Journal of Infection and Public Health 15 (2022) 365–372

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: www.elsevier.com/locate/jiph

Original article

Clinical characteristics and outcome of coronavirus disease 2019 infection in patients with solid organ transplants: A systematic review and meta-analysis

Wen An[a,1], Qiuyang Wang[b], Tae-Eun Kim[c], Ju-Seop Kang[a,*,2]

[a] Department of Pharmacology & Clinical Pharmacology, College of Medicine, Hanyang University, Seoul, South Korea
[b] Department of Central China Research Institute of Health, Xinxiang Medical University, Xinxiang, China
[c] Department of Clinical Pharmacology, Konkuk University Hospital, Seoul, South Korea

ARTICLE INFO

Article history:
Received 6 October 2021
Received in revised form 3 January 2022
Accepted 6 February 2022

Keywords:
COVID-19
Solid organ transplantation
Meta-analysis
SOT

ABSTRACT

Background: Although many studies have reported cases of COVID-19 infection in transplant recipients, most of them only involve a small number of patients and narrow geographic areas. This study aims to investigate the clinical characteristics, morbidity, severity, and mortality of COVID-19 infection among solid organ transplant (SOT) recipients by meta-analysis.

Method: We performed a literature search using the databases PubMed, Web of Science, and Google Scholar as of November 26, 2020. We included randomized controlled trials and cohort studies, excluding case reports and small case series (n < 10). The pooled incidence proportion and 95% confidence intervals (CI) were used to estimate the combined results of forty-seven studies were included for the meta-analysis. Heterogeneity was assessed using I^2. Freeman-Tukey double arcsine transformation was used to stabilize the specific rate variance. Publication bias was using Egger's test.

Results: The morbidity rate of COVID-19 in SOT recipients was 2.10% [95% CI 1.35–3.01], and the proportion of severe infection was 22.46% [95% CI 15.74–29.90]. The mortality rate was 17.38% [95% CI 13.72–21.34]. In the analysis by transplanted organ, the proportion of patients with severe infection was highest in recipients of two or more transplants 48.85% [95% CI 11.88–86.38]. The mortality rate was highest in lung transplant recipients 25.12% [95% CI 16.94–34.00]. The most common symptoms of COVID-19 in SOT recipients were fever (73.39%), cough (58.90%), and respiratory symptoms (45.77%).

Conclusion: SOT was a risk factor for worse COVID-19 outcomes, although the morbidity of COVID-19 in SOT recipients was not markedly higher than the general population. These results may change when our understanding of the disease progress.

Introduction

In December 2019, the first case of coronavirus disease 2019 (COVID-19) was reported in Wuhan, China. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent, is a pathogenic virus capable of rapid person-to-person spread. As of December 1, 2020, the COVID-19 pandemic has affected over 60 million people, with over 1.4 million deaths worldwide [1]. Although many studies have identified risk factors associated with COVID-19 morbidity and mortality, such as old age, obesity, diabetes, cardiovascular disease, and chronic kidney disease [2], there are conflicting views on whether immunosuppression is a risk factor for morbidity and mortality associated with COVID-19 infection. While the U.S. Center for Disease Control and Prevention has stated that an immunocompromised state increases the risk for COVID-19 [3] and compromised immunity renders the host more vulnerable to viral infection, some argue that immunosuppression may limit the hyperinflammatory response to COVID-19 caused by cytokine storm

Abbreviations: SOT, solid organ transplant; COVID-19, coronavirus disease 2019; CI, confidence intervals; ICU, intensive care unit; PRISMA, Preferred Reporting Items and Meta-Analyses

* Corresponding author.
E-mail addresses: anwen@hanyang.ac.kr (W. An), 202034@xxmu.edu.cn (Q. Wang), tekim@kuh.ac.kr (T.-E. Kim), jskang@hanyang.ac.kr (J.-S. Kang).
[1] Orcid ID: 0000-0002-1895-1950
[2] Orcid ID: 0000-0002-5588-8663

https://doi.org/10.1016/j.jiph.2022.02.002

syndrome [4]. Furthermore, immunocompromised patients were not at an increased risk of contracting a viral infection or experiencing worse clinical outcomes in the epidemics of Middle East Respiratory Syndrome and SARS-CoV-1 [5].

Solid-organ transplant (SOT) recipients are at an increased risk of some opportunistic infections because immunisuppressants are administered to prevent rejection against transplanted organs. Although many people live with SOTs, information on the susceptibility to and clinical outcome of COVID-19 infection among these patients is lacking, and then it is difficult to make a decision for prevention and management of COVID-19 infected patients. Although many studies have reported on the association between COVID-19 and SOT, these cases are relatively small and from limited geographic areas. Thus, we performed a meta-analysis to delineate the clinical characteristics and outcomes such as mortality, morbidity and severity of COVID-19 infection in SOT recipients.

Methods

Search strategy

Articles published in English were selected from the online databases of PubMed, Web of Science, and Google Scholar as of November 26, 2020. The following terms, both separately and in combination, were used for the search: ("SARS-CoV-2" or "COVID-19" or "Novel coronavirus 2019" or "coronavirus disease 2019") and ("SOT" or "solid organ transplantation" or "kidney transplant" or "heart transplant" or "liver transplant" or "lung transplant").

Selection criteria

This meta-analysis and systematic review were screened by the Agency for Healthcare Research and Quality (AHRQ) and reported according to the meta-analysis guidelines (PRISMA). (Supplement Table S1) We included randomized controlled trials and cohort studies, case reports were excluded. We also excluded studies involving patients with suspected infection, such as chest imaging abnormalities and symptoms, and studies without RT-PCR detection.

In the meta-analysis, we only included articles with 10 or more patients to minimize the impact of small studies. The following variables were collected from the included studies: sample size, type of organ transplantation, symptoms, follow-up period, number of COVID-19 diagnoses, number of intensive care unit (ICU) residents, and all-cause mortality. After obtaining these results, we excluded studies focusing only on critical patient admissions, ICU admissions, mechanical ventilation, and all-cause mortality to avoid selection bias and heterogeneity.

Definition of endpoints

The severity of the study was based on whether to be admitted to the ICU. The mortality rate was determined by death regardless of other causes. Morbidity refers to the prevalence of COVID-19 infection in patients with SOT. The methodology of morbidity is the number of COVID-19 in SOT recipients/ the total number of covid-19 patients reported in the study.

Data abstraction

Two researchers (An and Wang) independently screened the articles' titles and abstracts to evaluate study eligibility. Data were extracted using a predesigned Microsoft Excel® worksheet. The following data were extracted from the studies: first author, year, sample size, study design, age of patients, transplanted organs, and outcome indicators. Disagreements were resolved by a third researcher (Kim and Kang).

Statistical analysis

All statistical analyses were performed using the R version 3.6.1. The pooled incidence proportion (i.e., cumulative incidence) and 95% confidence intervals (CI) were used to estimate the morbidity, severity, and mortality of COVID-19 in SOT recipients, as well as clinical symptoms. The Cochrane Q statistic and Higgins I^2 statistic were used to evaluate heterogeneity among the studies. Freeman-Tukey double arcsine transformation was used to stabilize the specific rate variance to minimize the impact of studies with extremely low or highly significant rates on overall estimates. When $I^2 < 50\%$, a fixed-effect model was used to estimate the risk. In contrast, the random-effects model was used when I^2 was $> 50\%$. Publication bias was estimated using a funnel plot and Egger's linear regression test. Sensitivity analyses were conducted to assess the impact of each study on the pooled effect.

Ethics statement

This study did not receive nor require ethics approval, as it does not involve human & animal participants. The IRB approval and Patient and Public Involvement were not required.

Results

Study selection and characteristics

A total of 1189 articles were retrieved based on the keywords. After screening the abstracts and titles of 1189 studies, 237 studies were selected for full-text evaluation. Among them, 190 studies were excluded owing to lack of sufficient data. Finally, a total of 47 studies were included in the meta-analysis: 37 articles were analyzed for clinical characteristics; 16 articles (kidney: 9; liver: 6; lung: 5; heart: 9) for morbidity analysis, 36 articles (kidney: 18; liver: 12; lung: 8; heart: 9; multi-organ: 4) for severity analysis; 41 articles (kidney: 31; liver: 15; lung: 11; heart: 12; multi-organ: 7) for mortality analysis (Fig. 1). The characteristics of the included studies are presented in Table 1.

Morbidity, severity, and mortality

The morbidity rate was investigated in 64,916 patients with SOT from 10 articles. The overall morbidity rate of COVID-19 in SOT recipients was 2.10% (95% confidence intervals [CI], 1.35–3.01) (Fig. 2A). When it was analyzed per organ, the COVID-19 morbidity rates of kidney 5.09% (95% CI 3.26–7.27), liver 0.61% (95% CI 0.05–1.55), lung 0.38% (95% CI 0.00–2.47), and heart transplant recipients 2.14% (95% CI 0.73–4.06), respectively (Fig. 3A).

The severity of infection was evaluated in 1574 patients with COVID-19 and SOT from 17 articles. The overall proportion of patients who experienced a severe clinical process resulting in admitting ICU admission was 22.46% (95% CI 15.74–29.90) (Fig. 2B). The proportion of patients with severe COVID-19 symptoms per organ was in the kidney 21.23% [95% CI 15.68–27.30], liver 7.41% [95% CI 0.84–17.52], lung 11.84% [95% CI 0.73–29.35], and heart transplant recipients 5.77% [95% CI 1.12–12.54], respectively. In the case of multi-organ transplant recipients, the proportion was 48.85% (95% CI 11.88–86.38), which was a markedly higher proportion than that in single organ transplant recipients (Fig. 3B).

The overall mortality rate of COVID-19 in SOT recipients among 2161 patients with COVID-19 and SOT in 18 articles was 17.38% (95% CI 13.72–21.34) (Fig. 2C). When analyzed per organ, the COVID-19 mortality rates of kidney 18.74% (95% CI 15.20–22.52), liver 11.80% (95% CI 8.56–15.33), lung 25.12% (95% CI 16.94–34.00), and heart transplant recipients 18.87% (95% CI 12.07–26.43), respectively. The

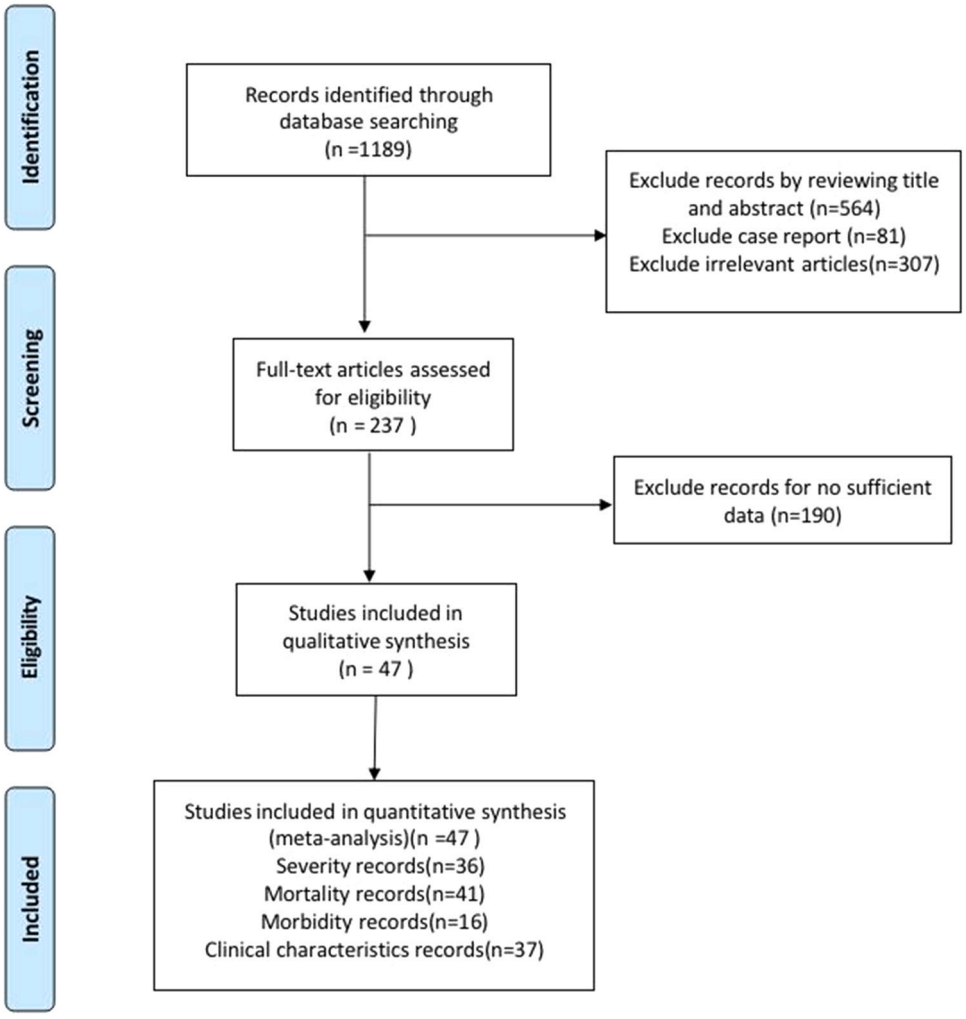

Fig. 1. Flow chart of study selection.

mortality rate of the multi-organ transplant recipients was 5.28% (95% CI 0.00–18.95) (Fig. 3C).

Clinical characteristics of COVID-19 infection in SOT recipients

The clinical characteristics of COVID-19 infection in SOT recipients were evaluated in 2064 patients from 37 articles. The most common symptoms of SOT recipients with COVID-19 infection were fever 73.39% [95% CI 68.95–77.63], cough 58.90% [95% CI 54.09–63.62], and other respiratory symptoms 45.77% [95% CI 41.01–50.56], respectively. Fatigue 34.85% [95% CI 26.83–43.28], diarrhea 31.48% [95% CI 26.77–36.38], and myalgia 30.92% [95% CI 24.47–37.74] were reported in the SOT recipients with COVID-19 infection, respectively. Headache and vomiting were reported in 10–20% of SOT recipients with COVID-19 infection. Those patients with abdominal pain 4.28% (95% CI 0.90–9.26) and sore throat 9.16% (95% CI 4.59–14.80)were reported. The results are presented in Table 2.

Discussion

To our knowledge, this is the first meta-analysis to report the morbidity, severity, and mortality of COVID-19 among SOT recipients. Our study showed that the mortality rate of COVID-19 in SOT recipients was 17.38%, which is approximately eight times higher than that in the population. This result is roughly the same as the mortality rate of COVID-19 in SOT recipients reported in the previous narrative review of 21% (n = 39)[6], 25.64% (n = 403)[7], and 18.6% (n = 2772)[8]. The Globally, as of December 1, 2020, the mortality rate has been reported to be 2.3%. Although there were differences by country, the mortality rate generally has not been reported to exceed 4.0%. In cases of diabetes mellitus, a known risk factor for COVID-19, the mortality rate because of COVID-19 has been reported to be 10–20%, which is comparable to the results of this study. In our study, the morbidity rate of COVID-19 in SOT recipients was 2.10%. Compared to the global morbidity rate reported by the World Health Organization[9], it seems similar to that in the general population. However, morbidities differ across countries and some countries show much higher morbidity: the morbidity rate of the US is 4.6% as of December 1, 2020. Considering this, we believe that SOT recipients are not more susceptible to COVID-19 than the general population.

Although there was no marked difference in morbidity by transplanted organs, the proportion of severe COVID-19 infection in multi-organ transplant recipients was significantly higher than that in SOT recipients. Interestingly, the mortality rate was not substantially higher than that in SOT recipients. Consistent with the clinical course of severe COVID-19 infection leading to respiratory failure and acute respiratory distress syndrome, the mortality rate was highest in lung transplant recipients.

It has been shown that SOT patients have severe peripheral lymphopenia and have a low frequency of IFN-γ, IL-2, IFN-γ/

Table 1
Characteristics of the studies in the meta-analysis.

No.	Study	Country	Age (mean), years	Sex (M/F)	COVID-19 positive	Died	Patients admitted to ICU	Number of SOT recipients with COVID-19				
								Kidney	Liver	Lung	Heart	multi-organ
1	Pereira et al.[15]	USA	57	53/37	90	16	27	47	13	17	9	NA
2	Hoek et al.[16]	Netherlands	59	18/5	23	5	2	15	1	3	2	NA
3	Ravanan et al.[17]	England	NA	387/210	597	154	NA	470	64	13	23	22
4	Yi et al.[18]	USA	54.8	13/8	21	1	7	13	3	2	NA	4
5	Roberts et al.[19]	USA	61.5	23/9	52	5	11	20	4	2	5	NA
6	Cavagna et al.[20]	North Italy	NA	10/4	14	2	0	6	NA	3	5	NA
7	Iacovoni et al.[21]	North Italy	65	20/6	26	7	5	NA	NA	NA	26	NA
8	Abrishami et al.[22]	Iran	47.66	9/3	12	8	10	12	NA	NA	NA	NA
9	Chaudhry et al.[23]	USA	61	32/29	47	8	13	39	1	4	5	NA
10	Ruiz et al.[24]	Spain	71	14/4	18	5	2	8	6	NA	4	NA
11	Tschopp et al.[25]	Swiss	56	15/6	21	2	5	12	5	1	1	NA
12	Fung et al.[26]	USA	56.5	4/6	10	0	3	7	1	1	1	NA
13	Akdur et al.[27]	Turkey	NA	162/374	9	0	NA	NA	NA	NA	NA	NA
14	Verma et al.[28]	UK	39	5/0	5	NA	NA	NA	NA	NA	NA	NA
15	Passamonti et al.[29]	Italy	NA	NA	5	1	NA	2	2	NA	1	NA
16	Verleden et al.[30]	Belgium	52.5	7/3	10	1	1	NA	NA	10	NA	NA
17	Felldin et al.[31]	Sweden	56	NA	53	5	8	31	8	5	5	4
18	Caillard et al.[32]	France	61.6	NA	279	43	88	268	NA	NA	NA	NA
19	Al-Darzi et al.[33]	USA	59	5/1	6	NA	NA	NA	NA	NA	NA	NA
20	Gaston et al.[34]	USA	60	12/13	25	7	10	23	2	NA	NA	NA
21	Coll et al.[35]	Spain	61	512/266	778	4	84	423	110	54	69	1
22	Alberici et al.[36]	Italy	NA	NA	21	5	NA	21	NA	NA	NA	NA
23	Nair et al.[37]	USA	57	6/4	10	3	5	10	NA	NA	NA	NA
24	Devresse et al.[38]	Belgium	57	12/10	22	2	2	22	NA	NA	NA	NA
25	Lubetzky et al.[39]	USA	57	38/16	54	7	NA	54	NA	NA	NA	NA
26	Bossini et al.[40]	Italy	60	42/11	53	15	10	53	NA	NA	NA	NA
27	Demir et al.[41]	Turkey	44.9	20/20	40	5	7	40	NA	NA	NA	NA
28	Abolghasemi et al.[42]	Iran	49	62.5%	24	10	12	24	NA	NA	NA	NA
29	Monfared et al.[43]	Iran	52	15/7	22	6	NA	22	NA	NA	NA	NA
30	Rivinius et al.[44]	Germany	58.6	17/4	21	7	NA	NA	NA	NA	21	NA
31	Elias et al.[45]	France	NA	NA	66	16	15	66	NA	NA	NA	NA
32	Molaei et al.[46]	Iran	59.6	8/2	10	2	4	10	NA	NA	NA	NA
33	Lum et al.[47]	USA	48.5	22/19	41	4	9	41	NA	NA	NA	NA
34	Benotmane et al.[48]	France	62.2	37/12	49	9	14	49	NA	NA	NA	NA
35	Shrivastava et al.[49]	USA	NA	NA	39	9	13	39	NA	NA	NA	NA
36	Crespo et al.[50]	Spain	62	265/149	414	109	50	414	NA	NA	NA	NA
37	Cravedi et al.[51]	Italy	62	94/50	144	46	NA	144	NA	NA	NA	NA
38	García-Cosío et al.[52]	Spain	59.5	10/3	13	4	1	NA	NA	NA	13	NA
39	Caraffa et al.[53]	USA	67	5/1	6	2	2	NA	NA	NA	6	NA
40	Saez-Giménez et al.[54]	Spain	62.8	26/18	44	17	4	NA	NA	44	NA	NA
41	Messika et al.[55]	France	50.4	19/16	35	5	13	NA	NA	35	NA	NA
42	Lee et al.[56]	USA	NA	NA	38	7	8	NA	38	NA	NA	NA
43	Loinaz et al.[57]	Spain	58	14/5	19	2	1	NA	19	NA	NA	NA
44	Becchetti et al.[58]	Switzerland	65	40/17	57	7	4	NA	57	NA	NA	NA
45	Colmenero et al.[59]	Spain	65.34	71.2%	111	20	12	NA	111	NA	NA	NA
46	Webb et al.[60]	USA	60	102/49	151	28	43	NA	151	NA	NA	NA
47	Malekhosseini et al.[61]	Iran	46.4	67/18	85	17	19	NA	NA	NA	NA	NA

IL-2-producing T cells against membrane antigens. SOT patients have a degree of delayed immunity and are unable to achieve a strong immune response immediately, as evidenced by a lower rate of IgG seroconversion and frequency of cytokine-producing T cells[10]. This may be related to the long-term use of immunosuppressants in SOT patients, which will aggravate the COVID-19 infection after SOT patients are infected with COVID-19. The presence of this condition is a challenge for SOT patients infected with COVID-19 during the acute infection period. Inflammatory markers as well as IL-6, a risk factor for COVID-19-related mortality in hospitalized patients, are significantly increased in SOT patients[11]. Therefore, SOT patients infected with COVID-19 have a high level of mortality. Lung transplantation exhibited high mortality among the five transplant types, which may be related to the fact that the SARA-COV-2 viral target ACE2 receptors are mostly distributed in alveolar epithelial cells, alveolar space, and primary bronchus[12].

Even though, the morbidity and severity of COVID infection in lung SOT patients is lower than other organ SOT patients but is highest in mortality of COVID infections in lung SOT patients. Therefore, we believe that we need to be very careful care in managing COVID-19 infection in lung SOT patients. Heart transplant recipients had the lowest proportion of severity.

The clinical manifestations of COVID-19 in SOT recipients were not different from those in the general population; however, the patients experiencing respiratory distress were over 40%, which was relatively higher than the 24–26% reported in other meta-analyses involving patients with COVID-19 in the general population [13,14]. We found significant heterogeneity among some studies, and the following reasons may account for this. First, this study did not address the clinical history and characteristics of individual transplant recipients. Susceptibility to opportunistic infection among SOT recipient changes over time and the susceptibility and outcome of COVID-19 are likely to differ across transplant recipient dependent upon the period of transplantation and the type of immunosuppressive regimen. Second, this study did not consider other risk factors for COVID-19, such as age, obesity, and comorbidities.

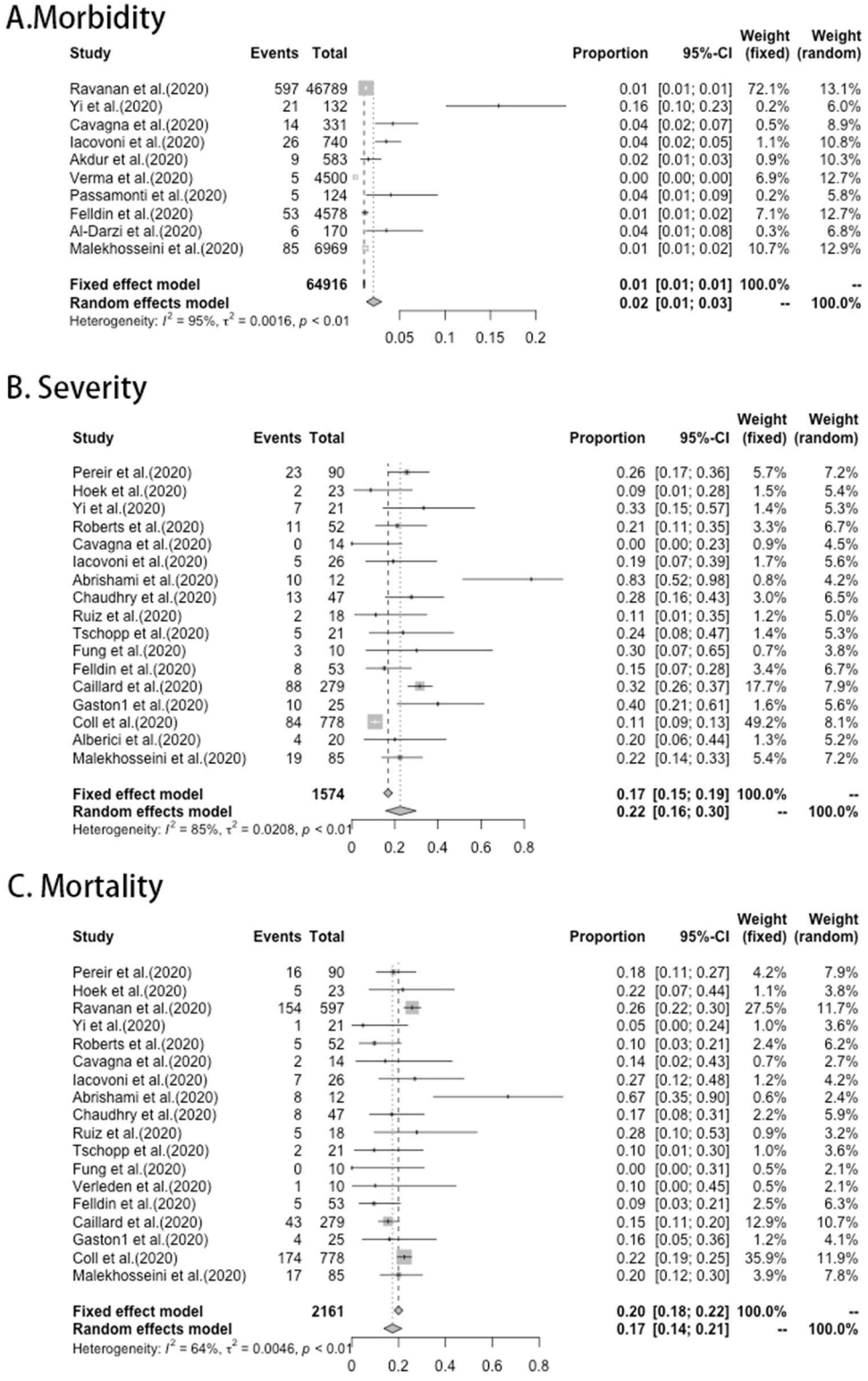

Fig. 2. The forest for morbidity(A), severity(B), and mortality(C) of SOT patients.

Third, there are still a small number of patients who have not been discharged at the time of publication, affecting mortality accuracy. Finally, it may be related to the lack of uniformity in treatment and hospitalization management. Although almost all articles adopted measures to reduce the dosage of immunosuppressants, calcineurin inhibitors, etc., in combination with antiviral and symptomatic treatment (mechanical ventilation, etc.), there was heterogeneity in the kinds of medication administered to individual patient between and within groups. On the other hand, all the inpatients in the study were required to meet the hospitalization standards set by their respective hospitals before they could be admitted for treatment. There were many differences in the hospitalization standards of each

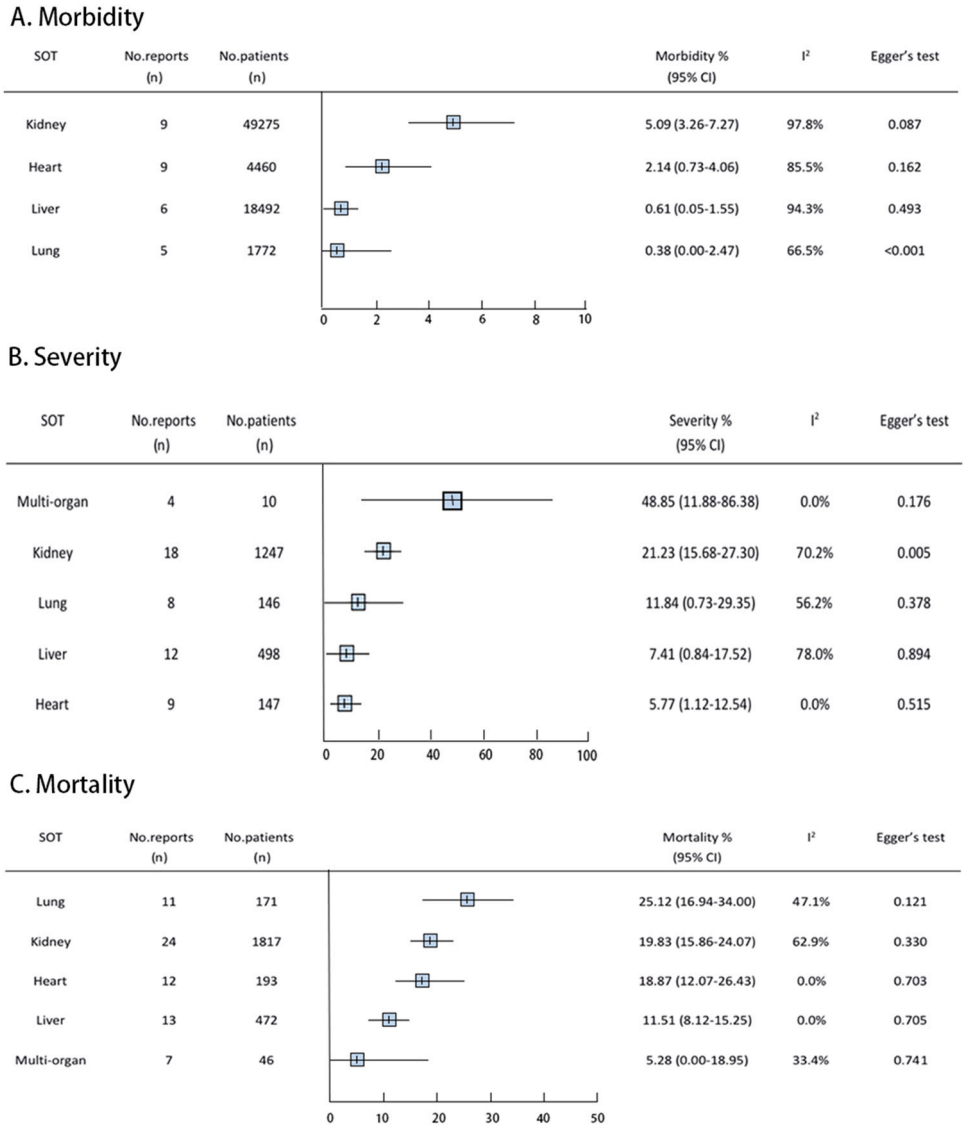

Fig. 3. The forest for morbidity(A), severity(B), mortality(C), and clinical characteristics(D) of COVID-19 patients in per-organ.

Table 2
Results of meta-analysis in clinical characteristics.

No.	Type of analysis	Reports	Patients	95% CI	I^2	Egger's test
1	Fever	36	2054	0.7339 [0.6895; 0.7763]	73.9	0.732
2	Cough	36	1914	0.5890 [0.5409; 0.6362]	71.0	0.164
3	Respiratory system	34	2003	0.4577 [0.4101; 0.5056]	72.4	0.313
4	Abdominal pain	5	154	0.0428 [0.0090; 0.0926]	15.4	0.090
5	Vomiting	14	478	0.1476 [0.0901; 0.2145]	66.0	0.052
6	Headache	11	592	0.2005 [0.1361; 0.2727]	64.2	0.599
7	Sore throat	5	147	0.0916 [0.0459; 0.1480]	26.3	0.022
8	Myalgias	20	824	0.3092 [0.2447; 0.3774]	72.3	0.105
9	Fatigue	10	360	0.3485 [0.2683; 0.4328]	52.3	0.865
10	Diarrhea	25	1198	0.3148 [0.2677; 0.3638]	60.0	0.247

study, which led to significant heterogeneity between the studies. Despite these limitations, we believe that the large sample size of various publications can attenuate our limitations to some extent.

In conclusion, we conducted a systematic review and meta-analysis of the symptoms and outcomes of the SOT receptor covid-19. Based on this review and meta-analysis, we concluded that although the incidence rate of COVID-19 in SOT recipients is not significantly higher than that of the general population. Once patients with SOT are infected with COVID-19, COVID-19 is a risk factor for worse prognosis, and the mortality and severity are also higher. These results may change when our understanding of the disease progress.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

CRediT authorship contribution statement

Wen An and Qiuyang Wang designed the model and the computational framework and analysis the data. Ju-seop Kang was involved in planning and supervised the work. Tae-Eun Kim discussed the results and commented on the manuscript.

Conflict of interest

The authors have no conflicts of interest to declare.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2022.02.002.

References

[1] ⟨https://covid19.who.int/?gclid=CjwKCAiA8Jf-BRB-EiwAWDtEGtGy30myGkh6lL-Pxkjt_ZlkKnvv4wsa3nmm3hQb9QmkxVyAyLLhmhoCRD0QAvD_BwE⟩ (accessed December 1, 2020).

[2] Carethers JM. Insights into disparities observed with COVID-19. J Intern Med 2020. https://doi.org/10.1111/joim.13199

[3] ⟨https://covid.cdc.gov/covid-data-tracker⟩ (Accessed Dec 1, 2020).

[4] Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033–4. https://doi.org/10.1016/s0140-6736(20)30628-0

[5] Chan JW, Ng CK, Chan YH, Mok TY, Lee S, Chu SY, Law WL, Lee MP, Li PC. Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS). Thorax 2003;58:686–9. https://doi.org/10.1136/thorax.58.8.686

[6] Nacif LS, Zanini LY, Waisberg DR, Pinheiro RS, Galvao F, Andraus W, et al. COVID-19 in solid organ transplantation patients: a systematic review. Clinics 2020;75:e1983. https://doi.org/10.6061/clinics/2020/e1983

[7] Aziz H, Lashkari N, Yoon YC, Kim J, Sher LS, Genyk Y, et al. Effects of coronavirus disease 2019 on solid organ transplantation. Transpl Proc 2020;52:2642–53. https://doi.org/10.1016/j.transproceed.2020.09.006

[8] Raja MA, Mendoza MA, Villavicencio A, Anjan S, Reynolds JM, Kittipibul V, et al. COVID-19 in solid organ transplant recipients: a systematic review and meta-analysis of current literature. Transpl Rev 2021;35:100588. https://doi.org/10.1016/j.trre.2020.100588

[9] WHO Coronavirus Disease (COVID-19) Dashboard, ⟨https://covid19.who.int/⟩ (accessed Dec 14,2020).

[10] Fava A, Donadeu L, Sabe N, Pernin V, Gonzalez-Costello J, Llado L, et al. SARS-CoV-2-specific serological and functional T cell immune responses during acute and early COVID-19 convalescence in solid organ transplant patients. Am J Transpl 2021. https://doi.org/10.1111/ajt.16570

[11] Belsky JA, Tullius BP, Lamb MG, Sayegh R, Stanek JR, Auletta JJ. COVID-19 in immunocompromised patients: a systematic review of cancer, hematopoietic cell and solid organ transplant patients. J Infect 2021;82:329–38. https://doi.org/10.1016/j.jinf.2021.01.022

[12] Croci GA, Vaira V, Trabattoni D, Biasin M, Valenti L, Baselli G, et al. Emergency lung transplantation after COVID-19: immunopathological insights on two affected patients. Cells 2021:10. https://doi.org/10.3390/cells10030611

[13] Alimohamadi Y, Sepandi M, Taghdir M, Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. J Prev Med Hyg 2020;61:E304–12. https://doi.org/10.15167/2421-4248/jpmh2020.61.3.1530

[14] Pormohammad A, Ghorbani S, Baradaran B, Khatami A, Mansournia J.T.; R, Kyriacou MA;, et al. N.C. clinical characteristics, laboratory findings, radiographic signs and outcomes of 61,742 patients with confirmed COVID-19 infection: a systematic review and meta-analysis. Micro Pathog 2020;147:104390. https://doi.org/10.1016/j.micpath.2020.104390

[15] Pereira MR, Mohan S, Cohen DJ, Husain SA, Dube GK, Ratner LE, et al. COVID-19 in solid organ transplant recipients: Initial report from the US epicenter. Am J Transpl 2020(20):1800–8. https://doi.org/10.1111/ajt.15941

[16] Hoek RAS, Manintveld OC, Betjes MGH, Hellemons ME, Seghers L, Van Kampen JAA, Caliskan K, van de Wetering J, van den Hoogen M, Metselaar HJ, et al. COVID-19 in solid organ transplant recipients: a single-center experience. Transpl Int 2020;33:1099–105. https://doi.org/10.1111/tri.13662

[17] Ravanan R, Callaghan CJ, Mumford L, Ushiro-Lumb I, Thorburn D, Casey J, et al. SARS-CoV-2 infection and early mortality of waitlisted and solid organ transplant recipients in England: a national cohort study. Am J Transpl 2020;20:3008–18. https://doi.org/10.1111/ajt.16247

[18] Yi SG, Rogers AW, Saharia A, Aoun M, Faour R, Abdelrahim M, et al. Early experience With COVID-19 and solid organ transplantation at a US high-volume transplant center. Transplantation 2020;104:2208–14. https://doi.org/10.1097/TP.0000000000003339

[19] Roberts MB, Izzy S, Tahir Z, Jarrah Al, Fishman A;, El Khoury JA;. J. COVID-19 in solid organ transplant recipients: dynamics of disease progression and inflammatory markers in ICU and non-ICU admitted patients. Transpl Infect Dis 2020;22:e13407. https://doi.org/10.1111/tid.13407

[20] Cavagna L, Seminari E, Zanframundo G, Gregorini M, Di Matteo A, Rampino T, et al. Calcineurin inhibitor-based immunosuppression and COVID-19: results from a multidisciplinary cohort of patients in Northern Italy. Microorganisms 2020:8. https://doi.org/10.3390/microorganisms8070977

[21] Iacovoni A, Boffini M, Pidello S, Simonato E, Barbero C, Sebastiani R, et al. A case series of novel coronavirus infection in heart transplantation from 2 centers in the pandemic area in the North of Italy. J Heart Lung Transpl 2020;39:1081–8. https://doi.org/10.1016/j.healun.2020.06.016

[22] Abrishami A, Samavat S, Behnam B, Arab-Ahmadi M, Nafar M, Sanei Taheri M. Clinical course, imaging features, and outcomes of COVID-19 in kidney transplant recipients. Eur Urol 2020;78:281–6. https://doi.org/10.1016/j.eururo.2020.04.064

[23] Chaudhry ZS, Williams JD, Vahia A, Fadel R, Parraga Acosta T, Prashar R, et al. Clinical characteristics and outcomes of COVID-19 in solid organ transplant recipients: a cohort study. Am J Transpl 2020;20:3051–60. https://doi.org/10.1111/ajt.16188

[24] Fernandez-Ruiz M, Andres A, Loinaz C, Delgado JF, Lopez-Medrano F, San Juan R, et al. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. Am J Transpl 2020(20):1849–58. https://doi.org/10.1111/ajt.15929

[25] Tschopp J, L'Huillier AG, Mombelli M, Mueller NJ, Khanna N, Garzoni C, et al. First experience of SARS-CoV-2 infections in solid organ transplant recipients in the Swiss transplant cohort study. Am J Transpl 2020;20:2876–82. https://doi.org/10.1111/ajt.16062

[26] Fung M, Chiu CY, DeVoe C, Doernberg SB, Schwartz BS, Langelier C, et al. Clinical outcomes and serologic response in solid organ transplant recipients with COVID-19: a case series from the United States. Am J Transpl 2020;20:3225–33. https://doi.org/10.1111/ajt.16079

[27] Akdur A, Karakaya E, Ayvazoglu Soy EH, Alshalabi O, Kirnap M, Arslan H, et al. Coronavirus disease (COVID-19) in kidney and liver transplant patients: a single-center experience. Exp Clin Transpl 2020;18:270–4. https://doi.org/10.6002/ect.2020.0193

[28] Verma A, Khorsandi SE, Dolcet A, Prachalias A, Suddle A, Heaton N, et al. Low prevalence and disease severity of COVID-19 in post-liver transplant recipients-a single centre experience. Liver Int 2020;40:1972–6. https://doi.org/10.1111/liv.14552

[29] Passamonti SM, Cannavo A, Trunzo V, Caporale V, Buonocore R, DeFeo TM. Solid organ transplantation in the coronavirus disease 2019 era: "the great bet" in the North Italy transplant program area. Transpl Proc 2020;52:2631–6. https://doi.org/10.1016/j.transproceed.2020.07.001

[30] Verleden GM, Godinas L, Lorent N, Van Bleyenbergh P, Dupont L, Delcroix M, et al. COVID-19 in lung transplant patients: a case series. Am J Transpl 2020;20:3234–8. https://doi.org/10.1111/ajt.16212

[31] Felldin M, Softeland JM, Magnusson J, Ekberg J, Karason K, Schult A, et al. Initial report from a Swedish high-volume transplant center after the first wave of the COVID-19 pandemic. Transplantation 2021;105:108–14. https://doi.org/10.1097/TP.0000000000003436

[32] Caillard S, Anglicheau D, Matignon M, Durrbach A, Greze C, Frimat L, Thaunat O, Legris T, Moal V, Westeel PF, et al. An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants. Kidney Int 2020;98:1549–58. https://doi.org/10.1016/j.kint.2020.08.005

[33] Al-Darzi W, Aurora L, Michaels A, Cowger J, Grafton G, Selektor Y, et al. Heart transplant recipients with confirmed 2019 novel coronavirus infection: the detroit experience. Clin Transpl 2020;34:e14091. https://doi.org/10.1111/ctr.14091

[34] Gaston DC, Malinis M, Osborn R, Peaper DR, Landry M, Juthani-Mehta M, et al. Clinical implications of SARS-CoV-2 cycle threshold values in solid organ transplant recipients. Am J Transpl 2020. https://doi.org/10.1111/ajt.16357

[35] Coll E, Fernandez-Ruiz M, Sanchez-Alvarez JE, Martinez-Fernandez JR, Crespo M, Gayoso J, et al. COVID-19 in transplant recipients: the Spanish experience. Am J Transpl 2020. https://doi.org/10.1111/ajt.16369

[36] Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A, et al. Management of patients on dialysis and with kidney transplantation during the SARS-CoV-2 (COVID-19) pandemic in Brescia, Italy. Kidney Int Rep 2020;5:580–5. https://doi.org/10.1016/j.ekir.2020.04.001

[37] Nair V, Jandovitz N, Hirsch JS, Nair G, Abate M, Bhaskaran M, et al. COVID-19 in kidney transplant recipients. Am J Transpl 2020(20):1819–25. https://doi.org/10.1111/ajt.15967

[38] Devresse A, Belkhir L, Vo B, Ghaye B, Scohy A, Kabamba B, et al. COVID-19 infection in kidney transplant recipients: a single-center case series of 22 cases from belgium. Kidney Med 2020;2:459–66. https://doi.org/10.1016/j.xkme.2020.06.001

[39] Lubetzky M, Aull MJ, Craig-Schapiro R, Lee JR, Marku-Podvorica J, Salinas T, et al. Kidney allograft recipients, immunosuppression, and coronavirus disease-2019:

a report of consecutive cases from a New York City transplant center. Nephrol Dial Transpl 2020;35:1250–61. https://doi.org/10.1093/ndt/gfaa154
[40] Bossini N, Alberici F, Delbarba E, Valerio F, Manenti C, Possenti S, et al. Kidney transplant patients with SARS-CoV-2 infection: the brescia renal COVID task force experience. Am J Transpl 2020;20:3019–29. https://doi.org/10.1111/ajt.16176
[41] Demir E, Uyar M, Parmaksiz E, Sinangil A, Yelken B, Dirim AB, et al. COVID-19 in kidney transplant recipients: a multicenter experience in Istanbul. Transpl Infect Dis 2020;22:e13371. https://doi.org/10.1111/tid.13371
[42] Abolghasemi S, Mardani M, Sali S, Honarvar N, Baziboroun M. COVID-19 and kidney transplant recipients. Transpl Infect Dis 2020;22:e13413https://doi.org/10.1111/tid.13413
[43] Monfared A, Dashti-Khavidaki S, Jafari R, Jafari A, Ramezanzade E, Lebadi MK, Haghdar-Saheli Y, Aghajanzadeh P, Khosravi M, Movassaghi A, et al. Clinical characteristics and outcome of COVID-19 pneumonia in kidney transplant recipients in Razi hospital, Rasht, Iran. Transpl Infect Dis 2020;22:e13420. https://doi.org/10.1111/tid.13420
[44] Rivinius R, Kaya Z, Schramm R, Boeken U, Provaznik Z, Heim C, Knosalla C, Schoenrath F, Rieth A, Berchtold-Herz M, et al. COVID-19 among heart transplant recipients in Germany: a multicenter survey. Clin Res Cardiol 2020;109:1531–9. https://doi.org/10.1007/s00392-020-01722-w
[45] Elias M, Pievani D, Randoux C, Louis K, Denis B, Delion A, et al. COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. J Am Soc Nephrol 2020;31:2413–23. https://doi.org/10.1681/ASN.2020050639
[46] Molaei H, Khedmat L, Nemati E, Rostami Z, Saadat SH. Iranian kidney transplant recipients with COVID-19 infection: clinical outcomes and cytomegalovirus co-infection. Transpl Infect Dis 2020:e13455. https://doi.org/10.1111/tid.13455
[47] Lum E, Bunnapradist S, Multani A, Beaird OE, Carlson M, Gaynor P, et al. Spectrum of coronavirus disease 2019 outcomes in kidney transplant recipients: a single-center experience. Transpl Proc 2020;52:2654–8. https://doi.org/10.1016/j.transproceed.2020.09.005
[48] Benotmane I, Perrin P, Vargas GG, Bassand X, Keller N, Lavaux T, et al. Biomarkers of cytokine release syndrome predict disease severity and mortality from COVID-19 in kidney transplant recipients. Transplantation 2021;105:158–69. https://doi.org/10.1097/TP.0000000000003480
[49] Shrivastava P, Prashar R, Khoury N, Patel A, Yeddula S, Kitajima T, et al. Acute kidney injury in a predominantly African American cohort of kidney transplant recipients with COVID-19 infection. Transplantation 2021;105:201–5. https://doi.org/10.1097/TP.0000000000003498
[50] Crespo M, Mazuecos A, Rodrigo E, Gavela E, Villanego F, Sanchez-Alvarez E, et al. Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. Transplantation 2020;104:2225–33. https://doi.org/10.1097/TP.0000000000003413
[51] Cravedi P, Mothi SS, Azzi Y, Haverly M, Farouk SS, Perez-Saez MJ, et al. COVID-19 and kidney transplantation: results from the TANGO international transplant consortium. Am J Transpl 2020;20:3140–8. https://doi.org/10.1111/ajt.16185
[52] Garcia-Cosio MD, Flores Hernan M, Caravaca Perez P, Lopez-Medrano F, Arribas F, Delgado Jimenez J. Heart transplantation during the COVID-19 pandemic: follow-up organization and characteristics of infected patients. Rev Esp Cardiol 2020;73:1077–80. https://doi.org/10.1016/j.rec.2020.08.011
[53] Caraffa R, Bagozzi L, Fiocco A, Bifulco O, Nadali M, Ponzoni M, Carrozzini M, Toscano G, Fraiese AP, Metra M, et al. Coronavirus disease 2019 (COVID-19) in the heart transplant population: a single-centre experience. Eur J Cardiothorac Surg 2020;58:899–906. https://doi.org/10.1093/ejcts/ezaa323
[54] Saez-Gimenez B, Berastegui C, Barrecheguren M, Revilla-Lopez E, Los Arcos I, Alonso R, et al. COVID-19 in lung transplant recipients: a multicenter study. Am J Transpl 2020. https://doi.org/10.1111/ajt.16364
[55] Messika J, Eloy P, Roux A, Hirschi S, Nieves A, Le Pavec J, et al. COVID-19 in lung transplant recipients. Transplantation 2021;105:177–86. https://doi.org/10.1097/TP.0000000000003508
[56] Lee BT, Perumalswami PV, Im GY, Florman S, Schiano TD, Group CS. COVID-19 in liver transplant recipients: an initial experience from the US epicenter. 1176-1178 e1172 Gastroenterology 2020;159. https://doi.org/10.1053/j.gastro.2020.05.050
[57] Loinaz C, Marcacuzco A, Fernandez-Ruiz M, Caso O, Cambra F, San Juan R, Justo I, Calvo J, Garcia-Sesma A, Manrique A, et al. Varied clinical presentation and outcome of SARS-CoV-2 infection in liver transplant recipients: Initial experience at a single center in Madrid, Spain. Transpl Infect Dis 2020;22:e13372. https://doi.org/10.1111/tid.13372
[58] Becchetti C, Zambelli MF, Pasulo L, Donato MF, Invernizzi F, Detry O, Dahlqvist G, Ciccarelli O, Morelli MC, Fraga M, et al. COVID-19 in an international European liver transplant recipient cohort. Gut 2020(69):1832–40. https://doi.org/10.1136/gutjnl-2020-321923
[59] Colmenero J, Rodriguez-Peralvarez M, Salcedo M, Arias-Milla A, Munoz-Serrano A, Graus J, Nuno J, Gastaca M, Bustamante-Schneider J, Cachero A, et al. Epidemiological pattern, incidence, and outcomes of COVID-19 in liver transplant patients. J Hepatol 2021;74:148–55. https://doi.org/10.1016/j.jhep.2020.07.040
[60] Webb GJ, Marjot T, Cook JA, Aloman C, Armstrong MJ, Brenner EJ, et al. Outcomes following SARS-CoV-2 infection in liver transplant recipients: an international registry study. Lancet Gastroenterol Hepatol 2020;5:1008–16. https://doi.org/10.1016/s2468-1253(20)30271-5
[61] Ali Malekhosseini S, Nikoupour H, Gholami S, Shamsaeefar A, Arasteh P, Kazemi K, et al. A report of 85 cases of COVID-19 and abdominal transplantation from a single center: what are the associated factors with death among organ transplantation patients. Transplantation 2021;105:90–9. https://doi.org/10.1097/TP.0000000000003470