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Effects of Coronavirus Disease 2019 on Solid Organ Transplantation

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ABSTRACT

Background. As the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a viral pandemic, data on the clinical characteristics and outcomes of patients with SARS-CoV-2 infection undergoing solid organ transplant are emerging. The objective of this systematic review was to assess currently published literature relating to the management, clinical course, and outcome of SARS-CoV-2 infection in liver, kidney, and heart solid organ transplant recipients.

Methods. We conducted a systematic review to assess currently published literature relating to the management, clinical course, and outcome of SARS-CoV-2 infection in liver, kidney, and heart solid organ transplant recipients. Articles published through June 2020 were searched in the MEDLINE, ClinicalTrials.gov, and PubMed databases. We identified 49 eligible studies comprising a total of 403 solid organ transplant recipients.

Results. Older age, male sex, and preexisting comorbidities, including hypertension and/or diabetes, were the most common prevailing characteristics among the solid organ transplant recipients. Clinical presentation ranged from mild to severe disease, including multiorgan failure and death. We found an overall mortality rate of 21%.

Conclusion. Our analysis suggests no increase in overall mortality or worse outcome in solid organ transplant recipients receiving immunosuppressive therapy compared with mortality in the general surgical population with SARS-CoV-2. Our findings suggest that transplant surgery and its immunosuppressive effects should not be a deterrent to proper surgical care for patients in the SARS-CoV-2 era.

THE World Health Organization (WHO) declared the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that causes coronavirus disease 2019 (COVID-19) a pandemic disease on March 11, 2020 [1], and as of September 5, 2020, the WHO reported 26,468,031 cases and 871,166 deaths related to SARS-CoV-2 infection globally [2]. Despite the extraordinary burden and stress the healthcare system is experiencing because of the disease, the vast majority of surgical care cannot be delayed or indefinitely withheld. Although current data on the clinical characteristics and outcomes of patients with SARS-CoV-2 infection undergoing surgery are sparse [3], it has been postulated that major surgery combined with SARS-CoV-2 infection may induce significant inflammatory stress, imparting an increased risk of postoperative complications and mortality [4,5].

Although many institutions are delaying elective surgeries, transplant surgeries are designated as tier 3b ("do not postpone") by the Centers for Medicare and Medicaid Services [6]. Despite this designation, these solid organ transplant (SOT) recipients represent an extremely vulnerable surgical cohort: in frequent contact with healthcare personnel, chronically immunosuppressed, and having other

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Table 1. Summary of Clinical Outcomes of Severe Acute Respiratory Syndrome Coronavirus 2–positive Solid Organ Transplant Recipients, by Study

SOT	Author [reference]	Location	No. of Cases (n)	Age and Sex	Comorbidities	Immunosuppressive Regimen	Time From Transplant	Initial Presentation (Symptoms)	Treatment	Clinical Course	Outcomes
Multiple SOT types	Tschopp et al [18]	Switzerland	21 Kidney (48%) Liver (24%) >1 organ (14%) Pancreas (5%) Lung (5%) Heart (5%)	Median 56 years 71% male	HTN (67%) DM (43%) Obesity (24%)	Tac (86%) Prednisone (43%) MMF (17%) CSA (10%) Aza (10%) mTOR (5%)	Median 47 months	Fever (76%), dry cough (57%), nausea (33%) and diarrhea (33%).	Immunosuppressant modified in 14 pts (67%); HCQ, azithromycin lopinavir/ritonavir	20 pts (95%) admitted 5 pts (25%) to ICU	16 pts (80%) discharged 3 pts (15%) remain hospitalized 2 pts (10%) died
	Fernández-Ruiz et al [11]	Spain	18 Kidney (44%) Liver (33%) Heart (22%)	Median 71 years 77% male	HTN (72%) DM (50%) Cirrhosis (28%) Obesity (11%)	Prednisone (67%) MMF/MPA (61%) Tac (56%) EVE (22%) CSA (17%) Aza (6%) mTOR (6%)	Median 9.3 years	Fever (83%), gastrointestinal symptoms (28%), respiratory failure (28%)	Lopinavir/ritonavir ± HCQ (50%) HCQ monotherapy (28%) Interferon-β (17%)	2 pts (11%) required ICU and invasive mechanical ventilation 4 pts (22%) developed progressive respiratory failure 1 (6%) pt had improvement in condition	5 pts died (28%) 5 pts (28%) remain hospitalized 8 pts (44%) discharged
	Pereira et al [8]	United States	90 Kidney (51%) Lung (19%) Liver (14%) Heart (10%) Heart-kidney (3%) Liver-kidney (1%) Kidney-pancreas (1%)	Median 57 years 59% male	HTN (64%) DM (46%) CKD (63%) Chronic lung disease (19%) Dialysis (6%) Obesity (6%) Cancer (3%) HIV (1%)	CNI (86%) MMF (72%) Steroid (59%) Aza (4%) Belatacept (6%) IVIG ± pheresis (3%) mTOR (7%)	Median 6.64 years	Fever (70%), cough (59%), dyspnea (43%), fatigue (28%), myalgias (24%), diarrhea (31%)	Immunosuppressant held or reduced in majority of hospitalized pts HCQ (91%) Azithromycin (66%) Remdesivir (3%) Tocilizumab (21%) Bolus steroid (24%)	22 (24%) required outpatient care 68 pts (76%) admitted; of these, 27 (30%) had severe disease requiring intubation or admission to ICU	16 pts (18%) died 37 pts (54%) discharged
	Travi et al [19]	Italy	13 Liver (54%) Kidney (31%) Heart/kidney (15%)	Median 59 years 69% male	HTN (54%) DM (31%)	Tac (54%) CSA (38%) MMF (38%) Steroid (46%) Belatacept (8%)	Median 5.3 years	Respiratory symptoms	62% had reduction or change to immunosuppressant medication HCQ (62%) HCQ + lopinavir/ritonavir (23%) Remdesivir (8%) High-dose steroids (23%) Tocilizumab (15%)	69% developed respiratory failure	1 pt died
	Fung et al [20]	United States	10 Kidney (70%) 7 Lung (10%) 1 Heart (10%) 1 Liver (10%) 1	Median 56.5 years 60% male 6	HTN, DM, cardiovascular disease	Triple immunosuppression (70%) 7	Median 6.1 years	Fever (80%), cough (80%), dyspnea (80%), myalgia (60%), fatigue (50%)	Immunosuppressive medications decreased in 8 (80%) 2 (20%) enrolled in RCT 3 (30%) with either HCQ, azithromycin, lopinavir/ritonavir, 7 (70%) abx	70% hospitalized 30% required ICU admission; all developed ARDS and shock	5 pts (50%) discharged 2 pts (20%) remain hospitalized
	Hoek et al [21]	Netherlands	23 Kidney (65%) 15 Heart (13%) 3 Lung (13%) 3 Liver (4%) 1 Kidney-heart (4%) 1	Mean 59 years 78% male 18	HTN (83%) 19, DM (43%) 10, obese (22%) 5	CNI + MMF (61%) 14 CNI, MMF + steroid (26%) 6 Steroid (4%) 1 EVE (4%) 1	<1 year (4%) >1 year (96%)	Fever (81%) 19, cough (71%) 16, dyspnea (59%) 14	57% remained on immunosuppressive medications 13 All hospitalized pts received abx HCQ (13%) 3	83% required hospitalization 19 13% monitored at home without additional treatment 3 2 pts (9%) admitted to ICU requiring ventilation	5 (22%) died 14 (61%) recovered and discharged 4 (17%) with clinical improvement
	Hsu et al [22]	Los Angeles, CA	1 heart/kidney	39 years, male	DM, HTN, obesity, chronic foot ulcer	Tac, MMF, prednisone	3 years	Fever, headache, sore throat, dry cough, dyspnea, fatigue, myalgias	HCQ Enrolled in clinical trial	Tac, prednisone, continued for entirety of illness course, MMF held starting SD 4 Presented to ED on SD 2; home quarantine SD 3; worsening symptoms and hospitalization SD 4, discharge SD 5; readmission SD 8; worsening hypoxia and transfer to ICU ID 9; transferred out of ICU; discharged SD 15	Alive, discharged

Table 1. (continued)

SOT	Author [reference]	Location	No. of Cases (n)	Age and Sex	Comorbidities	Immunosuppressive Regimen	Time From Transplant	Initial Presentation (Symptoms)	Treatment	Clinical Course	Outcomes
	Yi et al [23]	Houston, TX	21 Kidney (57%) 12 Liver (14%) 3 Lung (10%) 2 Heart-lung (5%) 1 Liver-kidney (5%) 1 Heart-kidney (5%) 1 Kidney-pancreas (5%) 1	Mean 54.8 years 62% male 13	90% with either HTN, DM, obesity, chronic lung disease, CVD	Triple immunosuppression (81%) 17	Median of 5.58 years	95% with fever, cough SOB 20 43% with diarrhea, vomiting, abdominal pain 9	Immunosuppressive medications adjusted daily based on organ type Azith ± HCQ, tolicuzimab remdesivir, ribavirin	33% treated as outpatients 7 67% hospitalized 14 50% hospitalized pts admitted to the ICU, 36% of hospitalized requiring ventilatory support 7 ICU, 5 vent	1 pt (5%) died (heart-kidney) 4 (19%) remain in ICU 6 (29%) discharged
Heart SOT	Holzhauser et al [24]	United States	2	Pt 1: 59 years/female Pt 2: 75 years/male	Pt 1: HTN, DM, CKD Pt 2: HTN, DM, CKD, and CAV	Pt 1: Tac, MPA Pt 2: CSA, MMF	Pt 1: 8 years Pt 2: 20 years	Pt 1: Fever, myalgia, fatigue, diarrhea, productive cough Pt 2: Fever, cough, diarrhea, fatigue, anorexia	Pt 1: Cefepime, vancomycin, oseltamivir, HCQ, tocilizumab, doxycycline, IVIG, lopinavir/ritonavir, micafungin, SMZ-TMP, tobramycin, linezolid Immunosuppressants held Pt 2: HCQ, tocilizumab, methylprednisolone MMF held	Pt 1: Respiratory failure, renal failure, and ARDS requiring intubation Pt 2: Required noninvasive respiratory support; clinical improvement over course of hospitalization	Pt 1: Died Pt 2: Alive, discharged
	Li et al [25]	China	2	Pt 1: 51 years/male Pt 2: 43 years/male	Pt 1: HTN Pt 2: Hyperlipidemia, IGT	Pt 1: Tac, MMF Pt 2: Tac, MMF	Pt 1: 17 years Pt 2: 3 years	Pt 1: Fever, chills, fatigue, anorexia, diarrhea Pt 2: Fever	Pt 1: Levofloxacin ribavirin, moxifloxacin, ganciclovir, IVIG, methylprednisolone, Umifenovir Pt 2: Ceftriaxone, ganciclovir, moxifloxacin, Umifenovir	Pt 1: Hospital admission MMF and Tac held 5 days Pt 2: Home quarantine followed by hospitalization for 5 days	Pt 1: Alive, discharged Pt 2: Alive, discharged
	Russell et al [26]	United States	1	3 years/female	EBV	Tac	25 months	Productive cough, rhinorrhea, nasal congestion	IVIG	Hospital admission; remained clinically stable with mild clinical course	Alive, discharged
	Latif et al [27]	United States	28	Median 64 years 79% male	HTN (71%) DM (61%), CAV (57%) Obesity (25%)	CNI (96%), MMF (68%) Steroid (68%) Sirolimus/EVE (18%)	Median 8.6 years	Fever (83%), dyspnea/cough (91%), gastrointestinal symptoms (48%)	22 pts (79%) had change in immunosuppressant medications on hospitalization HCQ (78%), High-dose steroid (47%) IL-6-ra (26%) HCQ (95%) Dexamethasone (55%) Tocilizumab (30%)	6 pts (21%) managed outpatient 22 pts (79%) hospitalized 7 pts (25%) required mechanical ventilation	7 admitted pts (25%) died 11 admitted pts (50%) discharged 4 admitted pts (18%) remain hospitalized
Kidney SOT	Alberici et al [28]	Italy	20	Not reported	Not reported	Not reported	Not reported	Not reported		4 pts (20%) admitted to ICU	5 pts (25%) died 3 pts (15%) discharged
	Banerjee et al [29]	England	7	Median age 54 years (range, 45-69) Pt 1: 48/male Pt 2: 67/female Pt 3: 54/female Pt 4: 65/male Pt 5: 69/female Pt 6: 54/male Pt 7: 45/male	Pt 1: HTN Pt 2: DM, HTN Pt 3: Post-transplant diabetes mellitus, CMV Pt 4: HTN, wheelchair bound Pt 5: DM, HTN Pt 6: HTN, hemolytic anemia Pt 7: HTN	Pt 1: Aza, prednisolone Pt 2: Tac, MMF, prednisolone Pt 3: Tac, MMF, prednisolone Pt 4: Tac, MMF, prednisolone Pt 5: Tac, MMF, prednisolone Pt 6: Tac, MMF Pt 7: Tac, Aza, prednisolone	Pt 1: 31 years Pt 2: 1 year Pt 3: 3 months Pt 4: 2 years Pt 5: 2 months Pt 6: 7 years Pt 7: 3 years (second transplant)	Respiratory symptoms (cough, shortness of breath) and fever Pt 5 presented with respiratory symptoms, fever plus vomiting and diarrhea	Pt 1: Aza, prednisolone continued Pt 2: MMF stopped; Tx with broad-spectrum abx in ICU; Tac d/c 1 day before death Pt 3: Tac and MMF stopped; Tx with broad-spectrum abx, oseltamivir; Empiric tx for pneumocystis with high-dose cotrimoxazole Pt 4: MMF stopped Pt 5: MMF stopped; Tx with doxycycline, piperacillin-tazobactam, paracetamol, furosemide, and blood transfusion Pt 6: MMF stopped Pt 7: Aza stopped, Tac dose reduced, prednisolone dose increased	Pt 1: Remained at home Pt 2: Hypoxic, transferred to ICU, required ventilation; developed AKI, severe metabolic acidosis Pt 3: Hypoxic on presentation, started on CPAP; rapid deterioration of respiratory status requiring ventilation Pt 4: Admitted to ICU; stepped down to medical ward Pt 5: Brief ICU stay for respiratory support, not intubated; stepped down to ward Pt 6: Developed AKI, continued to remain symptomatic, and MMF stopped Pt 7: Admitted, managed in the ward; developed severe AKI, required one hemodialysis session	Pt 1: Full recovery Pt 2: Died 12 days after hospitalization Pt 3: Alive, remains on ventilation Pt 4: Alive, requires 4 to 6 L oxygen to maintain saturation Pt 5: Alive, in inpatient ward Pt 6: Stayed at home; alive with continued cough and some flulike symptoms Pt 7: Alive, in inpatient ward

Arpali et al [30]	Turkey	1	28 years/female	Not reported	Tac and prednisone	6 months	Fever, malaise, sore throat, rhinorrhea	Continued on Tac and prednisone; oseltamivir given at second ED visit	Initially presented to ED, treated with amoxicillin, no SARS-CoV-2 testing done; presented following day to ED with high fever, swabbed for SARS-CoV-2, sent home; 6 days later, testing result positive and returned to hospital to be monitored; discharged after 24 hours	Alive, at home, reports no symptoms
Guillen et al [31]	Spain	1	50 years/male	HTN	Tac, EVE, prednisone	4 years (third deceased donor transplant)	Fever, vomiting	Ceftriaxone, azithromycin, ceftaroline, meropenem, lopinavir/ritonavir, HCQ, interferon-β, Tac and EVE held due to potential DDI	Presented to ED and discharged with presumptive viral gastroenteritis; presented to ED 5 days later with persistent fever and productive cough, dx with CAP; tested positive for SARS-CoV-2, was placed in isolation; respiratory status worsened, requiring intubation	Remains in ICU with respiratory support
Zhu et al [32]	China	1	52 years/male	Not reported	Tac, MMF, prednisone	12 years	Fatigue, dyspnea, tightness and chest pain, nausea, loss of appetite, intermittent abdominal pain, occasional dry coughs, fever, headache	Tac, MMF, prednisone discontinued; restarted at full dose 3 days prior to discharge Umifenovir, moxifloxacin, methylprednisolone, IVIG, interferon alpha, carbapenem, pantoprazole	Presented to fever clinic, laboratory findings and chest CT suggestive of SARS-CoV-2 Symptoms worsened at home and admitted to hospital on SD 8; required oxygen via NC; symptoms improved over course of hospitalization; discharged on SD 21	Alive, discharged to home
Marx et al [33]	France	1	58 years/male	Not reported	Belatacept, MMF, prednisone	3 years	Fever, mild dyspnea, cough	MMF and belatacept discontinued on admission to hospital; CSA started but plan to d/c this and restart MMF and belatacept at next date of infusion	Pt admitted to hospital; treated for possible bacterial superinfection but reported to have mild hospital course	Alive, resolution of fever and respiratory symptoms 5 days after discharge
Gandolfini et al [34]	Italy	2	Pt 1: 75 years/male Pt 2: 52 years/female	Pt 1: COPD, heart disease, HTN, obesity Pt 2: HTN	Pt 1: Tac, MMF, steroid Pt 2: Tac, MMF, steroid	Pt 1: 120 months Pt 2: 8 months	Cough, myalgia, fever, dyspnea	MMF and Tac were discontinued on the day of admission; both patients received hydroxychloroquine and lopinavir/ritonavir or darunavir/cobicistat Pt 2: Colchicine	Both patients required noninvasive ventilation Pt 1: Abrupt worsening of respiratory conditions and died 5 days after admission Pt 2: Respiratory symptoms worsened and received colchicine; respiratory symptoms improved after drug initiation	Pt 1: Died Pt 2: Alive, remained on noninvasive ventilation
Akalin et al [35]	United States	36	Median of 60 years 72% males	HTN (94%), DM (70%) History of smoking tobacco or current smokers (36%) CVD (17%)	Tac (97%) Prednisone (94%) MMF (86%)	Not reported	Fever (58%), diarrhea (22%)	Of hospitalized pts: Antimetabolite held in 86% Tac held in 21% HCQ (86%) 21% received leronlimab on a compassionate-use basis 7% received tocilizumab	8 pts (22%) in stable condition were monitored at home 28 pts (78%) were admitted to the hospital; 11 pts (39%) received mechanical ventilation, 6 pts (21%) received renal replacement therapy	10 (28%) pts died, including 2 pts who had been monitored as outpatients 12 pts (43%) remained hospitalized 10 pts (36%) hospitalized discharged to home
Chen et al [36]	China	1	49 years/male	HTN	Tac, MMF, prednisone	7 years	Loss of appetite, fever	MMF, Tac, and prednisone held Umifenovir, methylprednisolone, moxifloxacin, IVIG, ribavirin	Progressive worsening of cough, shortness of breath, hypoxic, fever; required inhaled oxygen and transferred to respiratory intensive care; symptoms gradually improved over course of hospitalization	Alive, discharged to home
Fontana et al [37]	Italy	1	61 years/male	CKD, malignancy, coagulopathy, Parkinson disease	CSA, steroid	15 years	Fever/chills	CSA held, steroid increased HCQ, tocilizumab, azithromycin, meropenem	Remained hemodynamically stable throughout hospitalization	Alive, discharged to home

Table 1. (continued)

SOT	Author [reference]	Location	No. of Cases (n)	Age and Sex	Comorbidities	Immunosuppressive Regimen	Time From Transplant	Initial Presentation (Symptoms)	Treatment	Clinical Course	Outcomes
	Zhang et al [38]	China	5	Mean 45 years 80% male 4	HTN (40%), 2 DM (40%), 2 Malignancy (20%), 1	MMF, CNI, and steroid (80%) 4	Range of 2 months to 4 years	Fever (100%), cough (100%), myalgia/ fatigue (60%), 3 Sputum (60%) 3	Oseltamivir or arbidol (100%) Abx (20%) 1 IVIG (20%) 1	Immunosuppressant modified after symptom onset All pts hospitalized; resolution of symptoms in 4 (80%) None required intubation or ICU admission	2 (40%) discharged 3 (60%) remain hospitalized
	Abrishami et al [39]	Iran	12	Mean 47.66 years 75% male	HTN (17%)	All on triple therapy (steroid, CNI/sirolimus, MMF/Aza)	Not reported	Fever (75%), cough (75%), dyspnea (42%)	HCQ, lopinavir/ritonavir, abx (100%) IVIG given if pt hypoxic	Immunosuppressant modified for all 100% pts hospitalized; 10 (83%) admitted to ICU; 90% in ICU were intubated	8 (67%) died 4 (33%) discharged
	Columbia University Kidney Transplant Program [40]	United States	15	Median 51 years 65% male 10	Not reported	Tac (93%) 14 MMF/MPA (80%) 12 Prednisone (67%) 10 Belatacept (13%) 2 Leflunomide (7%) 1 Aza (7%) 1	Median 49 months	Fever (87%), 13 Cough (60%), 9 Diarrhea (20%), 3 Myalgias (13%) 2	93% had immunosuppressant regimen changed 14 HCQ ± azithromycin (87%) 13 Tocilizumab (7%) 1	4 (27%) required intubation 6 (40%) developed AKI	2 (13%) died 8 (53%) discharged 6 (40%) remain hospitalized
	Nair et al [41]	United States	10	Median 57 years 60% male 6	HTN (100%), majority also with DM	Tac + MMF/MPA (90%) 9 Steroid (70%) 7 7	Median 7.7 years	Fever, cough, myalgia, fatigue, diarrhea	Hospitalized patients had antimetabolite agent stopped HCQ + azithromycin (100%) Antibiotic (60%)	90% hospitalized 9 5 (50%) admitted to ICU 5 (50%) developed acute kidney injury.	3 (30%) died 7 (70%) discharged
	Zhu et al [32]	China	10	Age between 24 and 65 years 80% male	HTN, CAD, COPD, atrial fibrillation, HF (60%)	Tac (90%) MMF (90%) Steroid (70%) CSA (10%) Mizoribine (10%)	6 mo to 12 years	Fever (90%), cough (90%), shortness of breath (90%), fatigue (90%), diarrhea (30%)	Immunosuppressant medication modified in 90% Methylprednisolone (80%) IVIG (70%) Antiviral (100%)	Mild symptoms in 20% Severe symptoms in 50% Critical symptoms in 30% 100% received NC 30% required noninvasive mechanical ventilation None underwent intubation	80% recovered 1 (10%) remained hospitalized 1 (10%) died
	Machado et al [42]	Brazil	1	69 years/male	HCV, DM, HTN	Tac, MMF, prednisone	6 years	Fever, fatigue, confusion, diarrhea, decreased urine output	MMF held, Tac decreased, prednisone increased on hospitalization HCQ, nitazoxanide, ceftriaxone, azithromycin	Developed mild AKI and severe metabolic acidosis; did not require supplemental oxygen; improved over course of hospitalization	Alive, discharged
	Kim et al [43]	Korea	2	Pt 1: 37 years/male Pt 2: 56 years/male	Not reported	Pt 1: Tac, MMF, prednisolone Pt 2: Tac, MMF, prednisolone	Pt 1: 4 years Pt 2: 8 years	Pt 1: Fever, cough, rhinorrhea, diarrhea, and decreased urine output Pt 2: Asymptomatic	Pt 1: MMF, tac held; Lopinavir/ritonavir and HCQ Pt 2: MMF held; HCQ with azithromycin	Pt 1: Improvement in clinical course and kidney function; did not require supplemental oxygen Pt 2: Remained hemodynamically stable with mild symptoms (cough); did not require supplemental oxygen	Pt 1: Recovered Pt 2: Recovered
	Seminari et al [44] Wang et al [45]	Italy China	1 1	50 years/male 49 years/male	HTN, DM HTN, DM	Tac, MMF CSA, MMF, prednisone	4 years 2 years	Fever, cough Fever, respiratory symptoms	Ceftriaxone Immunosuppressant medications continued Lopinavir/ritonavir, ribavirin, interferon-α2b, methylprednisolone	Improvement in clinical course Required supplemental oxygen; respiratory status improved over course of admission	Alive, discharged Recovered
	Billah et al [46]	United States	1	44years/M	Not reported	Tac, MMF, prednisone	7 years	Dyspnea	Immunosuppressant medications continued Methylprednisolone	Developed AKI requiring dialysis; Intubated for respiratory failure	Remains both dialysis and ventilator dependent
	Cheng et al [47]	China	2	Pt 1: 48 years/male Pt 2: 65 years/female	Pt 1: Not reported Pt 2: Not reported	Pt 1: Tac, MMF, prednisone Pt 2: Tac, MMF, prednisone	Pt 1: 11 years Pt 2: 9 years	Pt 1: Fever, chest tightness Pt 2: Fever, cough, chest tightness, myalgia	Pt 1: Immunosuppressant medications held; methylprednisolone Pt 2: Immunosuppressant medications held; moxifloxacin, Umifenovir, IVIG, methylprednisolone	Pt 1: Symptomatic supportive treatment with improvement in clinical course Pt 2: Respiratory symptoms initially deteriorated; required supplementary oxygen; gradual improvement in clinical course	Pt 1: Alive, discharged Pt 2: Alive, discharged

	Crespo et al [48]	Spain	16	Median 73.6 years 75% male 12	HTN (88%) 14, DM (50%) 8, heart disease (50%) 8, obesity (44%) 7, malignancy (31%) 5, lung disease (19%) 3	CNI (88%) 14 prednisone (81%) 13, MMF (50%) 8, mTOR (31%) 5, TCDA (19%) 3	Not reported	Fever (100%), dyspnea (75%) 12 myalgia (50%) 8, diarrhea (25%) 4	Tac held in 70%, MMF and mTOR held in all 16 Abx (88%), 14 HCQ (81%) 13, steroid (38%) 6 ritonavir-lopinavir/darunavir (31%), 5 tocilizumab (25%) 4	15 pts (94%) hospitalized 6 pts (40%) required ICU admission	8 pts (53%) died
	Ning et al [49]	China	1	29 years/male	HTN	MMF, CSA, methylprednisolone	2 years	Fever/chills, fatigue	Immunosuppressant medications continued SMZ-TMP, moxifloxacin, lopinavir/ritonavir	Developed oliguria and hyponatremia; clinical course improved over course of admission	Resolution and discharge
	Bush et al [50]	United States	1	13 years/male	Chronic severe constipation, rectal prolapse, cecostomy, colostomy with colonic resection	Sirolimus, MMF	6 years	Rhinorrhea, cough, fever	MMF and sirolimus reduced Antibiotics	Required NC; remained hemodynamically stable	Alive, discharged to home
	Kumar et al [51]	United States	1	50 years/male	HIV, HTN, asthma, steatohepatitis	Tac, MMF	14 months	Fever/chills, nasal congestion, cough	Not reported	Not admitted, enrolled in COVID home monitoring program	Health improved to baseline
Liver SOT	Maggi et al [52]	Italy	2	Pt 1: 61 years/male Pt 2: 69 years/M	Pt 1: Not reported Pt 2: HIV	Basiliximab, prednisolone, and Tac	Pts developed SARS-CoV-2 infection during hospitalization for transplant	Pt 1: Fever POD 9 Pt 2: Not reported	Not reported	Pt 1: Presented with fever POD 9 but with normal chest x-ray findings Pts 2: Tested positive for SARS-CoV-2 on POD 22	Pt 1: Alive Pt 2: Died on POD 30
	Bhoori et al [53]	Italy	3	>65 years/male	HTN, hyperlipidemia, DM (100%)	CSA (67%) Tac (33%)	>10 years	Respiratory symptoms similar to CAP	Not reported	100% required supplementary oxygen at admission but rapidly developed severe respiratory distress syndrome that required mechanical ventilation	100% died between 3 and 12 days after the onset of pneumonia Authors report 3 recently (within last 2 years) transplanted patients with positive test result for SARS-CoV-2 (on full imuunosuppression); all experienced uneventful course of disease (no further details about this cohort provided)
	D'Antiga et al [54]	Italy	3	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	None developed clinical pulmonary disease	Not reported
	Qin et al [55]	China	1	37 years/male	Not reported	Tac, glucocorticoid	Pt developed SARS-CoV-2 infection during hospitalization for transplant	Fever following chemoembolization on day 3 of hospitalization; persistent fever noted 2 days after transplant (transplant occurred on day 7 of hospitalization)	Osteltamivir, rh-GCSF, IVIG started after confirmation of infection Tac and glucocorticoids titrated to lower dose and then increased on day 40 of hospitalization given concerns for acute cellular rejection	Presented with fever following hepatic arterial chemoembolization; continued to have persistent fever 2 days following embolization; RT-PCR confirmed infection; fever subsided on day 33 of hospitalization	Alive, discharged to home
	Lagana et al [56]	United States	1	6 months/female	Not reported	Not reported	Pt developed SARS-CoV-2 infection during hospitalization for transplant	Respiratory distress, fever, diarrhea Notably, donor tested positive on POD 2 (symptoms not reported)	HCQ	Fever with increased work of breathing on POD 4; admitted to ICU	Pt remained in hospital with mild respiratory symptoms
	Huang et al [57]	China	1	59 years/male	Hepatitis B	Tac, MMF	3 years	Fever, cough, chills, fatigue, diarrhea, jaundice, ascites, splenomegaly	Nebulized α-interferon, umifenovir, lopinavir/ritonavir, methylprednisolone, albumin, blood, plasma, IVIG; multiple antimicrobials, including caspofungin, voriconazole, piperacillin tazobactam, cefoperazone -sulbactam, meropenem Tac and MMF dosages halved due to DDI with lopinavir/ritonavir	Respiratory failure on day 4 of hospitalization, placed on NC; hypoxemia worsened requiring intubation; on day 12, blood cx positive for *Candida*, pleural fluid positive for *Pseudomonas*; ECMO on day 15 due to worsened respiratory status; condition deteriorated to multiorgan failure	Pt died on day 45 of admission

Table 1. (continued)

SOT	Author [reference]	Location	No. of Cases (n)	Age and Sex	Comorbidities	Immunosuppressive Regimen	Time From Transplant	Initial Presentation (Symptoms)	Treatment	Clinical Course	Outcomes
	Bin et al [58]	China	1	50 years/male	Not reported	Tac	3 years	Fever	Umifenovir, lopinavir/ritonavir, methylprednisolone, IVIG, alpha interferon, antibiotics Tac held on admission to hospital; increased to full dose on discharge	Pt became progressively dyspneic requiring NC on day 5 of hospitalization; symptoms resolved on day 21; discharged after 4 weeks of hospitalization	Alive, at home
	Lee et al [59]	United States	38	Median 60 years	For hospitalized pts (n = 24): CKD (71%) 17 HTN (71%), 17 DM (50%), 12 cardiovascular disease (42%), 10 obesity (42%),10	For hospitalized pts (n = 24): Tac (96%) 23 CSA (4%) 1 MPA (54%) 13 Steroid (50%) 12	Not reported	Gastrointestinal symptoms (42%) 10	Immunosuppression was decreased in 79% of hospitalized patients 19 18 (75%) received HCQ + azithromycin 5 (21%) received glucocorticoid 8 (33%) received anticoagulant	63% hospitalized 18 (75%) required supplemental oxygen 8 (33%) required mechanical ventilation	7 (29%) died 3 (13%) remain hospitalized 14 (58%) discharged
	Patrono et al [60]	Italy	10	Pt 1: 69 years/male Pt 2: 59 years/male Pt 3: 56 years/male Pt 4: 58 years/male Pt 5: 64 years/female Pt 6: 64 years/male Pt 7: 64 years/male Pt 8: 62 years/male Pt 9: 75 years/male Pt 10: 85 years/female	Pt 1: None Pt 2: Obesity Pt 3 through Pt 10: Not reported	Pt 1: MMF, Tac, prednisone Pt 2: Tac, EVE Pt 3: Tac, EVE Pt 4: MMF, Tac, prednisone Pt 5: Tac, prednisone Pt 6: MMF, Tac Pt 7: MMF, Tac Pt 8: MMF, Tac Pt 9: MPA, Tac Pt 10: Tac	Pt 1: 5 days Pt 2: 8 months Pt 3: 3 years Pt 4: 2 months Pt 5: 4 years Pt 6: 8 years Pt 7: 9 years Pt 8: 11 years Pt 9: 11 years Pt 10: 22 years	Pt 1: Cough Pt 2: Fever, diarrhea, dyspnea Pt 3: Fever, odonyphagia, cough Pt 4: Asymptomatic Pt 5: Fever, anorexia, diarrhea Pt 6: Fever Pt 7: Fever Pt 8: Fever Pt 9: Fever, diarrhea, myalgia, cough Pt 10: Asymptomatic	6 patients were administered HCQ, 3 high-dose steroids, and 2 antivirals (lopinavir/ritonavir and darunavir/ritonavir) 6 patients were administered HCQ, 3 high-dose steroids and 2 antivirals (lopinavir/ritonavir and darunavir/ritonavir) 6 (60%) HCQ, 3 (30%) high dose steroids, 2 (20%) antivirals	Pt 1: Asymptomatic Pt 2: Required supplemental oxygen; gradual symptom improvement Pt 3: Mild symptoms followed by dyspnea requiring supplemental oxygen; clinical course improved Pt 4: Tested positive 2 months after discharge for transplant Pt 8: Contracted infection during hospitalization for head trauma Pt 10: Incidentally found to be positive Pt 5-7, 9: Not reported	Pt 1: Alive Pt 2: Alive Pt 3: Alive Pt 4: Alive Pt 5: Alive Pt 6: Alive Pt 7: Alive Pt 8: Died (unrelated to SARS-CoV-2) Pt 9: Died Pt 10: Alive
	Hammami et al [61]	United States	1	63 years/male	ESRD, DM, HTN, HF, PVD	Tac	10 years	Fever, dry cough, fatigue, headache	HCQ, ceftriaxone, azithromycin, cefepime, vancomycin, tocilizumab	Waxing and waning fever; day 10 of hospitalization developed pleuritic chest pain and severe periumbilical pain, with improvement after tocilizumab; remained afebrile thereafter	Alive
	Modi et al [62]	United States	1	32 years/male	HIV	Tac, MMF, prednisone	7 years	Fatigue, fever, headache, dry cough	MMF held, Tac reduce, prednisone continued HCQ	Admitted with mild symptoms which gradually improved over course of hospitalization	Discharge home
	Morand et al [63]	France	1	4 years/female	EBV	Tac	5 months	Rhinitis, fever, cough	Tac dose reduced Antipyretic	Improvement in clinical symptoms during hospitalization	Recovered

Abbreviations: Abx, antibiotics; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; Aza, azathioprine; CAD, coronary artery disease; CAP, community-acquired pneumonia; CAV, cardiac allograft vasculopathy; CNI, calcineurin inhibitor; CMV, cytomegalovirus; CPAP, continuous positive airway pressure; CSA, cyclosporine; Cx, culture; CMV, cytomegalovirus; CVD, cardiovascular disease; Dx, diagnosis; d/c, discontinued; DDI, drug–drug interaction; DM, diabetes mellitus; EBV, Epstein-Barr virus; ED, emergency department; ESRD, end-stage renal disease; EVE, everolimus; HCQ, hydroxychloroquine; HCV, hepatitis C virus; HF, heart failure; HIV, human immunodeficiency virus; HTN, hypertension; ICU; intensive care unit; IGT, impaired glucose tolerance; IL-6-ra, interleukin 6 receptor antagonist; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; MPA; mycophenolate acid; mTOR, mammalian target of rapamycin; NC, nasal cannula; Pt(s), patient(s); POD, postoperative day; PVD, peripheral vascular disease; RCT, randomized controlled trial; rh-GCSF, recombinant human granulocyte colony-stimulating factor; SD, symptom day; SMZ-TMP; sulfamethoxazole-trimethoprim; Tac, tacrolimus; TCDA, T-cell–depleting agents; Tx, treatment.

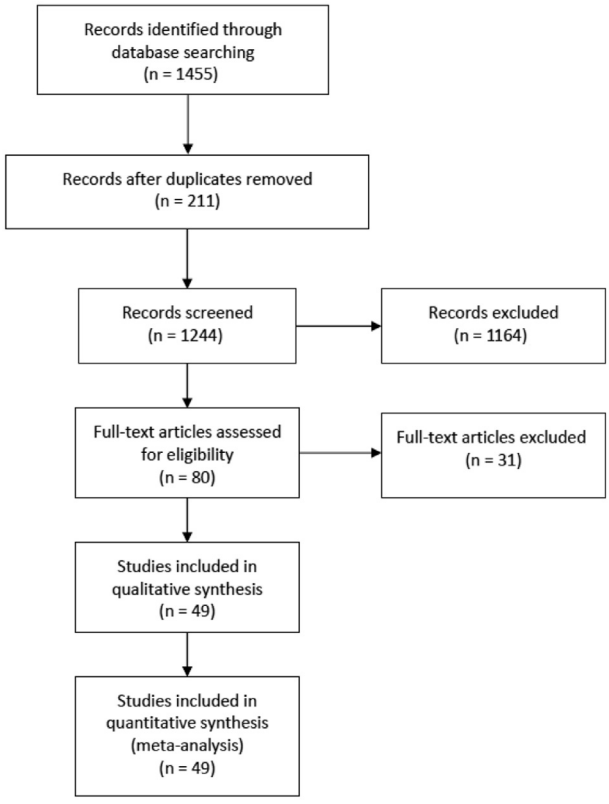

Fig 1. PRISMA flowchart.

concomitant medical conditions [7,8]. The surgical management and outcomes of SARS-CoV-2 in SOT recipients remain unclear [9], because published reports on SARS-CoV-2 positive SOT recipients and their outcomes are limited and largely unknown [9–11]. Case reports from Asia, Europe, and the United States suggest a wide range in severity of clinical symptoms from mild and nonspecific to severe respiratory distress and pneumonia [11–13]. Furthermore, reports of atypical presentations with an absence of respiratory symptoms may confound the diagnosis [12–14].

Although the American Society of Transplant Surgeons has recommended best practice guidelines for transplantation in the SARS-CoV-2 era, regional and institutional variation in transplant practice persists [15,16]. In addition, limitation and regional variance in testing pose a significant difficulty in the early identification of suspected SARS-CoV-2 cases in SOT recipients. A recent survey of 111 transplant centers in the United States found a marked reduction in transplant activity despite the tier 3b designation, a wide variation in SARS-CoV-2 testing practices, and substantial differences in the use of off-label and investigational therapies for treatment [17].

There is an urgent need to better understand the effects of SARS-CoV-2 on SOT recipients. We reviewed published literature in this rapidly evolving field to examine the current management practice; the clinical course of the disease; and the outcomes of SARS-CoV-2 infection in liver, kidney, and heart SOT recipients.

MATERIALS AND METHODS

We conducted a review of SARS-CoV-2 infection in SOT recipients according to the recommended Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.

Study Search

Articles published through June 6, 2020, were searched in the MEDLINE, ClinicalTrials.gov, and PubMed databases. A combination of the following Medical Subject Heading terms was used to identify articles discussing SARS-CoV-2 infection in solid organ transplant recipients: "coronavirus," "SarsCov," "SarsCov2," "SARS-Cov-2," "Severe Acute Respiratory Syndrome," "COVID," "COVID-19," "kidney," "heart," "liver," "solid organ transplant," "transplant," "transplantation," "outcome," and "immunosuppressant."

Inclusion and Exclusion Criteria

Only case reports, case series, and prospective and retrospective cohort studies published between 2019 and 2020 were included for final analysis and discussion. No restriction was placed on the publication status of the article. All non-English, investigational, animal, in vitro, and cadaveric studies were excluded. In addition, book chapters, conference abstracts, review articles, management guidelines, and any article that did not include discussion of clinical course, treatment, or outcomes of SARS-CoV-2 infection in SOT recipients were also excluded.

Data Collection and Analysis

Articles were screened independently by the authors. Any disagreements were reconciled through discussion between reviewers. Data extracted from each article included study type, year and month of publication, study country, number of patient cases, SOT type (heart, kidney, liver, or multiple), patient demographics, presence of comorbidities, immunosuppressant medications, time from transplant to initial presentation, initial presenting symptoms, treatment, clinical course, and outcomes (Table 1). Reporting of all of the above variables was not a requirement for article inclusion, and any unavailable variables were documented as "not reported." Data were reported using the median and interquartile range (IQR) for non-normally distributed continuous variables and absolute counts and percentages for categorical variables.

RESULTS

Study Selection

A total of 1455 citations were identified in the initial search. After removing 211 duplicates, a total of 1244 studies were screened by title and abstract (Fig 1). Studies were excluded if they did not mention SOT, SARS-CoV-2 infection, or associated clinical course and outcomes or did not fulfill the inclusion criteria. After excluding 1164 studies, we completed a full-text assessment of the remaining 80 studies. Forty-nine studies were included in our final analysis after the exclusion of 31 studies after a full-text screen. Exclusion of these 31 studies at the full-text review included the following reasons: discussed management and recommendations (n = 10), review

Table 2. Characteristics of Total Solid Organ Transplant Recipients With Severe Acute Respiratory Syndrome Coronavirus 2 Infection

	No.	%
Location		
United States	249	57.51%
Italy	55	12.7%
China	26	6%
Organ transplanted		
Kidney	252	58.2%
Liver	89	20.6%
Heart	51	11.8%
Other organ*	42	9.6%
Sex		
Male	264	61.0%
Comorbidity		
HTN	249	57.5%
DM	159	36.7%
Obesity	44	10.2%
CKD	77	17.8%
Immunosuppressive		
Tac	160	37.0%
CNI	122	28.2%
Prednisone or other steroid	217	50.1%
MMF/MPA	214	49.4%
Other immunosuppressive†	125	28.8%

Abbreviations: CKD, chronic kidney disease; CNI, calcineurin inhibitor; DM, diabetes mellitus; HTN, hypertension; MMF, mycophenolate mofetil; MPA, mycophenolic acid; Tac, tacrolimus.

*Includes lung, pancreas, and multiple solid organ transplant.

†Includes mammalian target of rapamycin, belatacept, leflunomide, mizoribine, cyclosporine, azathioprine, intravenous immunoglobulin/pheresis, basiliximab, T-cell–depleting agents, CNI + MMF, and triple therapy.

articles (n = 6), discussed impact of pandemic on transplant program volumes (n = 3), descriptive studies (n = 3), non-English (n = 1), discussed non-SOT transplant (n = 1), did not discuss SOT (n = 2), discussed SARS-CoV-2 infection in transplant surgeon or donor (n = 2), discussed investigational therapy (n = 1), discussed immunologic response (n = 1), or discussed non–transplant-related guideline (n = 1).

Study Characteristics

Of the 49 studies included, 22 were case reports, 8 were case series, and 19 were cohort studies. Four studies discussed heart SOT, 25 discussed kidney SOT, 12 discussed liver SOT, and 8 included multiple SOTs. A total of 433 SOTs were reported among all studies (Table 2). The most common SOT was the kidney with 252 (58.2%), followed by liver with 89 (20.6%), heart with 51 (11.8%), lung with 24 (5.5%), and pancreas with 1 (0.2%). Seventeen individuals (3.9%) received more than one SOT. A majority were men (n = 264; 61%). The median age was 54 years (IQR, 45-64), and the median time from transplant was 48 months (IQR, 12-108). Overall mortality was reported as 21% (Table 3).

Characteristics, Clinical Course, and Outcomes by SOT Type

Kidney. Among the 25 studies reporting solely kidney SOT, 150 recipients with SARS-CoV-2 infection were identified. Ninety-five (63.3%) were male. The most common comorbidities were hypertension (55.3%) and diabetes mellitus (26.7%). Tacrolimus (52%), mycophenolate mofetil (MMF) (56%), and prednisone/steroid (64.7%) were the most commonly used maintenance immunosuppressants. Additional immunosuppressant regimens included unspecified calcineurin inhibitors (CNIs) (12%), mTOR inhibitors (4.6%), and belatacept (2%). Fever was the most common presenting symptom (71.3%), followed by cough (39.3%) and dyspnea (26%). Ninety-three individuals (62%) were hospitalized, and 10.7% developed acute kidney injury. Mechanical ventilation, supplemental oxygen, and transfer to an intensive care unit (ICU) for a higher level of care were required in 20%, 11.3%, and 19.3% of the individuals, respectively. Nearly half (46.7%) of those reported had their maintenance immunosuppressant reduced when the infection was suspected or confirmed. The most commonly used treatments were hydroxychloroquine (HCQ) (65.3%), antibiotics (43.3%), steroids (20.7%), and lopinavir/ritonavir (15.3%). Thirty-three patients were reported as alive (22%), discharged to home (n = 45; 30%), or remaining hospitalized (non-ICU, n = 27 [18%]; ICU, n = 3 [2%]), and 26% of individuals died (n = 39).

Liver. Fifty-three liver SOT recipients were identified from 12 studies reporting liver SOT, and males comprised 28.3% of the population (n = 15). Hypertension, chronic kidney disease, and diabetes were the most common comorbidities (39.6%, 32.1%, and 30.2%, respectively). Tacrolimus (79.2%), MMF/mycophenolic acid (MPA)

Table 3. Presentation, Clinical Course, and Outcome of Total Solid Organ Transplant Recipients

	No.	%
Initial presentation		
Fever	291	67.2%
Cough	220	50.8%
Gastrointestinal symptoms	120	27.7%
Dyspnea	169	39.0%
Asymptomatic	3	0.7%
Treatment		
Immunosuppressant modified	235	54.3%
Antibiotics	178	41.1%
HCQ	242	55.9%
Methylprednisolone or other steroid	78	18.0%
Clinical course		
Hospitalized	283	65.4%
Outpatient	50	11.5%
Respiratory failure	18	4.2%
Transfer to ICU	78	18.0%
Outcome*		
Death (all studies)	91	21.0%
Kidney	39	26.0%
Heart	8	24.2%
Liver	14	26.4%

Abbreviations: HCQ, hydroxychloroquine; ICU, intensive care unit.

*Death for all studies includes studies for multiple solid organ transplant (SOT) type, including those reporting lung, pancreas, and multiple SOT, whereas death for kidney, heart, and liver SOT recipients was determined solely from studies discussing each individual organ separately.

(39.6%), and steroids (35.8%) were the most commonly used maintenance immunotherapies. Fever and gastrointestinal symptoms were the 2 most common initial presenting symptoms, followed by cough (28.3%, 28.3%, and 18.9%, respectively). Thirty-four individuals (64.2%) were hospitalized, and 45.3% subsequently had their maintenance immunosuppressant medication reduced. HCQ and antibiotics were used in 39.6% and 39.6%, respectively, for treatment of SARS-CoV-2 infection. In addition, 47.2% of individuals required supplemental oxygen during hospitalization, and 14 (26.4%) individuals died after the onset of illness.

Heart. Thirty-three individuals who underwent heart SOT were reported in 4 studies; 25 (75.8%) were male. The most common comorbidities were hypertension (69.7%), diabetes (57.6%), and cardiac allograft vasculopathy (48.5%). The most commonly used maintenance immunotherapies were CNI (81.8%) and MMF/MPA (69.7%). Fever (81.8%), cough (94.8%), dyspnea (75.8%), and gastrointestinal symptoms (48.5%) were the most common initial presenting symptoms. Twenty-seven (81.8%) patients were hospitalized, and intubation/mechanical ventilation was required in 24.2% of those individuals. Twenty-four (72.7%) patients received HCQ, and high-dose steroids were administered to 15 patients (45.5%). Maintenance immunotherapy was modified in 75.8% of the cases. Fifteen (45.5%) were reported as discharged, and 24.2% of the individuals died during their illness.

DISCUSSION

As the number of SARS-CoV-2 infections continues to grow worldwide, clinical data in SOT recipients are emerging, and our study showed overall mortality of 21% with no substantial variations among the different types of SOT (Table 3). The mortality rate is in concordance with published data in terms of outcomes reported in patients undergoing acute care surgery and cancer surgery: Lei et al, Liang et al, and the COVIDSurg Collaborative group reported mortality in the general surgical population of 20.5%, 39%, and 23.8%, respectively [4,64,65].

Older age, male sex, and preexisting conditions such as hypertension and diabetes were the most common characteristics among the SOT recipients. As predicted, we saw a broad spectrum of clinical courses ranging from having only a few mild symptoms to multiorgan failure leading to death. Despite the concerns of atypical disease presentation in immunocompromised patients, the most common presenting symptoms were similar to general population symptoms [7,66,67]; however, there were some variations in the incidence of the initial presenting symptoms among the different SOT types (Table 1).

Modification of immunosuppressant therapy at confirmation or suspicion of SARS-CoV-2 infection was reported in 54.3% of the patients, reflecting individualized adjustment based on the severity of the disease, type of transplanted organ, interval time since transplant, and risk of rejection [8]. On a similar note, the American Association for the Study of Liver Diseases recently published management guidelines for liver transplant recipients in the COVID era [68]: continuing the routine immunosuppressive regimen in nonsymptomatic recipients and reducing the immunosuppression regimen, including prednisone, azathioprine, or MMF and CNI in symptomatic patients with COVID-19. Our study suggests that the current practice of reducing immunosuppression upon the diagnosis of SARS-CoV-2 infection appears to be an appropriate measure without causing significant short-term adverse effects on graft function while maintaining patient survival comparable to that of the general population.

The median time from transplant to infection was 48 months in our study; the majority of the studies focused on patients who had received SOTs many years ago. Although it is a small number, we identified 4 cases in which the SOT recipient contracted SARS-CoV-2 infection during the transplant perioperative period, and we found no significant difference in their initial presentation, clinical course, and outcome when compared with a cohort of patients who received a transplant more than 1 year ago.

Although our study provides a general overview of SOT recipients' clinical course and outcomes with SARS-CoV-2 infection, we recognize several limitations of the study. First, the inclusion of early case reports may be biased toward those with increased severity of disease and worse outcome, leading to publication bias with overinterpretation. Second, the inclusion of a mixed transplant population and a wide heterogeneity in study inclusion criteria may not be a true representation of the study samples and therefore precluded the ability to derive causality. Furthermore, data were based on absolute counts and therefore can be used only for descriptive purposes. Last, a certain degree of reporting bias inevitably played a role because SOT recipients are trained to be more vigilant with their health conditions and have a low threshold for seeking medical attention. This reporting bias could have led to more disease diagnosis in our study group than in the general population.

In conclusion, SARS-CoV-2 infection in SOT recipients in general appears to have similar presentation, clinical course, and outcome as in the general non-SOT surgical population. We found that the patient demographics, preexisting risk factors, and outcomes were similar within each SOT type, and we saw no substantial differences in mortality rate among the different SOT types. Although our data show that the overall short-term survival is about the same, long-term patient survival and graft function data are needed to fully understand the impact of COVID in SOT patients.

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