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Prognostic Factors in Patients with AKI and COVID-19

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Abbreviations:

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; AKI: Acute kidney injury; CT: computed tomography; rt-PCR: Reverse transcriptase-polymerase chain reaction; ICU: Intensive care unit; LDH: Lactate dehydrogenase; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; KDIGO: Kidney disease improving global outcomes; GGO: Ground-glass opacities; SD: Standard deviation; ROC: Receiver operating characteristic; PCT: Procalcitonin; AUC: Area under the curve; CI: Confidence interval; BMI: Body mass index; HR: Hazard ratio

ABSTRACT

Background: Acute kidney injury is challenging in the context of the COVID-19 pandemic. Up to 30 % of critically ill COVID-19 patients develop AKI. Thus, it is imperative to determine what factors may predict the likelihood of these patients developing more severe and potentially life-threatening conditions.

Objective: The aim of this study is to investigate the clinical and computed tomography features associated with poor prognostic factors in COVID-19 patients developing AKI. We also aimed to investigate chest CT score and its pattern in AKI patients in the COVID-19 setting.

Materials and Methods: 415 patients with COVID-19 pneumonia were enrolled. 64 patients have been excluded due to a history of chronic kidney disorders. Finally, 351 patients, including 100 AKI cases and 251 non-AKI cases, were enrolled. The chest CT images

and clinical data of them were reviewed and compared. The CT scores and the risk factors associated with disease severity were discussed.

Results: Compared with the non-AKI group, the AKI patients had older ages and a higher incidence of certain comorbidities, such as hypertension and cardiovascular disorders. In AKI patients, the value of inflammatory markers, e.g., CRP, LDH, PCT, and Lactate level were significantly higher than those of the ordinary patients ($P<0.05$). In addition, the AKI patients showed higher incidences of lymphopenia ($P=0.019$) and leukocytosis ($P=0.023$). In the AKI group, the CT-scores were significantly higher than those of the non-AKI group ($P < 0.001$), and severe CT- scores were mainly associated with AKI. ROC analysis showed that 71.4 % sensitivity and 90 % specificity for CT scores higher than 13 in the AKI group. Out of all measured parameters, CT-score and the level of PCT, lactate, and WBC were the most reliable factors for predicting mortality in AKI patients.

Conclusions: There are significant differences in clinical symptoms, laboratory examinations, and CT manifestations between the AKI and non-AKI patients in the COVID-19 setting. Many factors are associated with the severity of the illness, which can help clinicians assess patients' prognosis.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first reported in Wuhan, China, in December 2019 and rapidly spread worldwide [1].

Despite most COVID-19 symptoms being associated with pulmonary interstitium and alveolar injury, recent studies have indicated that some patients are likely to experience renal, cardiovascular, or neurological damages [1]. Among COVID-19's complications, acute kidney injury (AKI) has been reported in 0.5-7 % of cases and is associated with higher mortality [2]. Additionally, it has been estimated that 29% of COVID-19 critically ill patients develop AKI [3]. However, AKI may be underestimated in COVID-19 because creatinine values measured at baseline may not represent the actual pre-admission renal function [4].

A chest computed tomography (CT) scan is applied for assessing the severity and extent of disease in patients with COVID-19-related pulmonary involvement [5, 6]. CT scan manifestations in COVID-19 pneumonia include ground-glass opacity (GGO), consolidation, nodules, cavities, and bilateral involvement of several lobes, more prominently revealed in the lower lobes and peripheral area [7, 8].

The correlation between CT severity scores and clinical parameters in COVID-19 pneumonia has been assessed in different studies [9]. A significant challenge for physicians handling COVID-19 patients is predicting their prognosis. A relative outlook on the 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[10]. For instance, there is evidence that elevated lactate dehydrogenase (LDH) levels are reliable indicators of disease severity in COVID-19 patients as well as factors such as elevated CRP [11].

This study aims to evaluate the chest CT manifestations in COVID-19 patients with AKI and compare them with the CT scores and patterns of COVID-19 patients without AKI.

Since it is essential to identify risk factors of progression to serious life-threatening COVID-19 infection conditions, we also discussed the importance of different laboratory parameters as a prognostic factor in AKI in the COVID-19 setting. Finally, we investigate the probable correlation between chest CT findings and the stage of AKI.

METHODS

Study design and participants

A retrospective cohort study was conducted at Imam Hussein medical center, affiliated with Shahid Beheshti University of medical sciences. The study included all patients hospitalized from March 2020 to July 2020 with the diagnosis of COVID-19. Subjects' COVID-19 diagnosis was confirmed by reverse transcriptase-polymerase chain reaction (rt-PCR). The inclusion criteria were: 1- minimum age of 18 years, 2- peripheral oxygen saturation below 90% (measured via pulse oximetry), categorized as severe COVID-19. Chronic kidney disease was the exclusion criterion since these individuals are more likely to develop severe forms of COVID-19. The Imam Hussein medical ethics board authorized the study, and it was run in accordance with Helsinki's declaration. Considering AKI as the primary outcome, the secondary outcomes included are hospitalization duration, renal replacement therapy, and intensive care unit (ICU) admission.

Data Collection and Measurements

Demographics, clinical and laboratory data, as well as radiologic characteristics, were collected for all included patients from medical records. Under the supervision of the responsible physician, all data were recorded on a prepared sheet. Upon hospital admission, all patients underwent chest CT scans, which an experienced radiologist has reviewed. Afterward, the validity of the radiological interpretation has been evaluated by another radiologist.

Laboratory data consisted of complete blood counts, renal and liver function tests, and inflammatory markers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and serum lactate dehydrogenase, were recorded.

For AKI diagnosis, we referred to the 2012 kidney disease improving global outcomes (KDIGO) clinical practice guideline, in which AKI is defined as any of the following: an increase in serum creatinine level by ≥0.3 mg/dl within 48 hours or to ≥1.5 times from baseline measure (which is known or presumed to have occurred within the previous seven days), decrease urinary output to less than 0.5 ml/kg/h for 6 hours or more. If the serum creatinine is 1.5–1.9 times baseline or ≥0.3 mg/dl (≥26.5 mmol/l) increase or urine output <0.5 ml/kg/h for 6–12 hours, the patient would be categorized in stage 1 AKI. Stage 2 AKI is defined as serum creatinine 2.0–2.9 times baseline or <0.5 ml/kg/h for ≥12 hours. Finally, serum creatinine 3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dl (≥353.6 mmol/l) or the initiation of renal replacement therapy or urine output <0.3 ml/kg/h for ≥24 hours or anuria for ≥12 hours is recognized as stage 3 of AKI [12].

Chest CT interpretation

Based on the visual inspection score of 0 to 5 for each pulmonary lobe, a CT score was calculated based on the severity of pulmonary involvement. 0 was considered for no involvement, 1 for less than 5% of involvement, 2 for 5%-25%, 3 for 26%-49%, 4 for 50%-79%, and 5 for more than 75% lung injury. As a result, the total probable score ranged from zero to 25[13]. In a qualitative assessment, CT severity scores of 1–5, 6–14, and 15–25 were categorized as mild, moderate, and severe involvement, respectively.

STATISTICAL ANALYSIS

The statistical analysis was carried out using STATA version 14 (Texas, United States). The patients were categorized by whether or not they experienced AKI during their hospitalization. We reported mean ± standard deviation (SD) and median (interquartile range) for parametric and non-parametric data. The Kolmogorov-Smirnov test was applied if the parameters were not normally distributed. A Mann-Whitney U test was used on non-parametric variables, and a t-test was used on parametric variables for comparing the variables. The chi test was utilized on categorical variables that were reported as numbers(percentages). The P-value of less than 0.05 is considered significant.

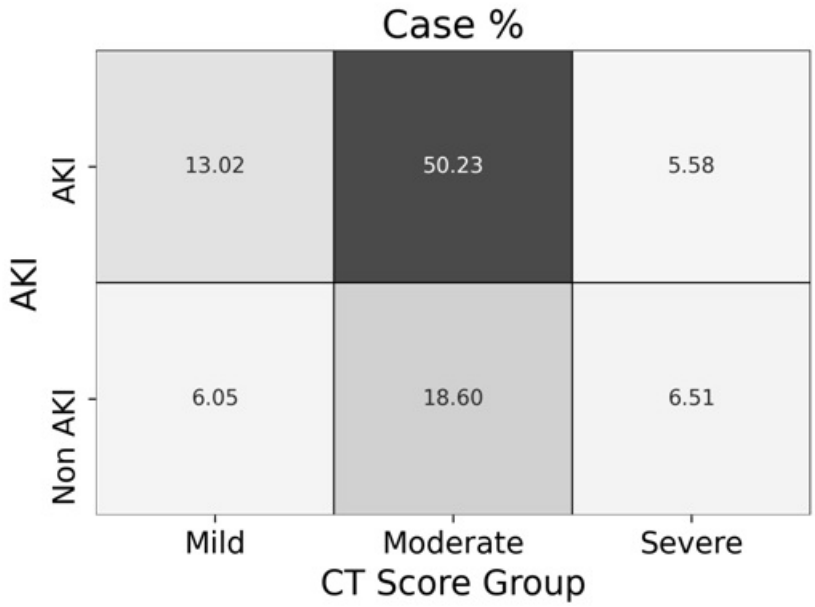

Figure 1: Contingency matrix (AKI vs. CT score group), values are presented in case percentage with respect to the total number of subjects per CT-score group in AKI and non-AKI patients.

COX proportional model was applied to assess the association of AKI occurrence and CT-scan scores to mortality. The crude association calculated using univariable analysis. Previously reported mortality risk factors were considered to assess the confounding effects of underlying conditions and demographics [14]. To identify the best predictors, variables with a P-value of less than 0.2 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. A P-value of less than 0.05 is considered significant.

The receiver operating characteristic (ROC) curves were used to identify mortality scores in the following subject groups: a. total subjects, b. non-AKI subjects, and c. AKI subjects. For instance, a classifier developed using CT scores achieved 80% specificity for all three subject groups, as shown in (Figure 2). In order to obtain quantitative results, the Area Under The Curve (AUC) of the ROCs was computed. The data in each of the groups are split

randomly into 80% train - 20% test batches. AUC is calculated from the test set after the classifier has been trained on the train set. This process is repeated 100 times for randomly obtained train-test splits to obtain statistics. The reported values (mean, Confidence Interval (CI), and the distribution comparison P-values) for AUCs of each ROC analysis is the outcome of distribution constructed via bootstrap sampling (to assure parametric distribution of the data) of these 100 AUC calculations.

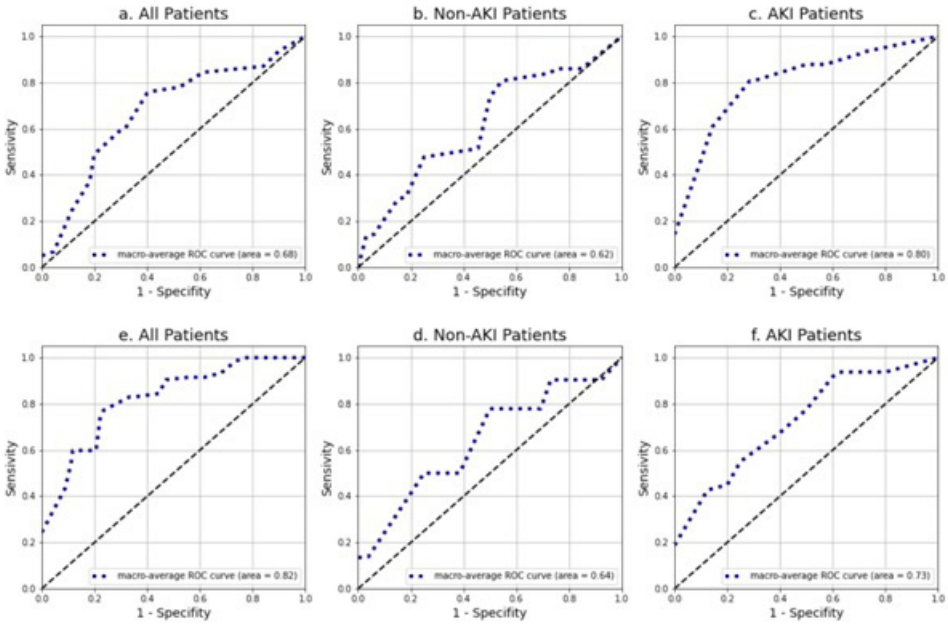

Figure 2: ROC analysis of: A- CT-score to predict mortality in the total cases, patients with AKI, and patients without AKI. (a: AUC = 0.68 [95% CI = 0.642- 0.678], b: AUC = 0.62 [95% CI = 0.548- 0.622], c: AUC = 0.80 [95% CI = 0.705- 0.756]). All mutual comparison of AUC-ROC distributions has P-value<0.001. B- The initial serum PCT level to predict mortality in the total cases, patients with AKI, and patients without AKI. (a: AUC = 0.82 [95% CI = 0.769- 0.800], b: AUC = 0.64 [95% CI = 0.614- 0.706], c: AUC = 0.73 [95% CI = 0.695- 0.754]). All mutual comparison of AUC-ROC distributions has P-value<0.001.

RESULTS

The study included 415 patients for a period of 5 months. 64 patients were excluded due to the history of chronic kidney disease and renal replacement therapy. One hundred patients were diagnosed with AKI. Two hundred and 51 patients were included in the control group.

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. Among all cases, sixty-three (18.10 %) experienced a critical condition and were admitted to the ICU. Patients diagnosed with AKI were significantly older compared to the control group (P=0.006). In addition, AKI was considerably more frequent in the male gender (P=0.010).

Regarding underlying conditions, hypertension and coronary artery disease were found to be more frequent in patients with AKI, and neurologic disorders were more common in control patients. The three most frequently reported clinical symptoms were dyspnea (72.08%), cough (66.09%), and fever (56.93%). Except for the higher prevalence of cough in the control group (71.31% vs. 53%, P=0.001), no significant differences in the prevalence of fever or dyspnea were observed (P=0.570, P=0.134, respectively). (Table 1) represents the demographic data, vital signs, and medical history of the patients.

Patients who experienced AKI had significantly higher baseline serum creatinine and urea levels (P<0.001). Also, inflammatory markers such as CRP, LDH, PCT, and lactate levels were considerably higher in this population (P<0.05). These patients had significantly higher white blood cell count (P=0.023) and lower lymphocyte count (P=0.019). The laboratory results are given in detail in (Table 2).

In the 351 patients involved, a mortality rate of 19.9% (70 patients) was reported, which was significantly higher in the AKI group (47% vs. 9,2%, P<0.001). Additionally, the length of hospitalization between groups was not statistically different (5 vs. 6 days, P=0.108). 63 (18.10%) out of all patients were admitted to the ICU, which was more prevalent in patients who experienced AKI compared to the control group (34.3% vs. 11.6%, P<0.001). Renal replacement therapy requirement was reported meaningfully higher in patients with AKI (11.0% vs. 0.8%, P<0.001).

Table 1: Demographic data, vital sign upon arrival characteristics, and medical history of patients with COVID-19

Characteristics		Total (n=351)	Without AKI (n=251)	With AKI (n=100)	P-value
Demographics					
Age (years)		61.51±17.80	57.18±16.96	72.50±15.05	0.006
Sex	Male	58.4	54.2	69.0	0.010
	Female	41.6	45.8	31.0	
Body Mass Index (kg/m^2)		26.44±3.97	26.56±3.78	26.13±4.42	0.055
Vital Signs					
Systolic Blood Pressure (mmHg)		119.97±48.87	117.58±13.95	126.14±89.73	0.311
Diastolic Blood Pressure (mmHg)		73.99±10.10	74.13±9.66	73.63±11.20	0.221
Pulse Rate (beats/min)		86.57±18.38	86.56±17.03	86.60±21.59	0.165
Respiratory Rate (breaths/min)		19.42±8.45	19.59±8.54	19.03±8.24	0.262
O_2 Saturation, %		89.70±7.74	90.48±7.25	87.87±8.58	0.187
Habitual History					
Non-smoker		314 (89.45)	226 (90.01)	88 (88.00)	0.574
Currently Smoking		37 (10.55)	25 (9.96)	12 (12.00)	
Past Medical History					
Hypertension (%)		99 (28.20)	60 (23.90)	39 (39.00)	0.005
Diabetes (%)		83 (23.64)	59 (23.50)	24 (24.00)	0.922
Coronary heart disease (%)		55 (15.67)	30 (12.00)	25 (25.00)	0.002
Neurologic disorders (%)		35 (9.97)	17 (6.77)	18 (18.00)	0.002
Chronic obstructive pulmonary disease/Asthma (%)		33 (9.40)	20 (7.97)	13 (13.00)	0.145
Malignancy (%)		29 (8.26)	21 (8.36)	8 (8.00)	0.910
Dyslipidemia (%)		21 (5.98)	14 (5.57)	7 (7.00)	0.612
Cirrhosis (%)		5 (1.42)	2 (0.79)	3 (3.00)	0.116

Table 2: Laboratory values of patients with COVID-19

Characteristics	Total (n=351)	Without AKI (n=251)	With AKI (n=100)	P-value
Serum creatinine, mg/dl	1.15 (0.83)	1.10 (0.30)	1.80 (0.90)	<0.001
Urea, mg/dl	35.00 (29.00)	30.77 (18.32)	62.15 (57.75)	<0.001
CRP, mg/L	43.00 (53.50)	38.50 (52.10)	54.00 (73.13)	0.010
ESR, mm/h	43.00 (40.00)	42.50 (42.00)	43.00 (37.00)	0.454
Lactate, mg/dL	18.00 (11.00)	18.00 (9.35)	22.55 (14.82)	0.016
PCT, ng/mL	0.68 (1.95)	0.28 (0.37)	0.70 (4.16)	<0.001
Ferritin, micg/L	502.45 (644.50)	350.45 (537.98)	633.00 (1392.90)	0.104
D-dimer, mg/L	828.00 (3755.00)	769.00 (1840.00)	1338.00 (5569.50)	0.469
Lactate dehydrogenase, Units/L	537.00 (264.50)	527.00 (262.00)	543.00 (349.00)	0.211
Troponin, ng/mL	0.02 (0.04)	0.02 (0.02)	0.03 (0.08)	0.056
AST, U/L	34.00 (27.00)	33.00 (24.00)	43.00 (35.00)	0.034
ALT, U/L	28.00 (25.90)	28.00 (24.00)	25.50 (27.75)	0.795
WBC 10^3, cells/micL	7.00 (4.90)	6.60 (4.33)	7.80 (7.40)	0.023
Lymphocyte count, cells/micL	1254.00 (722.00)	1290.80 (752.00)	1116.00 (753.00)	0.019

Median CT-score for total papulation were recorded as 10.00 (6.00), which was significantly higher in patients with critical conditions who were admitted to the ICU reported as 12.00 (7.50) compared to severe patients without ICU admission stated as 10.00 (5.25) (P=0.048). A score of 11.00 (6.50) was reported in patients with AKI and 10.00 (5.50) in patients without AKI (P=0.348).

The CT-score did not correlate significantly with the AKI stage (P=0.438). Additionally, the AKI stage has neither a statistically significant correlation with the pattern of involvement in chest CT nor the distribution of lesions (Table 3). (Figure 1) depicts the contingency matrix of different CT-score categories for both AKI and non-AKI patients. The chi-square test revealed a significant correlation between the CT-score stage and AKI (P= 0.024). Moreover, according to the post-hoc analysis, AKI is mainly discriminative between moderate and severe CT-score stages (P= 0.012). In other words, COVID-19 patients with severe CT-score are more likely to develop AKI.

As demonstrated in (Table 4), GGO is the most prevalent observed pattern in CT scans of all patients, and lung lesions were mainly distributed in the paracentral area. Also, pleural effusion was more frequently observed in AKI patients than in non-AKI cases (P=0.020).

As a result of stepwise COX regression analysis after adjusting for potential interfering baseline factors such as age, body mass index (BMI), smoking, and underlying conditions, AKI significantly increased the mortality (2.688 [1.329-5.33]), P=0.006). Furthermore, patients with a higher CT-score at baseline had a higher probability of mortality (1.076 [1.012-1.145], P=0.019). Also, mortality is significantly associated with increased age and history of malignancy (P=0.008 and P<0.001, respectively). Results from COX regression analysis are presented in (Table 5).

Table 3: Computed tomography findings of patients with AKI categorized by Stages

Characteristics	Stage 1	Stage 2	Stage 3	P-value
Pattern of involvement				
GGO, %	67.40	41.70	46.70	0.152
Consolidation, %	13.00	33.30	26.70	0.201
Plural effusion, %	21.70	16.70	33.30	0.548
Distribution of lesions				
Peri-Broncho vascular, %	28.30	16.70	33.30	0.613
Linear Opacity, %	2.20	0.00	6.70	0.532
Hazy Round, %	15.20	8.30	6.70	0.613
Perihilar, %	4.30	0.00	6.70	0.681
Pulmonary Fibrosis, %	2.20	8.30	0.00	0.389
CT-Score	10.00 (4.25)	12.00 (12.75)	13.00 (10.00)	0.788

Table 4: Computed tomography findings of patients

Characteristics	Total (n=351)	Without AKI (n=251)	With AKI (n=100)	P-value
Pattern of involvement				
GGO, %	63.04	64.15	60.50	0.603
Consolidation, %	22.5	24.37	18.30	0.308
Plural effusion, %	15.58	11.87	23.94	0.020
Distribution of lesions				
Peri-Broncho vascular, %	28.57	29.37	26.76	0.685
Hazy Round, %	14.29	15.19	12.33	0.707
Linear Opacity, %	3.46	3.80	2.74	0.982
Pulmonary Fibrosis, %	1.73	1.25	2.81	0.400
Perihilar, %	1.30	0.00	4.11	0.052

Table 5: Association of factors with mortality in COX proportional hazard regression model. The model was fitted based on the Schoenfeld residual test to evaluate the proportional hazard assumption with P=0.511.

Variable	Crude H.R.*, 95% CI	P-value	Adjusted H.R.*, 95% CI	P-value
Age (years)	1.041[1.023-1.059]	<0.001	1.031[1.008-1.054]	0.008
Sex	0.739[0.448-1.218]	0.236		
BMI (m^2/kg)	0.959[0.908-1.013]	0.134		
HTN	1.096[0.666-1.804]	0.718		
DM	0.770[0.428-1.386]	0.384		
Asthma/COPD	1.229[0.587-2.574]	0.584	1.840 [0.734-4.609]	0.193
CHD	0.953[0.509-1.784]	0.879		
Malignancy	1.942[1.028-3.670]	0.041	6.801 [2.842-16.275]	<0.001
Smoking	1.054[0.502-2.209]	0.890		
AKI	4.988[2.961-8.399]	<0.001	2.688 [1.329-5.434]	0.006
CT-score	1.084[1.015-1.157]	0.015	1.076 [1.012-1.145]	0.019

Based on ROC results, comparing the AUCs in (Figure 2) (b and c), the CT score was associated with a better mortality prognosis in patients with AKI than the non-AKI group (0.80 vs. 0.62 with P-value <0.001).

ROC analysis of the serum PCT value upon admission for mortality prognosis is presented in (Figure 2) (d, e, f) for three different subgroups: a-all patients, b-non-AKI patients, and c-AKI-patients. Based on the ROC results, the PCT level is an influential factor in prognosis mortality in AKI patients compared to the non-AKI group (0.73 vs. 0.64 with P-value <0.001).

The same ROC analysis is also conducted for the serum lymphocyte count, lactate level, and WBC count. The statistical measures for AUC of all ROC analyses (such as the mean and CI), applied for mortality prognosis in three different aforementioned subject groups, are presented in (Figure 3). As depicted, CT-score, serum PCT level, lactate level, and leukocytosis are all significantly more predictive of mortality prognosis for AKI patients than for the non-AKI group (All mutual comparisons between the AUC of different groups produce P-values<0.001). The most important prognostic factor among them is the CT score.

The cutoff values, sensitivity, and specificity of these prognostic factors are noted in (Table 6). CT-score 13 is associated with a sensitivity of 71.4 % and specificity of 90% to predict mortality among AKI patients, while this cutoff point is 0.65 with 100 % sensitivity and 37.5% specificity for PCT level. A lactate level of more than 39.3 predicts the poor prognosis in AKI patients with 60 % sensitivity and 100 % specificity. Ultimately, the WBC level of more than 13 is 50 % sensitive and 84.6 % specific in predicting the higher mortality in AKI patients.

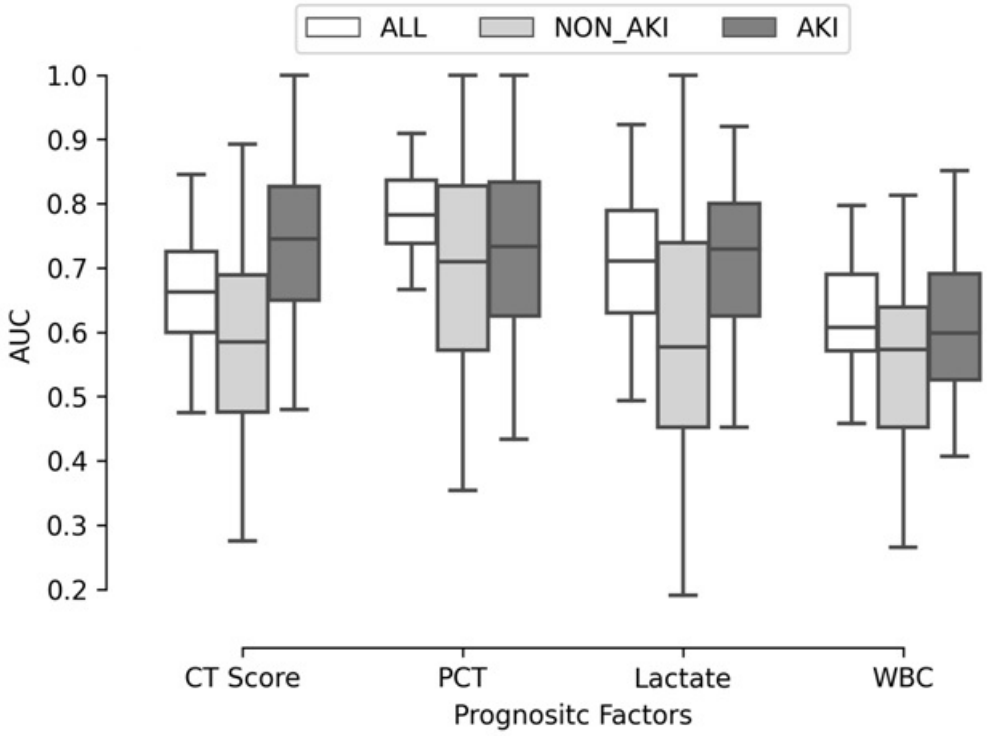

Figure 3: AUC distribution for mortality prognosis of three subject groups (All Patients, Non-AKI patients, and AKI patients) considering different prognostic factors as input parameter for computing ROC of patients classification into death-recovery classes.

Table 6: Most deterministic cutoff values, sensitivity, and specificity for different prognostic factors in the AKI group.

Prognostic factor	Cutoff value	Sensitivity (%)	Specificity (%)
CT-score	13	71.4	90
PCT level	0.65	100	37.5
Lactate level	39.3	60	100
WBC level	13.900	50	84.6

DISCUSSION

Patients with COVID-19 might also present with AKI or develop it during the hospitalization. Additionally, COVID-19 renal manifestations are considerably associated with a negative prognostic factor and higher mortality[15]. Among patients hospitalized because of COVID-19 diagnosis in our center, we observed a 28% AKI development during the hospitalization. In our study, AKI incidence is higher than in previously reported data from China and Italy and lower than from the united states [6]. This difference may be related to the prevalence of comorbidities in patients studied in different studies, or it could be due to racial differences. HTN, coronary heart disease, and neurological disorders were significantly more prevalent in patients with AKI and COVID-19. Consistently, our study findings demonstrate AKI to be more common in the elderly. Hansrivijit et al. also reported increasing age and hypertension as the possible predisposing factors for AKI in patients infected with SARS-CoV-2 in their meta-analysis [20].

Our findings revealed that DM was not more frequent in COVID-19 patients suffering from AKI. A possible disagreement between our findings and the correlation between DM and AKI in the literature may be caused by the fact that chronic renal failure patients have not been excluded from these studies [21].

In our analysis, one of the most evident death-related factors in COVID-19 patients was increasing age, which was in good agreement with other studies [18]. Several publications have associated malignancy with higher mortality in patients with COVID-19, and our data goes in the same direction as well [19]. Likewise, another death-related factor in COVID-19 cases was AKI. Surprisingly, smoking, asthma, and COPD did not play a notable role in increasing the mortality of COVID-19 patients. Altogether in our study, among all COVID-19 patients, mortality prognosis was determined mainly by age, malignancy, AKI, and CT-score.

Multiple laboratory parameters differed between the AKI and the non-AKI COVID-19 cases in our study. The increased CRP value in AKI may be related to cytokine storm resulting from viral invasion. In the COVID-19 and other infective disorders, a higher CRP level in patients with AKI indicates a poorer prognosis and more aggressive diagnosis [16]. COVID-19-associated lymphopenia might be a result of lymphocyte retention in the lung. Addi-

tionally, lymphocytes express the angiotensin-converting enzyme (ARS-CoV-2 receptor) on their surface [17]. The more prominent decrease of lymphocytes in the AKI patients in comparison with the non-AKI group suggests the immune system's inhibition due to already consumed immune cells [18]. This lymphopenia is critical in the disease exacerbation.

Although COVID-19 chest CT findings overlap with several other infectious or inflammatory lung processes, Chest CT is served as an accurate Para clinical tool evaluating the type and extent of lung lesions in COVID-19 patients. We assessed the severity of a patient's lung involvement based on the visual method on a total cumulative severity score basis. In general, the most observed pattern of lung involvement in COVID-19 pneumonia is as following: bilateral distribution of ground-glass opacities (GGO) with or without consolidation (known as the hallmark of COVID-19 pneumonia), reticulation, honeycombing, parenchymal bands, and air trapping[19]. GGO was the most common chest CT feature following consolidation in our analysis, observed in both groups' chest CT scans. The lung lesions of COVID-19 patients are predominantly located in the peripheral and subpleural area[20]; however, in our study, paracentral lesions were the most commonly observed chest CT lesions. This difference in lesion distribution makes the diagnosis more challenging and mislead the radiologist of the COVID-19 diagnosis in such patients. Thus, physicians should not always look for classic chest CT findings associated with COVID-19. Pleural effusion is one of the most significant chest CT findings of COVID-19 patients reported roughly in 20% [21] of the cases representing a poor prognostic factor. The prevalence of pleural effusion correlating COVID-19 is also based on the presence or absence of underlying medical conditions [22], which justifies the significantly higher occurrence rate of pleural effusion AKI than non-AKI COVID-19 patients.

Regarding the chest CT score in the COVID-19 context, different scoring systems have been proposed to assess the disease severity [23]. Here, we employed the lobar involvement scoring system (0–25) and observed higher mortality in patients with higher CT scores, consistent with previous studies [24, 25]. With or without AKI, high lung CT scores were a prognostic factor for COVID-19 patients, determining the severity of disease and extent of lung involvement. Additionally, AKI was more frequently associated with severe CT-scores in comparison with non-AKI patients. More importantly, a higher CT-score is more reliable for predicting mortality in patients with AKI. A number of studies reported different CT score cutoffs to determine severity prognosis for COVID-19. In Francone et al. study, CT score of ≥ 18 was associated with an increased mortality risk [26]. The CT score cutoff point was lower in our study, which could be attributed to the presence of comorbid conditions, including AKI, making the prognosis poor.

Consequently, we believe this score can be applied as a possible prognosis factor to distinguish severe AKI patients in the COVID-19 setting.

The serum PCT level has been shown to be associated with the severity of infectious diseases in previous studies [27]. In the COVID-19 context, elevated serum PCT levels may be employed as an early indicator of criticalness, worsening condition, and mortality [28]. In this study, we found that PCT is even more decisive for the prognosis of AKI patients in comparison to non-AKI COVID-19 cases. In order to improve the prognosis, physicians may consider admitting such patients to the ICU and providing closer follow-up. Additionally, among COVID-19 patients with AKI, serum PCT was considerably superior to CRP for predicting mortality.

Huang et al. mentioned the presence of leukocytosis as a reliable marker of COVID-19 severity and hospitalization [29]. Another study showed that leukocytosis on arrival might predict poor outcomes and ICU admission [30]. We found that leukocytosis is associated with higher mortality in AKI patients compared with non-AKI patients. The same pattern has been observed for higher lactate level approving their potential for predicting prognosis in AKI patients.

Our study is the first to discuss the prognostic factors in COVID-19 patients developing AKI. Our study has several 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 designed as a single-centered cohort. Third, the sample size was relatively small.

In conclusion, we found that AKI was a relatively common finding among patients hospitalized with COVID-19. Moreover, in addition to patients' clinical condition, CT score, PCT level, lactate level, and the presence of leukocytosis are applicable as possible prognosis factors to distinguish severe patients accurately. Providing more care to such patients can reduce mortality and improve outcomes. Consequently, clinicians should apply these parameters to assess COVID-19 severity in AKI patients in the very early stages to be able to treat them properly.

HIGHLIGHTS

- Acute kidney injury is a serious complication of COVID-19
- AKI is associated with poor prognostic and higher mortality in COVID-19
- A high CT-score is significantly related to higher mortality in AKI patients in the COVID-19
- In addition to CT score, the values of PCT, Lactate, and WBC are reliable prognostic factors
- It is highly recommended that regular assessments of AKI patients' severity be performed using such parameters

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