COVID-19 outbreak and the impact on renal disorders: A rapid review

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ABSTRACT

In this rapid review, we aimed to evaluate the effect of coronavirus disease 2019 (COVID-19) on renal functions and mortality of patients with kidney diseases. We searched MEDLINE, The Cochrane Library, Scopus, Embase, Web of Science, UpToDate, and TRIP databases using the following keywords: COVID-19, COVID19, 2019-nCoV, 2019-CoV, coronavirus, SARS-nCoV-2, urology, cancer, bladder, prostate, kidney, trauma, stone, neurogenic, and reconstructive. The initial search resulted in 495 records. After the primary screening of titles, abstracts, and full texts and removing duplicates, 10 articles were selected and included in this rapid review. Moreover, we performed meta-analysis of binary data for the outcomes with sufficient data. Owing to a high level of heterogeneity because of different study designs and contexts, we used a random model for the meta-analysis. Only 5 studies were eligible for the meta-analysis. In these studies, comprising 964 COVID-19 positive patients, the cumulative event rate of acute kidney injury (AKI) was 7.1% (95% confidence interval: 1.8%–24.5%, p<0.001, I2=92.4). Based on the qualitative synthesis of the 10 included studies, patients with COVID-19 and kidney diseases had higher risk of in-hospital mortality. If AKI occurs because of the novel coronavirus, the mortality rate will be very high. Therefore, we need further investigations and more studies to recognize the extent and the cause of renal involvement in COVID-19.

Keywords: COVID-19; kidney diseases; renal disorders; systematic review.

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Introduction

In December 2019, novel coronavirus pneumonia caused by COVID-19 occurred in Wuhan city, the capital of Hubei Province in China. The World Health Organization (WHO) declared it a global pandemic on March 11, 2020, after the disease spread quickly nationwide.[1] More than 1 million cases and 50,000 deaths have been reported until April 4, 2020.[2]

The main symptoms of COVID-19 are similar to those of patients with severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus infection, including fever, cough, and fatigue.[3,4] However, it has a wide spectrum of clinical presentations ranging from asymptomatic infection and mild upper respiratory tract illness, from common seasonal cold to severe interstitial and alveolar pneumonia.[5,6] COVID-19 can also affect multiple organs, such as the kidneys, heart, digestive tract, blood, and nervous system.[7]

Renal disorders are one of the complications seen in patients with the novel coronavirus infection.[8] Acute kidney failure (AKF) can probably happen by two mechanisms. The first mechanism is because of ACE2 receptor involvement in the renal cells. In the kidney, ACE2 is highly expressed in the brush border of the proximal tubular cells and, to a lesser extent, in podocytes but not in glomerular, endothelial, and mesangial cells.[6] Therefore, this virus can directly damage the kidney tissue by binding to ACE2, thereby leading to AKI.[9] The second mechanism in renal disturbances by COVID-19 is dehydration because of fever or decreased intake of fluids in the elderly.[8]

Wang et al.[10] conducted a study on kidney function in 116 patients with COVID-19 infection. In this study, 12 (10.8%) patients showed

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mild elevation of blood urea nitrogen (BUN) or creatinine and 8 (7.2%) showed trace or 1+ albuminuria. Therefore, AKI was uncommon. In contrast, findings of Cheng et al.[4] show the prevalence of kidney diseases on admission, and the development of AKI during hospitalization in patients with COVID-19 is high and is associated with in-hospital mortality.

In this rapid review, we examined the effect of COVID-19 on renal functions and mortality of patients with COVID-19 infection and kidney diseases.

Material and methods

Search methods for identification of studies

In this systematic review, we searched the electronic databases, including MEDLINE (PubMed, Ovid), The Cochrane Library, Scopus, Embase, Web of Science, UpToDate, and TRIP database, for studies published between 2019 and 2020. In addition, we searched Google Scholar, Google, Medscape, and Guidelines such as Scottish Intercollegiate Guidelines Network (SIGN), National Institute for Health and Care Excellence (NICE), WHO, Urological Associations (Asia, European, America, Canadian, Japanese, Australia, and New Zealand; American College of Surgeons; and European Surgical Association), and all in press and ongoing studies.

The search strategy included a combination of free and MeSH terms, such as COVID-19,COVID19, 2019-nCoV, 2019-CoV, coronavirus, SARS-nCoV-2, urology, cancer, bladder, prostate, kidney, trauma, stone, neurogenic, and reconstructive. The search strategy of PubMed is shown in Appendix 1.

Criteria for considering studies for this review

In this study, we included randomized controlled trials (RCTs), Quasi-RCTs, RCTs, prospective cohort studies, case-control studies, and cross-sectional studies.

Methods for screening search results

The articles were screened in terms of title, abstract, and full text; the articles that met the inclusion criteria were included in this study. Two subject specialists critically evaluated the studies and excluded the ones with low quality. Disagreements were resolved using the Delphi method.

Main Points:

- Kidney impairment is frequent in hospitalized patients with severe acute respiratory syndrome coronavirus infection.
- Kidney injury is associated with higher risk of death in these patients, and it is an indicator of patient mortality.
- Early detection of renal involvement and comprehensive protective treatments followed by effective interventions of acute kidney injury may help to reduce mortality and morbidity in patients with COVID-19 infection.

Assessment of methodological quality

Two independent reviewers assessed the methodological quality of the eligible studies using the JBI critical appraisal checklist form.[11] Three checklists for case report, cross-sectional, and cohort studies were used. The disagreement between the reviewers was resolved using the Delphi method. Because of the different number of questions in each checklist, the reviewers considered studies with a score of 70% and above as high quality.

Data extraction

We extracted demographic characteristics of the studies, including the date of publication, study design, age (years), country, and number of patients together with the outcomes assessed, numerical data for outcomes of interest, effect modifiers, prognostic factors, and disease severity. For meta-analysis, we extracted quantitative data of patients with AKI, elevated GFR, proteinuria, albuminuria, elevated BUN, and creatinine together with the sample sizes in the individual studies.

Meta-analysis

We performed meta-analysis of the binary data for the outcomes with sufficient data. High level of heterogeneity

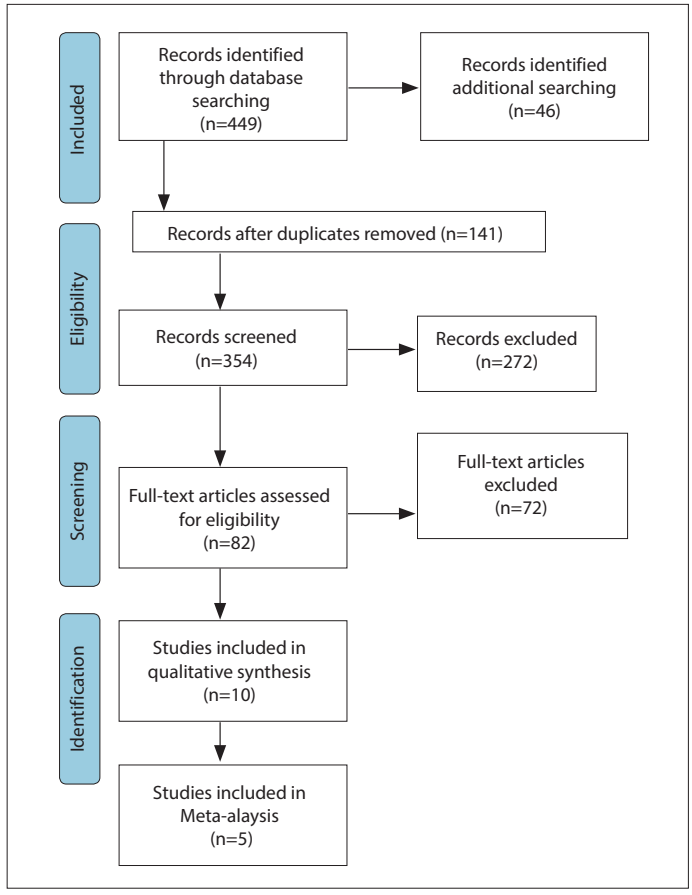

Figure 1. Search results, study selection, and inclusion process

was predicted because of the different study designs and contexts. Therefore, we used a random model for the meta-analysis.

Ethical considerations

This was a review study, and there was no need for ethical approval.

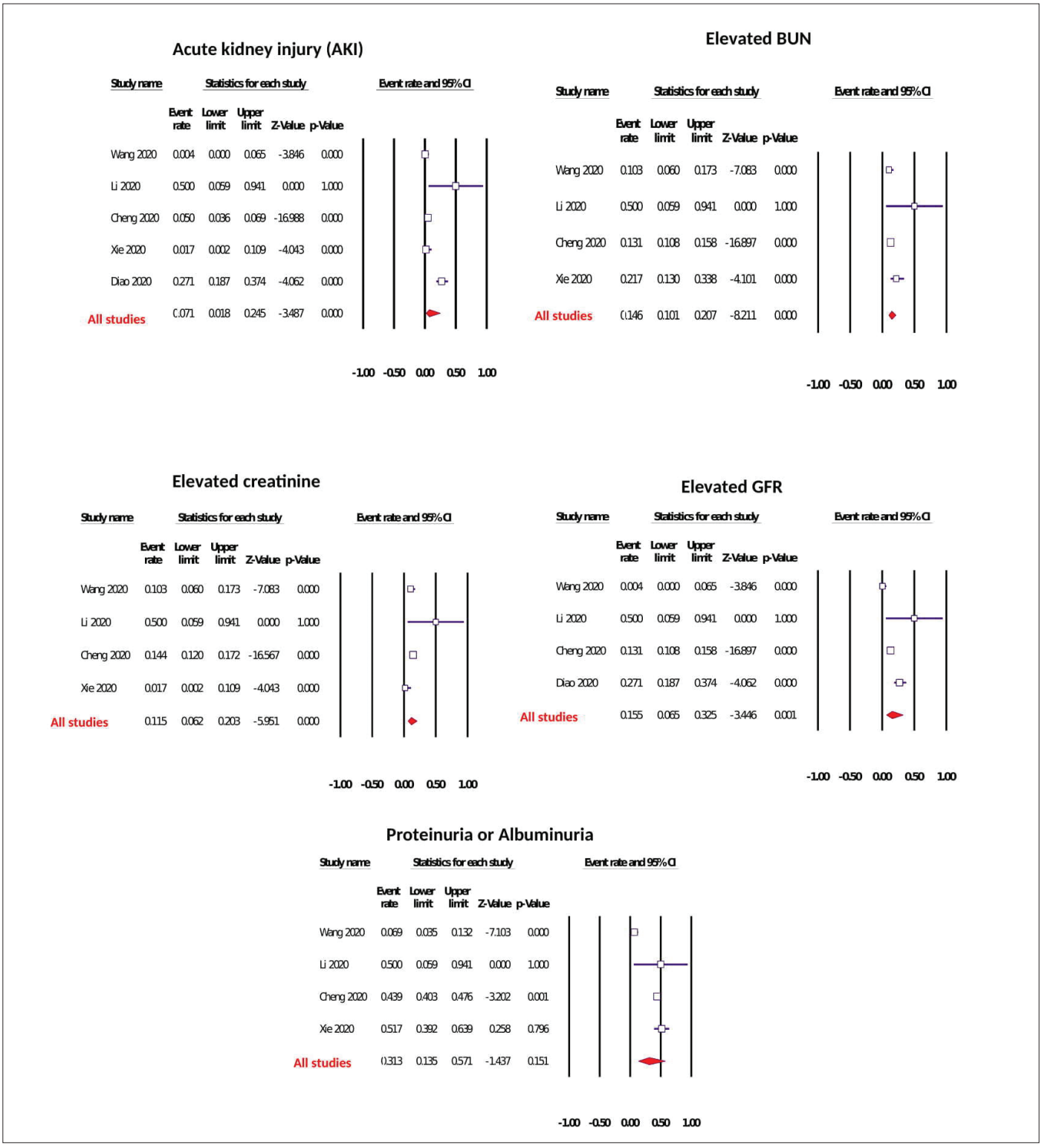

Figure 2. Cumulative adverse events in various outcomes

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Clinical and Research Consequences

Study inclusion

We rapidly reviewed the databases to find out the kidney disorders in patients with COVID-19 infection. This search strategy yielded 495 records. After the primary screening of titles, abstracts, and full texts and removing duplicates, 82 studies were selected for full text evaluation. Finally, 10 articles were included in this rapid review, and 5 studies were selected for the meta-analysis. A detailed flowchart for the selection is shown in Figure 1.

Characteristics of the included studies

All the 10 included studies comprising 2,085 patients were conducted in China; 1 of the included studies was a case report. The remaining were descriptive observational studies (2 cohort studies and 7 cross-sectional studies). Table 1 shows the characteristics of the included studies.

Results of the meta-analysis

Only 5 studies were eligible for the meta-analysis. In these studies comprising 964 COVID-19 positive patients, the cumulative event rate of AKI was 7.1% (95% confidence interval [CI]: 1.8%–24.5%, p<0.001, I2=92.4). In 4 studies comprising 904 COVID-19 positive patients, the cumulative event rate of patients with abnormal GFR was 15.5% (95% CI: 6.5%–32.5%, p=0.001, I2=84.6). In 4 studies comprising 879 COVID-19 positive patients, the cumulative event rate was 14.6% (95% CI: 10.1%–20.7%, p<0.001, I2=50.9) for elevated BUN level, 11.5% (95% CI: 6.2%–20.3%, p<0.001, I2=62.5) for elevated creatinine level, and 31.3% (95% CI: 13.5%–57.1%, p=0.15, I2=92.8) for proteinuria or albuminuria (Figure 2).

Methodological quality

A total of 10 included studies were appraised using the appropriate checklists on the basis of the study design. Furthermore, 6 of 10 studies scored above 70% (5 scored 75%, and 1 scored 87%), and the remaining scored less than the defined criteria (2 scored 62.5%, 1 scored 50%, and 1 scored 45%). The identification of confounders and the strategies to deal with the confounding factors were referenced in only 2 studies, and the questions in this regard had the lowest scores.

Review findings

Mortality in COVID-19 patients with kidney diseases

Mortality of the patients with COVID-19 infection was reported in 5 studies. In a study intending to explore the effects of SARS-CoV-2 infection on renal function, 7 (6.03%) patients transferred to the intensive care unit died of respiratory failure despite using invasive ventilation. None of these patients exhibited AKI.[12] Results of a case study by Li et al.[13] indicated that 1 of the 2 studied cases of renal transplant recipients with COVID-19 infection, who were 59 years old, died in the hospital. In this case, the symptoms quickly deteriorated, hypoxemia occurred rapidly, and renal function worsened gradually, resulting in death. This patient had a 5-year history of kidney transplantation. They concluded that AKI caused by coronavirus, as in these 2 patients, is common and mainly manifests as renal tubular injury. Cheng et al.[4] showed that during the study period, AKI occurred in 5.1% of the patients. Their research indicated that patients with kidney abnormalities, including elevated baseline serum creatinine (SCr), elevated baseline BUN, proteinuria, hematuria, and AKI (P<0.001), had a significantly higher risk for in-hospital death. In-hospital death occurred in 16.1% of patients in this study, and the median time to death was 6 days (interquartile range:3–12 days). Li et al.[1] assessed the kidney function in patients with COVID-19 infection and its relation to mortality. Their analysis showed that patients with COVID-19 infection who developed AKI had a ~5.3 times higher risk of mortality than those without AKI and much higher than that of comorbid chronic illnesses. Another study showed a higher prevalence of kidney impairment (hematuria, proteinuria, and kidney dysfunction) in hospitalized patients with COVID-19 infection. In addition, patients with kidney impairment had a higher risk of in-hospital death.[14]

COVID-19 impact on renal function

The results of our meta-analysis show that COVID-19 affects the kidney function in many ways, the most prominent being proteinuria, rise of BUN, and rise of GFR. The results also show a considerable rate of AKI in the COVID-19-infected patients (Figure 2).

One study assessed the effects of SARS-CoV-2 infection on renal functions in 116 hospitalized COVID-19-confirmed patients. Results of this study showed that although 12 patients (10.8%) without CKD showed a mild increase of BUN or SCr (<26 μmol/L within 48 h) and 8 patients (7.2%) showed trace or 1+ albuminuria after being infected with the virus, during the treatment of pneumonia, none of them met the AKI criteria. Therefore, acute renal impairment was uncommon in these patients.[12] Results from another study indicated that the SARS-CoV-2 virus directly infects human kidney tubules by inducing acute tubular damage ARF and probably also leads to urine transmission.[15] In a cross-sectional study on 60 patients, a high rate of positive urine protein was detected in patients with novel coronavirus pneumonia. In addition, the degree of the pulmonary lesion was positively related to the level of urine protein.[16] Results of a study exploring the potential mechanism of SARS-CoV-2 on AKI at the single-cell level showed that patients with AKI might be infringed by synergistic assaults from the virus-induced cytopathic effect and systemic inflammatory response, especially in severe and critical cases with positive viral RNA in blood samples and heavy proteinuria.[17] Another study assessed the

Table 1. Characteristics of included studies

	Study design			Participant characteristics					
Author (year)	**Study method**	**Country**	**Patient number**	**Effect modifiers**	**Prognostic factors**	**Disease severity**	**Age (years)**	**Outcomes assessed**	**Numerical data for outcomes of interest**
Wang, L 2020[12]	Cross-sectional	China	116	1. Changes of kidney-related clinical indicators 2. Detection results of SARS-CoV-2[a] RNA in urine sediment 3. Mortality of COVID-19	1. BUN (mmol/L), Cr (μmol/L), eGFR, 2. RNA in urine sediments 3. Disease severity, age, comorbidities.	59 (50.8%) were mild pneumonia, 46 (39.7%) were severe pneumonia, and 11 (9.5%) were ARDS	20–95	Acute renal impairment was uncommon in COVID-19. SARS-CoV-2 infection does not significantly cause obvious acute renal injury, or aggravate Chronic Renal Failure (CRF) in the patients with COVID-19 infection.	1. 12 (10.8%) patients with mild elevation of BUN or creatinine, and eight(7.2%) patients with trace or 1+ albuminura 2. RNA in urine sediments was positive in three patients without renal illness (3/48) and one patient with CRF (1/5). 3.Seven(6.03%) ARDS patients died of respiratory failure
Diao, B 2020[15]	Cross-sectional	China	85	Human kidney is a target for novel SARS-CoV-2 infection	1. eGFR 2. SCr[e] 3. BUN 4. Histopathological examination	–	21–92	1. Renal function impairment is relatively common in COVID-19 patients. 2. Varying degrees of acute tubular necrosis, luminal brush border sloughing, and vacuole degeneration	27.06% of patients with COVID-9 had abnormal eGFR. Patients who are older (>60 years) or carry comorbidities more easily developed ARF (65.22% vs. 24.19%, P<0.001; 69.57% vs. 11.29%, P<0.001, respectively).
Li, Q 2020[13]	Case Report	China	2	1.Changes of kidney-related clinical indicators 2. Mortality of COVID-19 in Patients with transplanted kidney	1. BUN (mmol/L), Cr (μmol/L), eGFR, 2. Patients mortality at the time of hospitalization	In one patient, the kidney condition recovered, and the patient was discharged. The next patient died in the hospital.	59 and 37 years	In one patient, the kidney condition recovered, and the patient was discharged. The next patient died in the hospital.	

Y. Cheng 2020[4]	Cohort	China	701	1. Prevalence of AKI[b] in patients with COVID-19. 2. Kidney disease and death in patients infected with COVID-19	1. Acute kidney injury stage 2. In-hospital death 3. proteinuria 4. hematuria 5. BUN 6. SCr	73 (10.4%) patient admission to intensive care unit 97 (13.4%) patient administration of mechanical ventilation	50–71	Analysis demonstrated that patients with kidney disease had a significantly higher risk for in-hospital death.	1. SCr elevated in 14.4%, 2. BUN were elevated in 13.1%, 3. 43.9% of patients had proteinuria, 4. 118(26.7%) had hematuria 5. 113(16.1%) In-hospital death 6. 36 (5.1%) acute kidney injury: 13(1.9%) Stage 1 9 (1.3%) Stage 2 14 (2%) Stage 3
Xie, Z 2020[16]	Cross-sectional	China	60	Relationship between clinical characteristics of the 60 novel coronavirus cases with renal injury (Upro positive)	1. Laboratory finding(ALT, AST, Glb[f], SCr, LDH, lymphocyte, and CRP), 2. pulmonary HRCT finding	All patients Admission to ordinary ward	–	High rate of Upro positive was detected in novel coronavirus patients. The degree of pulmonary lesion is positively related to the level of Upro.	Upro+ group and Upro- group: level of ALT [P=0.048), AST[P=0.001], Glb [P=0.001], SCr [P=0.002], serum CRP[P=0.001], blood lymphocyte [P=0.014] and LDH [P=0.013], moderate grade of HRCT imaging change (P=0.037).
Xu, D 2020[17]	Cross-sectional	China	15	Survey mechanism of SARS-CoV-2 on AKI at the single-cell level	1. ACE2 Expression 2. TMPRSSs genes	–	–	AKI may be infringed by synergistic assaults from the virus-induced cytopathic effect and systemic inflammatory response, especially in severe patients.	ACE2 expression in kidney cells suggesting that the kidney may be an important target Organ for SARS-CoV-2 and high expression of ACE2 and kidney-disease-related genes in Occidental donors relative to Asian donors, occidental populations with SARS-CoV-2 infection might be a higher risk of kidney injury.

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Zhou, F 2020[5]	Cohort	China	191		Not assessed	Probably Cr>1.5	18–87	Acute kidney injury: total: 28 (15%) nonsurvivors: 27 (50%) survivors: 1 (1%) P<0·0001	
Hong, X 2020[18]	Cross-sectional	China	12	The incidence of early renal injury in COVID-19	CRP and NER[g]	UMA[h],A1M[i], IGU[j],TRU[k]	Not mentioned	Early renal injury was common in patients with COVID-19. Combined detection of UMA, A1M, IGU, and TRU was helpful for the diagnosis of early renal injury in COVID-19.	abnormal rates of eGFR, Ccr, and UACR were 66.7%, 41.7%, and 41.7%, respectively
Li, Z 2020 [1]	Cross-sectional	China	193		Proteinuria, hematuria		57	Acute kidney injury: total: 55 (28%) non severe: 12 (9%) severe:43 (66%)	1. 88/147 (60%) patients exhibited proteinuria, and 71/147 (48%) exhibited hematuria. 2. Blood urea nitrogen (BUN): 59/193 (31%) patients exhibited an elevated level of BUN 3. Plasma creatinine (SCr): 43/193 (22%) patients exhibited an elevated level of SCr 4. 39/192 (20%) patients exhibited an elevated level of UA[l] and 128/182 (70%) exhibited an elevated level of DD[m]. 5. Computed tomography data: 106/110 patients exhibited radiographic abnormalities of kidney.
Cheng, Y 2020[14]	Cohort	China	710				51–71	During the study period, AKI occurred in 3.2% patients. Patients with kidney impairment have higher risk for in-hospital death.	110 of 710 pts: high creatinine level

[a]SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; [b]AKI: acute kidney injury. [c]BUN: blood urea nitrogen; [d]Cr: creatinine; [e]SCr: serum creatinine; [f]Glb: globulin; [g]NER: neutrophil ratio; [h]UMA: urine microalbumin; [i]A1M: α1-microglobulin; [j]IGU: urine immunoglobulin-G; [k]TRU: urine transferring; [l]UA: uric acid; [m]DD: D-dimer

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incidence of COVID-19 with early renal injury in 12 patients diagnosed with COVID-19. Of these, 2 were severely ill patients, 8 were general patients, and 2 were light patients. The results suggested that the more severe is the infection, the more obvious is the early renal injury, and this injury can often cause hypokalemia and hyponatremia.[18] In a study of 191 patients with COVID-19 infection, AKI was reported in 28 (15%) patients (1 [1%] among survivors and 27 [50%] among nonsurvivors). Based on the results of this study, AKI occurred 9 days after the onset of illness in the survived patient.[5]

On the basis of results of the included studies, patients with COVID-19 infection and kidney diseases had higher risk of in-hospital mortality, ranging between 6.03%[12] and 50%[13] (1 of the 2 study cases). Results also indicated that AKI was common in the patients with COVID-19 although one of the studies declared that it was uncommon. It is true that kidney is not a common organ for novel coronavirus infection, and AKI is not a typical finding of this virus, but if AKI occurs because of this virus, the mortality rate will be very high.

Limitations of the study

Because COVID-19 is a novel disease, different aspects of the disease and their impact on different organs such as kidney are still unclear. Lack of high-quality evidence was the major limitation of this study. In addition, since the origin of the disease was in China and most of the available studies were from this country, we faced limitations in comparing the effect of COVID-19 on patients with kidney diseases in different contexts and healthcare systems. In addition, because of the small number of studies and different study settings, we faced high levels of heterogeneity in the meta-analysis.

Conclusion

Although COVID-19 primarily involves the respiratory tract, kidney impairment is frequent in hospitalized patients with SARS-CoV-2 infection. Kidney injury is associated with a higher risk of death in these patients, and it is an indicator of patient mortality. This is important because early detection of renal involvement and comprehensive protective treatments followed by effective interventions of AKI may help to reduce mortality and morbidity in patients with COVID-19 infection.

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Appendix 1. Search Strategy of PubMed

Search	Query	Items found
#1	Search "Coronavirus"[Mesh]	11,536
#2	Search (((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]	14,292
#3	Search ("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word])	16,918
#4	Search "Urology"[Mesh]	11,320
#5	Search (Urology[Text Word]) OR Urological[Text Word]	43,289
#6	Search ((("Urology"[Mesh]) OR ((Urology[Text Word]) OR Urological[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	2
#7	Search "Kidney"[Mesh]	346,989
#8	Search (Kidney[Text Word]) OR renal[Text Word]	1,060,963
#9	Search (Kidney[Text Word]) OR renal[Text Word]	1,060,963
#10	Search ("Kidney"[Mesh]) OR ((Kidney[Text Word]) OR renal[Text Word])	1,065,720
#11	Search ((("Kidney"[Mesh]) OR ((Kidney[Text Word]) OR renal[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	712
#12	Search "Renal Dialysis"[Mesh]	112,465
#13	Search ((Hemodialysis[Text Word]) OR Hemodialyses[Text Word]) OR Dialysis[Text Word]	178,878
#14	Search ("Renal Dialysis"[Mesh]) OR (((Hemodialysis[Text Word]) OR Hemodialyses[Text Word]) OR Dialysis[Text Word])	179,628
#15	Search ((("Renal Dialysis"[Mesh]) OR (((Hemodialysis[Text Word]) OR Hemodialyses[Text Word]) OR Dialysis[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	38
#16	Search "Calculi"[Mesh]	55,322
#17	Search ((stone[Text Word]) OR Calculi[Text Word]) OR Calculus[Text Word]	76,446
#18	Search ("Calculi"[Mesh]) OR (((stone[Text Word]) OR Calculi[Text Word]) OR Calculus[Text Word])	84,730
#19	Search ((("Calculi"[Mesh]) OR (((stone[Text Word]) OR Calculi[Text Word]) OR Calculus[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	10
#20	Search "Urinary Bladder"[Mesh]	49,977
#21	Search (Bladder[Text Word]) OR "Urinary Bladder"[Text Word]	184,960
#22	Search ("Urinary Bladder"[Mesh]) OR ((Bladder[Text Word]) OR "Urinary Bladder"[Text Word])	184,960
#23	Search ((("Urinary Bladder"[Mesh]) OR ((Bladder[Text Word]) OR "Urinary Bladder"[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	6
#24	Search "Nephrotomy"[Mesh]	4685
#25	Search ((Nephrotom*[Text Word]) OR "Kidney Incision*"[Text Word]) OR Nephrostom*[Text Word]	7676
#26	Search ("Nephrotomy"[Mesh]) OR (((Nephrotom*[Text Word]) OR "Kidney Incision*"[Text Word]) OR Nephrostom*[Text Word])	7676
#27	Search ((("Nephrotomy"[Mesh]) OR (((Nephrotom*[Text Word]) OR "Kidney Incision*"[Text Word]) OR Nephrostom*[Text Word]))) AND (("Coronavirus"[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	0
#28	Search "Urologic Diseases"[Mesh]	744,694
#29	Search ((((("Urologic Disease*"[Text Word]) OR "Urological Disease*"[Text Word]) OR "Urinary Tract Disease*"[Text Word])	1181

Appendix 1. Search Strategy of PubMed (Continued)

Search	Query	Items found
#30	Search ("Urologic Diseases"[Mesh]) OR (((((“Urologic Disease*”[Text Word]) OR “Urological Disease*”[Text Word]) OR “Urinary Tract Disease*”[Text Word]))	745,018
#31	Search (((“Urologic Diseases”[Mesh]) OR (((((“Urologic Disease*”[Text Word]) OR “Urological Disease*”[Text Word]) OR “Urinary Tract Disease*”[Text Word]))))) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	73
#32	Search “Prostate”[Mesh]	35,602
#33	Search prostate*[Text Word]	203,139
#34	Search (“Prostate”[Mesh]) OR prostate*[Text Word]	203,139
#35	Search (((“Prostate”[Mesh]) OR prostate*[Text Word])) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	6
#36	Search “Neoplasms”[Mesh]	3,300,837
#37	Search (((cancer[Text Word]) OR tumor[Text Word]) OR Neoplasm[Text Word]) OR Neoplasms[Text Word]	3,776,942
#38	Search (“Neoplasms”[Mesh]) OR ((((cancer[Text Word]) OR tumor[Text Word]) OR Neoplasm[Text Word]) OR Neoplasms[Text Word])	4,202,868
#39	Search (((“Neoplasms”[Mesh]) OR ((((cancer[Text Word]) OR tumor[Text Word]) OR Neoplasm[Text Word]) OR Neoplasms[Text Word]))) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	656
#40	Search “Reconstructive Surgical Procedures”[Mesh]	205,265
#41	Search (reconstructive[Text Word]) OR “Reconstructive Surgical Procedures”[Text Word]	75,665
#42	Search (“Reconstructive Surgical Procedures”[Mesh]) OR ((reconstructive[Text Word]) OR “Reconstructive Surgical Procedures”[Text Word])	227,523
#43	Search (((“Reconstructive Surgical Procedures”[Mesh]) OR ((reconstructive[Text Word]) OR “Reconstructive Surgical Procedures”[Text Word]))) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	3
#44	Search “Wounds and Injuries”[Mesh]	894,238
#45	Search (trauma*[Text Word]) OR Injur*[Text Word]	1,364,965
#46	Search ((“Wounds and Injuries”[Mesh])) OR ((trauma*[Text Word]) OR Injur*[Text Word])	1,661,050
#47	Search (((((“Wounds and Injuries”[Mesh])) OR ((trauma*[Text Word]) OR Injur*[Text Word])))) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word])))	226
#48	Search “Emergencies”[Mesh]	39,958
#49	Search (Emergency[Text Word]) OR Emergencies[Text Word]	302,234
#50	Search (“Emergencies”[Mesh]) OR ((Emergency[Text Word]) OR Emergencies[Text Word])	319,948
#51	Search (((“Emergencies”[Mesh]) OR ((Emergency[Text Word]) OR Emergency[Text Word]))) AND ((“Coronavirus”[Mesh]) OR ((((((Coronavirus[Text Word]) OR covid-19[Text Word]) OR covid19[Text Word]) OR 2019-CoV[Text Word]) OR 2019-nCoV[Text Word]) OR SARS-CoV-2[Text Word]))	332