18%)                                                 |                        |                                   |
| Pereira et al. 21       | 24 April                        | All inpatients and outpatients with COVID-19 confirmed by RT-PCR                  | Two multiple solid organ transplant centers, New York City, United States                 | 13 March to 3 April | 51                    | Death or ICU admission 13/51 (25%)                                                        |                      |                                                                           |                        |                                   |
| Sánchez-Alvarez et al. 12 | 27 April            | Inpatients and outpatients who tested positive for COVID-19 entered to COVID-19 Registry of Spanish Society of Nephrology | Health centers across the Autonomous Communities of Spain                                | 18 March to 11 April | 286 (~269 hospitalized, ~122 recovered or died) | Age (y) median 60 ± 13 Sex: males ~100/~286 (66%) ACEI/ARB ~110/286 (39%) | Death ~53/122 (43%) (for in-center HD ~138/230 [80%]) | Death ~3/286 (9%) | ICU admission ~25/286 (9%) | Steroids ~110/286 (39%) | Interferon ~16/286 (6%) | Tocilizumab ~23/286 (8%) |
| Vistoli et al. 19       | 3 June                          | Reported COVID-19-positive inpatients and outpatients according to survey of kidney transplant centers, Italy | Up to 17 March | 60 (57 hospitalized) | Transplanted between 1 February and 15 March 3/60 (5%) | Death 11/57 (19%) | ICU 17/57 (30%) | (Continued on following page) |}

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study                        | Online publication date in 2020 | Study population                                      | Setting                             | Timeframe in 2020                  | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|------------------------------|---------------------------------|-------------------------------------------------------|-------------------------------------|------------------------------------|-----------------------|-------------------------|------------------------|----------|-------------------------|------------------|
| Rodriguez-Cubillo et al.23   | 12 June                         | Confirmed COVID-19 (RT-PCR) referred to a kidney transplant center | Kidney transplant center, Madrid, Spain | 15 March to 24 April; follow-up to 19 May | 29 (29 recovered to discharge or died) | ● Age (y) median 66 (IQR 59–72) | ● Symptomatic           | ● Death 6/29 (21%); with AKI 4/14 (29%); patients treated with cyclosporin strategy 3/2 (13%); people treated with IS minimization 3/6 (50%) | ● Switched to ciclosporin and prednisolone 23/29 (79%) | ● HOQ 22/29 (92%) |
|                              |                                 |                                                       |                                     |                                    |                       | ● Sex: male 17/29 (59%) | ● Fever 20/29 (69%) | ● Renal failure 13/24 (54%) | ● Antibiotics 29/29 (100%) | ● Glucocorticoids 12/24 (50%) |
|                              |                                 |                                                       |                                     |                                    |                       | ● Time since transplant (mo) median 90 (IQR 26–171) | ● Cough 17/29 (59%) | ● Mechanical ventilation 9/24 (38%) | ● CYC 60 (100%) | ● LPV/r 8/24 (33%) |
|                              |                                 |                                                       |                                     |                                    |                       | ● Comorbidities: diabetes 11/29 (38%); obesity 15/29 (52%) | ● Dyspnea 14/29 (48%) | ● ICU admission 4/24 (17%) | ● Tacrolimus 9/29 (31%) | ● Tocilizumab 8/24 (33%) |
|                              |                                 |                                                       |                                     |                                    |                       | ● Baseline IS: tacrolimus 19/29 (66%); ciclosporin 6/29 (21%); mTORi 8/29 (28%); azathioprine 1/29 (3%); prednisolone 23/29 (79%) | ● Diarrhea 14/29 (48%) | ● Mechanical ventilation | ● Anticoagulation 24/29 (83%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Age: ≥65 y 12/24 (50%) | ● AKI 14/29 (48%) | ● Antiproliferative stopped 23/29 (100%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Sex: male 11/24 (46%) | ● Oxygen requirement 7/29 (24%) | ● mTORi stopped 8/29 (100%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Comorbidities: diabetes 12/24 (50%) | ● CXR no changes 11/29 (46%) | ● Glucocorticoids 12/24 (50%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Deceased donor 23/24 (96%) | ● D-dimer (ng/ml) median 1429 (IQR 754–2358) | ● Mechanical ventilation 5/29 (17%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● DGF 12/24 (50%) | ● Ferritin (ng/ml) median 647 (IQR 348–1682) | ● Recovery from mechanical ventilation 3/5 (60%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Acute rejection 2/24 (8%) | ● LDH (iu/l) median 488 (IQR 360–712) | ● Recovery from mechanical ventilation 3/5 (60%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Baseline IS: prednisone 24/24 (100%); tacrolimus 24/24 (100%); MMF 21/24 (88%); mTORi 2/24 (8%) | ● Pneumonia 22/24 (92%) | | | |
| Pascual et al.13             | 19 June                         | Inpatients with confirmed COVID-19 (RT-PCR) within 60 d of kidney transplantation, entered to COVID-19 Registry of Spanish Society of Nephrology | 12 transplant centers, Spain | 17 March to 18 April | 24 (of 265 transplants within 60 d) (do not specify how many recovered to discharge) | ● Age: ≥65 y 12/24 (50%) | ● Fever 15/24 (63%) | ● Death 11/24 (46%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Sex: male 11/24 (46%) | ● Cough/thrombocytopenia 14/24 (58%) | ● Renal failure 13/24 (54%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Comorbidities: diabetes 12/24 (50%) | ● Dyspnea 14/24 (58%) | ● Mechanical ventilation 9/24 (38%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● Deceased donor 23/24 (96%) | ● Pneumonia 22/24 (92%) | ● ICU admission 4/24 (17%) | | |
|                              |                                 |                                                       |                                     |                                    |                       | ● DGF 12/24 (50%) | ● Lymphopenia 24/24 (100%) | | |
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|---------------------------------|---------|-------------------|-----------------------|------------------------|----------------------|----------|------------------------|------------------|
| Chen et al. | 23 June Inpatients with confirmed COVID-19 (RT-PCR) in addition to radiographic evidence | Single center, New York City, United States | 18 March to 10 April | 30 (29 recovered to discharge or died) | ● Age (y) mean 56 ± 12  
● Sex: males 16/30 (53%)  
● Race: African descent 22/30 (73%), Hispanic 5/30 (17%), Caucasian 2/30 (7%), Asian 1/30 (3%)  
● BMI (kg/m²) mean 28.7 (SD 6.9)  
● Time since transplant (y) median 7 (IQR 4–14)  
● Deceased donor 18/30 (60%)  
● Cause of ESRD: hypertension 13/30 (43%), diabetes 11/30 (38%), HIV 2/30 (7%), ADPKD 2/30 (7%), SLE 2/30 (7%)  
● Comorbidities: diabetes 14/30 (47%), vascular diseases 11/30 (37%), obesity 10/30 (33%), asthma/COPD 0/30 (0%)  
● Baseline creatinine (mg/l) median 1.3 (IQR 1.0–1.8)  
● CKD stage: 3 14/30 (47%), 4 1/30 (3%), 2/30 (7%)  
● Baseline IS: tacrolimus 26/30 (87%), ciclosporin 3/30 (10%), MMF 12/30 (40%), prednisone 30/30 (100%)  
● Baseline tacrolimus level (ng/ml) mean 7.0 (SD 5.6) | ● Fever 22/30 (73%)  
● Cough 20/30 (67%)  
● GI symptoms 13/30 (43%)  
● Oxygen requirement 27/30 (90%)  
● Intubated pre-hospital/in ED 2/30 (7%)  
● AKI 23/30 (77%)  
● Creatinine (mg/ml) median 1.8 (IQR 1.4–2.7)  
● LDH (units/l) median 294 (238–427)  
● CRP (mg/l) median 76 (IQR 44–147)  
● ESR (mm/h) median 72 (IQR 58–80)  
● Ferritin (µg/l) median 979 (IQR 422–1977)  
● D-dimer (µg/ml) median 2900 (IQR 1053–5142) | ● Deaths 6/29 (21%)  
● Mechanical ventilation 7/30 (23%)  
● RRT 4/30 (13%)  
● Ischaemic stroke 2/30 (7%) | ● CNI withheld 29/29 (100%)  
● MMF withheld 12/30 (100%)  
● High-dose MP 18/30 (60%) | ● HCQ + AZM 30/30 (100%) |
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study                  | Online publication date in 2020 | Study population                                                                 | Setting                              | Timeframe in 2020 | Total number of cases | Patient characteristics                                                                 | Clinical presentation                                                                 | Outcomes                                                                 | Baseline IS adjustment | COVID-19 therapy               |
|------------------------|---------------------------------|----------------------------------------------------------------------------------|--------------------------------------|-------------------|-----------------------|------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------|---------------------------------|
| Bossini et al. 25       | 6 July                           | Symptomatic inpatients and outpatients assessed either in ED or clinic with confirmed COVID-19 (RT-PCR) | Kidney transplant outpatient center and 3 admitting hospitals, Brescia, Italy | 1 March to 16 April | 53 (45 hospitalized; 42 recovered to discharge or died) | Age (y) median 60 (IQR 50–67)                                                                 | Temperature >37.5°C 51/53 (96%)                                                                 | Inpatients only:        | Death 15/42 (36%), due to ARDS 14/15 (93%), due to likely bacterial sepsis 1/15 (7%) | MMF withheld 42/53 (93%) (including all outpatients) | MMF reduced 42/53 (93%) |
| Mehta et al. 28         | 23 June                          | Attendees to ED with confirmed COVID-19 (RT-PCR) of 44 who reported symptoms to an outpatient monitoring system | Kidney transplant center, New York City, United States | 15 March to 12 April | 34 (33 recovered to discharge or died) | Age (y) median 59 (IQR 53–84)                                                                 | Time from symptoms to presentation (d) median 8 (IQR 5–10)                                                                 | Deaths 6/33 (18%)       | MMF withheld 26/33 (79%)         | HOQ 33/34 (97%)                  |

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|---------------------------------|------------------|---------|------------------|----------------------|------------------------|-----------------------|----------|----------------------|-----------------|
|       |                                 |                  |         |                  |                      | (9%), other 5/53 (9%), not determined 17/53 (32%) | *GI symptoms 9/53 (17%)* | *ARDS 27/45 (60%)* | *Creatinine increase compared with baseline (%) – 8 (IQR 20 to 7) from 1 center = 28 patients* | *Glucocorticoid dose unchanged 11/45 (24%)* | *Outpatients:* |
|       |                                 |                  |         |                  |                      | Comorbidities: diabetes 11/53 (21%), cardiac diseases 10/53 (18%), previous DVT 4/53 (8%), other 4/53 (8%) | *CXR: no infiltrates 1/39 (3%), bilateral infiltrates 27/39 (69%)* | *ICU 10/45 (22%)* | *Creatinine increase compared with baseline (%) – 8 (IQR 20 to 7)* | *MMF withdrawn & CNI halved 4/8 (50%)* | *Prophylactic heparin 23/45 (51%)* |
|       |                                 |                  |         |                  |                      | Time since transplant (y) median 9 (IQR 4–16) | *Time from symptoms to presentation (d) median 7 (IQR 4–10)* | *Mechanical ventilation 9/45; 8/9 (89%) died* | *Low-dose MMF maintained 1/8 (13%)* | *mTORi withdrawn & CNI halved 1/8 (13%)* |
|       |                                 |                  |         |                  |                      | Deceased donor 48/53 (91%) | *WCC (10⁹/l) median 5.6 (IQR 4.1–7.4)* | *LOS (d) median 11 (IQR 7–18)* | *CNI halved 1/8 (13%)* | *Started or increased to MP or equivalent 16mg 3/8 (38%)* |
|       |                                 |                  |         |                  |                      | Induction IS: ATG 17/38 (45%), basiliximab 14/38 (37%), alemtuzumab 6/38 (18%), other 1/38 (3%) | *Neutrophils (10⁹/l) median 4.1 (IQR 2.9–6.8)* | *Ferritin (μg/dl) median 433 (IQR 284–872)* | *Glucocorticoid dose unchanged 5/8 (62%)* | *Glucocorticoid dose 18/45 (40%)* |
|       |                                 |                  |         |                  |                      | *Baseline IS: tacrolimus 31/53 (58%), cyclosporin 17/53 (32%), MMF 32/53 (60%), mTORi 6/53 (11%), glucocorticoid 30/53 (57%)* | *Lymphocytes (10⁹/l) median 0.6 (IQR 0.4–1.1)* | *LDH (units/l) median 263 (IQR 213–323)* | *CRP (mg/l) median 39 (IQR 16–103)* | *CNI halved 1/8 (13%)* |
|       |                                 |                  |         |                  |                      | *Baseline creatinine (mg/dl) median 1.8 (IQR 1.5–2.4)* | *Creatinine increase compared to baseline (%) median 21 (IQR 7–30)* | *Fibrinogen (mg/dl) median 540 (IQR 380–625)* | *Started or increased to MP or equivalent 16mg 3/8 (38%)* | *Glucocorticoid dose unchanged 5/8 (62%)* |
| Study       | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|------------|---------------------------------|------------------|---------|-------------------|-----------------------|------------------------|-----------------------|----------|------------------------|-----------------|
| Cravedi et al.17 | 10 July                        | Inpatients with confirmed COVID-19 (RT-PCR) participating in the TANGO consortium (www.tangoxstudy.com) (excluded patients included in prior publications) | 12 transplant centers across the United States (5), Italy (4), and Spain (2) | 2 March to 15 May | 144 (do not specify how many recovered to discharge) | Ages (y) median 62 (IQR 52–69) | Sex: male 94/144 (65%) | Race: Hispanic 56/144 (40%), White 43/144 (31%), African American 35/144 (25%) | Comorbidities: diabetes 75/144 (52%), obesity 71/144 (49%), heart disease 41/144 (28%), lung disease 27/144 (19%), cancer 22/144 (15%), smoking history 39/144 (27%), HIV 3/144 (2%), ACEI 20/144 (14%), ARB 24/144 (17%) | Cause of ESRD: diabetes 43/144 (30%), glomerular disease 26/144 (19%), hypertension 20/144 (14%), PKD 13/144 (9%) | Time since transplant (y) median 5 (IQR 2–9), <1 y 23/144 (16%) | Deceased donor 112/144 (78%) | Baseline IS: tacrolimus 131/144 (91%), MMF 111/144 (77%), everolimus 11/144 (8%), prednisolone 125/144 (89%) | D-dimer (ng/ml) median 414 (IQR 101–677) | Fever 96/144 (67%) | Dyspnea 97/144 (68%) | Diarrhea 55/144 (38%) | Myalgia 76/144 (53%) | Symptoms onset to admission (d) median 6 (IQR 3–8) | WCC (10⁹/L) median 6.4 (IQR 4.8–8.3) | Lymphocytes (x10⁹) median 0.9 (IQR 0.5–3.1) | Creatinine (mg/dl) median 1.5 (IQR 1.1–1.9) | CRP (mg/l) median 41 (IQR 12–125) | Ferritin (μg/l) median 1280 (IQR 523 - 2620) | D-dimer (μg/ml) median 1.12 (0.62–2.00) | L-6 (ng/ml) 37 (8–95) | Procalcitonin (ng/ml) median 0.3 (IQR 0.1–1.0) | Death 46/144 (32%), by age (y) >60 vs <60 OR 1.07 (95% CI 1.02–1.14) | Tacrolimus withheld 32/131 (25%) | Steroid increased 95/126 (78%) | HCQ 101/144 (70%) | Antibiotics 106/144 (74%) | Tocilizumab 19/144 (13%) | Remdesivir 9/144 (6%) | LP/Vir 7/144 (5%) | DRV/IRM 3/144 (2%) | Darunavir-cobisetvir 1/144 (1%) |

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study                        | Online publication date in 2020 | Study population                                                                                     | Setting                                                                                                           | Timeframe in 2020 | Total number of cases | Patient characteristics                                                                                           | Clinical presentation                                                                 | Outcomes                                                                                                         | Baseline IS adjustment | COVID-19 therapy                                                                                      |
|------------------------------|---------------------------------|------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------|-----------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|------------------------|-------------------------------------------------------------------------------------------------------------------|
| Chaudhry et al.26             | 12 July                         | All inpatient and outpatient SOT recipients with confirmed COVID-19 (RT-PCR)                         | 5 hospitals within a quaternary care academic institution, Michigan, United States                                 | 20 March to 18 April | 38 (26 hospitalized)  | • Age (y): median 61.5 (IQR 52–70)                                                                                  | • Cough 23/38 (61%)                                                                  | • Age: males 26/38 (68%)                                                                                          |                       | • Fever 22/38 (58%)                                                                                          |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Sex: Black 31/38 (82%)                                                                                         | • Dyspnea 21/38 (55%)                                                              | • Race: Black 31/38 (82%)                                                                                     |                       | • Mechanical ventilation 11/38 (29%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Altered mentation 7/38 (18%)                                                     | • Comorbidities: COPD 5/38 (13%), CKD 35/38 (92%), heart failure 8/38 (21%), coronary artery disease 3/38 (8%), diabetes 27/38 (71%), hypertension 37/38 (97%), malignancy 3/38 (8%), smoking history 7/38 (18%) |                       | • ARDS: mild 0/11 (0%), moderate 4/11 (36%), severe 7/38 (64%)                                                |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Diarrhea 20/38 (53%)                                                             | • Race: Black 31/38 (82%)                                                                                     |                       | • AKI requiring RRT 5/38 (13%)                                                                               |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Myalgia 15/38 (40%)                                                              | • Race: Black 31/38 (82%)                                                                                     |                       | • Hospital LOS (d) median 4 (IQR 2–20)                                                                         |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Symptom duration (d) median 7 (IQR 2–10)                                      | • Race: Black 31/38 (82%)                                                                                     |                       | • Secondary bacterial infection 7/38 (18%)                                                                      |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • WCC (10⁹/l) median 5.8 (IQR 4.7–8.8)                                         | • Race: Black 31/38 (82%)                                                                                     |                       | • Hospital LOS (d) median 4 (IQR 2–20)                                                                         |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Lymphocytes (10⁹/l) median 0.5 (IQR 0.4–0.8)                                   | • Race: Black 31/38 (82%)                                                                                     |                       | • Secondary bacterial infection 7/38 (18%)                                                                      |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • CRP (mg/dl) median 7.5 (IQR 2.4–13.5)                                        | • Race: Black 31/38 (82%)                                                                                     |                       | • Secondary bacterial infection 7/38 (18%)                                                                      |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Black 31/38 (82%)                                                                                         | • Abnormal CXR/CT chest 24/38 (64%)                                               | • Race: Black 31/38 (82%)                                                                                     |                       | • Secondary bacterial infection 7/38 (18%)                                                                      |
| Pérez-Sáez et al.14          | 12 July                         | Inpatients identified through national COVID-19 registry with confirmed COVID-19 (RT-PCR) who received tocilizumab based on individual hospital protocols for increased disease severity. All patients had at least one of the following: increased IL-6; increase in other inflammatory markers; rapidly progressive ARDS. | 29 hospitals, Spain (27 completed request for additional data)                                                | Up to 9 May (follow-up to 15 May)                               | 80 (of 468 included in the registry) (80 recovered to discharge or died)                                        | • Age (y): mean 59 (SD 12)                                                                                       | • Fever 65/80 (81%)                                                                                           | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab 80/80 (100%)                                                                                  |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Sex: Males 54/80 (68%)                                                                                          | • Dyspnea 46/80 (58%)                                                             | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Caucasian 71/80 (89%)                                                                                     | • ICU admission 24/80 (30%)                                                      | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Caucasian 71/80 (89%)                                                                                     | • NIV 33/80 (44%)                                                                | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Caucasian 71/80 (89%)                                                                                     | • Both CNI & MMF/mTORi withheld 63/80 (54%)                                      | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Caucasian 71/80 (89%)                                                                                     | • HCQ 79/80 (99%)                                                               | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |
|                              |                                 |                                                                                                      |                                                                                                                   |                   |                       | • Race: Caucasian 71/80 (89%)                                                                                     | • AZM 59/80 (74%)                                                               | • Death 26/80 (33%)                                                                                             |                       | • Tocilizumab > 1 dose 16/80 (20%)                                                                            |

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|-----------------|---------|------------------|----------------------|------------------------|----------------------|----------|-----------------------|-----------------|
|       |                               | Additional patients were identified after contacting centers |         |                  |                      | ACE/ARB 26/80 (33%), smoking history 17/80 (21%) | GI symptoms 38/80 (48%) | AKI 36/80 (45%) |         | Other antibiotic 61/80 (76%) | Steroids 64/80 (80%) |
|       |                               |                 |         |                  |                      | Cause of ESRD: diabetes 15/80 (19%), vascular 7/80 (9%), glomerular 17/80 (21%), PKD 14/80 (18%) | CXR changes 78/80 (88%) | AKI requiring dialysis 15/80 (19%) |         | i.v. lg 12/80 (15%) | Interferon 5/80 (6%) |
|       |                               |                 |         |                  |                      | Time since transplant (mo) median 72 (IQR 17 – 165) | Symptom onset to admission (d) median 4 (IQR 3–8) | Acute rejection 1/80 (1%) |         | LPV/r or remdesivir 38/80 (49%) | Anakinra 6/80 (8%) |
|       |                               |                 |         |                  |                      | Re-transplantation 21/80 (26%) | Follow-up time (d) median 25 d (IQR 17–35) |         |          |                     |                 |
|       |                               |                 |         |                  |                      | Induction: ATG 33/80 (41%) | Moderate/severe ARDS 6/80 (8%) |         |          |                     |                 |
|       |                               |                 |         |                  |                      | Baseline IS: CNI 66/80 (83%), prednisolone 73/80 (91%), MMF 64/80 (80%), mTORi 14/80 (18%) | Oxygen saturation (%) median 95 (IQR 91 – 97) | Follow-up time (d) median 25 d (IQR 17–35) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | WCC (10^9/l) mean 6.8 (SD 3.1) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | Lymphocytes (10^9/l) mean 0.8 (SD 0.6) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | CRP (mg/l) median 49 (IQR 10–49) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | Procalcitonin (ng/ml) median 0.24 (IQR 0.1–1.1) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | IL-6 (pg/ml) median 52 (IQR 33–110) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | LDH (units/l) median 335 (IQR 257–486) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | Ferritin (ng/ml) median 698 (IQR 395–1677) |         |          |                     |                 |
|       |                               |                 |         |                  |                      |                          | D-dimer (mcg/l) |         |          |                     |                 |

(Continued on following page)
| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|------------------|---------|-------------------|----------------------|------------------------|-----------------------|----------|------------------------|------------------|
| Demir et al. | 13 July | Inpatients and outpatients with confirmed COVID-19 (RT-PCR) | 5 transplant centers, Istanbul, Turkey | 1 February to 4 May (follow-up for at least 15 d) | 44 (1 excluded as “without typical findings”, 3 lost to follow-up; 39 hospitalized - do not specify how many recovered to discharge) | Age (y): mean 45 (SD 15) | Fever 25/40 (63%) | Death 5/40 (13%) | CNI withheld 11/38 (30.8%) | Favipiravir 18/40 (45%) |
| | | | | | | Sex: male 20/40 (50%) | Cough 30/40 (75%) | NIV 4/40 (10%) | Tocilizumab 5/40 (13%) |
| | | | | | | Cause of ESRD: hypertension 4/40 (10%), diabetes 2/40 (5%), chronic GN 13/40 (33%) | Dyspnea 21/40 (53%) | Mechanical ventilation 6/40 (15%) | Anakinra 3/40 (8%) |
| | | | | | | Comorbidities: lung disease 3/40 (8%), ACEI/ARB 18/40 (45%), hypertension 26/40 (65%) | Diarrhea 10/40 (25%) | Follow-up time (d) 32 (IQR 23–44) | Antibiotics 24/40 (60%) |
| | | | | | | Time since transplant (mo) median 75 (IQR 32–126) | Oxygen saturation (%) median 96 (IQR 93–98) | LOS (d) median 9 (IQR 5–12) | |
| | | | | | | Deceased donor 5/40 (13%) | Creatinine (mg/dL) median 1.6 (IQR 1.2–2.2) | | |
| | | | | | | Induction IS: ATLG 22/40 (55%), basiliximab 3/40 (8%) | WOC (10^9/l) median 5.2 (IQR 4.0–7.0) | | |
| | | | | | | Baseline IS: tacrolimus 31/40 (78%), cyclosporine 5/40 (13%), mTORi 4/40 (10%), mycophenolate 36/40 (90%), steroids 40/40 (100%) | Lymphocytes (10^9/l) median 0.7 (IQR 0.5–1.0) | | |
| | | | | | | | CRP (mg/l) median 45 (IQR 24–88) | | |
| | | | | | | | LDH (units/l) median 257 (IQR 198–370) | | |
| | | | | | | | D-dimer (ng/ml) median 720 (IQR 510–1734) | | |
| | | | | | | | Ferritin (ng/ml) median 358 (IQR 173–892) | | |

(Continued on following page)
| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|------------------|---------|------------------|----------------------|------------------------|----------------------|----------|------------------------|-----------------|
| Lubetzky et al.²² | 17 July | Consecutive inpatients and outpatients with confirmed COVID-19 (RT-PCR) | Transplant center, New York, United States | 13 March to 20 April | 54 (39 hospitalized, 37 recovered to discharge or died) | • Age (y): median 57 (range 29 – 83) | • Graft dysfunction 14/40 (35%) | • Fever 40/54 (74%) | • Death 7/39 (18%) | • Tacrolimus reduced 17/52 (33%) | • HCQ 31/39 (79%) |
| | | | | | | • Sex: male 38/54 (70%) | • Cough/upper respiratory tract symptoms 32/54 (59%) | • Mechanical ventilation 11/39 (28%) | Tacrolimus withheld 0/52 (0%) | Remdesivir 2/39 (5%) |
| | | | | | | • Race: white 17/54 (31%), Hispanic 17/54 (31%), black 13/54 (24%), Asian 6/54 (11%), Middle Eastern 1/54 (2%) | • Dyspnea 28/54 (52%) | • AKI 20/39 (51%) | MMF halved 15/52 (29%) | IL-6 receptor inhibitor 2/39 (5%) |
| | | | | | | • BMI (kg/m²): (median) 28 (IQR 18 – 43) | • Fatigue/Myalgia 23/54 (43%) | • AKI: resolved 9/20 (45%), partially resolved 5/20 (25%), not resolved 6/20 (30%), dialysis dependent at follow-up 3/20 (15%) | MMF withheld 24/52 (46%) | Convalescent plasma 1/39 (3%) |
| | | | | | | • Comorbidities: diabetes 16/54 (30%), cardiovascular disease 19/54 (35%), stroke 4/54 (7%), lung disease 8/54 (15%), antihypertensives 50/54 (93%), ACEI/ARB 19/54 (37%), smoking 12/54 (22%) | • D-dimer (ng/ml) median 394 (IQR 278 – 589) | Additional steroid 5/54 (9%) | • Azithromycin 7/39 (18%) |
| | | | | | | • Baseline creatinine (mg/dl) mean 1.5 (SD 0.7) | • Time symptoms to diagnosis (d): mean 8 (SD 6) | • Remained steroid free 29/32 (91%) | • Doxycycline 8/39 (21%) | • Dexamethasone 1/39 (3%) |
| | | | | | | • Cause of ESRD: hypertension 11/54 (20%), diabetes 14/54 (26%), GN 13/54 (24%), lupus 2/54 (4%), PKD 3/54 (6%) | Inpatients: | | Outpatient: |
| | | | | | | • Time since transplant (y): median 4.7 (range 0.3 – 35) | | • Complete symptom resolution 14/15 (93%) | • HCQ 1/15 (7%) | • Azithromycin 5/15 (33%) |
| | | | | | | • Deceased donor 17/54 (31%) | | Follow-up (d) median 29 (range 5 – 53) | • Doxycycline 1/15 (7%) | |
| | | | | | | • IS induction: T-cell depleting agent 39/54 (72%) | | | | |
| | | | | | | • Baseline IS: steroids 22/54 (41%), CNI 52/54 (96%), belatacept 1/54 (2%), MMF 52/54 (96%), mTORi 2/54 (4%) | | | | |
| | | | | | | • Baseline creatinine (mg/dl) mean 1.5 (SD 0.7) | | | | |

(Continued on following page)
| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|------------------|---------|-------------------|-----------------------|------------------------|-----------------------|----------|------------------------|-----------------|
| Bell et al.15 | 21 July (posted) | Notified confirmed COVID-19 as identified through the Scottish Renal Registry through linkage to Health Protection Scotland | Scotland, UK (100% patient- and unit-level coverage) | Up to 31 May | 24 (of 3286 functioning kidney transplants) | • Age (y): 20–44 4/24 (17%), 45–64 12/24 (50%), 65–74 5/24 (21%), ≥75 3/24 (13%) | • Ferritin (ng/ml) median 1498 (IQR 383–2646) | • Death 7/24 (29%) |
| | | | | | | • Sex: male 13/24 (54%) | • IL-6 (pg/ml) median 8 (IQR 4.5–92) | | | |
| | | | | | | • Cause of ESRD: GN 3/24 (13%), interstitial 12/24 (50%), Multi-system 3/24 (13%), diabetes 3/24 (13%) | • Procalcitonin (ng/ml) median 0.3 (IQR 0.1–0.6) | | | |
| | | | | | | • Time since transplant (y): <1 0/24 (0%), ≥1 10 14/24 (58%) | • AKI 20/39 (51%) | | | |
| | | | | | | • Scottish Index of Multiple Deprivation: 1 (most deprived) 7/24 (29%), 5/24 (21%), 4/24 (17%), 5/24 (21%), 3/24 (13%) | | | |
| Mohamed et al.20 | 31 July | Consecutive inpatients and outpatients with confirmed COVID-19 (RT-PCR) | Kidney transplant center, London, UK | Up to end of April | 28 (of 1434 functioning transplants) (25 hospitalized – 26 recovered to discharge or died); comparison with 32 patients active on transplant waiting list (of 321) (14 hospitalized) | • Healthcare-associated infection 2/28 (7%) | • Death 9/25 (36%); (vs 5/14 (36%) on waiting list) | • MMF withdrawal 1/21 (5%) | • RECOVERY trial (dexamethasone arm) 1/25 (4%) |
| | | | | | | • Donor: deceased 22/28 (79%) | • ICU 5/25 (20%); died 4/5 (80%) | | | |
| | | | | | | • BMI (kg/m²) median 28 (range 19–38) | • RT 2/25 (8%) | | | |
| | | | | | | • Comorbidities: diabetes 10/28 | | | | |

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|------------------|---------|------------------|-----------------------|------------------------|-----------------------|----------|-----------------------|----------------|
| Kates et al.10 | 7 August | Any inpatient or outpatient SOT recipient with confirmed COVID-19 (RT-PCR) reported through an electronic case report form | >50 transplant centers, >98% United States | 7 March to 15 April; all cases followed-up for 28 d | 318 kidney-only or kidney-pancreas recipients | Age (y) 56 (IQR 46–66) | Healthcare-associated infection 39/318 (12%) | Deaths within 28 d 57/318 (18%) | IS modified 241/318 (76%) | CQ/HQD 197/318 (62%) |
| | | | | | | Sex: male 186/318 (59%) | Fever 186/318 (59%) | Hospitalization 254/318 (80%) | AZM 110/318 (35%) |
| | | | | | | Race: Asian/Pacific Islander 18/318 (6%), black 150/318 (47%), white 130/318 (41%), other/unknown 20/318 (6%), Hispanic ethnicity 59/318 (19%) | Cough 235/318 (74%) | ICU 107/254 (42%) | Anti-IL-6 39/318 (12%) |
| | | | | | | Geographic location: United States – Northeast 151/318 (48%), Midwest 72/318 (23%), South 46/318 (15%), West 44/318 (14%), international 5/318 (2%) | Dyspnea 187/318 (59%) | Mechanical ventilation 87/254 (34%) | High-dose steroids 35/318 (11%) |
| | | | | | | | GI symptoms 156/318 (49%) | Vasopressors 74/254 (29%) | Convalescent plasma 10/318 (3%) |
| | | | | | | | WCC (x 10^9/l) median 5.8 (IQR 4.3–8.4) (not reported in 34/318 [11%]) | AKI 130/318 (41%) | Protease inhibitor 9/318 (3%) |
| | | | | | | | Baseline creatinine (μmol/l) median 155 (range 68–356) | Anti-CD20 59/318 (19%) | Remdesivir 9/318 (3%) |
| | | | | | | | AKI 7/25 (28%) | Anti-CD40 39/318 (12%) |
| | | | | | | | Creatinine (μmol/l) 255 (range 58–566) | Anti-IL-2 39/318 (12%) |
| | | | | | | | Hb (g/l) median 108 (range 81–157) | Anti-IL-8 39/318 (12%) |
| | | | | | | | WCC (10^9/l) median 6.8 (range 3.0–18.0) | Anti-IL-10 39/318 (12%) |
| | | | | | | | Neutrophils (10^9/l) median 5.5 (range 1.0–17.0) | Anti-IL-12/23 39/318 (12%) |
| | | | | | | | Lymphocytes (10^9/l) median 0.6 (range 0.2–1.7) | Anti-IL-18 39/318 (12%) |
| | | | | | | | CRP (mg/l) median 85 (range 7–367) | Anti-IL-19 39/318 (12%) |
| | | | | | | | CXR ground-glass shadowing or consolidation 19/25 (76%) | Anti-L-34 39/318 (12%) |

(Continued on following page)
### Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|-------------------------------|------------------|---------|-------------------|-----------------------|------------------------|-----------------------|----------|------------------------|-----------------|
| Benotmane et al.29 | 10 August | Consecutive inpatients with COVID-19 diagnosed by RT-PCR or typical CT chest lesions | Kidney transplant center, Strasbourg, France | 4 March to 7 April; followed-up to 13 May | 40 | • Age (y) median 64 (QQR 55–68) | • Fever 38/40 (96%) | • Deaths 9/40 (23%) | • MMF/MPA withdrawal 34/34 (100%) | • AZM 26/40 (65%) |
| | | | | | | • Sex: male 31/40 (78%) | • Cough 31/40 (78%) | • Severe disease (oxygen requirement >6 l/min or ICU admission or death) | • CNI withdrawal 15/35 (43%) | • Other antibiotics 40/40 (100%) |
| | | | | | | • BMI (kg/m²) median 30 (QQR 24–33) | • Dyspnea 28/40 (70%) | | • LPVR 1/40 (3%) | | • HCQ 15/40 (38%) |

- Time since kidney transplant (y) median 5 (QQR 2–10)
- Transplanted in 2020 9/318 (3%)
- Comorbidities: coronary artery disease 68/318 (21%), heart failure 30/318 (9%), diabetes 170/318 (54%), CKD 134/318 (42%), haemodialysis 25/318 (8%), chronic lung disease 29/318 (9%), malignancy 8/318 (3%), HIV 5/318 (2%), BMI >30 kg/m² 116/318 (37%)
- ≥2 of age >65 y, heart failure, chronic lung disease and obesity 53/318 (17%)
- Baseline IS: CNI + antiproliferative + steroid 176/318 (55%), CNI + steroid 49/318 (15%), CNI + antiproliferative 39/318 (12%), mTORi regimen 16/318 (5%), other 64/318 (20%)
- Recently augmented IS 26/318 (8%)
- Blood type: A 95/318 (34%), B 49/318 (18%), AB 14/318 (5%), O 118/318 (43%)

- Neutrophils (x 10⁹/l) 4.3 (3.1–6.3) (not reported in 34/318 [11%])
- Lymphocytes (x10⁹/l) 0.7 (0.4–1.0) (not reported in 34/318 [11%])
- CT chest: abnormal 207/271 (76%); not performed 47/318 (15%)
- Bloodstream infection 17/318 (5%)

- New RRT 42/318 (13%)
- Acute rise in LFT >3x ULN 21/318 (7%)
- Acute MI 7/318 (2%)
- VTE 8/318 (3%)
- Bacterial pneumonia 23/318 (7%)

- Deaths 9/40 (23%)
- MMF/MPA withdrawal 34/34 (100%)
- CNI withdrawal 15/35 (43%)
- Other antibiotics 40/40 (100%)

- LPVR 1/40 (3%)
- HCQ 15/40 (38%)

- Clinical trial 23/318 (5%)
- Other experimental treatments 18/318 (4%)

Benotmane et al.29
10 August
Consecutive inpatients with COVID-19 diagnosed by RT-PCR or typical CT chest lesions
Kidney transplant center, Strasbourg, France
4 March to 7 April; followed-up to 13 May
40

V Mahalingasivam et al.: COVID-19 and Kidney Transplantation
Kidney International Reports (2021) 6, 24-45

(Continued on following page)
Table 2. (Continued) Summary of clinical data and outcomes from all included studies listed by order of online publication date

| Study | Online publication date in 2020 | Study population | Setting | Timeframe in 2020 | Total number of cases | Patient characteristics | Clinical presentation | Outcomes | Baseline IS adjustment | COVID-19 therapy |
|-------|--------------------------------|------------------|---------|------------------|-----------------------|------------------------|-----------------------|----------|------------------------|-----------------|
| Ravanan et al. | 11 August | SOT recipients with functioning graft as of 1 February with notified COVID-19 (RT-PCR) as identified through the NHS Blood and Transplant registry with linkage to Public Health England and the NHS Digital Tracing Service | England, UK | 1 February to 20 May | 489 (of 33,972 kidney-only or kidney-pancreas recipients): compared with 188/4241 patients active on the waiting list | • Comorbidities: cardiovascular disease 16/40 (40%), respiratory disease 9/40 (23%), diabetes 19/40 (48%); ACEI/ARB 15/40 (38%)<br>• Time since kidney transplant (y): median 7 (IQR 3–15)<br>• Induction IS: ATG 18/40 (44%), anti-CD25 19/40 (46%), none 3/40 (7%)<br>• Baseline IS: tacrolimus 21/40 (53%), ciclosporin 14/40 (35%), MMF/MPA 34/40 (85%), mTORi 6/40 (15%), azathioprine 1/40 (3%), corticosteroids 23/40 (58%), belatacept 2/40 (5%), eculizumab 1/40 (3%)<br>• Diarrhea 12/40 (30%)<br>• Neurological symptoms 15/40 (38%)<br>• RT-PCR negative 2/40 (5%); subsequent serology positive 2/2 (100%)<br>• Viral load (log copies/reaction) 5.2 (3.8–6.7)<br>• Death 18/40 (45%)<br>• mTORi withdrawal 6/6 (100%)<br>• Belatacept delayed 1/2 (50%)<br>• High-dose corticosteroids 14/40 (35%) | death) 18/40 (45%)<br>• RNAemia 8/31 (26%)<br>• Seropositivity 31/31 (100%) (survivors only >14 d)<br>• Tocilizumab 4/40 (10%) | • Deaths 12/489 (26%) (vs 18/188 [10%] in waitlisted patients) |
in only a few studies, in a small number of patients. Eleven studies reported the use of an anti–interleukin-6 therapy. Pérez-Sáez et al.\textsuperscript{14} described the experience of tocilizumab use based on inpatient cases entered to the Spanish Society of Nephrology registry.

Outcomes

Inpatient mortality was calculated where possible as a proportion from patients with completed outcomes (i.e., death or recovery to discharge), with the intention of reducing bias by misclassification of patients who remain hospitalized but may die later. In the largest national registry reports, mortality was 43% among mostly inpatients with completed outcomes in Sánchez-Álvarez et al.\textsuperscript{12} from Spain up until April 11, and 26% in mostly inpatients reported by Ravanan et al.\textsuperscript{11} from England up until May 20, although the number of patients who may subsequently recover from both studies was not known. In the largest multicenter series, Cravedi et al.\textsuperscript{17} reported 32% mortality in 144 inpatients, although it did not specify how many recovered to discharge, whereas Kates et al.\textsuperscript{10} reported 28-day mortality as 18% from its dataset in which 254 of 318 patients were hospitalized. Of other studies from which inpatient mortality could be calculated, mortality was 7 of 39 patients (18%) in Lubetzky et al.\textsuperscript{22} across New York, 6 of 29 patients (21%) in both Rodriguez-Cubillo et al.\textsuperscript{24} in Madrid and Chen et al.\textsuperscript{27} in New York City, 15 of 42 patients (36%) in Bossini et al.\textsuperscript{25} in Brescia, and 9 of 25 patients (36%) Mohamed et al.\textsuperscript{20} in London.

Cravedi et al.\textsuperscript{17} found 7% increased mortality in people aged >60 years compared with those aged ≤60 years. In subgroup reports from the national registry in Spain, Pascual et al.\textsuperscript{15} reported 46% mortality among patients within 60 days of transplantation, whereas Pérez-Sáez et al.\textsuperscript{14} reported 33% mortality among patients with severe COVID-19 treated with tocilizumab.

The proportion of patients requiring intensive care was variable, from 9% of inpatients across Spain according to early registry data,\textsuperscript{12} to 42% of inpatients in the large multicenter series report by Kates et al.\textsuperscript{10} including 34% requiring mechanical ventilation.\textsuperscript{10}

Acute kidney injury was common, ranging from 41% in Kates et al.\textsuperscript{10} with 13% requiring extracorporeal renal replacement therapy, to 53% in Mehta et al.,\textsuperscript{28} although none required renal replacement therapy. There were very few reports of acute rejection, with only 1 case of 318 in Kates et al.\textsuperscript{10} Benotmane et al.\textsuperscript{26} reported RNAemia in 26% and seropositivity in 100% of survivors.

DISCUSSION

Our systematic review of the early literature up to August 11, 2020, suggests that kidney transplant recipients hospitalized with COVID-19 experience poor outcomes, especially in the early post-transplant period.

The limitations of the literature so far require appreciation. Over time, published studies evolved from reports from a small number of centers, to larger multicenter studies and national registries. To reduce bias by smaller studies, we reported only those studies with completed outcomes for at least 20 kidney transplant recipients with confirmed COVID-19. Small studies may be more likely to be published by centers who accumulate more complex or unwell patients or by centers who are affected particularly unfavorably, both of which may introduce important bias; they may also exert a period effect, reflecting more overwhelming circumstances in the earlier stages of the pandemic.

Variation in reported mortality also could be due to strong period effects, with differences in thresholds for hospitalization, availability of resources, and management practices. Data from Sánchez-Álvarez et al.\textsuperscript{12} found mortality of 43% from the Spanish Society of Nephrology COVID-19 registry in which 94% were inpatients. However, this is likely to be exaggerated as this was an early report based on data reported up to April 11, and approximately 147 patients remained alive but not yet recovered so were not included in our mortality calculation; fewer patients were admitted to intensive care compared with other reports which also may be an important period effect related to stretched resources.

The other large national registry report was Ravanan et al.\textsuperscript{11} who identified all solid organ transplant recipients from the National Health Service Blood and Transplant and linked this to confirmed COVID-19 cases through Public Health England and the National Health Service Digital Tracing Service. Of more than 30,000 prevalent kidney or kidney-pancreas recipients in England, there were 489 cases of COVID-19 of whom 128 died (26%) up to May 20.\textsuperscript{11} This was compared with deaths in 18 of 188 (10%) patients waitlisted for transplantation but this comparison should be treated with caution, as many of these will have been in-center hemodialysis patients with more access to testing for milder or asymptomatic disease than transplant recipients in the community during the period of study. It was not possible to distinguish inpatients and outpatients from the available data sources, but as data were collected up to May 20, most cases were likely to be inpatients.

Large multicenter series were published by Cravedi et al.\textsuperscript{17} and Kates et al.\textsuperscript{10} Cravedi et al.\textsuperscript{17} reported data for inpatients with COVID-19 from centers in Italy, Spain, and the United States already participating in the TANGO consortium, an
international network formed initially to investigate the recurrence of glomerular disease after transplantation. Kates et al.\textsuperscript{10} reported outcomes from a registry hosted by the University of Washington to which cases were submitted from >50 centers, >98% of which were from United States after invitations through the American Society of Transplantation and American Society of Transplant Surgeons.\textsuperscript{10} Entered data were not independently verified and its representativeness is uncertain as the extent to which cases from participating centers were systematically submitted is not known, with the authors acknowledging susceptibility to bias.

Studies from the United States reported high proportions of black patients, although no study investigated for associations between ethnicity or other socioeconomic factors with outcomes. From all solid organ transplant recipients in England, 38 of 129 Asian recipients (30%) and 27 of 95 (28%) black recipients died, compared with 79 of 334 white recipients (24%). In total, 2.4% of Asian recipients and 3.6% of black recipients have been diagnosed with COVID-19, compared with 1.0% of white recipients.\textsuperscript{11}

The withdrawal of antiproliferative drugs such as mycophenolate, an inhibitor of T- and B-cell proliferation, was practiced almost universally, in keeping with expert consensus for even mild disease.\textsuperscript{30,31} Our review highlighted the myriad of different management strategies used in different centers, including antivirals, hydroxychloroquine, corticosteroids, and tocilizumab. Establishing the effectiveness of therapies requires well-designed clinical trials; as high-risk patients, kidney transplant recipients may benefit from both prophylactic and therapeutic trials. The RECOVERY trial demonstrated mortality benefit in treatment with dexamethasone 6 mg daily for patients with COVID-19 requiring oxygen in June 2020, with the World Health Organization consequently recommending the use of systemic corticosteroids in severe and critical cases.\textsuperscript{6,12} The RECOVERY trial has stopped recruiting patients to its lopinavir/ritonavir arm because of lack of benefit.\textsuperscript{13} Few patients in studies were reported to have been treated with remdesivir.

Acute kidney injury was seen in several studies, although not all studies reported their definition and alternative terminology such as “renal failure” was also mentioned. Acute kidney injury is not uncommon in COVID-19, and its pathophysiology remains uncertain, but direct parenchymal infection and microangiopathy mediated by complex inflammatory processes have been suggested.\textsuperscript{34} In transplant kidneys, there may be additional mechanisms, such as acute rejection from underimmunosuppression, or calcineurin inhibitor toxicity through drug-drug interactions (e.g., lopinavir/ritonavir); however, there were few reports of acute rejection in our review, but there may have been less investigation for this because of unwillingness to augment immunosuppression if it were diagnosed; we did not identify any histopathological series; and case reports of biopsies are prone to bias so systematic cross-sectional or longitudinal study designs would need to be considered. Studies in the coming months and years will need to address the longer-term impact of COVID-19 on graft function and permanent graft loss.

Pascual et al.\textsuperscript{13} reported deaths in almost half the patients in Spain who acquired COVID-19 within 60 days of transplantation (11 of 24 [of 265 transplants in total] up to April 18. Nearly all were recipients of deceased donor transplants with delayed graft function reported in half, but the authors did not report whether SARS-CoV-2 infection was acquired in health care settings or in the community. Although these findings are alarming, it will also have been affected by period effects from the start of the pandemic and there may now be opportunities to better minimize transmission in acute transplantation through planning and infrastructure. Several deceased- and live-donor programs were suspended with the aim of preventing high-risk patients acquiring SARS-CoV-2 infection perioperatively, limiting the use of lymphocyte-depleting antibodies as induction agents or in treatment of severe rejection, and avoiding use of limited inpatient resources. As services are restored, outcomes should be audited closely, and the risks and benefits should be nevertheless considered on an individualized basis given the apparent increased risk with heightened immunosuppression.

As the pandemic continues, we will need to use more systematic national and international registries with appropriate control groups and linkage to other sources, such as community test results and hospital records, to allow timely, large-scale analyses that can better inform policies and practices. Serological surveys of transplant recipients using validated antibody assays could be valuable in capturing the prevalence of asymptomatic and mild infection that did not result in inpatient admission or community viral RNA testing; such surveys will be important to obtain more accurate mortality and hospitalization estimates, follow-up potential longer-term complications, and identify the factors that are associated with more favorable outcomes.

**Limitations**

In the absence of available data, we were unable to undertake time-to-event analysis, therefore we report mortality as a proportion of patients with completed outcomes to avoid misclassification of patients who remain hospitalized but may die after surviving the
study period. However, this might be biased in the opposite direction if most of those who remained hospitalized were patients who were slowly recovering and more likely to survive.

Our searches included studies in English or Chinese only, with studies meeting inclusion criteria from France, Italy, Spain, Turkey, the United Kingdom, and the United States only. Searches in more languages may have resulted in a broader perspective, including more experiences in middle-income economies. As well as studies from Europe and North America, there were studies published from China and Iran from early in the pandemic that did not fulfill our criteria for inclusion because of smaller numbers of confirmed cases. It would be beneficial to obtain updated reports from centers such as these, as well as others in Africa, Asia, and Latin America.

The Newcastle-Ottawa Quality Assessment Scale was of limited value in objective quality assessment. It is designed to be semi-quantitative, but the crude equivalence of all the constituent assessment items may be misleading.

**CONCLUSION**

Our review of the literature in the early phase of the COVID-19 epidemic suggests that hospitalized kidney transplant recipients with COVID-19 are at a high risk of death. The quality of observational data is improving. Detailed and comprehensive data collection through registries and linkage with health records will be necessary to conduct analyses of risk factors for adverse outcomes, not least given the risks of stopping immunosuppression. Indeed, to optimize clinical care, we should ensure that nonhospitalized patients are included and existing registries are supported and commissioned to answer important questions that affect screening and management.

We are reassured that we have developed a reproducible search strategy that can be effectively redeployed at appropriate intervals during the pandemic and beyond to be able to conduct meta-analyses of accumulating data in the future.

**DISCLOSURE**

All the authors declared no competing interests.

**ACKNOWLEDGMENTS**

We are grateful to the authors of Manganaro et al., Kates et al., and Mohamed et al. for providing additional data and clarifications as requested.

Insilica, LLC, owners of Sysrev, gifted the review team a grant worth $2000 total to support screening and data extraction. This research did not receive any other specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**SUPPLEMENTARY MATERIAL**

**Supplementary Material S1.** Initial search. Tables S1 and S1.1–S1.4 and Appendices S1.5–S1.8.

**Supplementary Material S2.** Updated searches. Tables S1 and S2.1, Appendices S2.2 and S2.3, and Table S2.4.

**Supplementary Material S3.** Example data request.

**REFERENCES**

1. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382:1199–1207.

2. Miller IF, Becker AD, Grenfell BT, Metcalf CJ E. Disease and healthcare burden of COVID-19 in the United States. *Nat Med*. 2020;26:1212–1217.

3. 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.

4. Phua J, Weng L, Ling L, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir Med*. 2020;8:506–517.

5. Alhazzani W, Möller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med*. 2020;46:854–887.

6. RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19—Preliminary Report [e-pub ahead of print]. *N Engl J Med*. https://doi.org/10.1056/nejmoa2021436. Accessed September 19, 2020.

7. Linares L, Cofán F, Cervera C, et al. Infection-related mortality in a large cohort of renal transplant recipients. *Transplant Proc*. 2007;39:2225–2227.

8. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *ACP J Club*. 1995;123:A12–A13.

9. Deeks JJ, Dinnes J, D’Amico R, et al. Evaluating non-randomised intervention studies. *Health Technol Assess (Rocky)*. 2003;7:1–173. iii–x.

10. Kates OS, Haydel BM, Florman SS, et al. COVID-19 in solid organ transplant: a multi-center cohort study [e-pub ahead of print]. *Clin Infect Dis*. doi:https://doi.org/10.1093/cid/ciaa1097. Accessed September 9, 2020.

11. Ravanan R, Callaghan CJ, Mumford L, et al. SARS-CoV-2 infection and early mortality of waitlisted and solid organ transplant recipients in England: a national cohort study. *Am J Transplant*. 2020;20:3008–3018.

12. Sánchez-Álvarez JE, Fontán MP, Martín CJ, et al. Status of 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.

13. Pascual J, Meliili E, Jiménez-Martín C, et al. COVID-19–related mortality during the first 60 days after kidney transplantation. *Eur Urol*. 2020;78:641–643.
14. Pérez-Sáez MJ, Blasco M, Redondo-Pachón D, et al. Use of tocilizumab in kidney transplant recipients with COVID-19 [e-pub ahead of print]. *Am J Transplant*. https://doi.org/10.1111/ajt.16192. Accessed September 19, 2020.

15. 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.

16. Manganaro M, Baldovino S, Besso L, et al. First considerations on the SARS-CoV-2 epidemic in the Dialysis Units of Piedmont and Aosta Valley, Northern Italy. *J Nephrol*. 2020;33:393–395.

17. Cravedi P, Mothi SS, Azzi Y, et al. COVID-19 and kidney transplantation: results from the TANGO International Transplant Consortium. *Am J Transplant*. 2020;20:3140–3148.

18. Boyarsky BJ, Chiang TPY, 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.

19. Vistoli F, Furian L, Maggiore U, Caldara R, Cantaluppi V. COVID-19 and kidney transplantation: an Italian Survey and Consensus. *J Nephrol*. 2020;33:867–880.

20. Mohamed IH, Chowdary PB, Shetty S, et al. Outcomes of renal transplant recipients with SARS-CoV-2 infection in the eye of the storm [e-pub ahead of print]. *Transplantation*. https://doi.org/10.1097/tp.0000000000003406. Accessed September 9, 2020.

21. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: Initial report from the US epicenter. *Am J Transplant*. 2020;20:1800–1808.

22. Lubetzky M, Aull MJ, Craig-Schapiro R, et al. Kidney allograft recipients, immunosuppression, and coronavirus disease-2019: a report of consecutive cases from a New York City transplant center. *Nephrol Dial Transplant*. 2020;35:1250–1261.

23. Rodríguez-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.

24. Demir E, Uyar M, Parmaksiz E, et al. COVID-19 in kidney transplant recipients: A multicenter experience in Istanbul [e-pub ahead of print]. *Transpl Infect Dis*. https://doi.org/10.1111/tid.13371. Accessed August 15, 2020.

25. 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.

26. Chaudhry ZS, Williams JD, Vahia A, et al. Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: a cohort study. *Am J Transplant*. 2020;20:3051–3060.

27. Chen TY, Farghaly S, Cham S, et al. COVID-19 pneumonia in kidney transplant recipients: focus on immunosuppression management. *Transpl Infect Dis*. 2020;22:e13378.

28. 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. *Transpl Infect Dis*. 2020:e13383.

29. Benotmane I, Gautier Vargas G, Wendling M, et al. In-depth virological assessment of kidney transplant recipients with COVID-19. *Am J Transplant*. 2020;20:3162–3172.

30. Kronbichler A, Gauckler P, Windpessl M, et al. COVID-19: implications for immunosuppression in kidney disease and transplantation. *Nat Rev Nephrol*. 2020;16:365–367.

31. Maggiore U, Abramowicz D, Crespo M, et al. How should I manage immunosuppression in a kidney transplant patient with COVID-19? An ERA-EDTA DESCARTES expert opinion. *Nephrol Dial Transplant*. 2020;35:899–904.

32. World Health Organization. Corticosteroids for COVID-19: living guidance, 2 September 2020. World Health Organization; 2020. License: CC BY-NC-SA 3.0 IGO. Available at: https://apps.who.int/iris/handle/10665/334125. Accessed December 8, 2020.

33. Griffin S. Covid-19: Lopinavir-ritonavir does not benefit hospitalized patients, UK trial finds. *BMJ*. 2020;370:m2650.

34. Batlle D, Soler MJ, Sparks MA, et al. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. *J Am Soc Nephrol*. 2020;31:1380–1383.