Original Article

Patients with Chronic Kidney Disease Have Higher Acute Kidney Injury Morbidity than those without after SARS-CoV-2 Infection

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Abstract

Background and Objectives: Chronic kidney disease (CKD) and acute kidney injury (AKI) increase the risk of serious disease and mortality in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-infected patients. This study evaluated the occurrence and outcome of AKI in CKD and non-CKD patients infected with SARS-CoV-2. **Subjects and Methods:** We retrospectively analyzed the medical records of 845 patients with SARS-CoV-2 infection regarding the occurrence and outcome of AKI in a coronavirus disease-2019 (COVID-19)-designated hospital in Wuhan, China, from December 31, 2019, to March 20, 2020. **Results:** Of the 845 COVID-19 patients, 91 had CKD and 754 had no CKD (non-CKD), of whom 22 and 14 developed AKI, respectively. Finally, 36 patients were included in the analysis. Older patients and those with cardiovascular or cerebrovascular diseases were more likely to develop AKI. More CKD patients progressed to critical illness (72.73%) than non-CKD patients (57.14%), but the degree of AKI in CKD patients was lesser than that in non-CKD patients. Higher urea nitrogen, creatinine, and proteinuria levels were observed in CKD patients. More non-CKD patients were treated with human albumin than CKD patients. The survival probability of CKD patients was lower than that of non-CKD patients, but it was not statistically significant. **Conclusion:** There were significant differences in the incidence rate of AKI after SARS-CoV-2 infection between CKD and non-CKD patients, and the clinical manifestations and treatments of AKI also differed. These results highlight the necessity of variable treatment methods for optimal clinical management.

Key words: Acute kidney injury, chronic kidney disease, coronavirus disease-2019, severe acute respiratory syndrome coronavirus 2

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INTRODUCTION

The second outbreak of coronavirus disease-2019 (COVID-19) highlights considerable public health problems. The mortality rate of respiratory syndrome coronavirus-2 (SARS-CoV-2)-infected patients after acute kidney injury (AKI) is consistently high (60%–90%).[1,2] An early study found that chronic kidney disease (CKD) is a

risk factor for severe COVID-19 and death,[2] indicating that CKD might be a risk for SARS-CoV-2 infection and death.

Several studies have reported the incidence and severity of AKI in COVID-19 patients,[3-5] but the clinical manifestations of CKD developing AKI after SARS-CoV-2 infection are not well-described, hindering treatment. Therefore, we aimed to identify the clinical characteristics and prognosis of AKI in SARS-CoV-2-infected patients and compare the clinical features of patients with and without CKD to provide a clinical reference for treating these patients.

SUBJECTS AND METHODS

Study design and participants
This retrospective single-center study was performed in one of the largest designated hospitals for patients with severe COVID-19. Patients infected with SARS-CoV-2 and treated at the hospital from December 31, 2019, to March 20, 2020, were included. All patients were diagnosed with SARS-CoV-2 infection based on the Diagnosis and Treatment Protocols for Novel Coronavirus Pneumonia (Trial Version 7) guidelines.[6] Patients undergoing maintenance dialysis or renal transplantation were excluded. Clinical outcomes were monitored through May 5, 2020. This study followed the guidelines of the Declaration of Helsinki and was approved by the institutional ethics board of our institution.

Data sources
Data on the baseline characteristics, clinical manifestations, laboratory results, treatments, and outcomes were obtained from the hospital's health information system and were recorded by standard electronic methods. The laboratory data consisted of renal function, electrolyte levels, and routine urine parameters.

Definitions
SARS-CoV-2-infected cases were clinically classified as mild, moderate, severe, or critical based on the Diagnosis and Treatment Protocols for Novel Coronavirus Pneumonia (Trial Version 7) guidelines.[6] The Kidney Disease: Improving Global Outcomes guidelines were used to diagnose and classify AKI and CKD.

Disease progression was based on lung computed tomography (CT) imaging and defined as the expansion of the infected lesion or the appearance of new lesions at the second checkup. No progression was defined as no obvious enlargement or shrinkage of the infected lesions compared with the last checkup or some lesions were enlarged and others slightly reduced without obvious change overall. Remission

was defined as the absorption or shrinkage of the infected lesion at the second checkup.

Statistics
Normally distributed data were expressed as means ± standard deviations, and a *t*-test was used for between-group comparisons. Nonnormally distributed data were represented by medians and interquartile ranges (P25, P75), and the Wilcoxon test was used for between-group comparisons. Fisher's exact test was used for categorical variables. The overall survival between the CKD–AKI and CKD groups was compared by Kaplan–Meier analysis with the log-rank test. SPSS version 23.0 (IBM Corp., Armonk, NY, USA) and RevMan version 5.3 (Cochrane Collaboration, The Nordic Cochrane, Copenhagen) were used for the statistical analyses. $P < 0.05$ was considered statistically significant.

RESULTS

Chronic kidney disease patients infected with severe acute respiratory syndrome coronavirus-2 developed acute kidney injury more frequently than did nonchronic kidney disease patients
In total, 845 patients were diagnosed with SARS-CoV-2 infection, of whom 91 (10.77%) had CKD and 22 (24.18%) had AKI. Of the 754 (89.23%) non-CKD patients, 14 (1.86%) had AKI. In total, 36 (4.26%) patients with SARS-CoV-2 infection developed AKI and were included in the analysis. These results suggest that patients with SARS-CoV-2 infection can develop AKI, and CKD patients were more likely to develop AKI after being infected [Figure 1].

Patients with severe acute respiratory syndrome coronavirus 2 infection who developed acute kidney injury were mainly elderly patients or those with cardiovascular and cerebrovascular diseases
The mean age of infected patients with AKI was 77.5 (66.5–85.75) years, and most were male. In total, 61.11% of patients had cardiovascular disease, 72.22% had cerebrovascular disease, 38.89% had diabetes, and 8.33% had cancer. The time from onset to admission for AKI was at least 1 week, with a mean of approximately 10 days. Angiotensin drugs were previously taken by 28% of the patients, and hypoglycemic drugs were previously taken by 13.89% of the patients.

Age, sex, time from onset to admission, and comorbidities did not differ between CKD and non-CKD patients. More CKD
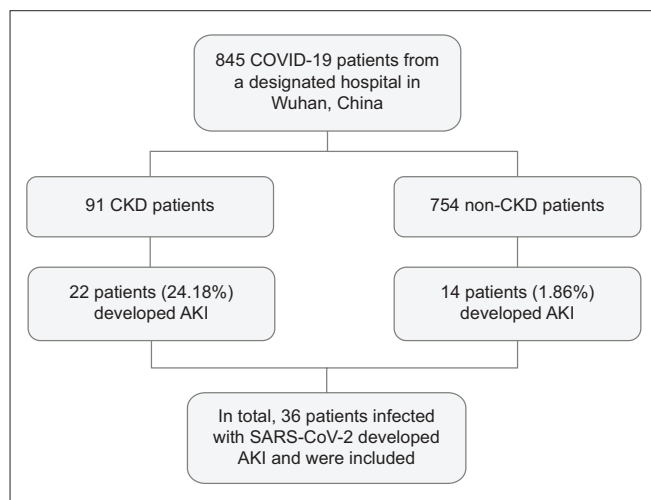
Figure 1: AKI morbidity in patients diagnosed with COVID-19 from a designated COVID-19 hospital in Wuhan, China. AKI: Acute kidney injury, COVID-19: Coronavirus disease-2019, CKD: Chronic kidney disease

patients took oral angiotensin drugs before admission, but the difference was statistically insignificant [Table 1].

More than 90% of the infected patients who developed acute kidney injury progressed to severe or critical illness

Cough (61.11%), fatigue (50%), decreased appetite (82.76%), and decreased urine output (78.13%) were the main clinical symptoms of infected patients who developed AKI, followed by fever (47.22%), chest tightness (25%), edema (14.29%), and sore throat (11.11%). The mean oxygen saturation (by finger pulse oximeter) was 96% at admission, which was lower than the reference range. After admission, the mean maximum body temperature was 39°C, and the mean minimum 24-hour urine output was 500.00 ml. Overall, 27.78% of the patients developed severe disease, and 66.67% developed critical illness. Regarding the AKI stage, 33.33%, 36.11%, and 30.56% of the infected patients were at Stage 1, Stage 2, and Stage 3, respectively.

Among SARS-CoV-2-infected patients who developed AKI, the urine output 24-hour after admission was significantly lower in non-CKD patients than in CKD patients. Furthermore, non-CKD patients had a higher frequency of decreased urine output (92.31%), decreased appetite (90.91%), and diarrhea (21.43%). Cough (72.73%), fatigue (59.09%), edema (17.65%), and increased nocturia (12.50%) were more frequent in CKD patients, but the differences were not statistically significant.

Regarding clinical classification, more CKD patients (72.73%) progressed to critical illness than non-CKD patients. The AKI classification suggests that 40.91% of CKD patients were at Stage 1, 36.36% at Stage 2, and 22.73% at Stage 3

AKI. However, the clinical classification of non-CKD patients trended oppositely with the AKI grade: 35.71% of patients progressed to severe illness and 57.14% progressed to critical illness, and 21.43% were at AKI Stage 1, 35.71% were at Stage 2, and 42.86% were at Stage 3 [Table 2]. It suggests that the relationship between the progression of CKD and AKI may not be as close as that of non-CKD patients.

Lung computed tomography of severe acute respiratory syndrome coronavirus-2-infected patients with acute kidney injury showed disease progression, and more than half had hematuria or proteinuria

Lung CT re-examination indicated that only 37.04% of patients had lung lesion absorption, 22.22% had no significant improvement, and 40.74% had disease progression. Overall, 57.90% of patients had hematuria, 57.15% had proteinuria, and 20% had pathological casts in the urine test. After admission, the highest urinary nitrogen and creatinine levels were significantly higher than the normal values.

Comparing non-CKD patients and CKD patients who developed AKI, we found that CKD patients had significantly higher basal urea nitrogen and creatinine levels ($P = 0.02$ and $P = 0.02$, respectively). The proportion of CKD patients with proteinuria was also higher than non-CKD patients ($P = 0.050$). Lung CT re-examination showed the proportions of progression, no change, and remission in non-CKD patients were similar. However, 46.67% of CKD patients showed progression, whereas 40% showed remission. More pathological casts were also seen in the urine of CKD patients, but these differences were statistically insignificant [Table 3].

More than half of severe acute respiratory syndrome coronavirus-2-infected patients who developed acute kidney injury died, and chronic kidney disease patients may have a higher mortality rate

Antibiotics (97.22%), Chinese medicine (88.89%), antiviral agents (86.11%), and human albumin (58.33%) were the primary treatment methods, followed by steroids (43.75%), diuretics (41.12%), and blood transfusion (31.25%). All three patients treated with continuous renal replacement therapy (CRRT) died. Overall, 41.67% of patients received noninvasive ventilation, 22.86% received invasive ventilation, and two patients (6.45%) received extracorporeal membrane oxygenation. Regarding outcomes, 44.66% of patients were discharged and 55.56% died.

Comparing non-CKD patients and CKD patients, we found that significantly more non-CKD patients were treated with

Table 1: Baseline characteristics of nonchronic kidney disease and chronic kidney disease patients with severe acute respiratory syndrome coronavirus-2 infection and acute kidney disease

	Patients included in the study (*n*=36)	Non-CKD patients infected with SARS-CoV-2 and develop AKI (*n*=14)	CKD patients who are infected with SARS-CoV-2 and develop AKI (*n*=22)	*P*
Demographic characteristics				
Average age (years)	77.5 (66.5-85.75)	78 (57.75-86.00)	77.50 (67.50-84.50)	0.922
Gender male, *n* (%)	23 (63.89)	7 (50.00)	16 (72.73)	0.152
Average days from onset to admission (days)	10 (7-20)	10.00 (7.00-18.50)	10.00 (2.75-21.00)	0.756
Comorbidities *n* (%)				
Chronic obstructive emphysema	3 (8.33)	0 (0.00)	3 (13.64)	0.216
Diabetes	14 (38.89)	5 (35.71)	9 (40.91)	0.518
Cardiovascular diseases	22 (61.11)	8 (57.14)	14 (63.64)	0.482
Cerebrovascular disease	26 (72.22)	4 (28.57)	6 (27.27)	0.611
Cancer	3 (8.33)	1 (7.14)	2 (9.09)	0.669
Medication history, *n* (%)				
Angiotensin (ACEI/ARB)	7 (28)	1 (9.09)	6 (42.86)	0.076
Hypoglycemic agents	5 (13.89)	3 (21.43)	2 (9.09)	0.287

P values were calculated by t-test or Wilcoxon test for continuous variables and by Fisher's exact test for categorical variables. CKD: Chronic kidney disease, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, AKI: Acute kidney disease, ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker

human albumin infusion than CKD patients. Moreover, non-CKD patients were more likely to receive hormone therapy ($P = 0.050$). Regarding outcomes, CKD patients had a higher mortality rate (68.18%) than non-CKD patients (35.71%), but the difference was not statistically significant [Table 4].

Survival analysis showed that the overall 1- and 2-month survival rates of CKD patients were lower than those of non-CKD patients, but the differences were not statistically significant [Figure 2].

DISCUSSION

In this study, we investigated the clinical characteristics and prognosis of AKI in SARS-CoV-2-infected patients. We found that 4.26% of patients diagnosed with SARS-CoV-2 infection in a COVID-19-designated hospital in Wuhan, China, had AKI, consistent with a previous study,[7] but lower than that reported by Chan *et al.*[8] and Cheng *et al.*[2] This difference may be related to the lack of monitoring urine volume and fewer reviews of renal function in COVID-19 patients for various pandemic-related reasons.

Most SARS-CoV-2-infected patients with AKI were male and older than those without AKI.[8] However, there were no differences in age or sex between CKD and non-CKD patients in our study, which might be due to all included patients being infected with SARS-CoV-2 and developing AKI. Although age and sex are risk factors for SARS-CoV-2 infection, there were no differences between CKD and non-CKD patients who were infected.
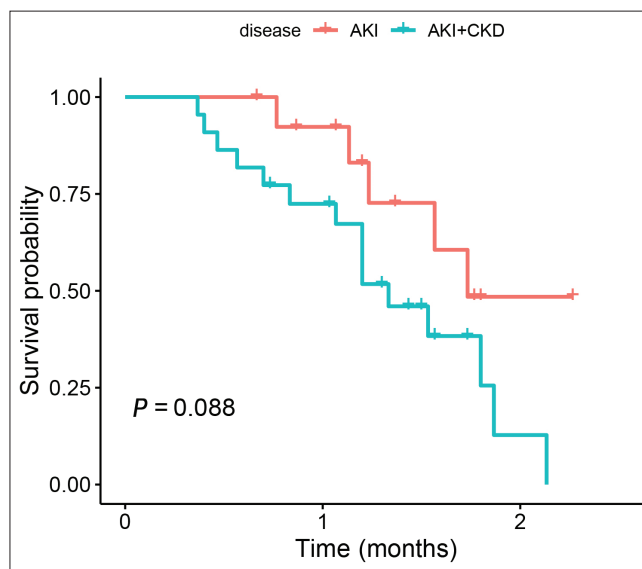

Figure 2: Kaplan–Meier survival rate estimations of CKD and non-CKD patients with SARS-CoV-2 infection and AKI. SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2, AKI: Acute kidney injury, CKD: Chronic kidney disease

Many SARS-CoV-2-infected patients who developed AKI had cardiovascular, cerebrovascular disease, or diabetes. A previous study reported that most SARS-CoV-2-infected patients had diabetes.[1] Thus, it is hypothesized that SARS-CoV-2 infection combined with circulatory system diseases has a greater effect on the kidney.

The duration from onset to admission of patients with SARS-CoV-2 infection who developed AKI was at least 1 week. The oxygen saturation level at admission was lower than normal, consistent with a previous study.[2] It was speculated that patients with AKI progressed rapidly, and

Table 2: Clinical characteristic comparisons between chronic kidney disease and nonchronic kidney disease patients with severe acute respiratory syndrome coronavirus-2 infection and acute kidney disease

	Patients included in the study (n=36), n (%)	Non-CKD patients infected with SARS-CoV-2 and develop AKI (n=14), n (%)	CKD patients who are infected with SARS-CoV-2 and develop AKI (n=22), n (%)	P
Symptoms				
Fever	17 (47.22)	6 (42.86)	11 (50.00)	0.470
Cough	22 (61.11)	6 (42.86)	16 (72.73)	0.075
Sore throat	4 (11.11)	2 (14.29)	2 (9.09)	0.510
Fatigue	18 (50.00)	5 (35.71)	13 (59.09)	0.153
Chest tightness	9 (25.00)	2 (14.29)	7 (31.82)	0.218
Loss of appetite	24 (82.76)	10 (90.91)	14 (77.78)	0.356
Diarrhea	4 (11.11)	3 (21.43)	1 (4.55)	0.153
Edema	4 (14.29)	1 (9.09)	3 (17.65)	0.482
Decreased urine output	25 (78.13)	12 (92.31)	13 (68.42)	0.120
Increased nocturia	2 (7.41)	0 (0.00)	2 (12.50)	0.342
Signs				
Average SPO$_2$ on admission (%)	96.00 (88.75-97.00)	94.50 (85.00-97.75)	96.00 (90.00-96.00)	0.973
Average SBP (mmHg)	133.47±21.44	132.93±22.01	133.82±21.60	0.905
Average DBP (mmHg)	74.53±10.81	77.64±9.62	72.55±11.26	0.171
Average temperature at admission (°C)	36.6 (36.5-37.2)	36.50 (36.40-37.30)	36.70 (36.50-37.20)	0.535
Maximum temperature after admission (°C)	39.00 (38.45-39.55)	39.00 (38.40-39.90)	39.00 (38.45-39.45)	0.735
Basic 24-h urine output at admission (ml)	1175.00 (737.50-1975.00)	1000.00 (700.00-1200.00)	1600.00 (750.00-2200.00)	0.222
Minimum urine output 24 h after admission (ml)	500.00 (287.50-950.00)	355 (60-662.50)	635.00 (425-1000)	0.031
Clinical typing				
Mild	0 (0.00)	0 (0.0)	0 (0.0)	0.627
Moderate	2 (5.56)	1 (7.14)	1 (4.55)	
Severe	10 (27.78)	5 (35.71)	5 (22.73)	
Critical	24 (66.67)	8 (57.14)	16 (72.73)	
Acute kidney injury grade				
Stage 1	12 (33.33)	3 (21.43)	9 (40.91)	0.348
Stage 2	13 (36.11)	5 (35.71)	8 (36.36)	
Stage 3	11 (30.56)	6 (42.86)	5 (22.73)	

P values were calculated by t-test or Wilcoxon test for continuous variables and Fisher's exact test for categorical variables. CKD: Chronic kidney disease, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, AKI: Acute kidney disease, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

the disease may have already progressed to a serious level before admission. In our study, after admission, the mean maximum body temperature reached 39°C, which may also be related to a higher likelihood of severe or critical disease progression among AKI patients. In addition to the typical clinical manifestations of pneumonia during hospitalization, the AKI patients also had characteristics of kidney disease, such as decreased appetite, reduced urine output, and edema, indicating that the kidney is a major target of SARS-CoV-2 attack.

Antiviral agents, antibiotics, Chinese medicine, and human albumin were the main treatments for AKI, consistent with the treatment for SARS-CoV-2-infected patients. Three patients were treated with CRRT with poor results. A previous study suggested that CRRT treatment could improve AKI.[9] In severe acute respiratory syndrome, the Middle East respiratory syndrome, and sepsis infections, CRRT has been proven

to be an effective treatment. In particular, on the 7th day of sepsis, using 6 L/h high throughput hemodiafiltration can effectively remove interleukin 6 and improve multiple organ failure. However, the therapeutic effect of CRRT on AKI development after SARS-CoV-2 infection remains questionable.

The clinical characteristics of AKI in patients with SARS-CoV-2 infection emphasize the AKI risk in elderly patients and those with cardiocerebrovascular disease or low oxygen saturation levels on admission. Kidney-related routine tests should be performed on admission, and specialized tests should be performed if signs of AKI appear. Finally, more treatments for kidney disease should be administered to SARS-CoV-2-infected patients who develop AKI.

The clinical manifestations of non-CKD patients with AKI and SARS-CoV-2 infection were more similar to AKI

Table 3: Laboratory result comparisons between nonchronic kidney disease and chronic kidney disease patients with severe acute respiratory syndrome coronavirus-2 infection and acute kidney disease

	Patients included in the study (*n*=36)	Non-CKD patients infected with SARS-CoV-2 and develop AKI (*n*=14)	CKD patients who are infected with SARS-CoV-2 and develop AKI (*n*=22)	*P*
Compare the second lung CT with the first lung CT, *n* (%)§				
Progress	11 (40.74)	4 (33.33)	7 (46.67)	0.456
No change	6 (22.22)	4 (33.33)	2 (13.33)	
Remission	10 (37.04)	4 (33.33)	6 (40.00)	
Urine routine, *n* (%)*				
Hematuria				
Negative	8 (42.11)	3 (37.5)	5 (45.45)	0.212
1+	2 (10.53)	2 (25.00)	0 (0.00)	
2+ ~ 3+	9 (47.37)	3 (37.50)	6 (54.55)	
Proteinuria				
Negative	9 (42.86)	6 (75.00)	3 (23.08)	0.046
1+	4 (19.05)	0 (0.00)	4 (30.77)	
2+ ~ 4+	8 (38.10)	2 (25.00)	6 (46.15)	
Microalbuminuria				
<0.15	10 (52.63)	6 (75.00)	4 (36.36)	0.115
≥0.15	9 (47.37)	2 (25.00)	7 (63.64)	
Pathological cast	4 (20.00)	0 (0.00)	4 (33.33)	0.102
Renal function				
Highest BUN value after admission (mmol/L)	21.44±11.01	19.33±9.44	22.78±11.92	0.367
The highest average Scr value after admission (minimum–maximum) (μmol/L)	187 (126.75-262.75)	170.50 (114.75-263.50)	193.00 (142.75-263.75)	0.346
The average basic BUN value after admission (minimum–maximum) (mmol/L)	6.15 (4.50-7.88)	5.00 (3.43-6.98)	6.65 (5.28-9.83)	0.020
The basic Scr value after admission (minimum–maximum) (μmol/L)	82.31±29.44	68.29±18.31	91.23±31.98	0.020
Electrolyte (mmol/L)				
Potassium	4.18±0.87	4.16±0.98	4.20±0.81	0.888
Calcium	2.15±0.17	2.09±0.14	2.19±0.18	0.107
Phosphorus	1.06 (0.86-1.29)	1.00±0.26	1.22±0.47	0.118
Magnesium	0.89 (0.81-1.00)	0.85 (0.80-0.96)	0.90 (0.84-1.03)	0.297
Total carbon dioxide	24.53±3.57	24.68±3.20	24.43±3.85	0.840

§*The second lung CT results of nine patients were missing, *The routine urine results of 15 patients were missing. The P values were calculated by t-test or Wilcoxon test for continuous variables, and Fisher's exact test for categorical variables. CKD: Chronic kidney disease, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, AKI: Acute kidney disease, BUN: Blood urea nitrogen, sCr: Serum creatinine, CT: Computed tomography*

symptoms, such as decreased appetite and urine output. The frequency of diarrhea in non-CKD patients was slightly higher than that in CKD patients, and significantly more non-CKD patients were treated with human albumin than CKD patients. Thus, diarrhea caused by SARS-CoV-2 infection as well as the imbalances between water and electrolytes caused by reduced food intake may cause AKI in patients with non-CKD. Active nutritional support may improve the outcome of these patients.

The clinical classification of non-CKD patients was consistent with the AKI grade, suggesting that the degree of AKI in non-CKD patients may directly affect the severity of the clinical condition. In contrast, although many CKD patients progressed to critical illness, the trend was not consistent with the distribution of AKI grade, suggesting that diseases other than AKI affect disease progression in CKD patients.

CKD patients were significantly more likely to develop AKI than non-CKD patients. A previous study showed that SARS-CoV-2 mainly combines with angiotensin-converting enzyme 2 (ACE2) to invade human cells.[10] In addition to human type II alveolar epithelial cells and ciliary cells, cardiac endothelial cells and renal tubular cells also express ACE2.[11] Subsequently, Pan *et al.* performed single-cell sequencing analysis and found that the SARS-CoV-2-binding proteins, ACE2, and transmembrane protease serine 2 were abundantly expressed on renal tubular cells and

Table 4: Treatment and outcome comparisons between nonchronic kidney disease and chronic kidney disease patients with severe acute respiratory syndrome coronavirus-2 infection and acute kidney disease

	Patients included in the study (*n*=36), *n* (%)	Non-CKD patients infected with SARS-CoV-2 and develop AKI (*n*=14), *n* (%)	CKD patients who are infected with SARS-CoV-2 and develop AKI (*n*=22), *n* (%)	*P*
Treatment				
Antiviral	31 (86.11)	11 (78.57)	20 (90.91)	0.287
Antibiotic	35 (97.22)	14 (100.00)	21 (95.45)	0.611
Hormone	14 (43.75)	8 (75.00)	6 (30.00)	0.049
CRRT	3 (8.33)	1 (7.14)	2 (9.09)	0.669
Diuretics	15 (41.12)	6 (46.15)	9 (28.57)	0.565
Hypoglycemic agents	13 (33.33)	4 (28.57)	6 (27.27)	0.611
Angiotensin agents	2 (6.67)	0 (0.00)	2 (11.76)	0.313
Human albumin	21 (58.33)	12 (85.71)	9 (40.91)	0.009
Blood transfusion	10 (31.25)	3 (23.08)	7 (36.84)	0.335
Mechanical ventilation				
Noninvasive ventilation	15 (41.67)	5 (35.71)	10 (45.45)	0.411
Invasive ventilation	8 (22.86)	5 (35.71)	3 (13.64)	0.127
ECMO	2 (6.45)	1 (9.09)	1 (5.00)	0.591
Chinese medicine	32 (88.89)	14 (100.00)	18 (81.82)	0.124
Outcome				
Cure	16 (44.66)	9 (64.29)	7 (31.82)	0.058
Death	20 (55.56)	5 (35.71)	15 (68.18)	

The P values were calculated by t-test or Wilcoxon test for continuous variables, and Fisher's exact test for categorical variables. CKD: Chronic kidney disease, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, AKI: Acute kidney disease, CRRT: Continuous renal replacement therapy, ECMO: Extracorporeal membrane oxygenation

podocytes, suggesting that the SARS-CoV-2 might directly damage several kinds of inherent kidney cells.[12] However, this hypothesis needs further verification. CKD patients themselves have primary or secondary kidney disease with varying degrees of cell damage, such as glomerular podocytes, mesangial cells, endothelial cells, and tubule cells. Su *et al.* conducted pathological examinations on the kidneys of those who died from SARS-CoV-2 infection.[13] Under electron microscopy, coronavirus particles were found in the proximal tubular endothelial cells, podocytes, and distal renal tubules. Furthermore, fluorescent analyses of the SARS-CoV-2 showed positive for coronavirus particles, confirming that the coronavirus was SARS-CoV-2. These results indicate that the SARS-CoV-2 might increase the impact on the kidneys to varying degrees and become a potential cause of AKI, regardless of primary or secondary CKD.

CKD patients infected with SARS-CoV-2 and with AKI had the worst prognosis. The basic health of CKD patients was below average, most of which had diseases, such as chronic obstructive pulmonary disease, diabetes, cardiovascular disease, cerebrovascular disease, and malignant tumors. A previous study indicated that CKD patients also had long-term chronic inflammation and internal environmental disturbance.[14] However, SARS-CoV-2 activates the innate immune system, which induces the secretion of inflammatory factors by macrophages and dendritic cells.[15] In severe cases,

it can lead to inflammatory factor storms.[16] Therefore, after CKD patients are infected with the SARS-CoV-2, the virus may exacerbate the attack on the kidneys and internal environmental disturbances caused by oxidative stress products, inflammatory factors, and other pathological products. All of these factors increase the mortality rate of patients with AKI. Consistent with this, patients infected with SARS-CoV-2 may present with hypoxemia, acid–base balance disorder, respiratory failure, and sepsis.

This study has several limitations. First, SARS-CoV-2-infected patients who developed AKI may have more urine abnormalities, but not all patients underwent urine tests. Second, because of the inconvenience of data collection due to special reasons during the pandemic, the sample size was small and some results showed a trend without statistical differences. Third, whether the renal function of infected patients will recover or develop into a chronic issue remains unknown.

CONCLUSION

CKD and non-CKD patients have significantly different AKI incidence rates after being infected with SARS-CoV-2. After AKI occurred, the clinical manifestations and treatment of those with and without CKD also differed. Moreover, the mortality rate of CKD patients may also be higher. These results highlight the importance of variable treatment

methods in clinical management. For non-CKD patients with SARS-CoV-2 infection, timely fluid replacement and nutritional support may alleviate or slow down disease development. For patients with CKD, better monitoring and control of primary or secondary kidney disease and preventing AKI might be more effective.

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Conflicts of interest

Fei Xiong is an Editorial Board Member of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of this editor and his research groups.

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