



# Chronic kidney disease and clinical outcomes in patients with COVID-19 in Japan

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## Abstract

**Background** Identifying predictive factors for coronavirus disease 2019 (COVID-19) is crucial for risk stratification and intervention. Kidney dysfunction contributes to the severity of various infectious diseases. However, the association between on-admission kidney dysfunction and the clinical outcome in COVID-19 patients is unclear.

**Methods** This study was a multicenter retrospective observational cohort study of COVID-19 patients, diagnosed by polymerase chain reaction. We retrospectively analyzed 500 COVID-19 patients (mean age:  $51 \pm 19$  years) admitted to eight hospitals in Japan. Kidney dysfunction was defined as a reduced estimated glomerular filtration rate ( $<60$  mL/min/1.73 m<sup>2</sup>) or proteinuria ( $\geq 1$  + dipstick proteinuria) on admission. The primary composite outcome included in-hospital death, extracorporeal membrane oxygenation, mechanical ventilation (invasive and noninvasive methods), and intensive care unit (ICU) admission.

**Results** Overall, 171 (34.2%) patients presented with on-admission kidney dysfunction, and the primary composite outcome was observed in 60 (12.0%) patients. Patients with kidney dysfunction showed higher rates of in-hospital death (12.3 vs. 1.2%), mechanical ventilation (13.5 vs. 4.0%), and ICU admission (18.1 vs. 5.2%) than those without it. Categorical and multivariate regression analyses revealed that kidney dysfunction was substantially associated with the primary composite outcome. Thus, on-admission kidney dysfunction was common in COVID-19 patients. Furthermore, it correlated significantly and positively with COVID-19 severity and mortality.

**Conclusions** On-admission kidney dysfunction was associated with disease severity and poor short-term prognosis in patients with COVID-19. Thus, on-admission kidney dysfunction has the potential to stratify risks in COVID-19 patients.

**Keywords** Kidney dysfunction · Clinical outcome · COVID-19

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## Introduction

The coronavirus disease 2019 (COVID-19) is a novel respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in China in December 2019 [1]. To date, the virus has rapidly spread to at least 200 countries, causing more than 4,800,000 deaths as of October 8, 2021, according to the World Health Organization (<https://covid19.who.int>). The rapidly increasing number of COVID-19 patients, especially those who are critically ill or terminal, poses enormous challenges to public health care systems. Therefore, identifying prognostic factors associated with the risk of severe or critical outcomes in COVID-19 patients is crucial.

Kidney dysfunction is a potential factor contributing to the severity and prognosis of various infections, such as pneumonia and urinary tract infections [2, 3]. For example, the pneumonia-related mortality rate is significantly higher in patients with kidney dysfunction than in patients without it [4]. Therefore, diagnosing manifestations of kidney dysfunction may help stratify risks in COVID-19 patients. However, the clinical impact of on-admission kidney dysfunction on COVID-19 patients remains unclear. Therefore, we investigated whether kidney dysfunction in the early phase of COVID-19 is associated with increased COVID-19 severity and mortality.

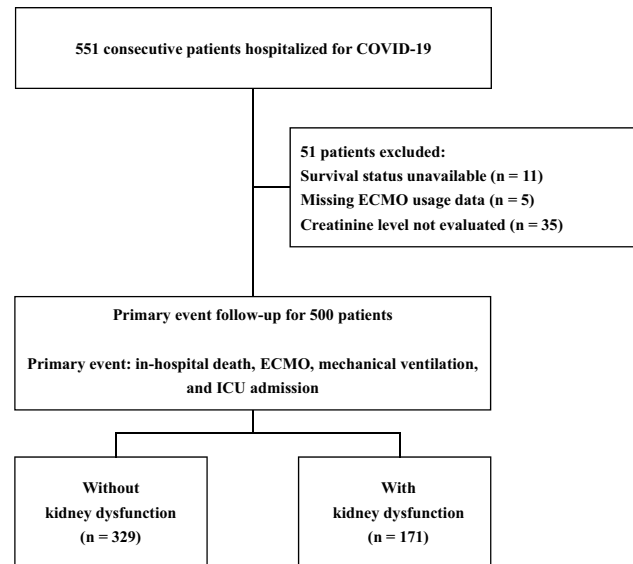
## Materials and methods

### Study design and patient population

This study was a multicenter retrospective observational cohort study of COVID-19 patients, diagnosed by polymerase chain reaction. The following eight hospitals in Japan contributed patient data: The Jikei University Hospital, Saitama Medical University Hospital, Fujisawa City Hospital, Kanagawa Cardiovascular and Respiratory Center, Yokosuka City Hospital, Kanagawa Prefectural Ashigarakami Hospital, Yokohama City University Hospital, and Yokohama City University Medical Center.

Five hundred and fifty-one COVID-19 patients admitted between February 5, and December 31, 2020, were enrolled. Patients whose survival status could not be obtained ( $n = 11$ ), who exhibited missing extracorporeal membrane oxygenation (ECMO) usage data ( $n = 5$ ), or those lacking a creatinine concentration evaluation ( $n = 35$ ) were excluded. Thus, the final analysis included 500 patients (Fig. 1).

Kidney dysfunction was defined as a reduced estimated glomerular filtration rate (eGFR;  $< 60 \text{ mL/min/1.73 m}^2$ )



**Fig. 1** Study flow chart. COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit

or proteinuria ( $\geq 1 +$  dipstick proteinuria) on admission according to the criteria published by the organization Kidney Disease: Improving Global Outcomes [22], and eGFR was calculated using the formula promulgated by the Japanese Society of Nephrology [23]. Immunosuppressed patients were defined as those with (1) primary immunodeficiency or (2) secondary immunodeficiency, e.g., aplastic anemia, multiple myeloma, leukemia, or human immunodeficiency virus infection. All data were collected retrospectively from clinical records. The medical histories were based on information obtained by the attending doctors, medications on admission, and medical information from other hospitals.

The study protocol was approved by the Institutional Review Board of Yokohama City University Medical Center, who also waived the written informed consent requirement. The study followed the Declaration of Helsinki and the ethical standards of the responsible committee on human experimentation.

### Outcome definitions

The primary composite outcome comprised in-hospital death, ECMO, mechanical ventilation (invasive and noninvasive methods), and intensive care unit (ICU) admission. In addition, the primary composite outcome was assessed for the entire study population and compared between patients with and without kidney dysfunction.

## Statistical analyses

Statistical calculations were performed using JMP Pro® 15 (SAS Institute Inc., Cary, NC, USA). The data were expressed as means  $\pm$  standard deviations with normal distribution, as medians (25th–75th percentile) with skewed distributions for continuous variables, and as frequencies and percentages for categorical variables. Continuous variables were compared using the Student *t* test or Mann–Whitney *U* test, as appropriate. Categorical comparisons were performed using Fisher's exact test. Univariate and multivariate logistic regression analyses were used to evaluate factors associated with the primary outcomes. The factors included in the multivariate analysis were determined based on our previous study [24] and previously reported factors involved in COVID-19 prognosis [11–15]. Odds ratios (ORs) and 95% confidence intervals (CIs) were analyzed using logistic regression models. Statistical significance was a two-sided *p* value of  $< 0.05$ .

## Results

### Patient characteristics

Table 1 presents the baseline characteristics of COVID-19 patients; the mean age was  $51 \pm 19$  years, and 61.2% of the patients were male. On admission, 34.2% of the patients had kidney dysfunction. They were older, had a higher systolic blood pressure, heart rate, and body temperature than those without kidney dysfunction. In addition, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, and a history of cardiovascular or cerebrovascular disease were more prevalent in patients with kidney dysfunction than in those without it. Immunodeficiency complications were also significantly more common in patients exhibiting kidney dysfunction than in those who did not. Patients with kidney dysfunction took angiotensin II receptor blockers,  $\beta$ -blockers, antidiabetic drugs, and statins on admission more frequently than those without it. Furthermore, they had higher leukocyte and neutrophil counts, higher aspartate transaminase (AST),  $\gamma$ -glutamyl transpeptidase, blood glucose, total bilirubin, and C-reactive protein (CRP) levels, a decreased platelet count, as well as lower total protein and albumin levels than patients without renal disorders.

### The primary composite outcome

Of all examined patients, the primary composite outcome was observed in 60 (12.0%) patients. Regarding the individual components, there were 25 (5.0%) in-hospital deaths,

eight (1.6%) patients received ECMO, 36 (7.2%) patients required mechanical ventilation, and 48 (9.6%) patients were admitted to the ICU, among the entire study population.

The primary outcome rates were significantly higher in patients with kidney dysfunction ( $n = 43$ ) than in patients without it ( $n = 17$ ) (25.2 vs. 5.2%,  $P < 0.0001$ ; Fig. 2). The incidences of in-hospital death (12.3 vs. 1.2%,  $P < 0.0001$ ), ECMO (2.9% vs. 0.9%,  $P = 0.09$ ), mechanical ventilation (13.5 vs. 4.0%,  $P < 0.0001$ ), and ICU admission (18.1 vs. 5.2%,  $P < 0.0001$ ) were higher in patients with kidney dysfunction than in those without it. We further divided the patients into several stages using their eGFR and proteinuria, respectively, and evaluated the occurrence of the primary endpoint. Patients were divided into three groups according to their eGFR (eGFR  $> 60$  mL/min/1.73 m<sup>2</sup>;  $n = 396$ , 45–59 mL/min/1.73 m<sup>2</sup>;  $n = 58$ , and  $< 45$  mL/min/1.73 m<sup>2</sup>;  $n = 46$ ) and were evaluated for the primary outcome rate, which was significantly different among the three groups (8.3%, 20.7%, and 32.6%,  $P < 0.0001$ ; Fig. 3). For dipstick proteinuria, there were only 7 patients with a urinary protein of 2+ or higher. Therefore, we divided the patients into two groups according to their dipstick proteinuria (0 or  $\pm$ ;  $n = 204$ , and  $\geq 1$ ;  $n = 99$ ). The primary outcome rates was significantly higher in patients with proteinuria than in those without (29.3% and 6.9%,  $P < 0.0001$ ; Fig. 4).

### Factors associated with the primary composite outcome

The univariate regression analysis revealed that the following on-admission conditions and parameters were significantly associated with a higher risk of the primary composite outcome (Table 2): advanced age ( $\geq 65$  years), male sex, higher systolic blood pressure, a body temperature of  $\geq 37$  °C, hypertension, diabetes mellitus, a history of cerebrovascular or cardiovascular disease, an immunosuppressed condition, the use of  $\beta$ -blockers and antidiabetic medication, kidney dysfunction, the neutrophil count, as well as levels of hemoglobin, AST, total bilirubin, total protein, albumin, glucose, total cholesterol, and CRP (Supplementary Table).

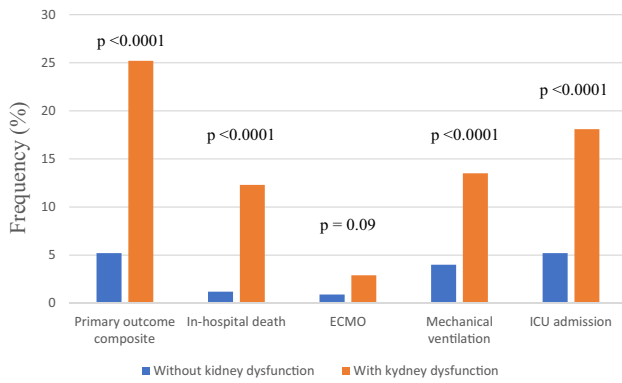
After adjusting for relevant factors (age, sex, hypertension, diabetes mellitus, history of cerebrovascular or cardiovascular disease, chronic obstructive pulmonary disease, an immunosuppressed condition, and on-admission serum albumin and CRP levels), the multivariate logistic regression analysis identified that on-admission kidney dysfunction was significantly and independently associated with the primary composite outcome in COVID-19 patients (OR: 2.35, 95% CI: 1.14–4.86,  $P = 0.02$ ; Table 3). We performed an additional multivariate regression analysis with the limited number of explanatory variables to avoid overfitting (age, sex, hypertension, diabetes mellitus, and history of cerebrovascular or cardiovascular disease),

**Table 1** Baseline characteristics of COVID-19 patients

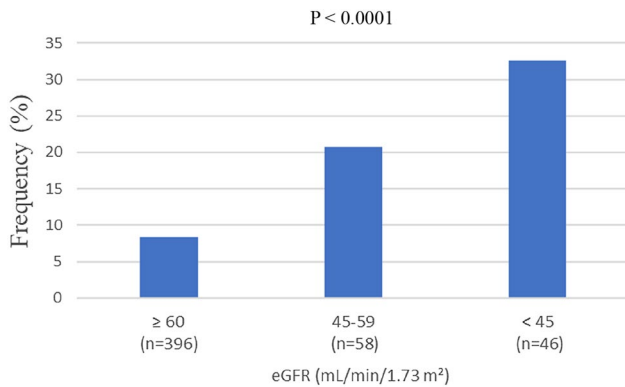
Characteristics	Total (n=500)	Without kidney dysfunction (n=329)	With kidney dysfunction (n=171)	P value
Age, years	53 ± 18	48 ± 17	63 ± 16	<0.0001
Male sex, %	61.2	56.2	70.8	0.002
Height, cm (male)	171 ± 7	172 ± 6	171 ± 8	0.53
Height, cm (female)	159 ± 8	159 ± 7	160 ± 11	0.89
Body mass index, kg/m <sup>2</sup> (male)	24.3 ± 4.2	24.1 ± 4.0	24.6 ± 4.4	0.45
Body mass index, kg/m <sup>2</sup> (female)	22.5 ± 4.1	22.3 ± 4.0	23.3 ± 4.2	0.06
Systolic blood pressure, mm Hg	127 ± 21	124 ± 19	132 ± 24	0.0001
Diastolic blood pressure, mm Hg	80 ± 15	79 ± 14	81 ± 18	0.18
Heart rate, beats/min	86 ± 16	84 ± 16	89 ± 16	0.002
Body temperature ≥ 37 °C, %	51.6	44.1	66.1	<0.0001
Comorbidities				
Hypertension, %	33.6	20.3	47.4	<0.0001
Diabetes mellitus, %	16.8	11.9	26.3	<0.0001
Cerebrovascular or cardiovascular disease, %	7.6	4.0	14.6	<0.0001
Chronic obstructive pulmonary disease, %	5.6	4.0	8.8	0.03
Currently smoking, %	10.3	11.7	7.7	0.21
Immunosuppressed condition, %	5.6	3.3	9.9	0.002
Medication on admission				
ACE-I, %	2.0	1.2	3.5	0.08
ARB, %	13.4	7.6	24.6	<0.0001
Direct renin inhibitor, %	0.2	0	0.6	0.14
Calcium channel blocker, %	16.8	10.9	28.2	<0.0001
β-blocker, %	6.6	4.6	10.6	0.01
Antidiabetic drugs, %	11.2	8.5	16.5	0.008
Statin, %	14.6	10.3	22.9	0.0002
Laboratory data on admission				
Leukocytes, 10 <sup>9</sup> /L	4.9 (3.8–6.3)	4.7 (3.7–6.1)	5.1 (4.1–7.0)	0.003
Neutrophils, 10 <sup>9</sup> /L		2.9 (1.9–4.0)	3.5 (2.4–5.2)	<0.0001
Platelets, 10 <sup>9</sup> /L	195 (158–241)	200 (169–250)	175 (145–225)	0.006
Hemoglobin, g/dL	14.2 (12.7–15.4)	14.2 (12.9–15.3)	14.3 (11.8–15.8)	0.17
AST, IU/L	27 (21–40)	25 (19–34)	33 (25–50)	0.0001
ALT, IU/L	23 (15–41)	22 (14–40)	25 (17–42)	0.05
γ-GTP, IU/L	35 (19–65)	31 (17–55)	42 (25–84)	0.02
Total bilirubin, mg/dL	0.59 ± 0.35	0.57 ± 0.31	0.64 ± 0.41	0.04
Total protein, g/dL	6.97 ± 0.78	7.04 ± 0.83	6.84 ± 0.63	0.007
Albumin, g/dL	3.83 ± 1.92	3.98 ± 2.32	3.53 ± 0.61	0.01
Glucose, mg/dL	103 (90–124)	97 (88–115)	111 (90–140)	<0.0001
Total cholesterol, mg/dL	180 ± 44	184 ± 40	173 ± 51	0.29
eGFR, mL/min/1.73m <sup>2</sup>	76 ± 26	87 ± 19	55 ± 25	–
CRP, mg/dL	1.4 (0.3–5.5)	0.8 (0.2–3.0)	4.5 (0.9–10.8)	<0.0001
Urine protein (303 patients)				
–, %	38.6	58.2	0	–
Trace, %	28.7	41.8	10.3	
1+, %	30.4	0	73.0	
2+, %	1.3	0	3.2	
3+, %	1.0	0	2.4	

ACE-I angiotensin-converting enzyme inhibitor, ALT alanine aminotransferase, ARB angiotensin II receptor blocker, AST aspartate transaminase, CRP C-reactive protein, eGFR estimated glomerular filtration rate, γ-GTP γ-glutamyl transpeptidase

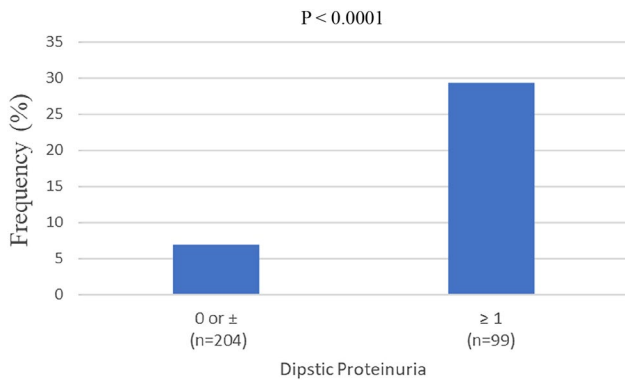
The values are numbers (percentages), means ± standard deviations, or medians (25th–75th percentile range). P values compare patients with and without kidney dysfunction



**Fig. 2** Primary composite outcome of COVID-19 patients with and without kidney dysfunction. *ECMO* extracorporeal membrane oxygenation, *ICU* intensive care unit



**Fig. 3** Primary outcome rates in three groups divided by the patients' eGFR. *eGFR* estimated glomerular filtration rate



**Fig. 4** Primary outcome rates in two groups divided by the patients' proteinuria

which demonstrated that on-admission kidney dysfunction was still significantly associated with the primary composite outcome (OR: 3.93, 95% CI: 2.07–7.45,  $P < 0.0001$ ; Table 4).

**Table 2** Univariate logistic regression analysis for the primary composite outcome

Variables	Univariate analysis		
	OR	95% CI	P value
Age, ≥ 65 years	6.90	3.79–12.57	<0.0001
Male	2.06	1.12–3.80	0.02
Body mass index, per 1 kg/m <sup>2</sup>	1.02	0.95–1.08	0.62
Systolic blood pressure, per 10 mm Hg	1.27	1.22–1.43	0.0001
Diastolic blood pressure, per 10 mm Hg	1.01	0.85–1.21	0.87
Heart rate, per 10/min	1.18	0.99–1.39	0.052
Body temperature ≥ 37 °C	1.87	1.08–3.34	0.03
<b>Comorbidities</b>			
Hypertension	2.32	1.33–4.04	0.003
Diabetes mellitus	3.22	1.78–5.83	0.0001
Cerebrovascular or cardiovascular disease	3.43	1.55–7.20	0.002
Chronic obstructive pulmonary disease	2.11	0.82–5.44	0.12
Currently smoking	n/a	n/a	n/a
Immunosuppressed condition	3.91	1.68–9.10	0.002
Kidney dysfunction on admission	6.17	3.45–11.48	<0.0001
<b>Medication on admission</b>			
ACE-I	1.86	0.39–8.98	0.44
ARB	1.54	0.76–3.14	0.23
Calcium channel blocker	1.83	0.94–3.41	0.06
β-blocker	3.12	1.37–7.09	0.007
Antidiabetic drugs	2.30	1.13–4.66	0.02
<b>Laboratory data on admission</b>			
Leukocytes, per 10 <sup>9</sup> /L	1.29	1.18–1.42	<0.0001
Neutrophils, per 10 <sup>9</sup> /L	1.37	1.24–1.52	<0.0001
Platelets, per 10 <sup>11</sup> /L	0.83	0.56–1.16	0.32
Hemoglobin, per 1 g/dL	0.79	0.69–0.89	0.0001
AST, per 10 IU/L	1.14	1.05–1.25	0.004
ALT, per 10 IU/L	1.05	0.99–1.11	0.12
γ-GTP, per 10 IU/L	1.01	0.98–1.03	0.48
Total bilirubin, per 1 mg/dL	3.35	1.72–6.53	0.0004
Total protein, per 1 g/dL	0.29	0.18–0.47	<0.0001
Albumin, per 1 g/dL	0.11	0.06–0.20	<0.0001
Glucose, per 100 mg/dL	1.62	1.35–1.95	<0.0001
Total cholesterol, per 10 mg/dl	0.73	0.57–0.88	0.0003
CRP, per 1 mg/dL	1.24	1.18–1.31	<0.0001

*ACE-I* angiotensin-converting enzyme inhibitor, *ALT* alanine aminotransferase, *ARB* angiotensin II receptor blocker, *AST* aspartate transaminase, *CI* confidence interval, *CRP* C-reactive protein, *ECMO* extracorporeal membrane oxygenation, *ICU* intensive care unit, *OR* odds ratio, *γ-GTP* γ-glutamyl transpeptidase

The primary composite outcome comprises in-hospital death, ECMO, mechanical ventilation, and ICU admission

**Table 3** Multivariate logistic regression analyses for the primary composite outcome

Variables	Multivariate analysis		
	OR	95% CI	P value
Age, $\geq 65$ years	2.84	1.33–6.05	0.007
Male sex	1.87	0.82–4.29	0.14
Hypertension	0.74	0.63–2.87	0.45
Diabetes mellitus	1.19	0.54–2.60	0.66
History of cerebrovascular or cardiovascular disease	1.32	0.48–3.66	0.59
Chronic obstructive pulmonary disease	0.97	0.29–3.26	0.96
Immunosuppressed condition	1.54	0.53–4.48	0.42
Albumin, per 1 g/dL	0.34	0.16–0.71	0.004
CRP, per 1 mg/dL	1.13	1.06–1.20	0.0001
Kidney dysfunction	2.35	1.14–4.86	0.02

CI confidence interval, CRP C-reactive protein, ECMO extracorporeal membrane oxygenation, ICU intensive care unit, OR odds ratio

The primary composite outcome comprises in-hospital death, ECMO, mechanical ventilation, and ICU admission

**Table 4** Multivariate logistic regression analyses for the primary composite outcome with more clinically relevant factors

Variables	Multivariate analysis		
	OR	95% CI	P value
Age, $\geq 65$ years	5.18	2.65–10.09	<0.0001
Male sex	2.16	1.09–4.28	0.02
Hypertension	0.76	0.38–1.50	0.42
Diabetes mellitus	1.53	0.77–3.05	0.22
History of cerebrovascular or cardiovascular disease	1.37	0.54–3.47	0.50
Kidney dysfunction	3.93	2.07–7.45	<0.0001

CI confidence interval, ECMO extracorporeal membrane oxygenation, ICU intensive care unit, OR odds ratio

The primary composite outcome comprises in-hospital death, ECMO, mechanical ventilation, and ICU admission

## Discussion

Overall, 34.2% of COVID-19 patients had on-admission kidney dysfunction, which was significantly associated with in-hospital death, mechanical ventilation, ICU admission, and the primary composite outcome. Furthermore, after adjusting for clinically relevant variables in the multivariate analysis, kidney dysfunction was the independent predictor of the primary composite outcome in COVID-19 patients. Thus, to our knowledge, this is the first study in Japan to identify the potential relevance of on-admission

kidney dysfunction as a predictive marker for poor short-term outcomes in COVID-19 patients.

## On-admission kidney dysfunction prevalence

In this study, 34% of COVID-19 patients had on-admission kidney dysfunction. Furthermore, patients with COVID-19 are more likely to exhibit kidney dysfunction than the general population [5], and this outcome is generally consistent with previous reports from Western countries [6, 7]. However, the exact cause of on-admission kidney dysfunction in COVID-19 patients remains unclear. One plausible explanation is pre-existing chronic kidney disease (CKD). Although we could not obtain accurate pre-existing CKD data on the examined study population, the prevalence of hypertension and diabetes, the leading causes of CKD, were relatively high [8, 9]. This observation suggests that CKD prevalence was also high in COVID-19 patients with on-admission kidney dysfunction in our study. Another potential explanation is that the time between COVID-19 onset and hospitalization affected the patients' kidney function. In this study, all participating facilities were advanced medical institutions, and some patients had been transferred in from other primary medical institutions. Previous reports indicate that SARS-CoV-2 causes acute kidney injury through a systemic inflammatory response [10]. Therefore, it is conceivable that the systemic inflammation in SARS-CoV-2-infected patients had substantially progressed before they were admitted to the participating hospitals, and, as a result, several patients had already developed on-admission kidney dysfunction. Notably, patients with kidney dysfunction presented with significantly higher on-admission CRP levels than those without it.

## Factors associated with COVID-19 severity and prognosis

Previous systematic reviews on COVID-19 have found that advanced age, male sex, hypertension, diabetes mellitus, a history of cerebrovascular or cardiovascular disease, chronic obstructive pulmonary disease, and malignancy contributed significantly to COVID-19-associated increased severity and poor prognosis [11–13]. Consistent with these findings, we found that these epidemiological and comorbidity factors were generally and significantly related to increased COVID-19 severity (Table 2). A meta-analysis on COVID-19 described the association between abnormalities in specific laboratory biomarkers and poor outcomes [13–15]. Indeed, inflammatory and metabolic biomarkers, such as an increased leukocyte count and elevated levels of AST, total serum protein, and on-admission CRP, were strong determinants of COVID-19 severity and a poor outcome in our study (Table 2). These results are consistent with previous reports [13–15].

Furthermore, we demonstrated that kidney dysfunction was significantly associated with in-hospital adverse events in COVID-19 patients. This association remained unchanged after adjusting for COVID-19 risk factors previously reported, including advanced age, male sex, hypertension, diabetes mellitus, a history of cerebrovascular or cardiovascular disease, chronic obstructive pulmonary disease, immunosuppression, and on-admission serum albumin and CRP levels. Overall, this result indicates that on-admission kidney dysfunction may help stratify risks in COVID-19 patients.

### Mechanisms of kidney dysfunction in COVID-19 patients

The mechanisms of kidney dysfunction in patients with COVID-19 are likely to be multifactorial, with direct effects derived from SARS-CoV-2 infection of the renal tissues and indirect mechanisms, such as the systemic inflammation caused by the viral infection.

Recently, SARS-CoV-2 has been shown to utilize angiotensin-converting enzyme 2 (ACE2) receptor, a type I membrane protein widely expressed in various human organs, including in the kidney's glomerular visceral and tubular epithelial cells, as a receptor for cell entry [16]. In addition, several postmortem studies have revealed the presence of viral particles in both the visceral and tubular epithelium [17, 18]. These findings indicate that SARS-CoV-2 directly infects kidney cells via the ACE2 receptor. However, kidney dysfunction in patients with COVID-19 may also arise through indirect mechanisms from SARS-CoV-2 infection. In this context, several hospitalized COVID-19 patients developed acute respiratory distress syndrome from pneumonia [19], and the resultant severe hypoxemia may be a leading cause of tubular epithelial damage [13]. Respiratory and gastrointestinal disorders associated with COVID-19 infection also cause hemodynamic disturbances derived from changes in vascular fluid volume, potentially leading to kidney dysfunction [7]. Furthermore, SARS-CoV-2-induced cytokines and chemokines may cause tubular and endothelial dysfunction and promote systemic vascular permeability. Elevated cytokine and chemokine levels have been reported in patients with COVID-19 [20, 21], and excessive cytokine production plays a pivotal role in promoting the severity and poor outcomes in COVID-19 patients.

In the present study, on-admission kidney dysfunction in hospitalized COVID-19 patients was significantly and independently associated with increased COVID-19 severity and poor short-term prognosis, even after adjusting for potential confounders. Therefore, particular attention should be given to COVID-19 patients with on-admission kidney dysfunction, irrespective of their comorbidities or laboratory findings. Early detection of kidney dysfunction and application of therapeutic strategies, such as appropriate

hemodynamic support and avoidance of nephrotoxic drugs, may help improve the prognosis of patients with COVID-19.

### Limitations

This study had several limitations. First, this was a retrospective analysis with a relatively small study population, and clinical data after discharge were lacking. In this context, the number of patients with the primary composite outcome was small; therefore, we should emphasize that our multivariate regression analysis is overfit and the statistical difficulties cannot be ruled out. Second, accurate baseline urinalysis data were not available for approximately 40% of the patients in this study, potentially underestimating the number of COVID-19 patients with on-admission kidney dysfunction. Third, the time between the onset of SARS-CoV-2 infection and hospitalization was not evaluated. Further investigations with more extended follow-up periods, sufficient clinical data, and adequate statistical power are required to address the clinical impact of on-admission kidney dysfunction on long-term clinical outcomes in COVID-19 patients.

### Conclusions

On-admission kidney dysfunction was associated with disease severity and poor short-term prognosis in patients with COVID-19. Thus, on-admission kidney dysfunction has the potential to stratify risks in COVID-19 patients.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s10157-022-02240-x>.

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**Data availability** The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

**Conflict of interest** The authors have declared no competing.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted (IRB approval number B201200036) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Not applicable.

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