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Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia

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ABSTRACT

Background Some patients with COVID-19 pneumonia also present with kidney injury, and autopsy findings of patients who died from the illness sometimes show renal damage. However, little is known about the clinical characteristics of kidney-related complications, including hematuria, proteinuria, and AKI.

Methods In this retrospective, single-center study in China, we analyzed data from electronic medical records of 333 hospitalized patients with COVID-19 pneumonia, including information about clinical, laboratory, radiologic, and other characteristics, as well as information about renal outcomes.

Results We found that 251 of the 333 patients (75.4%) had abnormal urine dipstick tests or AKI. Of 198 patients with renal involvement for the median duration of 12 days, 118 (59.6%) experienced remission of pneumonia during this period, and 111 of 162 (68.5%) patients experienced remission of proteinuria. Among 35 patients who developed AKI (with AKI identified by criteria expanded somewhat beyond the 2012 Kidney Disease: Improving Global Outcomes definition), 16 (45.7%) experienced complete recovery of kidney function. We suspect that most AKI cases were intrinsic AKI. Patients with renal involvement had higher overall mortality compared with those without renal involvement (28 of 251 [11.2%] versus one of 82 [1.2%], respectively). Stepwise multivariate binary logistic regression analyses showed that severity of pneumonia was the risk factor most commonly associated with lower odds of proteinuric or hematuric remission and recovery from AKI.

Conclusions Renal abnormalities occurred in the majority of patients with COVID-19 pneumonia. Although proteinuria, hematuria, and AKI often resolved in such patients within 3 weeks after the onset of symptoms, renal complications in COVID-19 were associated with higher mortality.

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The outbreak of coronavirus disease has rapidly evolved into a global pandemic.[1–7] This novel coronavirus is named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[8] The World Health Organization (WHO) officially named the disease caused by SARS-CoV-2 as coronavirus disease 2019 (COVID-19). The initial clinical sign for the detection of COVID-19 was pneumonia.[3] However, other organ damages were also reported.[6,9] Some cases of COVID-19 pneumonia presented with kidney injury,[4] and pathologic findings from autopsies also revealed renal damage from the corpses of patients with COVID-19[10]; thus, SARS-CoV-2 may include kidney tropism. In this study, we reported renal involvement and their early prognosis of patients with COVID-19 pneumonia admitted to Tongji Hospital in Wuhan, China, in terms of proteinuria, hematuria, and AKI.

METHODS

Study Design and Participants

For this retrospective, single-center study, we included adult patients from January 28 to February 9, 2020, at Tongji

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G.P. and Z.Z. contributed equally to this work.

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Hospital of Sino-French New City District, which was one of the designated hospitals solely for the treatment of patients with COVID-19 in Wuhan, China. The final follow-up for this study ended on February 23, 2020. All patients who were diagnosed as having COVID-19 pneumonia according to the Diagnosis and Treatment Protocols of Pneumonia caused by Novel Coronavirus (SARS-CoV-2) by the National Health Commission of China (Trial Version 7)[10] were screened. Specifically, the diagnosis criteria were as follows: (*1*) fever or respiratory symptoms, (*2*) leukopenia or lymphopenia, and (*3*) computed tomography (CT) scan showing radiographic abnormalities in lung. Those with two or more diagnosis criteria (lung involvement is necessary) and a positive result on high-throughput sequencing or RT-PCR assay were diagnosed as having COVID-19 pneumonia.[10] Exclusion criteria were as follows: (*1*) patients with CKD or suspected CKD, with at least one abnormal urine test including proteinuria and hematuria in the 3 months before admission; (*2*) patients with maintenance dialysis, renal transplantation, or peak serum creatinine of <53 μmol/L; (*3*) patients with time from onset of disease to admission date of >14 days, given that most patients achieved radiologic remission after 14 days from onset.[11] The study was approved by Tongji Hospital Ethics Committee of Huazhong University of Science and Technology (approval number TJ-C20200132). Informed consent was waived in the light of the urgency of data collection.

Data Collection and Measurements

We obtained demographic, epidemiologic, clinical, laboratory, and radiologic characteristics, and treatment and renal outcome data from electronic medical records. The data were reviewed by two physicians (G.P. and R.Z.). The onset date was defined as the day when the symptom was noticed. As of February 9, 2020, a total of 467 patients with COVID-19 were admitted and screened. A total of 333 patients with urine dipstick test on the first morning after admission, or with AKI on admission and during the hospital stay, were included in this study. Among the 333 patients, 82 patients without proteinuria or hematuria on admission and without AKI were excluded. Further, 53 patients without serial monitoring of urine dipstick tests were excluded. Finally, 198 patients with serial monitoring of urine dipstick tests, or with AKI, were included in the cohort (Supplemental Figure 1). It should be noted that 19 of the 35 patients with AKI and 235 of the 298 patients without AKI have been described previously by Cheng *et al.*[12]

Patients with possible COVID-19 pneumonia were admitted and quarantined, and throat swab samples were collected and detected in the hospital using a quantitative real-time RT-PCR to confirm SARS-CoV-2, as follows: A Viral Nucleic Acid Kit (Tianlong Science & Technology Co., Ltd., Xi'An, China) was used to extract nucleic acids from throat swab samples and a SARS-CoV-2 detection kit (DAAN GENE Co., Guangzhou, China) was used to detect the ORF1ab gene (nCovORF1ab) and the N gene (nCoV-NP) according to the manufacturer's instructions, using real-time RT-PCR. If the circulation threshold (Ct) values for both genes were >40 or had no typical amplification curves, and the internal control performed well, it was considered that the SARS-CoV-2 RNA was not present. If the Ct values for both genes were ≤ 40, the gene detection results were considered as positive. If only one gene had a Ct value of ≤ 40, and the other one had no typical amplification curve, a repeat experiment was performed, with consistent results considered as positive for SARS-CoV-2 RNA.

All patients were given a chest CT scan before or after admission to hospital, and a repeat chest CT scan was obtained at 5–10 day intervals. Laboratory data consisted of complete blood counts, liver and renal function, coagulation function, high-sensitivity C-reactive protein (CRP), erythrocyte sedimentation rate, and serum cytokines. Serial monitoring of these laboratory tests was performed for each patient according to the patient's clinical progress.

Significance Statement

Some cases of COVID-19 pneumonia have presented with kidney injury, and autopsy findings for patients with COVID-19 have revealed renal involvement. In this retrospective, single-center study of Chinese patients with COVID-19 pneumonia, 251 of 333 patients (75.4%) presented with renal complications, including proteinuria, hematuria, and AKI. After the median duration of 12 days of follow-up, nearly half of patients with AKI recovered from AKI within 3 weeks of onset of infection. However, patients with renal involvement had higher overall mortality (11.2%) compared with patients without renal involvement (1.2%). Adverse short-term outcomes of renal involvement were associated with severity of COVID-19 pneumonia. These findings indicate that although early renal abnormalities often resolve in such patients, intensive support and careful monitoring of severe or critical illness is appropriate for COVID-19 pneumonia with renal complications.

Definitions

COVID-19 pneumonia was classified into four types, namely, mild, moderate, severe, and critically ill, according to Diagnosis and Treatment Protocols of Pneumonia caused by Novel Coronavirus (SARS-CoV-2) by the National Health Commission of China (Trial Version 7).[10] Moderate COVID-19 pneumonia was defined as fever, respiratory syndrome, and radiologic lung findings.[10] Severe COVID-19 pneumonia was defined as meeting any of the following conditions: (*1*) respiratory rate ≥ 30 breaths/min, (*2*) oxygen saturation $\leq 93\%$ in a resting state, (*3*) Arterial oxygen partial pressure(PaO2) / Fractional inspired oxygen(FiO2) ratio ≤ 300 mm Hg, and (*4*) a 50% increase in chest radiologic abnormalities in 24–48 hours.[10,12] Critically ill COVID-19 pneumonia was defined as either (*1*) respiratory failure need for mechanical ventilation, (*2*) shock, or (*3*) organ failure need for ICU admission.[10,12]

For the diagnosis of AKI, we referred to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) definition

and the expanded criteria used by Yang *et al.*[13,14] First, we screened patients with suspected AKI using 2012 KDIGO definition as the major screening criteria. However, patients without previous baseline serum creatinine and those who did not meet the 2012 KDIGO criteria at admission but their increased serum creatinine was 1.5 times above the baseline with intervals longer than 7 days, would be excluded according to the 2012 KDIGO definition, which might potentially underestimate overall occurrence of AKI. For those who had no repeated serum creatinine within 7 days or with recovering AKI, we expanded the screening criteria to an increase or decrease in serum creatinine by ≥0.3 mg/dl during hospital stay. Second, these suspected AKI were reviewed on a case-by-case basis to confirm the diagnosis. The identification criteria included the 2012 KDIGO definition of AKI (KDIGO criteria). For those who had no repeated serum creatinine within 7 days or with recovering AKI, we expanded the identification criteria of AKI to an increase or decrease in serum creatinine by 50% during hospital stay (using serum creatinine concentration at admission as a baseline; we looked for increases or decreases in creatinine relative to this value), with or without oliguria. We defined renal recovery as serum creatinine decreasing to below threshold or to the baseline. The staging of AKI was on the basis of 2012 KDIGO criteria.[14]

Patients were considered to have prerenal AKI when the rise in serum creatinine concentration had been caused by low renal perfusion, and creatinine recovered rapidly to baseline after volume administration within 3 days.[15] Rhabdomyolysis was diagnosed on the basis of medical history, and elevated serum creatinine phosphokinase (CK) levels more than five times the upper limit of normal and/or serum myoglobin >150 ng/ml.[16,17] The elevations in CK were not caused by myocardial infarction, cerebral vascular disease, or neuromuscular disease. As no obstructive AKI was diagnosed, we classified the other AKI in this study as suspected intrinsic AKI, which might include acute tubular necrosis (ATN) and nephrotoxic AKI.

Patients with CKD were excluded. CKD was defined as eGFR<60 ml/min per 1.73 m^2 or urine microalbumin-creatinine ratio ≥30 μg/mg at least 3 months before admission.[18] If there was only one outpatient GFR <60 ml/min per 1.73 m^2, we evaluated CKD-related complications such as anemia and mineral and bone disorders. The patients who had CKD-related complications were considered as having suspected CKD and were also excluded.

Proteinuria and hematuria were defined as more than trace albumin or blood on urine dipstick tests, which were collected and detected on the first morning after admission and during the observation period. Remission of proteinuria and hematuria was defined as protein and blood were negative on urine dipsticks. Recovery of AKI was defined as complete recovery of kidney function.

Statistical Analyses

Data conforming to normal distribution were presented as mean±SD, or median and quartiles for non-normal distribution. Rate comparisons were performed by chi-squared test. *t* Test, Wilcoxon rank-sum test, Wilcoxon signed-rank test, or Kruskal–Wallis test were used to compare means across groups according to the number of group and distribution of variable. To estimate the degree of correlation between proteinuria or hematuria and clinical variables, Spearman rank correlation coefficient was used. Stepwise multivariate binary logistic regression was used to select and estimate the association between proteinuria, hematuria, or AKI remission and variables that were clinically relevant on grounds of professional knowledge and were statistically significant in preliminary univariate binary logistic regression. Specifically, variables with $P<0.05$ in the univariate analysis were entered into multivariate analysis to select the predictors (inclusion criterion was $P<0.05$ and exclusion criterion was $P<0.10$). Results are presented as odds ratios (ORs) with 95% confidence intervals (95% CIs) and *P* values. All statistical analyses were performed using SPSS version 20.0 software (IBM Corp.).

RESULTS

Baseline Characteristics

A total of 333 patients were included in the study. The mean of age was 56.3 years (Table 1), and 54.7% (182 of 333) patients were men. The median duration from onset to admission was 9 (7–11) days (Table 1). The prevalence of hypertension and diabetes was 32.2% (107 of 333) and 22.9% (76 of 333), respectively. Compared with moderate cases, patients with severe or critically ill COVID-19 pneumonia were older, more likely to experience dyspnea, and more likely to have hypertension, diabetes, and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) treatment history (Table 1).

Proteinuria, Hematuria, and AKI

On admission, of the 333 patients, 75.4% (251 of 333) patients had renal involvement, 65.8% (219 of 333) patients presented with proteinuria, and 41.7% (139 of 333) patients had hematuria (Table 1). The incidence of AKI in the overall cohort was 4.7% (22 of 467) by KIDGO criteria and 7.5% (35 of 467) by expanded criteria. Greater incidence of proteinuria (81.2% and 85.7%, respectively, versus 43.8%) and hematuria (39.1% and 69.6%, respectively, versus 33.3%) were demonstrated in patients with severe or critically ill COVID-19 pneumonia (Table 1). Among the 333 patients, the patients with AKI had higher incidence rate of proteinuria (88.6% versus 63.1%) and hematuria (60% versus 41.7%) compared with the non-AKI group (Supplemental Table 1). A total of 42.9% (24 of 56) critically ill cases developed AKI during the hospital stay (Table 1).

The number of patients with AKI was 22 by KDIGO criteria and 35 by expanded criteria (Table 2). According to KDIGO criteria, AKI occurred after admission in 19 (86.4%) of 22 patients with AKI. Rhabdomyolysis-induced

Table 1. Clinical characteristics of patients with COVID-19

Variables	All Patients	Moderate	Severe	Critically Ill	*P* Value
N	333	144 (43.2%)	133 (39.9%)	56 (16.8%)	
Days from onset	9 (7–11)	8 (6–11)	10 (7–11)	8 (6–11)	0.12[a]
Age, yr	56.3±13.4	50.9±12.5	58.1±12.3	63.1±11.0	<0.001[a]
Male patient, %	182/333 (54.7%)	67/144 (46.5%)	79/133 (59.4%)	36/56 (64.3%)	0.03[b]
Fever, %	301/333 (90.4%)	126/144 (87.5%)	123/133 (92.5%)	52/56 (92.9%)	0.16[b]
Cough, %	229/333 (68.8%)	98/144 (68.1%)	94/133 (70.7%)	37/56 (66.1%)	0.94[b]
Dyspnea, %	190/333 (57.1%)	71/144 (49.3%)	85/133 (63.9%)	34/56 (60.7%)	0.05[b]
Diarrhea, %	108/333 (32.4%)	42/144 (29.2%)	41/133 (30.8%)	25/55 (49.1%)	0.06[b]
Hypertension, %	107/332 (32.2%)	37/144 (25.7%)	43/133 (32.3%)	27/55 (49.1%)	0.003[b]
ACEI/ARB history, %	37/321 (11.5%)	12/143 (8.4%)	14/126 (11.1%)	11/52 (21.2%)	0.02[b]
ACEI/ARB	11/26	0/12	6/8	5/6	
Diabetes, %	76/332 (22.9%)	20/144 (13.9%)	32/133 (24.1%)	24/55 (43.6%)	<0.001[b]
SPO_2 (%)	93 (91.0–97.0)	97.0 (96.0–98.0)	92.0 (90.0–93.0)	89.5 (80.0–93.0)	<0.001[a]
Systolic BP, mm Hg	126 (115–138)	124 (114–132)	128 (116–141)	135 (118–145)	0.001[a]
Diastolic BP, mm Hg	78 (72–86)	77 (72–86)	78 (71–87)	79 (73–86)	0.76[a]
Blood sugar, mmol/L	6.6 (5.7–8.1)	6.0 (5.4–7.1)	6.9 (5.9–8.6)	7.8 (6.3–12.4)	<0.001[a]
CRP, mg/L	44.1 (16.3–90.8)	22.1 (7.5–45.3)	58.1 (32.5–101.4)	69.7 (42.9–119.6)	<0.001[a]
Erythrocyte sedimentation rate, mm/h	31.0 (18.0–58.8)	27.0 (14.3–50.3)	39.0 (22.0–64.0)	31.0 (22.0–58.0)	0.004[a]
ALT, U/L	24.0 (15.0–38.3)	20.0 (13.0–33.0)	26.0 (18.5–39.5)	29.0 (18.0–43.0)	0.001[a]
AST, U/L	31.0 (22.0–48.0)	24.0 (20.0–38.0)	33.0 (24.0–50.5)	40.5 (25.5–62.3)	<0.001[a]
HsTnI, pg/ml	5.4 (3.3–14.0)	4.6 (2.5–7.0)	4.8 (3.1–11.7)	11.4 (6.3–21.6)	<0.001[a]
NT-proBNP, pg/ml	139.0 (52.0–392.5)	76.0 (23.0–152.0)	157.5 (55.5–333.8)	372.5 (155.3–758.3)	0.002[a]
Serum albumin, g/L	34.5±4.7	36.6±4.9	33.6±4.2	32.9±4.3	<0.001[a]
BUN, mmol/L	4.3 (3.2–5.7)	3.9 (3.1–5.0)	4.4 (3.2–5.5)	5.9 (4.6–8.6)	<0.001[a]
SCR, μmol/L	70.0 (57.0–84.0)	66.5 (56.0–81.0)	69.0 (57.0–84.0)	77.0 (60.0–89.0)	<0.001[a]
Prothrombin time, sec	14.1 (13.5–14.8)	14.0 (13.2–14.5)	14.3 (13.5–14.9)	14.4 (13.8–14.9)	0.004[a]
D-dimer, mg/L	0.73 (0.40–1.33)	0.47 (0.32–1.10)	0.80 (0.57–1.33)	1.25 (0.64–5.90)	<0.001[a]
Neutrophils, 10^9/L	3.79 (2.57–5.45)	2.99 (2.14–4.13)	4.06 (2.84–5.56)	5.79 (3.79–8.59)	<0.001[a]
Lymphocytes, 10^9/L	0.86 (0.63–1.20)	1.01 (0.72–1.44)	0.78 (0.60–1.05)	0.55 (0.43–0.80)	<0.001[a]
Eosinophils, 10^9/L	0.00 (0.00–0.01)	0.00 (0.00–0.09)	0.00 (0.00–0.06)	0.00 (0.00–0.01)	<0.001[a]
Monocytes, 10^9/L	0.39 (0.28–0.51)	0.41 (0.30–0.53)	0.36 (0.26–0.52)	0.38 (0.22–0.49)	0.16[a]
Serum TNFα, pg/ml	8.6 (7.0–10.7)	8.1 (6.8–9.8)	9.3 (7.6–11.6)	9.3 (6.8–11.1)	0.09[a]
Serum IL-10, pg/ml	5.7 (5.0–10.2)	5.0 (5.0–8.1)	6.4 (5.0–10.4)	8.0 (5.0–15.1)	0.01[a]
Serum IL-6, pg/ml	19.9 (8.0–45.4)	13.2 (3.8–23.1)	27.1 (11.8–60.0)	32.8 (17.8–62.6)	<0.001[a]
Serum IL-2R, U/ml	669 (459–963)	546 (455–743)	766 (595–1050)	1026 (378–1260)	<0.001[a]
Proteinuria, %	219/333 (65.8%)	63/144 (43.8%)	108/133 (81.2%)	48/56 (85.7%)	<0.001[b]
Hematuria, %	139/333 (41.7%)	48/144 (33.3%)	52/133 (39.1%)	39/56 (69.6%)	<0.001[b]
AKI, %	35/333 (10.5%)	5/144 (3.5%)	6/133 (4.5%)	24/56 (42.9%)	<0.001[b]
Renal involvement, %	251/333 (75.4%)	89/144 (61.8%)	111/133 (83.5%)	51/56 (91.1%)	<0.001[b]
Death, %	29/333 (8.7%)	0	0	29/56 (52.8%)	<0.001[b]

Data are presented as a number and percentage or mean±SD or median (25th–75th percentiles); eosinophils are presented as median (fifth–95th percentiles). SPO_2, pulse oxygen saturation; ALT, alanine transaminase; AST, aspartate transaminase; HsTnI, high-sensitivity troponin; NT-proBNP, pro-brain natriuretic protein, N-terminal; SCR, serum creatinine.
[a]Kruskal–Wallis test.
[b]Wilcoxon rank-sum test.

AKI accounted for 18.2% (four of 22), but no prerenal AKI occurred. Suspected intrinsic AKI that accounted for 81.8% (18 of 22) was the most frequent form. Stage 2 comprised seven (31.8%) of 22 patients with AKI, and 50% (11 of 22) reached stage 3. The patients with AKI identified by the expanded criteria had more AKI occurrence on admission and more AKI in stage 1 than patients with AKI who met KDIGO criteria (Table 2).

Several clinical parameters were identified as being associated with proteinuria, hematuria, and AKI in patients with COVID-19 pneumonia at the time of admission, which were shown in Supplemental Tables 2– 4. Among 198 patients, one patient with AKI had a urine albumin-creatinine ratio of 238.7 μg/mg, and his urine protein electrophoresis showed a high proportion of the renal tubular protein (40.2%).

Renal Prognosis and Risk Factors

The clinical characteristics and treatment of the 198 patients followed up on are shown in Supplemental Table 4. The mean of age was 57.1 years, 57.1%

Table 2. Characteristics of patients with AKI according to two different criteria

Variables	KDIGO AKI Criteria	Expanded Criteria
N	22	35
AKI occurrence on admission	3/22 (13.6%)	13/35 (37.1%)
AKI occurrence during hospital stay	19/22 (86.4%)	22/35 (62.9%)
Classification		
Prerenal AKI	0/22 (0%)	2/35 (5.7%)
Rhabdomyolysis-induced AKI	4/22 (18.2%)	4/35 (11.4%)
Suspected intrinsic AKI	18/22 (81.8%)	29/35 (82.9%)
AKI stage		
1	4/22 (18.2%)	16/35 (45.7%)
2	7/22 (31.8%)	8/35 (22.9%)
3	11/22 (50.0%)	11/35 (31.4%)
AKI recovery (total)	4/22 (18.2%)	16/35 (45.7%)
Prerenal AKI recovery	—	2/2 (100%)
Rhabdomyolysis-induced AKI recovery	1/4 (25%)	1/4 (25%)
Suspected intrinsic AKI recovery	3/18 (16.7%)	13/29 (44.8%)
Stage 1 recovery	1/4 (25.0%)	12/16 (75.0%)
Stage 2 recovery	3/7 (42.9%)	4/8 (50.0%)
Stage 3 recovery	0/11 (0%)	0/11 (0%)
The mean time for AKI recovery	6 (5–8)[a]	6 (5–11)[a]
Total death	19/22 (86.4%)	20/35 (57.1%)
Death in prerenal AKI	0/0 (0%)	0/2 (0%)
Death in rhabdomyolysis-induced AKI	3/4 (75.0%)	3/4 (75.0%)
Death in suspected intrinsic AKI	16/18 (88.9%)	17/29 (58.6%)
Death in AKI stage 1	3/4 (75.0%)	4/16 (25.0%)
Death in AKI stage 2	6/7 (85.7%)	6/8 (75.0%)
Death in AKI stage 3	10/11 (90.9%)	10/11 (90.9%)

Data are presented as number and percentage.
[a]The unit of mean time for AKI recovery is day.

(113 of 198) patients were men, and the basic serum creatinine level was 74 μmol/L. A total of 98 (49.5%) of 198 patients presented with severe pneumonia and 37 (18.7%) of 198 had critical illness. Most patients received antibacterial therapy (84.8%, including moxifloxacin, levofloxacin, and cefoperazone-sulbactam), and many received antiviral therapy (umifenovir, 70.2%; lopinavir/ritonavir, 23.2%; ribavirin, 1.0%; remdesivir, 5.1%) and glucocorticoid therapy (71.7%, including at least one dose of dexamethasone in 5 mg or methylprednisolone in 20 mg, respectively).

The 198 patients were followed up on for a median duration of 12 days (Supplemental Table 5), during which 59.6% (118 of 198) patients with COVID-19 experienced pneumonia remission. Urine dipstick in 111 (68.5%) of 162 patients with proteinuria and in 44 (43.1%) of 102 patients with hematuria were reported as negative after follow-up (Table 3). According to KDIGO criteria, four (18.2%) of 22 patients with AKI achieved complete recovery of kidney function during the observation, including one of four patients with rhabdomyolysis-induced AKI, and three of 18 patients with suspected intrinsic AKI (Table 2). The mean time for AKI recovery was 6 days. The patients with AKI identified by the expanded criteria had higher rate of AKI recovery (45.7%, 16 of 35) and lower in-hospital mortality (57.1% versus 86.4%) than patients with AKI who met KDIGO criteria (Table 2). According to expanded criteria, patients with nonrecovered AKI presented with higher incidence of critical illness and severe pneumonia, and severe AKI (78.0% versus 25.0% in stage 2–3), compared with that in patients with recovered AKI (Table 4).

Stepwise multivariate binary logistic regressions were used to select significant predictors and estimate its ORs. Specifically, it showed that, compared with patients who achieved a decrease of CRP of $>$10 mg/L, patients whose decrease of CRP was $\leq$10 mg/L had a 9.20-fold odds (95% CI, 1.62 to 52.41) of proteinuric remission (Supplemental Table 6). Moderate versus critically ill, and severe versus critically ill groups had a 4.08-fold odds (95% CI, 0.58 to 28.55) and 41.18-fold odds (95% CI, 5.36 to 316.44) of proteinuric remission, respectively. Old age ($\geq$60 years) and ACEI/ARB treatment before admission were negative risk factors in proteinuric remission (old age: OR, 0.12 [95% CI, 0.02 to 0.70; ACEI/ARB: OR, 0.08 [95% CI, 0.01 to 0.68]) (Supplemental Table 6). Old age ($\geq$60 years), AKI, and ACEI/ARB treatment before admission were also negative risk factors in hematuric remission (old age: OR, 0.28 [95% CI, 0.08 to 0.90]; AKI: OR, 0.12 [95% CI, 0.02 to 0.81]; ACEI/ARB: OR, 0.11 [95% CI, 0.02 to 0.73]) (Supplemental Table 7). Moderate versus critically ill, and severe versus critically ill had a 1.05-fold

Table 3. Change in kidney function and biomarkers among participants in the follow-up study (n=198)

Variables	Patients before Follow-Up	Patients after Follow-Up	*P* Value
CRP, mg/L	56.2 (26.9–105.5)	3.9 (1.3–17.8)	<0.001[a]
Serum albumin, g/L	34.4±5.0	33.4±5.3	0.10[b]
BUN, mmol/L	4.7 (3.5–5.9)	4.6 (3.8–6.6)	0.07[a]
SCR, μmol/L	74.0 (61.0–89.0)	72.5 (60.0–85.0)	0.29[a]
Lymphocytes, 10^9/L	0.80 (0.59–1.12)	1.36 (0.87–1.82)	<0.001[a]
Eosinophils, 10^9/L	0.00 (0.00–0.06)	0.00 (0.07–0.29)	<0.001[a]
Serum IL-10, pg/ml	6.7 (5.0–13.1)	5.0 (5.0–5.2)	0.01[a]
Serum IL-6, pg/ml	24.3 (12.6–57.6)	4.8 (2.0–22.4)	0.008[a]
Serum IL-2R, U/ml	794 (552–1065)	505 (277–720)	<0.001[a]
Proteinuria			<0.001[a]
None	21/198 (10.6%)	132/198 (66.7%)	
±/+	146/198 (73.8%)	40/198(20.2%)	
++/+++	31/198 (15.6%)	4/198 (2.0%)	
Hematuria			<0.001[a]
None	89/198 (44.9%)	133/198 (67.2%)	
±/+	84/198 (42.4%)	33/198 (16.7%)	
++/+++	25/198 (12.6%)	10/198 (5.1%)	
AKI			<0.001[a]
No	163/198 (82.3%)	179/198 (90.4%)	
AKI stage 1	16/198 (8.1%)	6/198 (3.0%)	
AKI stage 2	8/198 (4.0%)	4/198 (2.0%)	
AKI stage 3	11/198 (5.6%)	9/198 (4.5%)	
Resolution on lung involvement		118/198 (59.6%)	
Death		29/198 (14.6%)	
Death in critically ill group		29/56 (51.8%)	

Data are presented as mean±SD or median (25th–75th percentiles) or as number and percentage. SCR, serum creatinine; ±/+, ± approximately 1+; ++/+++, 2+ approximately 3+.
[a]Wilcoxon signed-rank test.
[b]Paired *t* test.

odds (95% CI, 0.21 to 5.39) and 9.16-fold odds (95% CI, 1.53 to 54.97) of hematuric remission, respectively (Supplemental Table 7). Critical illness was the independently negative risk factor in the recovery of AKI in the multivariate analysis (OR, 0.03; 95% CI, 0.004 to 0.32) (Supplemental Table 8).

In the other 135 patients, 82 presented with no renal involvement at admission. The remaining 53 patients were lost to follow-up because they refused to or did not recheck urine analysis during follow-up. We compared the characteristics of the 53 patients lost to follow-up and 163 patients without AKI with follow-up. It showed no significant difference existing between the two groups (Supplemental Table 9). There was also no significant difference between the un-reported patients in this cohort and the overlapped patients in a previous cohort[12] (Supplemental Table 10).

Mortality

In this cohort study, 29 patients died during the observation period, out of 333 patients. All deaths occurred in patients with critical illness (Table 3). The patients with renal involvement, including hematuria, proteinuria, and AKI, had higher overall mortality (11.2%, 28 of 251) compared with that (1.2%, one of 82) of patients without renal involvement (Supplemental Table 11). No one with prerenal AKI died, whereas 75% (three of four) of patients with rhabdomyolysis-induced AKI died and 58.6% (17 of 29) of patients with suspected intrinsic AKI according to expanded AKI definition died (Table 2). The mortality was 25% (four of 16) in stage 1, 75% (six of eight) in stage 2, and 90.9% (ten of 11) in stage 3, respectively (Table 2). Among patients with proteinuric remission, no one died, whereas among patients without remission, nine (17.6%) of 51 died. There were no deaths among patients with hematuric remission; however, nine (20.3%) of 44 patients without remission died. Among patients with recovery of AKI, three (18.8%) of 16 died, whereas among patients with nonrecovery of AKI or new onset of AKI, 17 (89.5%) of 19 died (Supplemental Figure 2), suggesting that short-term outcomes of renal complications are associated with mortality in COVID-19 pneumonia.

DISCUSSION

Like Middle Eastern respiratory syndrome coronavirus (MERS-CoV), all coronaviruses have high renal involvement. The prevalence of proteinuria in this cohort study is similar to that reported in patients with MERS-CoV,[19] although a quantitative assessment of urinary protein excretion was not performed and patients with CKD were excluded. In the early phase (3 weeks after symptom onset) of MERS-CoV infection,

Table 4. Characteristics of patients in AKI nonrecovered and recovered group during follow-up periods

Variables	AKI Nonrecovery	AKI Recovery	*P* Value
N	19	16	
Days from onset	9 (7–14)	7 (5–12)	0.22[a]
Age	64.0±8.1	64.5±14.7	0.89[b]
Sex (male)	14/19 (73.7%)	8/16 (50.0%)	0.15[c]
Hypertension, %	9/19 (47.4%)	7/16 (43.8%)	0.83[c]
Diabetes, %	8/19 (42.1%)	6/16 (37.5%)	0.78[bc]
ACEI/ARB treatment history, %	4/19 (21.1%)	5/16 (31.3%)	0.49[c]
Glucocorticoids treatment, %	18/19 (94.7%)	13/16 (81.3%)	0.21[c]
Antibiotic treatment, %	19/19 (100.0%)	14/16 (87.5%)	0.11[c]
Umifenovir treatment, %	12/19 (63.2%)	8/16 (50.0%)	0.43[c]
Intravenous immunoglobulin therapy, %	9/19 (47.4%)	9/16 (56.3%)	0.60[c]
Continuous KRT, %	5/19 (26.3%)	1/16 (6.3%)	0.19[d]
Reexamined serum albumin, g/L	25.9±5.9	31.3±5.9	0.01[b]
Reexamined lymphocytes, 10^9/L	0.47 (0.32–0.85)	0.93 (0.35–1.45)	0.07[a]
Reexamined eosinophils, 10^9/L	0.03 (0.00–0.13)	0.04 (0.00–0.08)	0.67[a]
SCR of baseline, μmol/L	74.0 (61.0–89.0)	72.5 (60.0–85.0)	0.81[a]
COVID-19 grade			<0.001[a]
Moderate, %	1/19 (5.3%)	4/16 (25%)	
Severe, %	0/19 (0.0%)	6/16 (37.5%)	
Critically ill, %	18/19 (94.7%)	6/16 (37.5%)	
Stage of AKI			0.001[a]
Stage 1	4/19 (21.1%)	12/16 (75.0%)	
Stage 2	4/19 (21.1%)	4/16 (25.0)	
Stage 3	11/19 (57.9%)	0	
Classification of AKI			0.27[d]
Prerenal AKI	0/19 (0)	2/16 (12.5%)	
Rhabdomyolysis-induced AKI	3/19 (15.8%)	1/16 (6.3%)	
Intrinsic AKI	16/19 (84.2%)	13/16 (81.3%)	
Remission of proteinuria	1/7 (14.3%)	7/10 (70.0%)	0.05[d]
Remission of hematuria	1/7 (14.3%)	2/6 (33.3%)	0.56[d]

Data are presented as number and percentage, mean±SD, or median (25th–75th percentiles). SCR, serum creatinine.
[a]Wilcoxon rank-sum test.
[b]*t* test.
[c]Chi-square test.
[d]Fisher exact test.

proteinuria excretion is related to fever and systemic inflammatory status,[19] which is consistent with our results that half of proteinuria cases were mitigated with the recovery of pneumonia and systemic inflammation in 3 weeks after symptom onset. Therefore, we assume that proteinuria in early phase is probably transient febrile/illness-related proteinuria.

The high frequency of renal abnormalities in this study, including 75.4% with renal involvement, 65.8% with proteinuria, and 41.7% with hematuria, were similar to findings in other patients with critical illness, in which 67.4% had proteinuria and 77.5% had hematuria,[20] suggesting proteinuria and hematuria in COVID-19 is not different from patients with other critical illnesses. However, the incidence of AKI is lower.

About 7.5% (35 of 467) of the patients in the overall cohort had AKI according to the expanded criteria; and 45.7% of these patients had stage 1 AKI and 45.7% (16 of 35) achieved complete remission in 3 weeks after onset of disease. The mean time for AKI recovery was 6 days. When compared with patients with AKI who met KDIGO criteria, although the patients with AKI identified by the expanded criteria presented with more AKI on admission, they had a higher rate of AKI recovery and lower in-hospital mortality. As expanded criteria helped to identify the recovery of AKI, these data suggested that half of the early AKI in patients with COVID-19 was mild and easily recovered.

Using either KDIGO criteria or expanded criteria, suspected intrinsic AKI accounted for the most frequent form of AKI (>80%). Pathology from autopsies of patients with COVID-19 with renal function impairment demonstrated the direct evidence of intrinsic renal involvement, and revealed that the kidneys had varying degrees of ATN, luminal brush border sloughing, hyaline casts, microthrombi, and mild fibrosis in the interstitium, whereas severe glomerular injury and lymphocyte infiltration were absent,[10,21] suggesting the major form of intrarenal AKI in COVID-19 is ATN, which is consistent with the high proportion of renal tubular protein in urine findings. The high rate of resolution of proteinuria, hematuria, and AKI in the early stage (3 weeks after onset of symptom) is also consistent with the postmortem data that ATN appears to be

the most common cause. However, the mortality in patients with renal involvement, especially in those with no improvement of kidney function during the follow-up period (89.5%, 17 of 19), was extremely high in the early stage, suggesting that despite good short-term renal prognosis, renal complications in COVID-19 still remain associated with poor mortality.

Risk factors and causes of AKI in COVID-19 are diverse and multifactorial. On the basis of our multivariate binary regression analysis, we suggest that severity of pneumonia is the most important factor in development of AKI in patients with COVID-19. The fundamental pathophysiology of pneumonia in critically ill patients is severe acute respiratory distress syndrome, which has been identified as an independent risk factor associated with occurrence of AKI.[22] These data suggest it is necessary for intensively supporting and carefully monitoring patients with severe and critically ill pneumonia to ameliorate renal complications.

This study also has several limitations. First, the number of patients included in this study is limited, and there were some missing data. Second, because of the strain on medical resources in the epicenter of the COVID-19 outbreak, we could not get full laboratory support to obtain more sufficient evidence for evaluating the urine. Third, the duration of observation is not long enough to implement survival analysis to predict the probabilities for remission of renal damage in the long term and risks for mortality. Fourth, we did not detect SARS-CoV-2 in urine samples. Therefore, we could not assess correlations between urine virus and renal complications. Fifth, we did not have renal pathology data to assess the direct effect of the virus on renal outcomes. We did not detect biomarkers, such as urinary NGAL and KIM-1, to accurately distinguish prerenal AKI from ATN. Sixth, as the admission creatinine was used to define AKI in expanded criteria, some AKI at admission that did not resolve may have not been included, which might potentially overestimate overall recovery as well as underestimate severity in some patients (those with AKI at admission that continued to worsen).

In conclusion, despite high morbidity of renal involvement, the short-term renal prognosis of patients is good, as half of them achieved remission in 3 weeks after onset of symptoms. However, adverse short-term outcomes of renal involvement are also associated with mortality in COVID-19. Severity of pneumonia was identified as an independent negative prognostic indicator for renal complications. Therefore, the strategy on treatment and prevention of severe or critically ill pneumonia is appropriate for COVID-19–related renal complications.

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Dr. Xu, Dr. Yao, and Dr. Zeng designed the study. Dr. Pei, Dr. Liu, Dr. Zhang, Dr. Yu, Dr. Ma, Dr. Huang, and Dr. Liu collected the data. Dr. Pei, Dr. Zhang, and Dr. Zeng prepared figures and tables. Dr. Pei and Dr. Zhang contributed analytical tools. Dr. Pei, Dr. Zhang, and Dr. Zeng wrote the paper. Dr. Zeng and Dr. Yao conceived the project and supervised and coordinated all of the work.

DISCLOSURES

All authors declare that they have no competing interests, no support from any organization for the submitted work, and no financial relationships with any organizations that might have an interest in the submitted work.

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SUPPLEMENTAL MATERIAL

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Supplemental Table 1. Hematuria and proteinuria in the non-AKI group versus the AKI group.

Supplemental Table 2. The correlation between proteinuria and variables.

Supplemental Table 3. The correlation between hematuria and variables.

Supplemental Table 4. The correlation between AKI occurrence and variables.

Supplemental Table 5. Baseline and treatment characteristics among participants in the follow-up study (N=198).

Supplemental Table 6. Risk factors associated with proteinuria remission during follow-up periods.

Supplemental Table 7. Risk factors associated with hematuria remission during follow-up periods.

Supplemental Table 8. Risk factors associated with AKI recovery during follow-up periods.

Supplemental Table 9. Characteristics of patients lost to follow-up and patients with follow-up.

Supplemental Table 10. Comparison of unreported patients in this cohort and the overlapped patients in a previous cohort.

Supplemental Table 11. Mortality of the patients with renal involvement during follow-up periods.

Supplemental Figure 1. Schematic figure.

Supplemental Figure 2. Relationship between outcomes of renal involvement and mortality during follow-up periods.

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Supplementary Table 1. Hematuria and proteinuria in the non AKI group versus the AKI group

Variables	No AKI	AKI	*P*
Number	298	35	
Proteinuria			0.002[a]
none	110/298 (36.9%)	4/35 (11.4%)	
±/+	158/298 (53.0%)	24/35 (68.6%)	
++/+++	30/298 (10.1%)	7/35 (20.0%)	
Hematuria			0.007[a]
none	180/298 (58.3%)	14/35 (40.0%)	
±/+	94/298 (32.1%)	13/35 (37.1%)	
++/+++	24/298 (9.6%)	8/35 (22.9%)	

Data are presented as a percentage

a. Wilcoxon rank sum test

Supplementary Table 2. The correlation between proteinuria and variables

Variables	Spearman's rho	*P*	Variables	Spearman's rho	*P*
Gender (0,1)	-0.012	0.843	Blood sugar (mmol/L)	0.165	0.003
Age (years)	0.161	0.003	SBP (mmHg)	0.116	0.034
SPO2 (%)	-0.337	<0.001	DBP (mmHg)	0.047	0.396
Days from onset (days)	-0.046	0.405	HsTnI (pg/mL)	0.208	<0.001
Fever (0,1)	0.069	0.206	NT-proBNP (pg/mL)	0.159	0.039
Cough (0,1)	0.040	0.469	Hematuria	0.441	<0.001
Dyspnea (0,1)	-0.043	0.434	BUN (mmol/L)	0.303	<0.001
Diarrhea (0,1)	-0.024	0.662	SCR (μmol/L)	0.273	<0.001
Hypertension (0,1)	0.040	0.468	AKI (0,1)	0.207	<0.001
ACEI/ARB history (0,1)	0.009	0.870	Prothrombin time (s)	0.143	0.011
Diabetes (0,1)	0.111	0.044	D-dimer (mg/L)	0.210	<0.001
CRP (mg/L)	0.452	<0.001	Neutrophils (10^9/L)	0.211	<0.001
ESR (mm/h)	0.189	0.001	Lymphocytes (10^9/L)	-0.259	0.001
ALT (U/L)	0.205	0.001	Eosinophils (10^9/L)	-0.277	<0.001
AST (U/L)	0.409	<0.001	Serum IL-10 (pg/mL)	0.444	<0.001
Serum albumin (g/L)	-0.213	<0.001	Serum IL-6 (pg/mL)	0.412	0.001
Serum globin (g/L)	0.239	<0.001	Serum IL-2R (U/mL)	0.350	<0.001

Variables was defined as follows: Gender (0, female; 1, male); Fever (0, without fever; 1, with fever); Cough (0, without cough; 1, with cough); Dyspnea (0, without dyspnea; 1, with dyspnea); Hypertension (0, without hypertension; 1, with hypertension); ACEI/ARB (0, without ACEI/ARB treatment before the onset of the COVID-19; 1, with ACEI/ARB treatment before the onset of the COVID-19); Diabetes (0, without Diabetes; 1, with Diabetes); AKI (0, without AKI occurrence on admission or during the hospital stay;1, with AKI occurrence on admission or during the hospital stay); SBP, systolic blood pressure; DBP, diastolic blood pressure.

Supplementary Table 3. The correlation between hematuria and variables

Variables	Spearman's rho	*P*	Variables	Spearman's rho	*P*
Gender (0,1)	-0.012	0.843	Blood sugar (mmol/L)	0.117	0.037
Age (years)	0.170	0.002	SBP (mmHg)	0.090	0.102
SPO2 (%)	-0.189	0.001	DBP (mmHg)	0.036	0.512
Days from onset (days)	0.017	0.763	HsTnI (pg/mL)	0.325	<0.001
Fever (0,1)	0.131	0.017	NT-proBNP (pg/mL)	0.287	<0.001
Cough (0,1)	0.046	0.405	Proteinuria	0.441	<0.001
Dyspnea (0,1)	-0.001	0.981	BUN (mmol/L)	0.202	<0.001
Diarrhea (0,1)	-0.024	0.662	SCR (μmol/L)	0.171	0.002
Hypertension (0,1)	0.021	0.709	AKI (0,1)	0.162	0.003
ACEI/ARB history (0,1)	-0.009	0.874	Prothrombin time (s)	0.148	0.008
Diabetes (0,1)	0.139	0.012	D-dimer (mg/L)	0.141	0.013
CRP (mg/L)	0.252	<0.001	Neutrophils (10^9/L)	0.128	0.019
ESR (mm/h)	0.079	0.163	Lymphocytes (10^9/L)	-0.180	0.001
ALT (U/L)	0.031	0.065	Eosinophils (10^9/L)	-0.248	<0.001
AST (U/L)	0.187	0.002	Serum IL-10 (pg/mL)	0.284	<0.001
Serum albumin (g/L)	-0.152	0.005	Serum IL-6 (pg/mL)	0.248	0.001
Serum globin (g/L)	0.066	0.230	Serum IL-2R (U/mL)	0.228	0.004

Variables was defined as follows: Gender (0, female; 1, male,); Fever (0, without fever; 1, with fever); Cough (0,without cough; 1, with cough); Dyspnea (0,without dyspnea; 1, with dyspnea); Hypertension (0, without hypertension; 1, with hypertension); ACEI/ARB treatment history (0, without ACEI/ARB treatment before the onset of the COVID-19; 1, with ACEI/ARB treatment before the onset of the COVID-19); Diabetes (0, without Diabetes; 1, with Diabetes)； AKI (0, without AKI occurrence on admission or during the hospital stay;1, with AKI occurrence on admission or during the hospital stay); SBP, systolic blood pressure; DBP, diastolic blood pressure.

Supplementary Table 4. The correlation between AKI occurrence and variables

Variables	Spearman's rho	*P*	Variables	Spearman's rho	*P*
Gender (0,1)	0.056	0.304	Blood sugar (mmol/L)	0.194	0.001
Age (years)	0.200	<0.001	SBP (mmHg)	0.109	0.046
SPO2 (%)	-0.195	<0.001	DBP (mmHg)	0.025	0.654
Days from onset (days)	0.010	0.860	HsTnI (pg/mL)	0.301	<0.001
Fever (0,1)	0.012	0.333	NT-proBNP (pg/mL)	0.278	<0.001
Cough (0,1)	0.020	0.721	Proteinuria	0.207	<0.001
Dyspnea (0,1)	-0.039	0.479	Hematuria	0.162	0.003
Diarrhea (0,1)	0.097	0.076	BUN (mmol/L)	0.342	<0.001
Hypertension (0,1)	0.099	0.332	SCR (μmol/L)	0.256	<0.001
ACEI/ARB history (0,1)	0.155	0.005	Prothrombin time (s)	0.072	0.320
Diabetes (0,1)	0.140	0.011	D-dimer (mg/L)	0.247	<0.001
CRP (mg/L)	0.193	<0.001	Neutrophils (10^9/L)	0.239	<0.001
ESR (mm/h)	0.077	0.316	Lymphocytes (10^9/L)	-0.197	<0.001
ALT (U/L)	0.104	0.041	Eosinophils (10^9/L)	-0.160	0.003
AST (U/L)	0.194	0.001	Serum IL-10 (pg/mL)	0.137	0.084
Serum albumin (g/L)	-0.133	0.016	Serum IL-6 (pg/mL)	0.199	0.010
Serum globin (g/L)	0.114	0.038	Serum IL-2R (U/mL)	0.287	<0.001

Variables was defined as follows: Gender (0, female; 1, male,); Fever (0, without fever; 1, with fever); Cough (0, without cough; 1, with cough); Dyspnea (0, without dyspnea; 1, with dyspnea); Hypertension (0, without hypertension; 1, with hypertension); ACEI/ARB treatment history (0, without ACEI/ARB treatment before the onset of the COVID-19; 1, with ACEI/ARB treatment before the onset of the COVID-19); Diabetes (0, without Diabetes; 1, with Diabetes); SBP, systolic blood pressure; DBP, diastolic blood pressure.

Supplementary Table 5. Baseline and treatment characteristics among participants in the Follow-up Study (N=198)

Variables	Patients
Age (years)	57.1±13.4
Male patient, %	113/198 (57.1%)
SCR (μmol/L)	74 (61-89)
COVID-19 grade	
Moderate	63 (31.8%)
Severe	98 (49.5%)
Critically ill	37 (18.7%)
Hypertension, %	64/198 (32.3%)
ACEI/ARB treatment history, %	21/188 (11.2%)
Diabetes, %	46/198 (23.2%)
Days from admission to follow-up	12.0 (10.5-15)
Antibiotic treatment, %	168/198 (84.8%)
Arbidol treatment, %	139/198 (70.2%)
Lopinavir/ritonavir treatment, %	46/198 (23.2%)
Ribavirin treatment, %	2/198 (1.0%)
Remdesivir treatment, %	10/198 (5.1%)
Glucocorticoids treatment, %	142/198 (71.7%)
Intravenous immunoglobulin therapy, %	74/198 (37.4%)
Ventilator aid respiration, %	37/198 (18.7%)
Continuous renal replacement therapy (CRRT), %	6/198 (3.0%)

Data are presented as mean ± SD or median (25th–75th percentiles) or a percentage.

Supplementary Table 6. Risk factors associated with proteinuria remission during follow-up periods

Variable	Univariate analysis			Multivariate analysis[h]		
	OR	95% CI	*P*	OR	95% CI	*P*
Age (60 or above vs under 60) (n=162)	**0.199**	**(0.063, 0.626)**	**0.006**	**0.119**	**(0.020, 0.701)**	**0.019**
Gender (male vs female) (n=162)	0.966	(0.371, 2.509)	0.943			
AKI (yes vs no)[a] (n=162)	0.073	(0.023, 0.227)	<0.001			
Change of eosinophils count (1 vs 0)[b] (n=150)	2.601	(0.927, 7.299)	0.069			
Change of lymphocytes count (1 vs 0)[c] (n=153)	4.145	(1.484, 11.579)	0.007			
CRP grade (1 vs 0)[d] (n=131)	**9.895**	**(3.304, 29.636)**	**<0.001**	**9.203**	**(1.616, 52.413)**	**0.012**
Hypertension (with vs without) (n=162)	0.531	(0.205, 1.374)	0.192			
ACEI/ARB treatment history (1 vs 0)[e] (n=152)	**0.228**	**(0.068, 0.761)**	**0.016**	**0.076**	**(0.008, 0.684)**	**0.021**
Diarrhea (with vs without) (n=162)	0.464	(0.180, 1.194)	0.111			
Diabetes (with vs without) (n=162)	0.214	(0.080, 0.568)	0.002			
Days from onset (n=162)	1.054	(0.917, 1.212)	0.460			
Glucocorticoids treatment (with vs without) (n=162)	0.420	(0.117, 1.510)	0.184			
Antibiotic treatment (with vs without) (n=162)	0.868	(0.236, 3.195)	0.831			
Arbidol treatment (with vs without) (n=162)	1.216	(0.435, 3.397)	0.709			
Intravenous immunoglobulin therapy (with vs without) (n=162)	0.405	(0.157, 1.044)	0.061			
Bladder catheter (with vs without) (n=162)	0.063	(0.020, 0.203)	<0.001			
COVID-19 grade (reference=Critically ill) (n=162)			**<0.001**			**0.002**
Moderate (n=47)	11.727	(3.161, 43.512)	<0.001	4.081	(0.583, 28.550)	0.156
Severe (n=92)	**24.000**	**(6.583, 87.500)**	**<0.001**	**41.184**	**(5.360, 316.443)**	**<0.001**
Change of serum albumin (1 vs 0)[f] (n=135)	2.645	(0.886, 7.892)	0.081			
Recovery of lung (1 vs 0)[g] (n=145)	3.387	(1.100, 10.432)	0.034			

a. AKI (yes, with AKI occurrence on admission or during the hospital stay; no, without AKI occurrence on admission or during the hospital stay).

b. Change of eosinophils count (reexamined eosinophils was compared with initial eosinophils, 0, decreased or did not change; 1, increased)

c. Change of lymphocytes count (reexamined lymphocytes was compared with initial lymphocytes, 0, decreased or did not change; 1, increased)

d. CRP on follow-up (1, < or = 10mg/l; 0, >10mg/l)

e. 1, with ACEI or ARB treatment before the onset of the COVID-19; 0 without ACEI or ARB treatment before the onset of the COVID-19

f. Change of serum albumin (reexamined serum albumin was compared with initial serum albumin, 0, decreased; 1, increased or did not change)

g. Recovery of lung (reexamined degree of lung involvement was compared with initial degree of lung involvement, 0, no obvious recovery; 1, obvious recovery)

h. The number of cases included in the final multivariate logistic regression model is 120.

Supplementary Table 7. Risk factors associated with hematuria remission during follow-up periods

Variable	Univariate analysis			Multivariate analysis[h]		
	OR	95% CI	*P*	OR	95% CI	*P*
Age (60 or above vs under 60) (n=102)	**0.305**	**(0.119, 0.780)**	**0.013**	**0.276**	**(0.084, 0.903)**	**0.033**
Gender (male vs female) (n=102)	2.144	(0.882, 5.209)	0.092			
AKI (yes vs no)[a] (n=102)	**0.076**	**(0.019, 0.305)**	**<0.001**	**0.117**	**(0.017, 0.813)**	**0.030**
Change of eosinophils count (1 vs 0)[b] (n=94)	1.930	(0.685, 5.436)	0.213			
Change of lymphocytes count (1 vs 0)[c] (n=96)	2.211	(0.806, 6.062)	0.123			
CRP grade (1 vs 0)[d] (n=86)	2.210	(0.834, 5.854)	0.111			
Hypertension (with vs without) (n=102)	0.572	(0.229, 1.430)	0.232			
ACEI/ARB treatment history (1 vs 0)[e] (n=96)	**0.159**	**(0.037, 0.692)**	**0.014**	**0.106**	**(0.015, 0.725)**	**0.022**
Diarrhea (with vs without) (n=102)	0.370	(0.150, 0.912)	0.031			
Diabetes (with vs without) (n=102)	0.782	(0.304, 2.011)	0.610			
Days from onset (n=102)	1.075	(0.941, 1.228)	0.290			
Glucocorticoids treatment (with vs without) (n=102)	1.873	(0.746, 4.702)	0.181			
Antibiotic treatment (with vs without) (n=102)	0.514	(0.136, 1.947)	0.328			
Arbidol treatment (with vs without) (n=102)	1.120	(0.439, 2.857)	0.813			
Intravenous immunoglobulin therapy (with vs without) (n=102)	1.160	(0.470, 2.862)	0.747			
Bladder catheter (with vs without) (n=102)	0.103	(0.029, 0.366)	<0.001			
COVID-19 grade (reference=Critically ill) (n=102)			**0.001**			**0.011**
Moderate (n=34)	3.467	(1.125, 10.682)	0.030	1.050	(0.205, 5.385)	0.953
Severe (n=46)	**11.844**	**(3.364, 41.702)**	**<0.001**	**9.159**	**(1.526, 54.973)**	**0.015**
Change of serum albumin (1 vs 0)[f] (n=86)	1.227	(0.488, 3.088)	0.664			
Recovery of lung (1 vs 0)[g] (n=91)	1.298	(0.485, 3.472)	0.603			

a. AKI (yes, with AKI occurrence on admission or during the hospital stay; no, without AKI occurrence on admission or during the hospital stay).

b. Change of eosinophils count (reexamined eosinophils was compared with initial eosinophils, 0, decreased or did not change;1, increased)

c. Change of lymphocytes count (reexamined lymphocytes was compared with initial lymphocytes, 0, decreased or did not change; 1, increased)

d. CRP on follow-up (1, < or = 10mg/l; 0, >10mg/l)

e. 1, with ACEI or ARB treatment before the onset of the COVID-19; 0 without ACEI or ARB treatment before the onset of the COVID-19

f. Change of serum albumin (reexamined serum albumin was compared with initial serum albumin, 0, decreased; 1, increased or did not change)

g. Recovery of lung (reexamined degree of lung involvement was compared with initial degree of lung involvement, 0, no obvious recovery; 1, obvious recovery)

h. The number of cases included in the final multivariate logistic regression model is 96.

Supplementary Table 8. Risk factors associated with AKI recovery during follow-up periods

Variable	Univariate analysis			Multivariate analysis[f]		
	OR	95% CI	*P*	OR	95% CI	*P*
Age (60 or above vs under 60) (n=35)	1.212	(0.311, 4.730)	0.782			
Gender (male vs female) (n=35)	0.357	(0.087, 1.471)	0.154			
Change of eosinophils count (1 vs 0)[a] (n=32)	1.145	(0.270, 4.867)	0.854			
Change of lymphocytes count (1 vs 0)[b] (n=34)	1.270	(0.327, 4.930)	0.730			
Hypertension (with vs without) (n=35)	0.864	(0.227, 3.289)	0.831			
ACEI/ARB treatment history (1 vs 0)[c] (n=35)	1.705	(0.370, 7.854)	0.494			
Diarrhea (with vs without) (n=35)	0.540	(0.139, 2.093)	0.373			
Diabetes (with vs without) (n=35)	0.825	(0.211, 3.219)	0.782			
Glucocorticoids treatment (with vs without) (n=34)	0.361	(0.030, 4.418)	0.425			
Arbidol treatment (with vs without) (n=35)	0.583	(0.151, 2.256)	0.435			
COVID-19 grade (Critical ill vs Non-critical)[d] (n=35)	**0.033**	**(0.004, 0.317)**	**0.003**	**0.033**	**(0.004, 0.317)**	**0.003**
Change of serum albumin (1 vs 0)[e] (n=32)	0.709	(0.137, 3.660)	0.681			
Severity of AKI (stage 2+3 vs stage 1) (n=35)	0.089	(0.018, 0.432)	0.003			
Baseline creatinine (n=35)	0.995	(0.959, 1.031)	0.995			

a. Change of eosinophils count (reexamined eosinophils was compared with initial eosinophils, 0, decreased or did not change; 1, increased)

b. Change of lymphocytes count (reexamined lymphocytes was compared with initial lymphocytes, 0, decreased or did not change; 1, increased)

c. 1, with ACEI or ARB treatment before the onset of the COVID-19; 0 without ACEI or ARB treatment before the onset of the COVID-19

d. Among the 35 AKI patients, only 5 patients' COVID-19 grades were moderate and 6 patients' COVID-19 grades were severe. So these two levels were merged into a new level, i.e., non-critically.

e. Change of serum albumin (reexamined serum albumin was compared with initial serum albumin, 0, decreased; 1, increased or did not change)

f. The number of cases included in the final multivariate logistic regression model is 35.

Supplementary Table 9. Characteristics of patients lost to follow-up and patients with follow-up

Variables	Patients lost to follow-up	Patients with follow-up	*P*
Number	53	163	
SPO2	95 (92-98)	93 (91-96)	0.165[a]
Male patient, %	32/53 (60.4%)	91/163 (55.8%)	0.561[b]
Age	56.9±13.7	55.6±13.4	0.544[c]
Days from onset	8 (7-10)	9 (7-11)	0.369[a]
Fever, %	49/53 (92.5%)	148/163 (90.8%)	0.712[b]
Cough, %	38/53 (71.7%)	115/163 (70.6%)	0.077[b]
Dyspnea, %	22/53 (41.5%)	97/163 (59.5%)	0.022[b]
Diarrhea, %	16/53 (30.2%)	48/163 (29.4%)	0.918[b]
Hypertension, %	19/52 (36.5%)	47/163 (28.8%)	0.294[b]
ACEI/ARB history, %	6/52 (11.5%)	12/153 (7.8%)	0.416[b]
Diabetes, %	15/52 (28.8%)	32/163 (19.6%)	0.162[b]
Blood sugar (mmol/L)	6.6 (5.9-7.7)	6.6 (5.7-8.1)	0.696[a]
SBP (mmHg)	125 (116-134)	127 (115-140)	0.461[a]
DBP (mmHg)	78 (73-91)	78 (73-87)	0.560[a]
BUN	4.1 (3.4-5.8)	4.3 (3.4-5.4)	0.705[a]
SCR	72.0 (56.5-82.0)	71.0 (60.0-84.0)	0.684[a]
Lymphocytes (10^9/L)	0.81 (0.63-1.17)	0.85 (0.62-1.18)	0.594[a]
Eosinophils (10^9/L)	0.00 (0.00-0.07)	0.00 (0.00-0.06)	0.538[a]

Data are presented as a percentage or mean ± SD or median (25th–75th percentiles), eosinophils are presented as median (5th–95th percentiles)

a. Wilcoxon rank sum test; b. Chi-square test; c. *t* test

SBP, systolic diastolic blood pressure; DBP, diastolic blood pressure.

Supplementary Table 10. Comparison of un-reported patients in this cohort and the overlapped patients in a previous cohort

Variables	Un-reported patients	Reported patients	*P*
Number	79	254	
SPO2	95 (92-97)	93 (91-97)	0.165[a]
Male patient, %	48/79 (60.8%)	134/254 (52.8%)	0.212[b]
Age	54.1±13.5	56.8±13.3	0.112[c]
Days from onset	7 (5-10)	9 (7-12)	0.028[a]
Fever, %	66/79 (83.5%)	235/254 (92.5%)	0.018[b]
Cough, %	54/79 (68.4%)	175/254 (68.9%)	0.928[b]
Dyspnea, %	40/79 (50.6%)	150/254 (59.1%)	0.187[b]
Diarrhea, %	31/79 (39.2%)	77/254 (30.3%)	0.139[b]
Hypertension, %	26/79 (32.9%)	81/253 (32.0%)	0.882[b]
ACEI/ARB history, %	11/79 (14.1%)	26/243 (10.7%)	0.413[b]
Diabetes, %	15/79 (19.0%)	61/253 (24.1%)	0.344[b]
Blood sugar (mmol/L)	6.5 (5.7-7.8)	6.6 (5.6-8.6)	0.696[a]
SBP (mmHg)	124 (115-135)	128 (116-140)	0.066[a]
DBP (mmHg)	78 (70-86)	79 (73-87)	0.191[a]
BUN	4.1 (3.4-5.8)	4.3 (3.4-5.4)	0.497[a]
SCR	76.0 (58.0-85.0)	68.0 (56.0-84.0)	0.144[a]
Lymphocytes (10^9/L)	0.81 (0.59-1.25)	0.83 (0.60-1.18)	0.823[a]
Eosinophils (10^9/L)	0.00 (0.00-0.09)	0.00 (0.00-0.07)	0.323[a]
Proteinuria			0.132[a]
none	34/79 (43.0%)	80/254 (31.5%)	
±/+	36/79 (45.6%)	146/254 (57.5%)	
++/+++	9/79 (11.4%)	28/254 (11.0%)	
Hematuria			0.593[a]
none	49/79 (62.0%)	145/254 (57.1%)	
±/+	21/79 (26.6%)	86/254 (33.9%)	
++/+++	9/79 (11.4%)	23/254 (9.1%)	
AKI	11/79 (13.9%)	24/254 (9.4%)	0.257[b]

Data are presented as a percentage or mean ± SD or median (25th–75th percentiles), eosinophils are presented as median (5th–95th percentiles)

a. Wilcoxon rank sum test; b. Chi-square test; c. *t* test;

SBP, systolic diastolic blood pressure; DBP, diastolic blood pressure.

Note: This study has some overlap with a recently publish research with Kidney International (reference 12). However, our data collection was carried out independently to the KI study, and we were able to access a distinct group of patients. In our study, 254 patients in the total of 333 patients and 165 in the 198 patients with follow-up were included in the KI cohort (reference 12). The fact is that the Tongji Hospital System has three different branches: Main Campus, Optical Valley, and Sino-French New City, respectively. The data in the KI paper were collected via the remote HIS system by the physicians who worked in the Main Campus, while the data in this paper was collected via the local HIS system by the physicians who worked in the Sino-French New City branch of Tongji Hospital. Sino-French New City

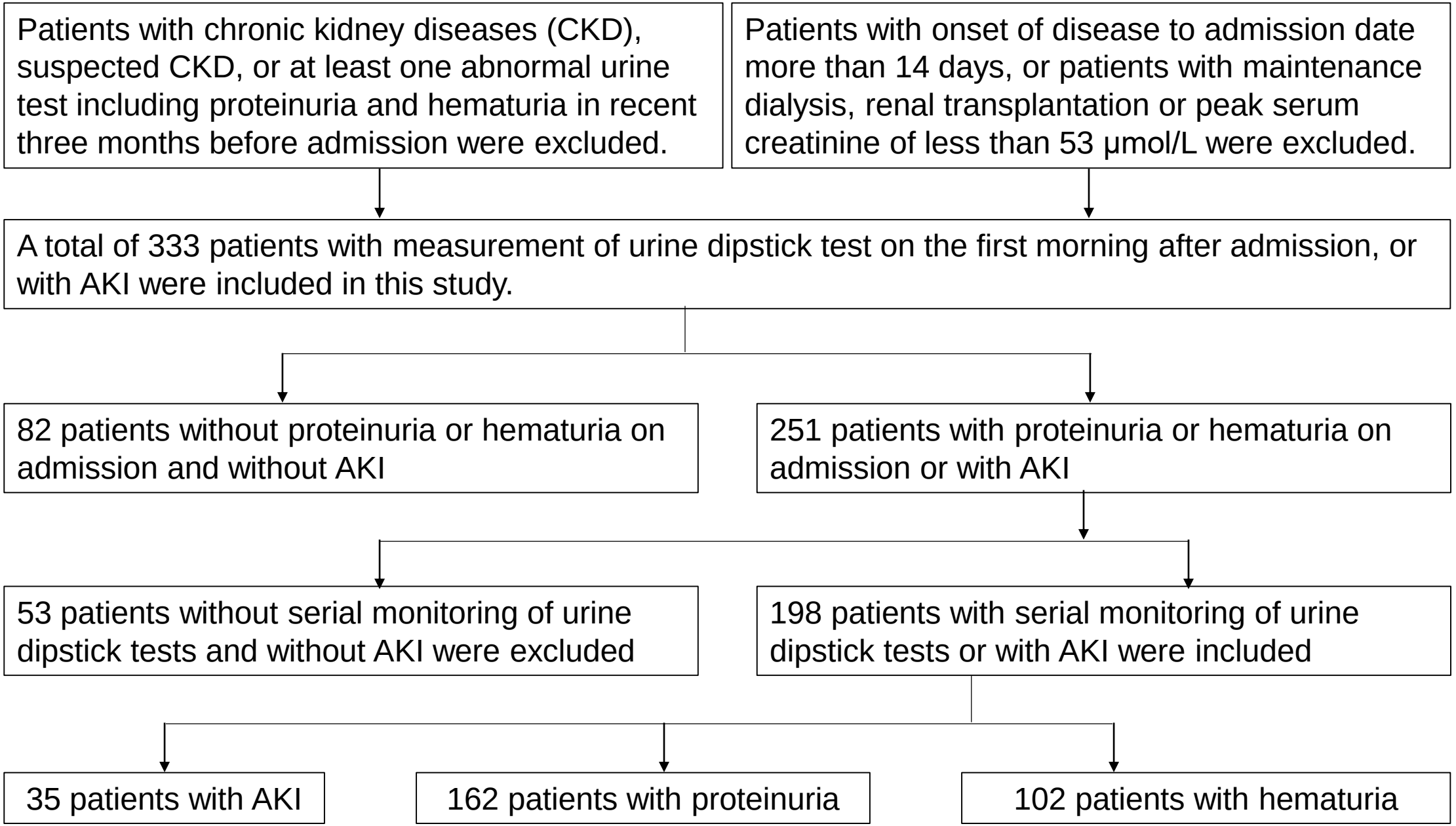
branch has been the main site of admission of COVID-19 patients under Tongji Hospital System. In addition, it is also the main site for the National Health Commission of China dispatched medical corps from other provinces. Two wards of the branch (100 beds) were exclusively managed by these medical corps in the early stage. It should be noted that there are rigorous regulations for the authorization of use of medical data in Tongji Hospital. The physicians assigned to this branch, including these medical corps, could only access to the local HIS system to collect medical data after rigorous application, including the data generated from the wards charged by these medical corps. Although the physicians who wrote the KI paper had access to the local HIS system, they did not obtain the data from these two wards at the point of preparing the KI study. Due to the access issue described above, 79 patients including 16 of the 35 AKI patients and 63 of the 298 non-AKI patients treated in these two wards were included in our study but not the KI study.

Supplementary Table 11. Mortality of the patients with renal involvement during follow-up periods

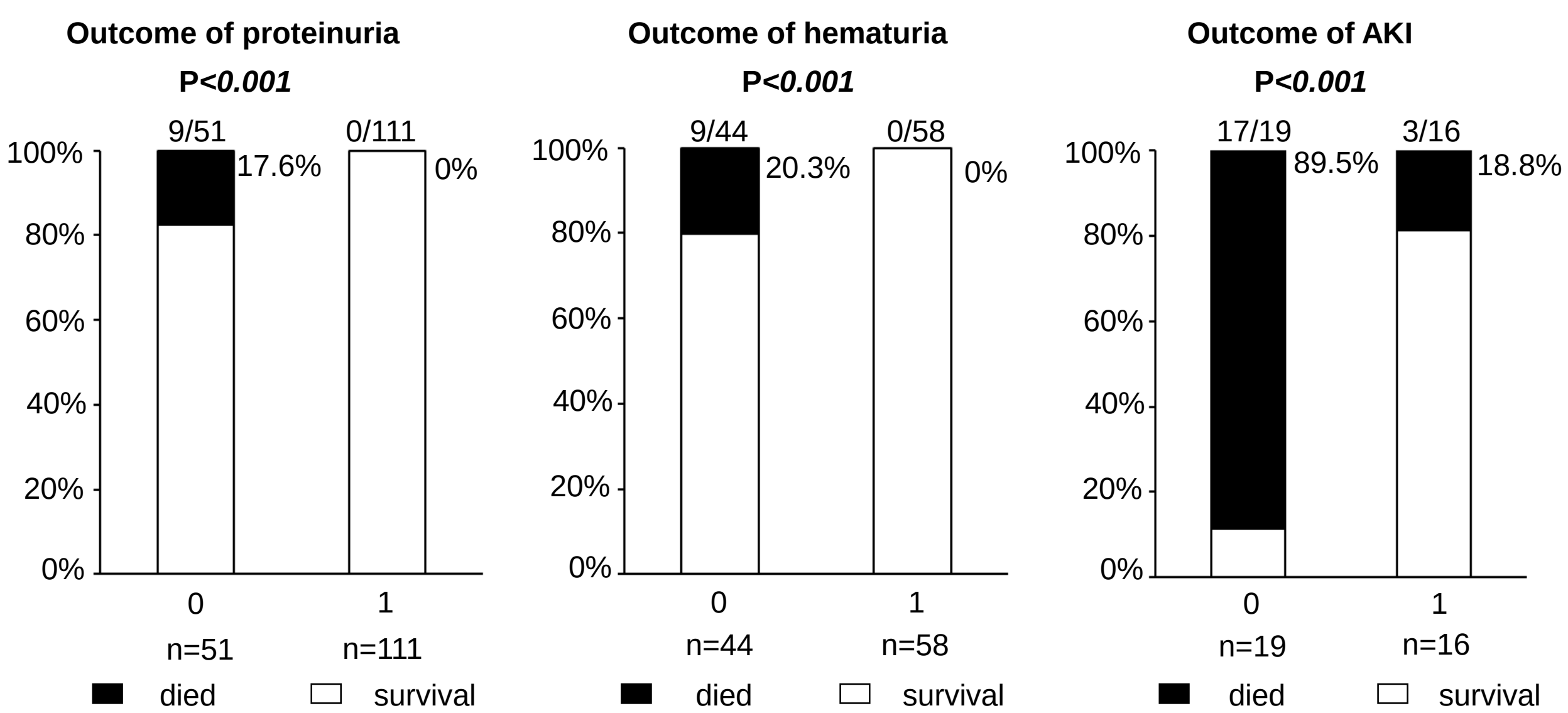
Variables	All patients	Survivor	Death	*P*
Proteinuria				0.005[a]
none	114/333 (34.2%)	112/114 (98.2%)	2/114 (1.8%)	
±/+	182/333 (54.6%)	160/182 (87.9%)	22/182 (12.1%)	
++/+++	37/333 (11.1%)	32/37 (86.5%)	5/37 (13.5%)	
Hematuria				<0.001[a]
none	194/333 (58.3%)	185/194 (95.4%)	9/194 (4.6%)	
±/+	107/333 (32.1%)	97/107 (90.7%)	10/107 (9.3%)	
++/+++	32/333 (9.6%)	22/32 (68.7%)	10/32 (31.3%)	
AKI				<0.001[b]
without	298/333 (89.5%)	289/298 (97.0%)	9/298 (3.0%)	
with	35/333 (10.5%)	15/35 (42.9%)	20/35 (57.1%)	
Renal involvement				0.006[b]
without	82/333 (24.5%)	81/82 (98.8%)	1/82 (1.2%)	
with	251/333 (75.5%)	223/251 (88.8%)	28/251 (11.2%)	

Data are presented as a percentage

a. Wilcoxon rank sum test; b. Chi-square test



Supplementary Figure 1. Schematic Figure



Supplementary Figure 2. Relationship between outcomes of renal involvement and mortality during follow-up periods. Results of Chi square test shows poor prognosis of proteinuria, hematuria and AKI and mortality were accompanied by higher mortality. For the outcome of proteinuria and hematuria , 0: deterioration or no remission; 1: remission, protein and hemoglobin were negative on serial monitoring of urine dipsticks test; for the outcome of AKI, 0: deterioration or no improvement of kidney function; 1: complete recovery of kidney function.