The incidence, risk factors and prognosis of acute kidney injury in severe and critically ill patients with COVID-19 in mainland China: a retrospective study

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Keywords: Corona Virus Disease 2019(Covid-19); Acute Respiratory Distress Syndrome(ARDS); Acute Kidney Injury(AKI); Intensive Care Unit(ICU); Mechanical Ventilation(MV)

Posted Date: July 30th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-50431/v1>

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Version of Record: A version of this preprint was published at BMC Pulmonary Medicine on November 9th, 2020. See the published version at <https://doi.org/10.1186/s12890-020-01305-5>.

Abstract

Background: Since the clinical correlates, prognosis and determinants of AKI in patients with Covid-19 remain largely unclear, we perform a retrospective study to evaluate the incidence, risk factors and prognosis of AKI in severe and critically ill patients with Covid-19.

Methods: We reviewed medical records of all adult patients (>18 years) with laboratory-confirmed Covid-19 who were admitted to the intensive care unit (ICU) between January 23rd 2020 and April 6th 2020 at Wuhan JinYinTan Hospital and The First Affiliated Hospital of Guangzhou Medical University. The clinical data, including patient demographics, clinical symptoms and signs, laboratory findings, treatment [including respiratory supports, use of medications and continuous renal replacement therapy (CRRT)] and clinical outcomes, were extracted from the electronic records, and we access the incidence of AKI and the use of CRRT, risk factors for AKI, the outcomes of renal diseases, and the impact of AKI on the clinical outcomes.

Results: Among 210 subjects, 131 were males (62.4%). The median age was 64 years (IQR: 56-71). Of 92 (43.8%) patients who developed AKI during hospitalization, 13 (14.1%), 15 (16.3%) and 64 (69.6%) patients were classified as stage 1, 2 and 3, respectively. 54 cases (58.7%) received CRRT. Age, sepsis, Nephrotoxic drug, IMV and elevated baseline Scr were associated with AKI occurrence. The renal recover during hospitalization among 16 AKI patients (17.4%), who had a significantly shorter time from admission to AKI diagnosis, lower incidence of right heart failure and higher P/F ratio. Of 210 patients, 93 patients deceased within 28 days of ICU admission. AKI stage 3, critical disease, greater age and minimum P/F <150mmHg independently associated with it.

Conclusions: Among patients with Covid-19, the incidence of AKI was high. age, sepsis, nephrotoxic drug, IMV and baseline Scr were strongly associated with the development of AKI. Time from admission to AKI diagnosis, right heart failure and P/F ratio were independently associated with the potential of renal recovery. Finally, AKI KIDGO stage 3 independently predicted the risk of death within 28 days of ICU admission.

Background

Since December 2019, the outbreak of coronavirus disease 2019 (Covid-19) has resulted in more than 10 million laboratory-confirmed cases and 499,913 death cases worldwide up to June 29th 2020 (1). The clinical manifestations of Covid-19 have been heterogeneous, ranging from asymptomatic viral carriers to critically ill cases (2,3). The clinical outcomes of critically ill cases have been poor, with the mortality rate being 61.5% within 28 days (4). Identification of the risk factors of death would be crucial to inform clinical decisions to guide early triage of patients for more intensive monitoring. Previous studies have documented that greater age and the presence of comorbidities correlated significantly with death in patients with Covid-19 (5). Few studies, however, have focused on the systemic complications and the clinical outcomes of Covid-19.

Acute kidney injury (AKI) is a heterogeneous disease and a common complication in critically ill patients. Severe respiratory infections such as Covid-19 might predispose to the development of AKI. Indeed, AKI reportedly correlated with poor clinical outcomes in patients with Covid-19 (2,3,4,6,7). Nonetheless, the clinical correlates, prognosis and determinants of AKI in patients with Covid-19 remain largely unclear. Early identification and intervention would help improve the clinical outcomes of patients with Covid-19 who were prone to develop AKI (8,9). Therefore, we performed a retrospective study to evaluate the incidence, risk factors and prognosis of AKI in severe and critically ill patients with Covid-19.

Methods

Patients

We reviewed medical records of all adult patients (>18 years) with laboratory-confirmed Covid-19 who were admitted to the intensive care unit (ICU) between January 23rd 2020 and April 6th 2020 at Wuhan JinYinTan Hospital and The First Affiliated Hospital of Guangzhou Medical University (designated hospitals for admitting patients with Covid-19). All patients met the criteria of having severe or critical Covid-19 according to the Chinese guidelines (10). The Ethics Committees of both hospitals approved the study protocol. Informed consent was waived due to the nature of the retrospective study.

Data extraction

The clinical data from 210 cases, including patient demographics, clinical symptoms and signs, laboratory findings, treatment [including respiratory supports, use of medications and continuous renal replacement therapy (CRRT)] and clinical outcomes, were extracted from the electronic records by two independent intensivists (LS and XZ) who subsequently cross-checked for data accuracy. The disagreement was further adjudicated by a third independent reviewer (YML). All data were entered into the computerized database for further statistical analyses.

Study definitions

Severe Covid-19 met any of the following: (1) Respiratory distress, $RR \geq 30$ times/min, with cyanosis; (2) Arterial finger oxygen saturation $\leq 93\%$ (air); (3) $PaO_2/FiO_2 \leq 300$ mmHg (1 mmHg = 0.133 kPa). Critical Covid-19 met any of the following: (1) Respiratory failure requires mechanical ventilation; (2) Shock; (3) Multiple organ failure requires ICU life support (10).

The definition, severity staging and clinical management of AKI were based on the *Kidney Disease: Improving Global Outcomes* (KDIGO) classification (9). The clinical management could also be amended as per the clinical needs at the discretion of the attending clinicians (11,12). Recovery of AKI was defined based on Acute Disease Quality Initiative (ADQI) 16 Workgroup:

(1) rapid sustained reversal: recovery from AKI within 48 h, (2) late sustained reversal: reversal after 48 hrs and sustained through 28 days after AKI diagnosis or hospital discharge, (3) relapsing AKI with complete recovery, (4) relapsing AKI without complete recovery and (5) never recovery. The first three categories were classified as complete renal recovery while the last two categories were classified as renal non-recovery (13).

Study outcomes

The study outcomes mainly consisted of the incidence of AKI and the use of CRRT . We also assessed the risk factors for AKI, the outcomes of renal diseases, and the impact of AKI on the clinical outcomes of Covid-19.

Statistical analysis

Continuous variables were expressed as the median and interquartile ranges (IQRs) and compared with Wilcoxon rank-sum test. Categorical variables were expressed as counts and percentages, and compared using chi-square test or Fisher's exact test as appropriate. The risk factors for AKI were screened with univariate logistic regression model, and the variables with P value of 0.10 or less were considered as the potential risk factors and further imported into the multivariate logistic regression analysis. The AKI and survivor risk model was established by calculating the regression coefficient (β), odds ratio (OR) and 95% confidence interval. The significance threshold was set at a 2-sided P value of less than 0.05. All statistical analyses were performed using R version 3.5.1 software (the R Foundation, USA) or SPSS version 17.0 (SPSS Inc., USA).

Results

Patient characteristics stratified by the severity of Covid-19

We included 210 patients with completed data, of whom 131 were males (62.4%). The median age was 64 years (IQR: 56-71). The patient characteristics as stratified by the disease severity are shown in **Table E1**. 60 patients were categorized as having severe disease and the remaining 150 patients as having critical disease upon admission to ICU. The gender and the age were comparable. Diabetes was more common in critical cases than in severe cases (24.7% vs 11.7%, $P=0.037$). There were, however, no significant differences for other comorbidities between severe and critical cases.

Overall, the most common respiratory support for severe cases consisted of conventional oxygen therapy (COT) and high-flow nasal cannula (HFNC), A significantly larger proportion of patients with critical disease were initiated with invasive mechanical ventilation (IMV). There was, however, no significant difference in the use of non-invasive mechanical ventilation (NIV) between severe and critical cases.

□**Table E1**□

Of the 210 patients, 194 patients were from Wuhan JinYinTan Hospital, and 16 patients were from The First Affiliated Hospital of Guangzhou Medical University. Right heart failure,

Hypoxemia, hypercapnia and higher levels of interleukin-6 were more common in patients from Wuhan JinYinTan Hospital (both $P < 0.05$). **Table E2**

The incidence of AKI and use of CRRT, and the Risk factors associated with AKI

Of 92 (43.8%) patients who developed AKI during hospitalization, 13 (14.1%), 15 (16.3%) and 64 (69.6%) patients were classified as having stage 1, 2 and 3 disease, respectively (**Table 1**). 54 cases (58.7%) received CRRT.

Patients with AKI were significantly more likely to be critical cases (97.8% vs. 50.9%, $P < 0.001$), have malignancy (10.9% vs. 3.4%, $P = 0.031$), develop sepsis (78.3% vs. 33.9%, $P < 0.001$), right heart failure (30.4% vs. 13.6%, $P = 0.003$) and disseminated intravascular coagulation (29.4% vs. 4.2%, $P < 0.001$). Significantly more critical cases than severe cases who received nephrotoxic drugs developed AKI (41.3% vs. 11.9%, $P < 0.001$). Patients with AKI more frequently received IMV (87.0% vs. 32.2%, $P < 0.001$) but less frequently received COT (2.2% vs. 33.1%, $P < 0.001$) and NIV (4.4% vs. 21.2%, $P < 0.001$). Furthermore, patients with AKI had markedly higher levels of serum creatinine (median: 75.5 vs. 67.1 $\mu\text{mol/L}$, $P = 0.002$), interleukin-6 (median: 17.9 vs. 12.3 pg/ml, $P < 0.001$) and serum ferritin (median: 2001.0 vs. 985.4 ng/ml, $P < 0.001$). Hypoxemia and hypercapnia were also more frequently identified in patients with AKI (both $P < 0.001$). In the multivariate regression model, greater age (OR 1.05, 95%CI 1.01-1.09), sepsis (OR 2.82, 95%CI 1.14-6.98), Nephrotoxic drug (OR 2.67, 95%CI 1.09-6.55), IMV (OR 9.72, 95%CI 2.93-32.24) and elevated baseline Scr (OR 1.01, 95%CI 1.00-1.02) were associated with AKI occurrence among patients with Covid-19. (**Table 2**)

Outcomes of renal diseases and impact of AKI on clinic outcomes

Of 92 patients with AKI, the renal function improved during hospitalization among 16 patients (17.4%), who had a significantly shorter time from admission to AKI diagnosis (median: 5 vs. 9 days, $P < 0.001$), lower incidence of right heart failure (56.3% vs. 25.0%, $P = 0.030$) and higher P/F ratio (median: 133.5 vs. 67.0, $P < 0.001$) than their counterparts (**Table 3**) (**Fig 1**)

Of 210 patients, 93 patients deceased within 28 days of ICU admission (ICU 28-day mortality: 44.3%), and non-survivors were more likely to be critical cases compared with severe cases (98.9% vs. 1.1%, $P < 0.001$). Significantly more non-survivors had sepsis (77.4% vs. 34.2%, $P < 0.001$) acute kidney injury stage 3 (52.7% vs. 12.8%, $P < 0.001$) and disseminated intravascular coagulation (28.0% vs. 5.1%, $P < 0.001$). CRRT was initiated significantly more frequently in non-survivors than in survivors (41.9% vs. 12.8%, $P < 0.001$).

IMV was initiated more frequently whereas COT and HFNC were initiated less frequently in critical cases (all $P<0.01$). Non-survivors had higher levels of interleukin-6 (median: 17.2 vs. 13.6 pg/ml, $P=0.031$) and serum ferritin (median: 2001.0 vs. 1000.7 ng/ml, $P<0.001$) compared with survivors. Hypoxemia and hypercapnia were also more common in non-survivors (both $P<0.001$). However, neither the use of nephrotoxic drugs nor the serum creatinine levels differed between survivors and non-survivors (**Table 4**). After adjusting for the potential confounding factors, having KDIGO stage 3 (OR:5.33, 95%CI: 1.15-24.65), critical disease (OR: 69.16, 95%CI: 5.86-815.79) , greater age (OR: 1.06, 95%CI: 1.02-1.11) and Min P/F <150 mmHg(OR: 15.21 , 95%CI: 4.72-49.07) independently predicted the death within 28 days of ICU admission(**Table 5**) (**Fig 2**).

Discussion

This is the first and largest, up to date, study which investigates the association between AKI and clinical outcomes in severe and critical patients with Covid-19. Among patients with Covid-19, the incidence of any AKI stages, AKI stage 1, 2, 3 was 43.8%, 14.1%,16.3% and 69.6%, respectively. age , sepsis, nephrotoxic drug, IMV and baseline Scr were strongly associated with the development of AKI. 58.7% of patients received CRRT, and only 17.4% of patients with AKI achieved recovery of the renal function, time from admission to AKI diagnosis, right heart failure and P/F ratio were independently associated with the potential of renal recovery. It is worth emphasizing that all dialysis-dependent AKI patients were treated with CRRT. Furthermore, greater age, severe hypoxemia, having severe AKI and critical Covid-19 independently predicted the risk of death within 28 days of ICU admission.

AKI has been a frequent complication among patients admitted to the ICU. A 2004–2012 systematic review that included large-scale cohort studies has estimated the global incidence of AKI to be 21.6% in adults (95% CI, 19.3 to 24.1), and 31.7% (95% CI, 28.6 to 35.0) in critical care settings, according to the KDIGO guideline (14). However, a recent study which enrolled 634 patients with ARDS demonstrated that an incidence rate of 68.3% for AKI after the onset of ARDS (15). In another observational study on the critically ill patients with 2009 influenza A (H1N1) viral pneumonia, the incidence of AKI reached to 51% (16). Our finding of the higher incidence of AKI (43.8%) in patients with Covid-19 therefore might have been attributable to the high incidence of ARDS during hospitalization.

Previous studies had demonstrated that greater age, sepsis and baseline Scr was associated with the development of AKI in adult patients(10,15,17,18,19,20,21), our results were consistence with this view. In recent years, the association between IMV and AKI in ARDS patients had attracted attention and became widely acceptable. Several studies had postulated that IMV might played a key role in the development of AKI due to the mechanisms of lung-kidney crosstalk(22,23), and lung protective ventilation strategy including low tidal volume ventilation, limited plateau pressure, and suitable PEEP level was postulated to decrease the risk of AKI(24). However, hypercapnia was very common in our patients, especially the patients with AKI. And it seemed to be difficult to correct even the patients had been intubated and received lung protective ventilation strategy, which was not displayed in our study. So the physicians had to relax restrictions on tidal volume and plateau pressure in a very constrained environment, especially at

the early stage of epidemic. And it might explain the reason IMV was the strongest risk factors associated with AKI in our study.

In our study, only 16 AKI patients (17.4%) had achieved recovery of renal function during the hospitalization, which was significantly lower than that reported in a previous study (39.3%)²⁵. Our analysis revealed that the delayed onset of AKI, the presence of right heart failure and lower oxygenation ratio were associated with an increased likelihood of having non-recovery of renal function. It was likely that patients with a delayed onset AKI would have a lengthy course of hospital management, including hemodynamic deterioration, use of drug with nephrotoxicity and the adverse impacts associated with lung-renal cross-talk during the course of ARDS development (18,19). Severe hypoxemia had been considered as a cause of chronic kidney disease and AKI(26,27,28). it seemed that the severity and duration of AKI likely depend on the severity and duration of hypoxemia. In our study, the overall incidence of right heart failure was similar with a previous study(29). Persistent right heart failure would lead to elevated central venous pressure and peripheral edema, which were risk factors of AKI in critically illness(30).

Several previous studies had demonstrated that AKI, especially severe AKI was associated with poorer clinical outcomes(15,18,31). The AKI-EPI study showed that patients with stage 1 AKI did not have a higher risk of mortality compared to patients without AKI(32). However, in our study, only AKI KDIGO stage 3 was associated with ICU 28 days mortality, patients with KDIGO stage 1 and 2 AKI did not have a higher mortality compared to patients without AKI.

To our knowledge, this is the first and largest study which investigates the incidence, risk factors of AKI, and the association between AKI and clinical outcomes in severe and critical patients with Covid-19. However, we acknowledge a number of limitations of the current study, which are in part due to the nature of retrospective study. We did not collect the ventilator parameters which might play a key role in lung-kidney crosstalk. We also did not access the cumulation of fluid balance per day due to the very constrained environment, and the result of our study needed further validation in the future study

Conclusion

In conclusion, Among patients with Covid-19, the incidence of AKI was high. age , sepsis, nephrotoxic drug, IMV and baseline Scr were strongly associated with the development of AKI. Time from admission to AKI diagnosis, right heart failure and P/F ratio were independently associated with the potential of renal recovery. Finally, AKI KIDGO stage 3 independently predicted the risk of death within 28 days of ICU admission.

Abbreviations

Covid-19: Corona Virus Disease 2019; ARDS: Acute Respiratory Distress Syndrome; AKI: Acute Kidney Injury; ICU: Intensive Care Unit; MV: Mechanical Ventilation; CRRT: continuous renal replacement therapy;

P/F: PaO₂/FiO₂; KIDGO: Kidney Disease: Improving Global Outcomes; ADQI: Acute Disease Quality Initiative; IQRs: interquartile ranges; OR: odds ratio; COT: conventional oxygen therapy; HFNC: high-flow nasal cannula; IMV: invasive mechanical ventilation; NIV: non-invasive mechanical ventilation.

Declarations

Acknowledgements

Not Applicable.

Authors' contributions

JXH, SYL, DYZ, NSZ and YML conceived and designed the study; ZHZ, WHL, MZ, LJ, CP, WZ, JAX, NSC, WJW, YHX, XSL and XQL collected and aggregated data; LS, SBC, XZ, WJG and HKW analyzed the data and wrote the manuscript. All authors read and approved the final manuscript.

Funding

The study was funded by the National Science and Technology Major Project (No.2017ZX10204401), National Natural Science Foundation of China (No.81970071), National Key Research and Development Program of China (No.2018YFC1200100), the Special Project of Guangdong Science and Technology Department (No.2020B111105001), and Natural Science Foundation of Guangdong (No.2020A1515011459). The funding body had no role in the study design, the collection, analysis or interpretation of the data.

Availability of data and materials

Data sharing will be considered only on a collaborative basis with the principal investigators, after evaluation of the proposed study protocol and statistical analysis plan.

Ethical approval and consent to participate

The Ethics Committees of Wuhan JinYinTan Hospital and the First Affiliated Hospital of Guangzhou Medical University approved the protocol (KY-2020-56.01/GY-2020-65). Since all data were anonymously used and this study does not contain protected health information, the ethics committee approved a waiver of the requirement for informed consent.

Consent for publication

Not Applicable.

Competing interests

None of the authors has any conflict of interest to report.

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Tables

Table 1. Clinical characteristics of patients with Covid-19 when stratified by the presence of AKI during hospitalization

Total		AKI	No AKI	
Characteristic	(N = 210)	(n = 92)	(n = 118)	<i>P</i> value
Age, median (IQR), yrs	64 (56-71)	65 (59-73)	62 (54-70)	0.021
Sex				0.186
Female	79 (37.6)	30 (32.6)	49 (41.5)	-
Male	131 (62.4)	62 (67.4)	69 (58.5)	-
Severity of Covid-19				<0.001
Severe	60 (28.6)	2 (2.2)	58 (49.2)	-
Critical	150 (71.4)	90 (97.8)	60 (50.9)	-
Comorbidities				
Hypertension	98 (46.7)	45 (48.9)	53 (44.9)	0.565
Diabetes	44 (21.0)	23 (25.0)	21 (17.8)	0.203
Cardiovascular diseases	23 (11.0)	9 (9.8)	14 (11.9)	0.632
Malignancy	14 (6.7)	10 (10.9)	4 (3.4)	0.031
Cerebrovascular disease	12 (5.7)	6 (6.52)	6 (5.1)	0.656
Chronic Kidney Disease	10 (4.8)	6 (6.52)	4 (3.4)	0.290
Chronic Obstructive Pulmonary Disease	5 (2.4)	2 (2.2)	3 (2.5)	NA
Connective Tissue Disease	2 (1.0)	2 (2.2)	0 (0.0)	NA
Complication				
Sepsis	112 (53.3)	72 (78.3)	40 (33.9)	<0.001
Right heart failure	44 (21.0)	28 (30.4)	16 (13.6)	0.003
Disseminated Intravascular Coagulation	32 (15.2)	27 (29.4)	5 (4.24)	<0.001
Treatment				
Drug with Nephrotoxicity	52 (24.8)	38 (41.3)	14 (11.9)	<0.001
Respiratory support: COT	41 (19.5)	2 (2.2)	39 (33.1)	<0.001
Respiratory support: HFN	22 (10.5)	6 (6.5)	16 (13.6)	0.099
Respiratory support: NIV	29 (13.8)	4 (4.4)	25 (21.2)	<0.001
Respiratory support: IMV	118 (56.2)	80 (87.0)	38 (32.2)	<0.001

Laboratory Findings				
Baseline serum creatinine (μmol/L)	69.7 (55.9-85.9)	75.5 (59.8-102.8)	67.1 (54.3-78.4)	0.002
Maximum PaCO ₂ (mmHg)	52.0 (39.0-73.8)	69.5 (46.8-81.3)	45.0 (38.3-57.5)	<0.001
Maximum PaCO ₂ ≥ 60mmHg	82 (39.05)	55 (59.78)	27 (22.88)	<0.001
Minimum PaO ₂ /FiO ₂ ratio (mmHg)	109.0 (65.0-207.7)	73.0 (62.8-138.6)	169.0 (74.3-217.5)	<0.001
Minimum PaO ₂ /FiO ₂ ratio <150mmHg	116 (55.24)	70 (76.09)	46 (38.98)	<0.001
Maximum IL-6 (pg/ml)	14.3 (9.9-24.9)	17.9 (12.6-33.5)	12.3 (8.9-19.6)	<0.001
Maximum serum ferritin (ng/ml)	1607.8 (786.2-2001.0)	2001.0 (1329.6-2001.0)	985.4 (581.8-2001.0)	<0.001

§ Right heart failure: defined according to the clinical diagnosis and ultrasonographic manifestations. & Drugs with Nephrotoxicity: mainly included aminoglycosides, glycopeptides and colistin. ^, Data were collected before the development of AKI among patients who had developed AKI; The most abnormal data during hospitalization were presented among patients who did not develop AKI. PaCO₂: arterial partial pressure of carbon dioxide; PaO₂/FiO₂ ratio: the ratio between the arterial partial pressure of oxygen and the inspiratory concentration of oxygen; Data in bold indicated the comparisons with statistical significance.

Table 2. Risk factors associated with acute kidney injury in the multivariate regression analysis among patients with Covid-19

Variables	β	p value	OR (95% CI)
Age	0.05	0.0064	1.05 (1.01-1.09)
Sepsis	1.04	0.0250	2.82 (1.14-6.98)
Drug with Nephrotoxicity	0.98	0.0316	2.67 (1.09-6.55)
Respiratory support: IMV	2.27	0.0002	9.72 (2.93-32.24)
Baseline SCR	0.01	0.0018	1.01 (1.00-1.02)
95%CI: 95% confident interval			

95%CI: 95% confident interval

Table 3. Clinical characteristics of patients with AKI who had improved renal function and those without during hospitalization

Table 3. Clinical characteristics of patients with AKI who had improved renal function and those without during hospitalization

Characteristic	Patient: with AKI (N = 92)	Improved (n = 16)	Not improved (n = 76)	P value
Age, median (IQR), y	65 (59-73)	63 (49-66)	65 (61-74)	0.065
Time from admission to diagnosis of AKI, (day)	9 (5-12)	5 (3-9)	9 (6-14)	<0.001
Sex				0.059
Female	30 (32.6)	2 (12.5)	26 (36.8)	-
Male	62 (67.4)	14 (87.5)	48 (63.2)	-
KDIGO staging				
1	13 (14.1)	3 (18.8)	10 (13.2)	0.850
2	15 (16.3)	3 (18.8)	12 (15.8)	=0.999
3	64 (69.6)	10 (62.5)	54 (71.1)	0.706
Comorbidities:				
Hypertension	45 (48.9)	8 (50.0)	37 (48.7)	0.924
Diabetes	23 (25.0)	6 (37.5)	17 (22.4)	0.341
Cardiovascular diseases	9 (9.8)	0 (0.0)	9 (11.8)	0.324
Malignancy	10 (10.9)	2 (12.50)	8 (10.5)	0.651
Cerebrovascular disease	12 (13.7)	12 (6.2)	0 (0.0)	=0.999
Chronic Kidney Disease	6 (6.5)	3 (18.8)	3 (4.0)	0.063
Chronic Obstructive Pulmonary Disease	2 (2.2)	1 (6.3)	1 (1.3)	NA
Connective Tissue Disease	2 (2.2)	0 (0.0)	2 (2.6)	NA
Complication				
Sepsis	72 (78.3)	10 (62.5)	62 (81.6)	0.178
Right heart failure	28 (30.4)	9 (56.3)	19 (25.0)	0.030
Disseminated Intravascular Coagulation	27 (29.4)	5 (31.3)	22 (29.0)	=0.999
Treatment				
CRR	52 (56.5)	9 (56.3)	43 (56.6)	0.981
Drug with Nephrotoxicity	38 (41.3)	7 (43.8)	31 (40.8)	0.827
Respiratory support: COT	2 (2.2)	1 (6.3)	1 (1.3)	NA
Respiratory support: HFV	6 (6.5)	0 (0.0)	6 (7.9)	NA
Respiratory support: NIV	4 (4.4)	1 (6.25)	3 (4.0)	NA
Respiratory support: EMV	80 (87.0)	14 (87.5)	66 (86.8)	=0.999
Laboratory Findings:				
Baseline serum creatinine (μmol/L)	75.5 (59.8-102.8)	88.6 (54.4-229.8)	72.3 (61.8-90.8)	0.169
Maximum PaCO ₂ (mmHg)	69.5 (46.8-81.3)	65.5 (51.7-76.0)	72.0 (46.8-82.0)	0.881
Maximum PaCO ₂ >= 60mmHg	55 (59.8)	9 (56.3)	46 (60.5)	0.751
Minimum PaO ₂ /FiO ₂ ratio (mmHg)	73.0 (62.8-138.6)	133.5 (106.0-230.0)	67.0 (62.0-88.8)	<0.001
Minimum PaO ₂ /FiO ₂ ratio <150mmHg	70 (76.1)	9 (56.3)	61 (80.3)	0.085
Maximum IL-6 (pg/ml)	17.9 (12.6-33.5)	18.0 (14.0-97.3)	17.9 (12.1-31.5)	0.323
Maximum serum ferritin (ng/ml)	2001.0 (1329.6-2001.0)	2001.0 (1922.2-2001.0)	2001.00 (1296.5-2001.0)	0.889

§ Right heart failure: defined according to the clinical diagnosis and ultrasonographic manifestations. & Drugs with Nephrotoxicity: mainly included aminoglycosides, glycopeptides and colistin. ^, Data were collected before the development of AKI among patients who had developed AKI: The most abnormal data during hospitalization

Table 4. Clinical characteristics of patients with AKI who had survived and those not

Total		Non-survivor		Survivor	
Characteristic	(N = 210)	(n = 93)	(n = 117)		<i>P</i> value
Age, median (IQR), yrs	64 (56-71)	66 (61-73)	62 (53-69)		0.002
Sex					0.997
	Female	79 (37.6)	35 (37.6)	44 (37.6)	-
	Male	131 (62.4)	58 (62.4)	73 (62.4)	-
Severity of Covid-19					<0.001
	Severe	60 (28.6)	1 (1.1)	59 (50.4)	-
	Critical	150 (71.4)	92 (98.9)	58 (49.6)	-
Comorbidities					
Hypertension		98 (46.7)	43 (46.2)	55 (47.0)	0.911
Diabetes		44 (21.0)	21 (22.6)	23 (19.7)	0.605
Cardiovascular diseases		23 (11.0)	10 (10.8)	13 (11.1)	0.934
Malignancy		14 (6.7)	9 (9.7)	5 (4.3)	0.119
Cerebrovascular disease		12 (5.7)	7 (7.5)	5 (4.3)	0.313
Chronic Kidney Disease		10 (4.8)	3 (3.2)	7 (6.0)	0.545
Chronic Obstructive Pulmonary Disease		5 (2.4)	2 (2.2)	3 (2.6)	NA
Connective Tissue Disease		2 (1.0)	1 (1.1)	1 (0.9)	NA
Complication					
Sepsis		112 (53.3)	72 (77.4)	40 (34.2)	<0.001
Acute kidney injury		92 (43.8)	65 (69.9)	27 (23.1)	<0.001
AKI KDIGO stage 1		13 (6.2)	6 (6.5)	7 (6.0)	0.889
AKI KDIGO stage 2		15 (7.1)	10 (10.8)	5 (4.3)	0.070
AKI KDIGO stage 3		64 (30.5)	49 (52.7)	15 (12.8)	<0.001
Right heart failure		44 (21.0)	25 (26.9)	19 (16.2)	0.060
Disseminated Intravascular Coagulation		32 (15.2)	26 (28.0)	6 (5.1)	<0.001
Treatment					

Continuous renal replacement therapy	54 (25.7)	39 (41.9)	15 (12.82)	<0.001
Drug with Nephrotoxicity	52 (24.8)	28 (30.1)	24 (20.51)	0.110
Respiratory support: COT	41 (19.5)	0 (0.00)	41 (35.04)	0.287
Respiratory support: HFN	22 (10.5)	3 (3.23)	19 (16.24)	0.002
Respiratory support: NIV	29 (13.8)	10 (10.75)	19 (16.24)	0.252
Respiratory support: IMV	118 (56.2)	80 (86.0)	38 (32.5)	<0.001
Laboratory Findings				
Baseline Scr(umol/L)	69.7 (55.9-85.9)	71.1 (58.4-90.8)	69.0 (54.4-81.3)	0.165
Maximum PaCO ₂ mmHg	52.0 (39.0-73.8)	71.0 (54.0-79.0)	43.0 (38.0-54.0)	<0.001
Maximum PaCO ₂ ≥ 60mmHg	82 (39.1)	61 (65.6)	21 (18.0)	<0.001
Minimum P/F mmHg	109.0 (65.0-207.7)	65.0 (58.0-75.9)	190.0 (130.0-220.0)	<0.001
Minimum P/F <150mmHg	116 (55.2)	82 (88.2)	34 (29.1)	<0.001
Maximum IL-6 (pg/ml)	14.3 (9.9-24.9)	17.2 (11.7-31.2)	13.6 (9.3-22.2)	0.031
Maximum serum ferritin (ng/ml)	1607.8 (786.2-2001.0)	2001.0 (1130.0-2001.0)	1000.7 (590.2-2001.0)	<0.001

Right heart failure: defined according to the clinical diagnosis and ultrasonographic manifestations. & Drugs with Nephrotoxicity: mainly included aminoglycosides, glycopeptides and colistin. ^, Data were collected before the development of AKI among patients who had developed AKI; The most abnormal data during hospitalization were presented among patients who did not develop AKI. PaCO₂: arterial partial pressure of carbon dioxide; PaO₂/FiO₂ ratio: the ratio between the arterial partial pressure of oxygen and the inspiratory concentration of oxygen

Data in bold indicated the comparisons with statistical significance.

Non-survivor: Deceased within 28 days of ICU admission

Table 5. Risk factors associated with deceased within 28 days of ICU admission in the multivariate regression analysis among patients with Covid-19

Variables	β	<i>p</i> value	OR (95% CI)
Age	0.06	0.0035	1.06 (1.02-1.11)
Severity of Covid-19: critical	4.24	0.0008	69.16 (5.86-815.79)
AKI stage 3	1.67	0.0321	5.33 (1.15-24.65)
Min P/F <150mmHg	2.72	0.0000	15.21 (4.72-49.07)

95%CI: 95% confident interval

Min P/F: Minimal PaO₂/FiO₂ ratio

Figures

Figure 1

Association between the minimal PaO₂/FiO₂ ratio, time from admission to AKI diagnosis, right heart failure and the outcomes of renal disorders in patients with Covid-19 who had acute kidney injury during hospitalization A (left). Association between the minimal PaO₂/FiO₂ ratio, time from admission to AKI diagnosis and the outcomes of renal disorder and the severity of acute kidney injury in patients with Covid-19 during hospitalization B(right). Association between the minimal PaO₂/FiO₂ ratio, time from admission to AKI diagnosis and the outcomes of renal disorders and the presence of right heart failure in patients with Covid-19 who had acute kidney injury during hospitalization KDIGO: Kidney Disease: Improving Global Outcomes Min P/F: Minimal PaO₂/FiO₂ ratio

Figure 2

The proportion of patients with Covid-19 when stratified according to the survival status and the staging of the acute kidney injury AKI: Acute kidney injury; G: stage

Supplementary Files

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- [SupplementResults1.pdf](#)