Roles of Clinical Features and Chest CT in Predicting the Outcomes of Hospitalized Patients with COVID-19 Developing AKI

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This research aimed to evaluate the clinical features and computed tomography (CT) scans associated with poor outcomes in COVID-19 patients with acute kidney injury (AKI). A total of 351 COVID-19 patients (100 AKI, 251 non-AKI) hospitalized at Imam Hossein Teaching Hospital affiliated to Shahid Beheshti University of Medical Sciences were included. To investigate the factors associated with in-hospital mortality in COVID-19 patients developing AKI, COX univariate and multivariate regression models were applied after controlling other confounding variables. C-reactive protein CRP, lactate, and procalcitonin levels were significantly higher in AKI patients than in non-AKI patients ($P < .05$). In addition, AKI patients had higher frequencies of lymphopenia and leukocytosis ($P < .05$). The troponin levels and WBC were the most significant factors for predicting mortality in patients with AKI. Our findings showed that AKI per se is much more important than any other prognostic factor affecting non-AKI patients. However, AKI patients with higher CRP, PCT, and lactate levels had a poor prognosis.

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Brief Communication

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a disease arising from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has been estimated that 29% of critically ill COVID-19 patients develop acute kidney injury (AKI).[1] A relative outlook on patients' prognosis can significantly influence patient care in a setting where many medical centers are closed to new patients. Poor prognosis has been associated with certain clinical symptoms and paraclinical signs in COVID-19.[2]

In this regard, this study investigated the laboratory values and clinical and chest CT scan scores in COVID-19 patients with AKI and compared them with COVID-19 patients without AKI. It also discussed the importance of different clinical and paraclinical parameters as predictive factors for patients with AKI in a COVID-19 setting.

MATERIALS AND METHODS

This retrospective cohort study was undertaken at Imam Hossein medical center, affiliated to Shahid Beheshti University of Medical Sciences. The research protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, with approval number

(RETECH.REC.1397.403). All procedures were carried out according to the relevant regulations and guidelines. Informed consent was obtained from all the participants. The study included all the patients hospitalized between August 2020 and January 2021 with a diagnosis of COVID-19. The diagnosis of COVID-19 was established by reverse transcriptase-polymerase chain reaction (rt-PCR). Our inclusion criteria were: 1) ≥ 18 years old; 2) peripheral oxygen saturation < 90%, classified as severe COVID-19. The exclusion criterion was chronic kidney disease (CKD) since these patients are more prone to severe forms of COVID-19. Imam Hossein Teaching Hospital medical ethics board authorized the study, and it was carried out following the Helsinki declaration.

Demographics, clinical and laboratory data, and radiologic characteristics were collected from the medical records of the study participants. Under the supervision of a chief physician, all the gathered data were recorded on datasheets. Upon hospital admission, all the patients underwent chest CT scans, which were reviewed by an experienced radiologist to confirm the diagnosis of COVID-19.

We referred to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines for clinical practice for the diagnosis of AKI, where it is defined as one or more of the following criteria: serum creatinine increase by ≥ 0.3 mg/dL within 48 hours or to ≥ 1.5 times from the first measurement (known or supposed to have happened within the recent seven days).[3]

A chest CT scan score was calculated based on the visual inspection score of 0 to 5 for each pulmonary lobe, with 0 (considered for no involvement), 1 (for < 5% of involvement), 2 (for 5 to 25%), 3 (for 26 to 49%), 4 (for 50 to 79%), and 5 (for > 75% lung injury). As a result, the total probable score ranged from zero to 25.[4] In the qualitative assessment, CT scores of 1 to 5 were categorized as mild, 6 to 14 as moderate, and 15 to 25 as severe involvement.

Statistical Analysis

Statistical analyses were carried out using STATA version 14. The patients were categorized by whether or not they experienced AKI during hospitalization. We reported mean ± SD for parametric data. The Kolmogorov-Smirnov test was applied if the parameters were not normally distributed. Concerning non-parametric variables, the Mann-Whitney U test and concerning parametric variables, the t-test was used to compare the variables. The chi-squared test was used for categorical variables reported as numbers (percentages). A P value < .05 was considered significant. COX proportional model was used to assess the association of clinical and paraclinical variables in AKI patients with mortality. The crude association was calculated using univariate analysis. Previously reported mortality risk factors were considered to assess the confounding effects of underlying conditions and demographics.[5] To identify the best predictors, variables with a P value < .2 were selected for analysis through a stepwise COX proportional hazard model. Based on Schoenfeld residual regressions, hazard ratios were calculated at a 95% confidence level using the proportional hazard assumption. P value < .05 was considered significant.

RESULTS

This research included 415 patients. Sixty-four patients were excluded due to a history of CKD and kidney replacement therapy. One hundred patients were diagnosed with AKI, and 251 did not develop AKI. The median duration of hospitalization was five days. The mean age of the patients was 61.51 ± 17.80 years, and 58.40% were male. Patients diagnosed with AKI were significantly older than those who did not develop AKI (P < .05). In addition, AKI was considerably more frequent in males (P < .05). The most common underlying conditions in patients with AKI were hypertension and coronary artery disease (P < .001). In addition, inflammatory markers such as CRP, PCT, and lactate levels were considerably higher in this population (P < .05). In addition, these patients had significantly lower lymphocyte counts and higher white blood cell counts (P < .05) (Table 1).

According to the stepwise COX regression analysis, patients with AKI and a higher CT score at baseline did not have higher odds of mortality. Furthermore, increased troponin and WBC levels were associated with increased mortality (P < .05). The results of the COX regression analysis are presented in Table 2.

DISCUSSION

Patients with COVID-19 might also present with AKI or develop it during hospitalization.

Table 1. Baseline Characteristics of AKI and Non-AKI Patients with COVID-19

Characteristics	Total (n = 351)	Without AKI (n = 251)	With AKI (n = 100)	*P*
Demographics and In-hospital Baseline Measures				
Age, y (mean ± SD)	61.51 ± 17.80	57.16 ± 17.00	72.55 ± 14.83	< .001
Sex, %				
Male	205 (58.40)	138 (55.00)	67 (67.00)	< .05
Female	146 (41.60)	113 (45.00)	33 (33.00)	
BMI, kg/m^2 (mean ± SD)	26.44 ± 3.97	26.58 ± 3.79	26.09 ± 4.38	> .05
Vital Signs				
Systolic Blood Pressure, mmHg (median (IQR))	120.00 (10.00)	120.00 (10.00)	110.00 (10.00)	> .05
Diastolic Blood Pressure, mmHg (median (IQR))	70.00 (10.00)	70.00 (10.00)	70.00 (10)	> .05
Pulse Rate, beats/min (median (IQR))	85.00 (14.00)	85.00 (12.00)	85.00 (20.00)	> .05
Respiratory Rate, breaths/min (median (IQR))	18.00 (4.00)	18.00 (4.00)	17.90 (6.00)	> .05
O_2 Saturation, % (median (IQR))	67.00 (48.13)	66.00 (46.20)	70.50 (49.05)	> .05
Habit History				
Smoking, %				
Yes	37 (10.50)	25 (10.00)	12 (12.00)	> .05
No	314 (89.5)	226 (90)	88 (88)	
Past Medical History				
Hypertension, %	99 (28.20)	61 (24.30)	38 (38.00)	< .05
Diabetes, %	83 (23.60)	59 (23.50)	24 (24.00)	> .05
Coronary Heart Disease, %	55 (15.70)	30 (12.00)	25 (25.00)	< .05
Neurologic Disorders, %	35 (10.00)	18 (7.20)	17 (17.00)	< .05
Chronic Obstructive Pulmonary Disease/Asthma, %	33 (9.40)	20 (8.00)	13 (13.00)	> .05
Malignancy, %	29 (8.30)	21 (8.40)	8 (8.00)	> .05
Dyslipidemia, %	21 (6.00)	15 (6.00)	6 (6.00)	> .05
Cirrhosis, %	5 (1.40)	2 (0.80)	3 (3.00)	> .05
Serum Cr, mg/dL (median (IQR))	1.10 (0.40)	1.10 (0.30)	1.80 (0.90)	<.001
Urea, mg/dL (median (IQR))	35.00 (29.00)	31.00 (17.70)	61.80 (57.48)	<.001
CRP, mg/L (median (IQR))	43.00 (53.50)	38.50 (53.00)	54.00 (73.13)	< .05
ESR, mm/h (median (IQR))	43.00 (40.00)	43 (42.00)	42.50 (37.50)	> .05
Lactate, mg/dL (median (IQR))	18.00 (11.00)	18.00 (9.35)	33.00 (14.30)	< .05
PCT, ng/mL (median (IQR))	0.32 (0.75)	0.28 (0.37)	0.70 (3.36)	<.001
Ferritin, micg/L (median (IQR))	450.00 (697.50)	366.00 (545.00)	623.00 (1393.00)	> .05
D-dimer, mg/L (median (IQR))	828.00 (3755.00)	769.00 (1840.00)	1338.00 (5569.50)	> .05
Lactate Dehydrogenase, Units/L (median (IQR))	537.00 (264.50)	527.00 (262.00)	543.00 (349.00)	> .05
Troponin, ng/mL (median (IQR))	0.02 (0.04)	0.02 (0.02)	0.03 (0.08)	> .05
AST, U/L (median (IQR))	34.00 (27.00)	33.00 (24.00)	43.00 (34.75)	< .05
ALT, U/L (median (IQR))	28.00 (25.90)	28.00 (24.45)	26.00 (27.00)	> .05
WBC 10^3, cells/μL	7.00 (4.90)	6.60 (4.33)	7.80 (8.20)	< .05
Lymphocyte Count, cells/μL	1254.00 (722.00)	1293.60 (739.00)	1124.50 (773.00)	< .05

Furthermore, kidney involvement during COVID-19 is significantly associated with a poor prognosis and increased mortality.[6,7] Among patients hospitalized with a COVID-19 diagnosis in our center, we observed a 28% rate of AKI development during hospitalization. In our study, the AKI incidence was higher than what had been reported from China and Italy but lower than that from the United States.[8] This disparity could be attributed to the different prevalence of comorbidities in study patients in or racial differences. Hypertension, coronary heart disease, and neurological disorders were more prevalent in COVID-19 patients with AKI. Consistently, our study findings demonstrated that AKI was more common in the elderly. Hansrivijit *et al.* also reported increasing age and hypertension as possible predisposing factors for AKI in patients with COVID-19 in their meta-analysis.[9]

Multiple laboratory parameters differed between COVID-19 cases without AKI and those with AKI, in our research. Increased CRP levels in AKI may

Table 2. Factors Related to In-hospital Mortality Based on Univariate and Multivariable Cox Proportional Hazards Regression Model in AKI Patient

Variables	Crude HR,* 95% CI	*P*	Adjusted HR, 95% CI	*P*
Age, y	1.020 (0.995 to 1.046)	> .05	-	-
Sex				
Female	Ref	-		
Male	1.014 (0.573 to 1.916)	> .05	-	-
BMI	0.990 (0.928 to 1.057)	> .05	-	-
Pulse Rate	1.016 (1.001 to 1.032)	< .05	-	-
Systolic Blood Pressure	0.981 (0.964 to 0.998)	< .05	-	-
Urea	1.004 (0.999 to 1.009)	> .05	-	-
Serum Cr	1.043 (0.880 to 1.273)	> .05	-	-
Troponin	1.576 (1.132 to 2.195)	< .05	1.682 (1.197 to 2.364)	< .05
WBC	1.033 (1.001 to 1.068)	< .05	1.098 (1.013 to 1.190)	< .05
CT Score	1.059 (0.986 to 1.137)	> .05		

*Hazard ratio
The model was fitted based on the Schoenfeld residual test for evaluating proportional hazards assumption with *P* equal 0.81.

be related to a cytokine storm caused by viral invasion.[10] COVID-19-related lymphopenia might be a result of lymphocyte retention in the lungs. Additionally, lymphocytes express the angiotensin-converting enzyme (ARS-CoV-2 receptor) on their surface.[11] The greater decrease in lymphocytes in the AKI patients compared to the non-AKI group suggests the immune system inhibition due to already consumed immune cells. This lymphopenia is critical in disease progression.

In the present study, among COVID-19 patients with AKI, mortality was determined mainly by troponin and WBC levels. Although age and CT scores had an impact on mortality in both AKI and non-AKI groups, [12] CT scores and age did not play a significant role in increasing mortality in the AKI group of COVID-19 patients. Arikan *et al.* reported that older age, male gender, and comorbidities were risk factors for patients with COVID-19 and AKI. The impact of acute kidney injury on patients' outcomes may vary due to differences in healthcare systems, geographical areas, or hospital capacities.[13] Huang *et al.* described leukocytosis as a reliable predictor of COVID-19 severity and hospitalization.[14] Another study showed that leukocytosis on admission might predict poor outcomes and ICU admission.[15] Our results showed that increased mortality was observed in patients with AKI who also had leukocytosis.

The purpose of this study was to assess the prognostic factors for AKI in COVID-19 patients. This research had some limitations. First, this study included only the severe cases of COVID-19. The laboratory parameters, as well as the distribution of the chest CT lesions, may be different in mild and moderate cases. Second, the study was planned as a single-centered cohort. Third, the sample size was relatively small.

CONCLUSION

The results showed that AKI itself is much more important than any other prognostic factor. The CT scores did not differ significantly between the two groups. In addition to the patients' clinical condition, troponin level and leukocytosis can be used as possible prognostic factors to determine severity of disease in COVID-19 with AKI. It is possible to improve patient outcomes and reduce mortality by providing additional care to these patients.

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