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Acute cardiac injury and acute kidney injury associated with severity and mortality in patients with COVID-19

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Abstract. – OBJECTIVE: To determine the incidence and risk factors for acute cardiac injury (ACI) and acute kidney injury (AKI), and then investigate their effect on severity and mortality in patients with COVID-19.

PATIENTS AND METHODS: A total of 1249 patients with COVID-19 were included in this retrospective study. Predictors of ACI and AKI were investigated. Multivariable-logistic regression models were used to determine the association of ACI (or AKI) with severity and mortality.

RESULTS: Median age of patients was 36 years and 61.9% were male. ACI and AKI were observed in 53 (4.2%) and 91 (7.3%) of patients, respectively. Patients with age > 60 years, chronic heart disease, decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission, and Lopinavir/Ritonavir use showed higher odds of ACI. Patients with age > 60 years, male, obesity, hypertension, chronic kidney disease, decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission showed higher odds of AKI. Increased Hs-cTnI (> 300 ng/L), Pro-BNP (> 2500 pg/ml) and decreased e-GFR (< 60 ml/min) revealed higher adjusted mortality.

CONCLUSIONS: ACI and AKI were not common in COVID-19 patients in Shanghai, China. However, patients with ACI/AKI had higher severity-rate and mortality-rate when compared to those without ACI/AKI.

Key Words:

Coronavirus disease 2019, Severe acute respiratory syndrome coronavirus-2, Acute cardiac injury, Acute kidney injury, Mortality.

Introduction

Since November 2019, the outbreak of novel coronavirus disease (COVID-19), which was identified to be caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global public health emergency[1]. Person-to-person transmission of SARS-CoV-2 has been confirmed, and asymptomatic infection patients have been identified as potential sources[2]. As of 7 December, there have been over 66.24 million cases and 1.52 million deaths reported globally since the start of the pandemic[3].

SARS-CoV-2 uses the SARS-CoV receptor angiotensin-converting enzyme 2 (ACE2) for entry and the serine protease TMPRSS2 for S protein priming[4]. Besides highly expressed in the lung, ACE2 also is highly expressed in the heart and the kidney, providing a mechanism for acute cardiac injury (ACI) and acute kidney injury (AKI)[5]. Although SARS-CoV-2 causes primarily respiratory problems, concurrent ACI and AKI cannot be ignored. A meta-analysis of 40 studies and 24,527 patients reported that the incidence of AKI was 10 % (95% CI 8%-13%) in COVID-19 patients[6]. Similarly, previous studies reported that ACI is a common condition (19.7%-27.8%) among hospitalized patients with COVID-19 in Wuhan, China[7,8].

A relatively low severity rate (3.0%) and mortality (0.6%) occurred in patients hospitalized with COVID-19, in Shanghai, China, a city "Four Early Principle" (early detection, early diagnosis, early isolation and early treatment) has been undertaken at the early time of the outbreak. However, little is known about the incidence and clinical significance of ACI and AKI in areas with low severity rate and mortality of hospitalized COVID-19 patients. Therefore, the aims of the present study are: (1) to describe the incidence of ACI and AKI of a cohort of COVID-19 patients

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in Shanghai, China, (2) to assess the risk factors for the development of ACI and AKI, and investigate their effect on severity rate and mortality of COVID-19 patients.

Patients and Methods

Participants

This retrospective study includes 1332 consecutive patients hospitalized with COVID-19 between January 20th 2020 and November 30th 2020, at Shanghai Public Health Clinical Center, a tertiary teaching hospital and the only designated hospital for adult patients with COVID-19 in Shanghai, China. Patient outcomes were followed up until November 30th 2020. Patients who did not yet have a definite outcome of mortality or discharge, i.e., patients who were still being treated were excluded (n=83). After these exclusions, the final analysis included 1249 patients.

Diagnostic Criteria

Patients with COVID-19 were confirmed through positive results for SARS-CoV2 nucleic acids of nasopharyngeal or throat swab specimens[9]. The SARS-CoV-2 nucleic acids were detected using an automatic magnetic extraction device and accompanying kit (Bio-Germ Medical Technology Co., Ltd, Shanghai, China). Severe patients were defined as any one of the followings[9]: (1) Respiratory rates $\geq$ 30/min; (2) Resting oxygen saturation $\leq$ 93%; (3) Oxygenation index $\leq$ 300 mmHg; (4) Require mechanical ventilation; (5) shock; (6) Combined with other organ failures and needed intensive care unit (ICU) admission. ACI was defined as an high-sensitivity troponin I (Hs-cTnI) serum concentration above the 99th percentile of the upper limit of normal (ULN)[10]. AKI was defined as an increase in serum creatinine by 0.3 mg/dL within 48 hours or a 50% increase in serum creatinine from the baseline within 7 days according to the Kidney Disease Improving Global Outcomes (KDIGO) clinical guidelines[11]. We did not have access to pre-admission baseline creatinine values for the majority of patients. Therefore, we considered the lowest creatinine level recorded during the hospital stay as the baseline, and then compared this "baseline" to the highest creatinine recorded.

Data Collection

All data were manually abstracted from electronic health records of Shanghai Public Health Clinical Center, and included demographics, comorbid conditions, laboratory test results, chest CT scans, medical management information, and clinical outcomes. The following parameters recorded at admission and during hospitalization: Hs-cTnI, myoglobin, pro-brain natriuretic peptide (Pro-BNP), creatine kinase MB (CKMB), creatinine, and estimated glomerular filtration rate (e-GFR).

Statistical Analysis

We computed mean and standard deviation (SD) for normal distribution descriptive variables, median and interquartile range (IQR) for non-normal distribution continuous variables, and percentages for qualitative variables. Differences in mean, median, and percentages were assessed using the Student's t-test, the Mann-Whitney test, and the Chi-Squared test, respectively. Demographic factors (age, sex, BMI) and comorbidities were considered the four essential covariates and were always included for adjustments in the multivariable model assessing the association between ACI/AKI and clinical outcomes (severity rate and mortality). We performed the survival estimates using the Kaplan-Meier method, comparing the survival curves according to the cardiac and renal parameters between the groups. Two-sided $p < 0.05$ was considered statistically significant. All data were analyzed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographic and Clinical Characteristics of Study Population

The demographic and clinical characteristics of study population are shown in Table I. The median age of patients was 36 (IQR 27-50) years, 61.9% were male, and 28.3% had obesity. The most commonly observed comorbidities were hypertension (11.4%) and diabetes (5.0%). The 1249 patients were grouped into severe cases (n=38) and non-severe cases (n=1211). Among 38 severe patients, 7 were dead, and 31 were discharged with recovery. The overall severity rate and mortality rate were respectively 3.0% and 0.6%. ACI and AKI were observed in 53 (4.2%) and 91 (7.3%) of patients, respectively. ACI was present on admission in 19/53 (35.8%) of patients, and another 34/53 (64.2%) of patients developed ACI during the hospital stay. Similarly, AKI was present on admission in 38/91 (41.8%) of patients, and another 53/91 (58.2%) of patients developed AKI during the hospital stay.

Table I. Characteristics of the study population.

	Total (n = 1249)	Non-severe group (n = 1211)	Severe group (n = 38)	*p*-value
Age (years)	36 (27-50)	36 (26-50)	64 (49-72)	< 0.001
Male gender, n (%)	773 (61.9%)	743 (61.4%)	30 (78.9%)	0.028
Obesity, n (%)	353 (28.3%)	334 (27.6%)	19 (50%)	0.003
Comorbidity, n (%)	227 (18.2%)	200 (16.5%)	27 (71.1%)	< 0.001
Hypertension	142 (11.4%)	122 (10.1%)	20 (52.6%)	< 0.001
Diabetes mellitus	63 (5.0%)	55 (4.5%)	8 (21.1%)	< 0.001
CHD	25 (2.0%)	19 (1.6%)	6 (15.8%)	< 0.001
CKD	7 (0.6%)	6 (0.5%)	1 (2.6%)	0.082
Initial laboratory findings				
Lymphocyte (10^9/L)	1.5 (1.1-2.0)	1.6 (1.2-2.0)	0.8 (0.5-1.1)	< 0.001
PCT (ng/mL)	0.10 (0.02-0.10)	0.10 (0.02-0.10)	0.10 (0.07-0.16)	< 0.001
CRP (mg/L)	0.5 (0.5-3.5)	0.5 (0.5-2.6)	37.1 (9.8-72.7)	< 0.001
ESR (mm/h)	25 (10-46)	24 (10-45)	58 (38-89)	< 0.001
ACI or AKI during hospitalization				
ACI, n (%)	53 (4.2%)	46 (3.8%)	7 (18.4%)	< 0.001
AKI, n (%)	91 (7.3%)	80 (6.6%)	11 (28.9%)	< 0.001
AKI and ACI, n (%)	6 (0.5%)	3 (0.2%)	3 (7.9%)	< 0.001
Clinical outcomes				
Severity rate	38 (3.0%)	—	—	—
Mortality	7 (0.6%)	—	7 (18.4%)	—

CHD = chronic heart disease, included but not limited to coronary artery disease, previous myocardial infarction, cardiac arrhythmias, congestive heart failure, and myocardiopathy; CKD = chronic kidney disease; PCT = procalcitonin; CRP = C-reactive protein; ESR = erythorcyte sedimentation rate; ACI = Acute cardiac injury; AKI=Acute kidney injury; The p values indicate differences between severe group and non-severe group.

Severe COVID-19 patients were significantly older, more likely to be male, and had a higher prevalence of obesity, and comorbidities when compared to patients with non-severe COVID-19. The severe patients had a lower lymphocyte, but notably higher PCT, CRP, and ESR than the non-severe cases. A higher prevalence of ACI and AKI was observed in severe COVID-19 patients compared to non-severe COVID-19 patients (Table I).

Predictors of ACI During Hospitalization

Predictors of ACI during hospitalization are summarized in Table II, including age > 60 years, chronic heart diseases (CHD), decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission, and Lopinavir/Ritonavir use. Patients with ACI had a higher prevalence of age > 60 years (28.3% *vs.* 10.4%, $p < 0.001$), CHD history (7.6% *vs* 1.8%, $p = 0.003$), lymphocyte < 1×10^9/L (35.9% *vs.* 17.2%, $p < 0.001$), CRP > 10 mg/L (34.0% *vs.* 14.6%, $p < 0.001$), PCT > 0.5 ng/mL (3.8% *vs.* 0.7%, $p=0.013$), ESR > 15 mm/h (83.0% *vs.* 57.8%, $p < 0.001$) on hospital admission, and more Lopinavir/Ritonavir use (24.5% *vs.* 9.3%, $p<0.001$) during hospitalization when compared to patients without ACI.

Predictors of AKI During Hospitalization

Predictors of AKI during hospitalization are summarized in Table III, including age > 60 years, male gender, obesity, hypertension, chronic kidney disease (CKD), decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission. Patients with AKI had a higher prevalence of age > 60 years (26.4% *vs.* 9.9%, $p < 0.001$), male gender (83.5% *vs.* 60.2%, $p < 0.001$), obesity (39.6% *vs.* 27.4%, $p=0.013$), hypertension (27.5% *vs.* 10.1%, $p < 0.001$), CKD history (6.6% *vs.* 0.1%, $p < 0.001$), lymphocyte < 1×10^9/L (28.6% *vs.* 17.2%, $p=0.007$), CRP > 10 mg/L (23.1% *vs.* 14.9%, $p=0.037$), PCT > 0.5 ng/mL (5.5% *vs.* 0.4%, $p < 0.001$), ESR > 15 mm/h (74.7% *vs.* 57.6%, $p=0.001$) on hospital admission when compared to patients without AKI.

Association between Cardiac/Renal Parameters and Clinical Outcomes

Severity rate (13.2% *vs.* 2.6%, $p < 0.001$) and mortality (3.8% *vs.* 0.4%, $p=0.032$) were significantly higher in patients with ACI when compared to patients without ACI. Similarly, severity rate (12.1% *vs.* 2.3%, $p < 0.001$) and mortality (3.3% *vs.* 0.3%, $p=0.011$) were significantly higher in patients with AKI when com-

Table II. Predictors of ACI during hospitalization.

Characteristic	No ACI (n = 1196)	ACI (n = 53)	*p*-value
Age > 60 years	124 (10.4%)	15 (28.3%)	< 0.001
Male gender	744 (62.2%)	29 (54.7%)	0.272
Obesity	335 (28.0%)	18 (34.0%)	0.346
Hypertension	136 (11.4%)	6 (11.3%)	0.991
Diabetes mellitus	61 (5.1%)	2 (3.8%)	0.666
CHD	21 (1.8%)	4 (7.6%)	0.003
Hospital admission			
WBC < 4×10^9/L	160 (13.4%)	9 (17.0%)	0.453
Lymphocyte < 1×10^9/L	206 (17.2%)	19 (35.9%)	< 0.001
Platelet < 100×10^9/L	24 (2.0%)	2 (3.8%)	0.378
Abnormal CRP (> 10 mg/L)	175 (14.6%)	18 (34.0%)	< 0.001
Abnormal PCT (> 0.5 ng/mL)	8 (0.7%)	2 (3.8%)	0.013
Hydroxychloroquine use	270 (22.6%)	11 (20.8%)	0.756
Lopinavir/Ritonavir use	111 (9.3%)	13 (24.5%)	< 0.001
Chinese medicine use	600 (50.2%)	28 (52.8%)	0.704

ACI = acute cardiac injury; CHD=Chronic heart disease (coronary artery disease, cardiomyopathy, and cardiac insufficiency); WBC = white blood count; CRP=C-reactive protein; PCT = procalcitonin; ESR = erythorcyte sedimentation rate; The p values indicate differences between No ACI group and ACI group.

pared to patients without AKI. The association between cardiac/renal parameters and clinical outcomes are shown in Table IV. On multivariate analysis, age > 60 years, male gender, BMI > 30 kg/m2, comorbidity, and abnormal peak hospitalization pro-BNP and creatinine were associated with severe COVID-19 (OR > 1; $p < 0.05$). The dynamic profile of cardiac and renal parameters in patients by severity of COVID-19 is illustrated in Figure 1. Severe COVID-19 patients had markedly higher levels of Hs-cTnI, MYO, and pro-BNP from baseline to 30 days after admission ($p < 0.05$), higher creatinine but lower e-GFR levels from baseline to 5 days after admission ($p < 0.05$) than non-severe patients (Figure 1). On multivariate analysis, age > 60 years, BMI > 30 kg/m^2, comorbidity, and abnormal peak hospitalization Hs-cTnI (OR=2.77; 95% CI 1.10-8.46; p=0.034), pro-BNP (OR=6.45; 95% CI 1.97-34.75; p=0.001), and e-GFR (OR=3.72; 95% CI 1.58-17.15; p=0.008) were associated with death. Kaplan-Meier curves for cumulative mortality during hospitalization in patients with different levels of cardiac and renal injury are

Table III. Predictors of AKI during hospitalization.

Characteristic	No AKI (n = 1158)	AKI (n = 91)	*p*-value
Age > 60 years	115 (9.9%)	24 (26.4%)	< 0.001
Male gender	697 (60.2%)	76 (83.5%)	< 0.001
Obesity	317 (27.4%)	36 (39.6%)	0.013
Hypertension	117 (10.1%)	25 (27.5%)	< 0.001
Diabetes mellitus	55 (4.8%)	8 (8.8%)	0.090
CKD	1 (0.1%)	6 (6.6%)	< 0.001
Hospital Admission			
WBC < 4×10^9/L	156 (13.5%)	13 (14.3%)	0.827
Lymphocyte < 1×10^9/L	199 (17.2%)	26 (28.6%)	0.007
Platelet < 100×10^9/L	24 (2.1%)	2 (2.2%)	0.936
Abnormal CRP (> 10 mg/L)	172 (14.9%)	21 (23.1%)	0.037
Abnormal PCT (> 0.5 ng/mL)	5 (0.4%)	5 (5.5%)	< 0.001
Abnormal ESR (> 15mm/h)	667 (57.6%)	68 (74.7%)	0.001
Hydroxychloroquine use	254 (21.9%)	27 (29.7%)	0.089
Lopinavir/Ritonavir use	111 (9.6%)	13 (14.3%)	0.149
Chinese Medicine use	583 (50.3%)	45 (49.5%)	0.869

AKI = acute kidney injury; CKD = chronic kidney disease; WBC = white blood count; CRP = C-reactive protein; PCT = procalcitonin; ESR = erythorcyte sedimentation rate; The p values indicate differences between No AKI group and AKI group.

Table IV. Association between biomarkers (cardiac and renal parameters) and clinical outcomes.

	Severe COVID-19 (Multivariate model)		Death (Multivariate model)	
	OR (90% CI)	*p*-value	OR (90% CI)I	*p*-value
Age > 60 years	4.02 (1.72-9.43)	0.001	6.05 (2.15-12.83)	0.004
Male gender	2.36 (1.07-5.20)	0.033	1.54 (0.30-7.99)	0.605
BMI > 30 kg/m^2	3.81 (1.59-7.82)	0.015	1.69 (1.12-3.57)	0.017
Comorbidity	6.62 (2.74-18.51)	< 0.001	6.49 (2.21-15.98)	< 0.001
Hospital Admission				
Abnormal Hs-TnI	2.46 (0.52-7.12)	0.247	0.69 (0.13-18.87)	0.490
Abnormal MYO	5.15 (0.17-45.26)	0.859	0.60 (0.12-16.25)	0.705
Abnormal Pro-BNP	1.40 (0.37-5.31)	0.622	1.46 (0.02-87.31)	0.856
Abnormal CKMB	3.50 (0.63-9.04)	0.108	0.64 (0.51-7.78)	0.401
Abnormal Creatinine	2.25 (0.54-4.89)	0.368	1.26 (0.35-7.28)	0.664
Abnormal e-GFR	1.02 (0.16-6.47)	0.982	2.18 (0.93-8.54)	0.146
Peak Hospitalization				
Abnormal Hs-TnI	3.60 (0.47-27.70)	0.218	2.77 (1.10-8.46)	0.034
Abnormal MYO	3.54 (0.80-15.57)	0.095	1.46 (0.02-87.31)	0.856
Abnormal Pro-BNP	5.49 (1.82-16.63)	0.003	6.45 (1.97-34.75)	0.001
Abnormal CKMB	1.15 (0.39-3.41)	0.791	0.92 (0.49-5.16)	0.958
Abnormal Creatinine	2.46 (1.10-6.23)	0.027	1.31 (0.37-8.25)	0.784
Abnormal e-GFR	1.71 (0.42-6.99)	0.458	3.72 (1.58-17.15)	0.008

OR = odds ratio; CI = confidence interval; Hs-TnI = High sensitivity Troponin I; MYO = myoglobin; Pro-BNP = pro-brain natriuretic peptide; CKMB=creatine kinase MB; e-GFR = estimated glomerular filtrateion rate.

illustrated in Figure 2. An increased Hs-TnI (> 300 ng/L) (HR=25, 95% CI=5-127, $p < 0.001$), increased pro-BNP (> 2500 pg/ml) (HR=275; CI%=61-1238; $p < 0.001$) and decreased e-GFR (< 60 ml/min) (HR=83; CI%=16-423; $p < 0.001$) were associated with a higher mortality.

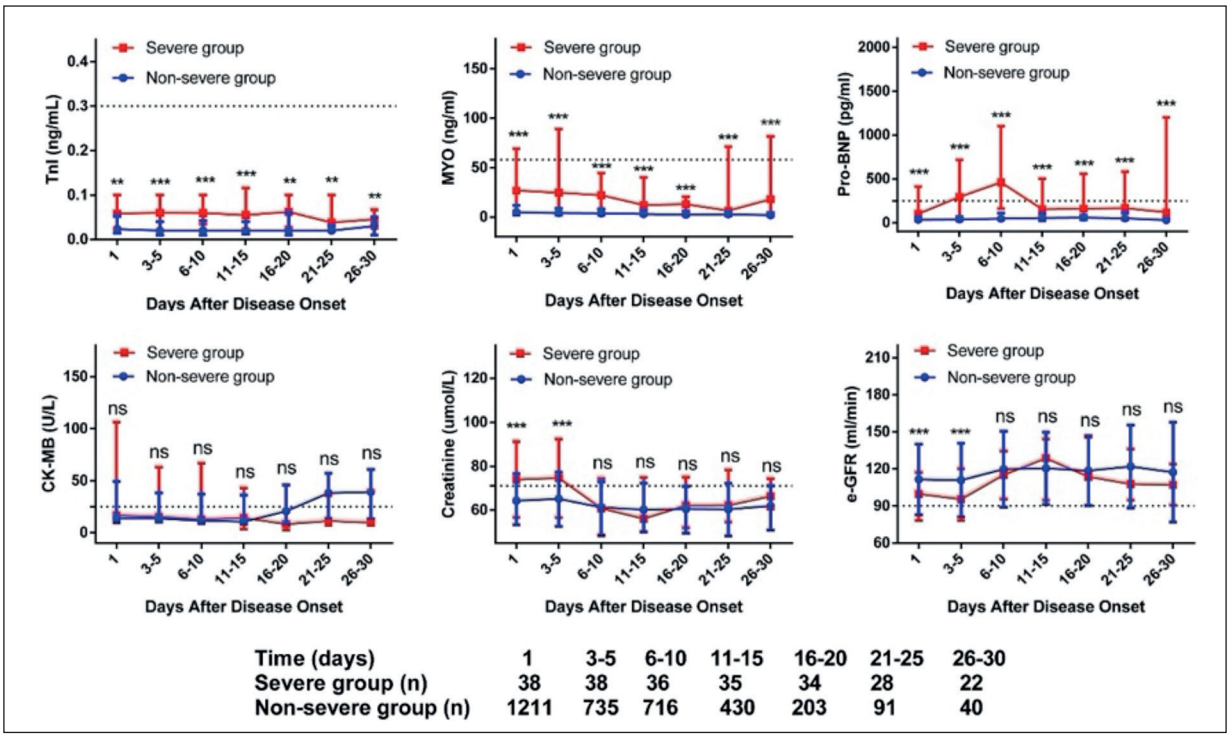

Figure 1. The dynamic profile of cardiac and renal parameters in patients by severity of COVID-19. The cardiac and renal parameters in the non-severe group (*blue line*) and severe group (*red line*) were analyzed at different time points after hospital admission. The cardiac and renal parameters are shown using median and IQR.

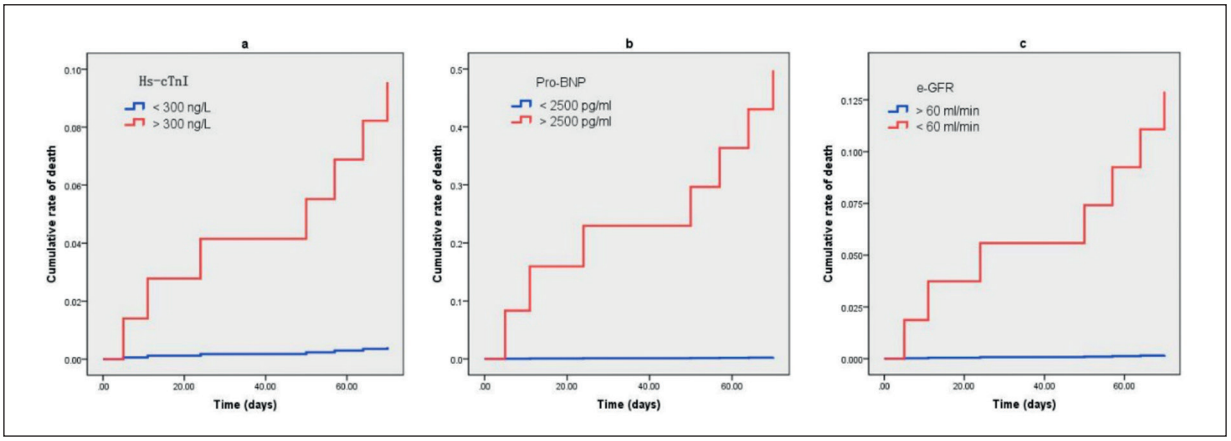

Figure 2. Kaplan-Meier curves for cumulative mortality during hospitalization in patients with different levels of cardiac and renal injury. An increased Hs-TnI (> 300 ng/L) (HR = 25, 95% CI = 5-127, $p < 0.001$), increased pro-BNP (> 2500 pg/ml) (HR = 275; CI % = 61-1238; $p < 0.001$) and decreased e-GFR (< 60 ml/min) (HR = 83; CI% = 16-423; $p < 0.001$) were associated with a higher mortality.

Discussion

Although COVID-19 is most well known for causing substantial respiratory pathology, it can also result in several extrapulmonary manifestations, including thrombotic complications, ACI, AKI, gastrointestinal symptoms, hepatocellular injury, and so on[12]. Even if reports on ACI and AKI in hospitalized COVID-19 patients are expanding, there is a dearth of clinical data regarding the incidence and the clinical significance of ACI and AKI in COVID-19 patients from areas with low severity rate and mortality of COVID-19. In Shanghai, China, the severity rate (3.0%) and mortality rate (0.6%) of COVID-19 weres very low, attributing to "Four Early Principle" has been undertaken at the early time of the outbreak. In this study, we assessed ACI and AKI among hospitalized COVID-19 patients in Shanghai, China, which is a representative city with low severity rate and mortality rate of COVID-19.

In this study, AKI is present in 7.3% of overall patients with COVID-19 and in 28.9% of severe patients with COVID-19. Our findings are similar to a meta-analysis reporting that AKI is present in 8.3% of overall patients with COVID-19 and in 19.9% of severe patients with COVID-19[13]. Our results correspond with the data from Case et al[14], who have demonstrated that the overall incidence of AKI in ICU patients ranges from 20% to 50%, higher than that of non-ICU patients. In this study, we found an increasing severity rate and mortality with progressively ACI or AKI in hospitalized patients with COVID-19. This effect on severity rate and mortality persisted despite adjusting for age, male, obesity, and comorbidities which has been shown to be the primary pathway for serious illness and mortality[15]. These findings are similar to the experience from an American cohort of 370 patients with COVID-19 with a high mortality (40.7%)[16], although our data is based on a cohort of 1249 COVID-19 patients with a low mortality (0.6%).

There are several mechanisms by which COVID-19 could impact the heart and the kidney. First, emerging evidence suggests the possibility of a direct cytopathic effect of SARS-CoV-2 on the heart and the kidney. ACE-2, the receptor for SARS-CoV-2 entry into human cells, is heavily expressed in tissues outside the lungs, including the heart and the kidneys[17]. Su et al[18] reported that immunostaining with SARS-CoV nucleoprotein antibody was positive in the renal tubules epithelium and podocytes. Second, the exaggerated cytokine release in response to viral infection, a condition known as cytokine release syndrome (CRS) or cytokine storm, is emerging as the mechanism leading to multiple-organ injury in COVID-19[19]. The concomitant presence of the cytokines storm and the pneumonia-related hypoxia could also determine myocardial and renal ischemia, since it alteres the oxygen supply-demand balance. Li et al[20] reported that the kinetic changes of cytokines are related with the prognosis of patients with severe COVID-19. Third, thrombotic microangiopathy leading to ACI and AKI is possible too. A generalized coagulopathy also appears to promote this thrombogenic condition.

Especially, arterial events, such as renal artery thrombosis or acute coronary syndrome were observed in COVID-19 patients[21].

The incidence of AKI in this study was much lower than the one previously reported from western countries. This could partly be due to a difference in the prevalence of severe COVID-19 patients. Cipriani et al[22] reported a higher rate of ACI (38% on admission, 46% during hospitalization) and mortality (18%), which may be explained by the characteristics of their population, represented by older (median 71 years) and comorbid patientshypertension (62%), dyslipidemia (36%), and diabetes (25%). Indeed, the median age of our patients (36 years) was notably lower than Cipriani et al[22] (71 years). In addition, the incidence of ACI in this study was much lower than previous studies from WuHan, China, in which, ACI has been reported in 12–30% in patients with COVID-19. This also could partly be due to a difference in the prevalence of old patients. Median age of our patients (36 years) was notably lower than Huang et al[23] (49 years) and Zhou et al[24] (56 years).

A meta-analysis explored the risk factors for COVID-19 patients to develop critical disease or death, and found that a Hs-cTnI > 28 pg/mL was associated to deterioration of the patient's condition OR=43.24, 95% CI (9.92, 188.49), $p < 0.001$[25]. We also found that the risk for mortality increases with the levels of Hs-cTnI and pro-BNP, reaching a plateau at a concentration of Hs-cTnI about 300 ng/L or pro-BNP > 2500 pg/ml. This is clinically important since an experts' consensus also suggested that the early evaluation and continued monitoring of cardiac damage (cTnI and proBNP) after hospitalization may identify patients with cardiac injury and predict COVID-19 complications[26]. Piccioni et al[27] also identified that a high value of high-sensitivity troponin represents a negative prognostic indicator in patients with COVID-19. Our results highlights the role of cardiac injury (HscTnI and pro-BNP) in the prediction of in-hospital mortality.

We saw higher adjusted odds of AKI in patients with age > 60 years, male gender, obesity, hypertension, CKD, decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission. Consistent with our results, Hansrivijit et al[13] identified that increasing age, diabetes, hypertension and elevated baseline serum creatinine levels are possible predisposing factors for AKI in patients infected with SARS-CoV-2. Nimkar et al[16] identified that increasing age, CKD, hyperlipidemia and being of African-American descent showed higher odds of AKI. However, we added that patients with decreased lymphocyte and increased CRP, PCT, and ESR on hospital admission were associated with a higher incidence of ACI and AKI even after the adjustments for other covariates. Decreased lymphocyte and increased CRP, PCT, and ESR suggested a more severe forms of cytokine storm and system inflammation, which is the mian cause for ACI and AKI in patients with COVID-19. Therefore, physicians should pay close attention to these patients as they are at significant risk of developing ACI and AKI.

Strengths of the study include the data's accuracy, that was manually extracted from patient charts, a relatively large cohort and using a systematic approach for multivariable analysis. The present study has the limitations inherent of singlecenter, retrospective, observational studies.Pre-admission creatinine values were not available in most of patients and thus a decision to use the lowest creatinine during the hospital stay as the patients' baseline creatinine values was made.

Conclusions

In summary, ACI and AKI were not common in COVID-19 patients in Shanghai, China, a representative city with low severity rate and mortality rate of COVID-19. The incidence of ACI and AKI is high in severe patients with COVID-19, but is much lower in non-severe cases. In this study, we confirmed that ACI and AKI had a significant impact on the severity rate and mortality among patients with COVID-19. Patients who developed ACI or AKI had a much higher mortality rate when compared to those without.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Declaration

Among 1249 patients in this study, 664 patients had been included in a previous report named "Efficacy Evaluation of Early, Low-Dose, Short-Term Corticosteroids in Adults Hospitalized with Non-Severe COVID-19 Pneumonia: A Retrospective Cohort Study" (Li Q, Li WX, Jin YP, et al. Infect Dis Ther 2020; 1-14).

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Authors' Contribution
Study concept and design: Qiang Li and Liang Chen. Data collection: Wei Xu, Ling Fei, ChenLu Huang, WeiXia Li, and XuDong Xie. Analysis and interpretation of data: Weixia Li, Wei Xu, ChenLu Huang, and Qiang Li. Drafting of the manuscript: Qiang Li. Critical revision of the manuscript: Liang Chen.

Consent for Publication
All authors read and approved the manuscript.

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Role of the Sponsor
The funding organizations are public institutions and had no role in the design and conduct of the study; collection, management, and analysis of the data; or preparation, review, and approval of the manuscript.

Availability of Data and Materials
We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality. The supporting data can be accessed from Qiang Li (corresponding author), E-mail: liqiang66601@163.com.

Ethics Approval and Consent to Participate
The study was approved by the Clinical Research Ethics Committee of the Shanghai Public Health Clinical Center. The study was conducted in accordance with the principles of the Helsinki Declaration of 1975, as revised in 1983.

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