

Clinical Analysis of Kidney Injury in Elderly Patients with COVID-19

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Abstract

Objective: The aim of the study was to analyze the clinical features of elderly patients with coronavirus disease 2019 (COVID-19) and to explore the relationship between COVID-19 patients and kidney injury. **Methods:** A total of 188 elderly patients with confirmed COVID-19 enrolled in this study were hospitalized for at least 1 week in the Central Theater Command General Hospital of Chinese People's Liberation Army from January 3, 2020 to March 14, 2020. The recorded information included clinical data and results of kidney-related laboratory tests. Retrospective analysis was performed. **Results:** The median age of the patients was 69 years (interquartile range 65–78, range: 60–97 years); 31.4% were 60–74 years old, and 68.6% were over 75 years old. A total of 12.8% and 18.6% of the patients were in critical and severe stages of COVID-19, respectively. The proportions of patients using mechanical ventilators and deaths were 9.5% and 8.5%, respectively. A total of 26.1% and 8.5% of the patients showed mild elevation of blood urea nitrogen (BUN) and serum creatinine (SCr) levels at admission. A total of 18.6% and 5.9% of the patients had elevated BUN and SCr 1 week after admission, respectively. A total of 3.1% of the patients were diagnosed with acute kidney injury, and 75% of those patients had chronic kidney disease before admission. Compared with the patients aged 60–74 years, those over 75 years exhibited significantly increased proportions of elevated BUN levels, critical illness, use of mechanical ventilated, and death. Multivariate logistic regression analysis revealed that an elevated BUN level at admission and 1 week after admission were independent risk factors for death in the elderly patients with COVID-19. **Conclusion:** There were more critical cases and a high mortality in elderly patients with COVID-19. An increased BUN level was an independent risk factor for death in elderly patients with COVID-19.

Key words: Blood urea nitrogen, coronavirus disease 2019, elderly, kidney injury, SARS-CoV-2

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 infection, poses severe challenges to people worldwide. People are generally susceptible to this virus, but the elderly bear the brunt. Studies have shown that COVID-19 patients who are older adults or have comorbidities such as hypertension, cardiovascular disease, diabetes, chronic

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respiratory disease, and chronic kidney disease (CKD) have worse outcomes and a higher mortality rate.^[1] Chen *et al.* reported 99 COVID-19 patients, of which 37% were patients over 60 years old.^[2] We summarized 87 patients with COVID-19 in the early stage of the Wuhan pandemic, and elderly patients accounted for 65%.^[3] Guan *et al.* found that 27% of patients with severe conditions were over 65 years old in 1099 patients with COVID-19.^[4] Liu *et al.* reported that the occupancy rate and death rate of COVID-19 patients over 60 years old in the intensive care unit (ICU) were higher than those of younger patients.^[5] A higher occurrence of kidney injury has been reported in patients with COVID-19. Large cohorts of hospitalized COVID-19 patients have showed that the incidence of COVID-associated acute kidney injury (AKI) is as high as 46%.^[6] The kidney pathology of COVID-19 patients includes acute tubular injury, glomerular fibrin thrombi, pigmented tubular casts, and collapsing focal segmental glomerulosclerosis.^[7,8] “Viral-like” particles have been observed in renal tissue samples by electron microscopy, and viral RNA has been identified in both glomerular and tubular compartments of kidney specimens.^[9] However, the link between viral presence and kidney injury remains unclear. There are also opposite reports that kidney damage is not common in COVID-19 patients.^[10] Wang *et al.* analyzed the clinical characteristics of 138 hospitalized patients with COVID-19; only 5 (3.6%) patients suffered from AKI, and three of them were in critical condition, indicating that kidney impairment was not common in these patients.^[11] According to our first-line experience, kidney impairment was also rare among young patients with COVID-19. The morbidity associated with CKD is 10.8%~13.4% in China,^[12,13] and the prevalence of CKD in people over 60 years old was 20% or even more.^[13] Moreover, elderly patients are more likely to suffer from kidney injury due to poor kidney reserve function, infection, high fever, insufficient blood capacity, etc., Therefore, is the kidney injury of patients with COVID-19 caused by SARS-CoV-2 infection or an underlying kidney disease of the patients? The answer to this question remains unclear and inconclusive. In this study, we collected 188 elderly (over 60 years of age) patients with COVID-19 and analyzed their basic clinical information, the occurrence of kidney damage, and their prognosis. The aim of this study was to explore the relationship between elderly patients with COVID-19 and kidney injury.

METHODS

Study design and participants

For this retrospective, single-center study, we recruited patients from January 03, 2020 to March 14, 2020, at the Central Theater Command General Hospital of Chinese People's Liberation Army in Wuhan, China. A total of 233 patients older than 60 years old were confirmed to have COVID-19.

Forty-three patients were excluded from this study due to a lack of serum creatinine (SCr) and blood urea nitrogen (BUN) at the 7th day after admission. Another two patients with maintenance hemodialysis were also excluded from the study. Finally, 188 patients were enrolled in this study. This study was approved by the Ethics Committee of Central Theater Command General Hospital, and written informed consent was obtained from the patients involved when data were collected retrospectively. All the authors reviewed the manuscript and vouch for the accuracy and completeness of the data and for the adherence of the study to the protocol. All the COVID-19 patients enrolled in the study were diagnosed according to the guidance provided by the National Health Commission of the People's Republic of China (NHC China).^[14] The diagnoses of COVID-19 patients were confirmed by SARS-CoV-2 nucleic acid detection or viral gene sequencing.

Procedures

The clinical characteristics, laboratory data, and outcome data were extracted from the electronic medical records of Central Theater Command General Hospital of Chinese People's Liberation Army. All information regarding age, sex, underlying comorbidities, clinical symptoms from onset to hospital admission, laboratory findings (routine urine and renal function at admission and renal function at 1 week after admission), and the use of mechanical ventilation were recorded. Clinical outcomes of the patients were followed up to March 14, 2020. All the data were entered into a computerized database and cross-checked by two physicians (Liu and Wang).

Definition and interpretation

The stages of disease severity were determined according to the guidelines for diagnosis and treatment of COVID-19 published by NHC China (7th Edition). (1) Mild cases were defined as follows: The clinical symptoms were mild, and there was no sign of pneumonia on imaging. (2) Moderate cases were defined as follows: Showing fever and respiratory symptoms with radiological findings of pneumonia. (3) Severe cases were defined as follows: adult patients meeting any of the following criteria: (i) respiratory distress (≥ 30 breaths/min), (ii) oxygen saturation $\leq 93\%$ at rest, and (iii) arterial partial pressure of oxygen/fraction of inspired oxygen ≤ 300 mmHg. Patients with chest imaging that showed obvious lesion progression within 24–48 h $> 50\%$ were managed as severe cases. (4) Critical cases were defined as follows: patients meeting any of the following criteria: Respiratory failure requiring mechanical ventilation, shock, or other organ failure requiring ICU care. According to the criteria of Kidney Disease, Improving Global Outcomes,^[15] AKI is defined as any of the following (not graded): increase

in the level of SCr by ≥ 0.3 mg/dl (≥ 26.5 $\mu\text{mol/L}$) within 48 h or increase in the level of SCr to ≥ 1.5 times the baseline, which is known or presumed to have occurred within the prior 7 days. The diagnostic criterion for elevated BUN was a level of BUN > 7.1 mmol/L (normal reference: 3.2–7.1 mmol/L); the diagnostic criterion for elevated SCr was a level of SCr > 106 $\mu\text{mol/L}$ (for males, normal reference: 53–106 $\mu\text{mol/L}$) or a level of SCr > 97 $\mu\text{mol/L}$ (for female, normal reference: 44–97 $\mu\text{mol/L}$).

Statistical analysis

SPSS software (Version 23) was used for statistical analysis in this study. Continuous variables are expressed as medians (interquartile ranges [IQRs]) and were compared with the Mann-Whitney *U*-test. Categorical variables are presented as numbers (%) and were compared with the Chi-square test and Fisher's exact test. The one-way ordered classified variables were compared with the rank sum test. Univariate logistic regression was used to analyze risk factors for death in elderly COVID-19 patients, and then the identified factors were analyzed by a multivariate logistic regression model with the "backward" method. The odds ratio and 95% confidence interval were reported. A significance level was considered statistically significant at $P < 0.05$.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Baseline characteristics

A total of 188 patients with COVID-19, aged 60–97 years [median: 69; IQR: 65–78; Table 1], were included in this study. Patients aged 60–74 accounted for 68.6% (129/188), and patients aged 75 and over accounted for 31.4% (59/188); 56.4% (106/188) of the COVID-19 patients were male. Critical, severe, and moderate or mild cases accounted for 13.3% (25/188), 20.7% (39/188), and 66.0% (124/188), respectively. A total of 11.7% (22/188) patients were treated with mechanical ventilation, and 9.0% (17/188) of the COVID-19 patients died [Table 1].

Kidney injury of the patients at admission

Nearly 23.9% (45/188) and 18.1% (34/188) of the elderly patients with COVID-19 had hematuria and proteinuria at admission. Forty-nine patients (26.1%) had an elevated BUN level, of whom 26.5% (13/49) had preexisting CKD.

Table 1: Baseline characteristics of patients hospitalized with coronavirus disease-2019

	n (%)
All patients	188
Sex	
Male	106 (56.4)
Female	82 (43.6)
Age (year), M (Q1, Q3)	69 (65, 78)
60–74	129 (68.6)
≥ 75	59 (31.4)
Comorbidities	
Hypertension	104 (55.3)
Diabetes	53 (28.2)
CKD	24 (12.8)
Severity of COVID-19	
Critical	25 (13.3)
Severe	39 (20.7)
Moderate or mild	124 (66)
Renal function at admission	
BUN (mmol/L), M (Q1, Q3)	4.8 (3.7, 6.6)
SCr ($\mu\text{mol/L}$), M (Q1, Q3)	66.5 (57.3, 80.0)
Mechanical ventilation	22 (11.7)
Death	17 (9.0)

COVID-19: Coronavirus disease 2019, BUN: Blood urea nitrogen, SCr: Serum creatinine, CKD: Chronic kidney disease

Sixteen patients (8.5%) had an elevated SCr level, of whom 43.8% (7/16) had preexisting CKD [Table 2].

The renal function of the elderly patients 1 week after admission

Around 18.6% (35/188) of the patients had an elevated BUN level 1 week after admission. Among those patients, 40.0%, 37.1%, 40.0%, and 34.3% were critically ill, had preexisting CKD, required mechanical ventilation, and died, respectively. A total of 5.9% (11/188) of the patients had an elevated SCr level, of whom 45.5%, 54.5%, 45.5%, and 45.5% were critically ill, had preexisting CKD, required mechanical ventilation, and died, respectively. Fourteen patients (10.7%) had an elevated BUN level after 1 week of admission, and their BUN level was normal at admission. Two patients (1.5%) had an elevated SCr level after 1 week of admission, while the level of SCr was normal at admission. Both patients were critical and severe cases and had preexisting CKD. One of them received mechanical ventilation treatment and died. Four patients (3.1%) met the diagnostic criteria of AKI. Of these patients, all four were critical or severe cases, three patients had preexisting CKD, three patients required mechanical ventilation, and two patients died [Table 3].

The different clinical characteristics between the two age groups

Compared with the 60–74 years old patients, those who were 75 years old and over exhibited higher BUN levels at

Table 2: Kidney injury at admission

	Hematuria, n (%)	Proteinuria, n (%)	BUN elevated, n (%)	BUN elevated, and SCr normal, n (%)	SCr elevated, n (%)
n (%)	45 (23.9)	34 (18.1)	49 (26.1)	34 (18.1)	16 (8.5)
Symptom, n (%)					
Fever	31 (68.9)	26 (76.5)	40 (81.6)	27 (79.4)	14 (87.5)
Vomiting	10 (22.2)	3 (8.8)	5 (10.2)	2 (5.9)	3 (18.8)
Diarrhea	4 (8.9)	6 (17.6)	6 (12.2)	2 (5.9)	5 (31.2)
Comorbidities, n (%)					
Hypertension	28 (62.2)	25 (73.5)	30 (61.2)	16 (47.1)	14 (87.5)
Diabetes	12 (26.7)	14 (41.2)	18 (36.7)	12 (35.3)	7 (43.8)
CKD	4 (8.9)	7 (20.6)	13 (26.5)	6 (17.6)	7 (43.8)

BUN: Blood urea nitrogen, SCr: Serum creatinine, CKD: Chronic kidney disease

Table 3: The changes of renal function 1 week after admission

	Elevated BUN, n (%)	Elevated SCr, n (%)	Normal BUN at admission, elevated now, n (%)	AKI, n (%)
n (%)	35 (18.6)	11 (5.9)	14 (7.4)	4 (3.1)
Clinical classification				
Critical	14 (40.0)	5 (45.5)	5 (31.2)	2 (50)
Severe	7 (20.0)	1 (9.1)	3 (18.8)	2 (50)
Moderate or mild	14 (40.0)	5 (45.5)	6 (42.9)	0
Comorbidities				
Hypertension	25 (71.4)	8 (72.7)	10 (71.4)	3 (75)
Diabetes	12 (34.3)	5 (45.5)	2 (14.3)	2 (50)
CKD	13 (37.1)	6 (54.5)	5 (35.7)	3 (75)
Mechanical ventilation	14 (40.0)	5 (45.5)	5 (35.7)	3 (75)
Death	12 (34.3)	5 (45.5)	4 (28.6)	2 (50)

BUN: Blood urea nitrogen, SCr: Serum creatinine, CKD: Chronic kidney disease, AKI: Acute kidney injury

admission and at 1 week after admission, a higher proportion of critical cases, more CKD comorbidities, a greater requirement for mechanical ventilator use, and a higher rate of death. In this study, AKI occurred in four patients, all of whom were over 75 years old [Table 4].

Results of univariate and multivariate logistic regression models

Univariate logistic regression models indicated that age, CKD comorbidities, a higher BUN level at admission, a higher SCr level at admission, and a higher BUN level at 1 week after admission were risk factors related to death in elderly patients with COVID-19. The analysis of the multivariate logistic regression model suggested that a higher BUN level at admission and a higher BUN level 1 week after admission were independent risk factors for death [Table 5].

DISCUSSION

This study shows that the main clinical symptom of elderly patients with COVID-19 was fever, which is the same as other reports. However, the proportion of vomiting and diarrheal symptoms and the proportion of hypertension, diabetes, and CKD comorbidities in this study were higher than those in

other reports.^[2,5,10,16] A clinical analysis of 1099 patients with COVID-19 found that the average age of the patients was 47 years old. Five percent of the patients entered the ICU, and 1.36% of the patients died,^[4] which was significantly lower than the results of our study (13.3% of patients with critically ill and 9.0% died). Liu *et al.* collected 78 patients with COVID-19; 14.1% of the patients deteriorated 2 weeks after admission, their average age was 66 years, and the average age of patients with stable or improved conditions was 37 years.^[17] Wu and McGoogan reported that the case fatality rate of COVID-19 patients over 80 years old was 14.8% (208/1408), and the case fatality rate of patients 70–79 years old was 8.0% (312/3918);^[18] their results were similar to those in our study. Elderly patients with COVID-19 were more susceptible to critical conditions, and their prognosis was worse.

Studies have shown that SARS-CoV-2 causes injury by binding to the ACE2 receptor in alveolar cells, and the kidneys also express the ACE2 receptor.^[19] Some pathology studies have indicated that patients with COVID-19 have varying degrees of kidney damage. Li *et al.* analyzed 59 cases of COVID-19 and found that the patients had varying degrees of kidney damage.^[20] Computed tomography (CT) imaging has

Table 4: Comparison between the two group

	60–74 years old (n=129), n (%)	≥75 years old (n=59), n (%)	P
Sex			
Male	68 (52.7)	38 (64.4)	0.13
Female	61 (47.3)	21 (35.6)	
Clinical classification			
Critical	10 (7.8)	14 (23.7)	0.003
Severe	29 (22.5)	6 (10.2)	
Moderate or mild	90 (69.8)	39 (66.1)	
Comorbidities			
Hypertension	67 (51.9)	37 (62.7)	0.17
Diabetes	32 (24.8)	21 (35.6)	0.13
CKD	9 (7.0)	15 (25.4)	0.01
Mechanical ventilation	8 (6.2)	9 (15.3)	0.045
Death	5 (3.9)	11 (18.6)	<0.01
AKI	0	4 (6.8)	
Symptoms			
Fever	90 (69.8)	34 (57.6)	0.10
Vomiting	5 (3.9)	5 (8.5)	0.19
Diarrhea	9 (7.0)	7 (11.9)	0.26

CKD: Chronic kidney disease, AKI: Acute kidney injury

Table 5: Results of univariate and multivariate logistic regression models

	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.12 (1.05–1.08)	<0.01	1.04 (0.96–1.13)	0.38
CKD	3.33 (1.01–10.05)	0.04	0.67 (0.08–5.86)	0.72
BUN level at admission	1.38 (1.21–1.57)	<0.01	1.46 (1.13–1.89)	<0.01
SCr level at admission	1.02 (1.01–1.04)	0.007	0.96 (0.92–1.01)	0.76
BUN level one week after admission	1.30 (1.13–1.48)	<0.01	1.22 (1.02–1.46)	0.03

CKD: Chronic kidney disease, BUN: Blood urea nitrogen, SCr: Serum creatinine, OR: Odds ratio, CI: Confidence interval

revealed that the CT value of the bilateral renal parenchyma is significantly lower than normal in those patients. This prompted clinicians to pay attention to kidney injury in COVID-19 patients. However, Wang *et al.* compared the renal function of patients with COVID-19 in the 1st week of admission and the 4th week after admission. The authors found that there was no significant difference in the changes of renal function. They suggested that SARS-CoV-2 infection does not cause kidney injury.^[10] We summarized the data of 87 patients with COVID-19, and we did not find serious kidney injury in the patients with COVID-19.^[3] The data of this study showed that 18.1%~26.1% of the elderly patients with COVID-19 were hospitalized with hematuria, proteinuria, elevated levels of BUN, and elevated levels of SCr, but all the patients exhibited inflammation and

stress conditions during the pandemic. Most of them had fever symptoms, combined with hypertension, diabetes, and CKD. Moreover, we found that the proportion of elevated BUN at admission was significantly disproportionate to the proportion of elevated SCr (26.1% vs. 8.5%) in the patients, and the two indicators were also disproportionate 1 week after admission (18.6% vs. 5.9%). Among the patients with elevated BUN levels at admission, the level of SCr was normal in 69.4% of the patients. Therefore, we believe that most of the elevated BUN may be related to nervousness, anxiety, malnutrition, insufficient calorie intake, and insufficient blood capacity in the elderly patients with COVID-19 during the early stage of the Wuhan pandemic. The level of BUN is not the best indicator of renal function. In most conditions, the evaluation of renal function is based on the level of SCr. The percentage of elevated SCr was stable and relatively low (8.5% and 5.9%) at admission and 1 week after admission. Among them, approximately 50% of patients were preexisting CKD (43.8% and 54.5%). The incidence of AKI was only 3.1%, and 75% of the patients had preexisting CKD. Logistic regression analysis also suggested that the BUN level (either at admission or at 1 week after admission) rather than the SCr level was an independent risk factor for death in elderly patients with COVID-19. Furthermore, the change in the BUN level may be closely related to the nervousness, anxiety, malnutrition, insufficient calorie intake, and insufficient blood capacity of elderly patients during the COVID-19 pandemic. All of the above clinical risk factors are preventable and treatable. Importantly, attention should be given to changes in BUN levels and their pathogenesis in elderly patients with COVID-19 during the pandemic.

Compared with the group aged 60–74 years, those aged 75 and over exhibited higher proportions of critical cases, mechanical ventilation use, and death. These findings suggest that COVID-19 is more severe with age. The level of BUN in patients aged 75 years and above was significantly increased, which reminded us to pay attention to the management of blood volume and calorie intake in elderly patients. Our results indicated that there was no statistically significant difference in SCr levels between the two different age groups, and there was no close relationship between serious conditions and kidney damage in elderly patients with COVID-19. However, there were only four cases of AKI diagnosed in our study, all of these patients were over 75 years old. This result suggested that patients over 75 years old may be more likely to develop AKI in the clinic.

CONCLUSION

In summary, the level of BUN in elderly patients with COVID-19 was significantly increased, and it was an

independent risk factor for death in elderly patients with COVID-19. The elderly patients with COVID-19 did not have serious kidney damage in our study. Although some elderly patients suffered from mild renal insufficiency, their prognosis was not too poor. However, elderly patients aged over 75 years were prone to AKI, and the status of malnutrition, insufficient calorie intake, and insufficient blood capacity of those patients should be closely monitored.

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Conflicts of interest

Qing-Li Cheng 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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