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Predicting hospital mortality in COVID-19 hemodialysis patients with developed scores

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Abstract

Various risk scores such as COVID-GRAM Critical Illness Risk Score (COVID-GRAM), quick COVID-19 Severity Index (qCSI), and systemic immune-inflammation index (SII) have been developed to determine critical illness in hospitalized patients. None of these risk scoring systems was evaluated in HD patients who indeed carry the highest risk of developing critical illnesses. We aimed to evaluate, in hemodialysis (HD) patients with COVID-19, the performance of these scoring systems for the need of intensive care unit (ICU) and mortality. The qCSI, COVID-GRAM, and SII scores of the patients at admission to hospital were calculated and grouped according to the scoring results. The primary outcome of the study was mortality and need of ICU. Critical illness was described as a composition of admission to the ICU, invasive ventilation, or death. It was determined that when the qCSI is over 6.5, the need for ICU increased 13.8 times and mortality increased 21.3 times. When the COVID-GRAM score is >157, the ICU need increased 14.7 times and the mortality increased 33.7 times. We found that the need for ICU increased 4.2 times and mortality increased 3.1 times when the SII score was >1145. These tests, which can be easily calculated, could be used to estimate the risk of developing critical illness among COVID-19 HD patients. Estimating the risk of critical illness could help to reduce mortality in HD patients.

1 | INTRODUCTION

Coronavirus Disease 2019 (COVID-19) caused by a novel coronavirus was declared as a pandemic by the World Health Organization (WHO) on March 2020.[1] Elderly population and patients with multiple comorbid diseases were more seriously affected by COVID-19. Hemodialysis (HD) patients due to weaker immune system, comorbid diseases, and older age are one of the most susceptible populations to COVID-19. HD patients visit the hospital or dialysis center routinely and stay in the same indoor environment with other patients and staff for 3–4 h each session, so it is difficult to prevent and control COVID-19. HD patients have a less efficient immune system that can alter their response to COVID-19. Therefore, it is not surprising that HD patients have increased mortality.[2–4] Studies have shown that mortality rate in HD patients is quite high.[5–7] Early detection of patients who are likely to develop critical illness is of great importance to reduce mortality. Various risk scores such as COVID-GRAM Critical Illness Risk Score (COVID - GRAM), quick COVID-19 Severity Index (qCSI), and systemic immune-inflammation index (SII) have been developed to determine critical illness in hospitalized patients. The success of these scores in predicting critical illness and mortality in hospitalized patients was found to be high. Easy application at the bedside is also the advantage of these scores.[8–11] None of these risk scoring systems are evaluated in HD patients who indeed carry the highest risk of developing critical illnesses.

In this study, we aimed to evaluate, in HD patients with COVID-19, the performance of these scoring systems including COVID-GRAM, qCSI, and SII for the need of intensive care unit (ICU) and mortality.

2 | MATERIALS AND METHODS

This study comprised 117 maintenance HD patients, hospitalized in Erzurum Regional Training and Research Hospital, the pandemic hospital in our region, between 22 March to 31 December 2020, and who were diagnosed COVID-19 based on positive real-time reverse transcription-polymerase chain reaction (rRT-PCR) assay of a specimen collected on a nasopharyngeal swab or chest computed tomography (CT) compatible in terms of COVID-19. The study was designed as a retrospective cohort study.

Demographic characteristics (age, gender), chronic diseases, complaints during hospitalization, vital signs at the time of admission, chest CT findings during hospitalization, discharge status, COVID-19 PCR test results, laboratory values such as white blood cell count (WBC, 10^3/μl), neutrophil count (10^3/μl), lymphocyte count (10^3/μl), neutrophil lymphocyte ratio (NLR), hemoglobin (g/dl), platelet count (10^3/μl), platelet lymphocyte ratio (PLR), mean platelet volume (MPV, fl), pH, lactate (mmol/L), alanine aminotransferase (ALT) (U/L), aspartate aminotransferase (AST, U/L), total bilirubin (mg/dl), lactate dehydrogenase (LDH, U/L), creatinine kinase (CK, U/L), blood urea nitrogen (BUN, mg/dl), creatinine (mg/dl), corrected calcium (mg/dl), phosphorus (mg/dl), albumin (g/L), total protein (gr/L), uric acid (mg/dl), international normalized ratio (INR), D-dimer (ng/ml), ferritin (ng/ml), C-reactive protein (CRP, mg/L), and procalcitonin (PCT, ng/ml) of the patients included in the study were recorded. Each record was checked independently by two clinicians.

Treatments given to patients during hospitalization (such as high-dose vitamin C, immune plasma, favipiravir, hydroxychloroquine, tocilizumab, antibiotic, and steroid use), intensive care unit needs, high flow oxygen needs, noninvasive mechanical ventilation needs, and intubation needs were retrospectively analyzed and recorded through the hospital's electronic recording system.

The NLR value was calculated by dividing the absolute neutrophil count by the number of lymphocytes, the PLR value by dividing the platelet count by the number of lymphocytes, and CRP/albumin value by dividing the CRP value by the albumin value.

2.1 | Risk scoring systems

Risk scores were calculated using baseline clinical data collected retrospectively from the patient cohort. The qCSI is a test predicting the risk of 24-h critical respiratory disease in hospitalized COVID-19 patients. The qCSI is a 12-point scale that uses only three variables available at the bedside: nasal cannula oxygen flow rate, respiratory rate, and minimum documented pulse oximetry. Patients are evaluated over 12 points and then assigned to four risk strata based on the following scores: 0–3 low risk, 4–6 low-intermediate risk, 7–9 high-intermediate risk, and >10 high risk.[11] COVID-GRAM is a scoring system that predicts the risk of critical illness in hospitalized COVID-19 patients and can be easily applied. Age, chest radiography (CXR) abnormality, dyspnea, hemoptysis and confusion, number of comorbid diseases, cancer history, NLR, LDH, and direct bilirubin levels are used to calculate the risk score. Patients are divided into three risk groups according to the score obtained, defined as low risk (<1.7%), medium risk (1.7% to 40.4%), high risk (≥40.4%). SII is calculated by $(N \times P)/L$ (N, P, and L represent neutrophil counts, platelet counts, and lymphocyte counts, respectively). The qCSI, COVID-GRAM, and SII scores of the patients at admission to hospital were calculated and grouped as described above according to the scoring results. The primary outcome of the study was mortality and need of ICU. Critical illness was described as a composition of admission to the ICU, invasive ventilation, or death.

2.2 | Statistical analysis

All of the statistical analysis were performed by SPSS software (version 22.0, SPSS Inc., Chicago, IL, USA). The compliance of the variables to normal distribution was examined by visual (histogram and probability graphics) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Descriptive analyses were given as means and standard deviations for normally distributed variables. Independent group t test (Student's t test) was used to compare two groups, and Mann–Whitney U test was used when the conditions were not met. One-way analysis of variance and Tukey HSD test, one of the multiple comparison tests, were used for comparison of three or more groups. When the conditions were not met, the Kruskal–Wallis test and the multiple comparison Bonferroni–Dunn test were used. Chi-square and Fisher's exact test methods were used in the analysis of categorical data. p value less than 0.05 was considered to have statistical significance. Receiver operating system (ROC) curve analysis was performed for diagnostic decision-making features. The ratio closest to the sum value of maximum sensitivity and specificity was regarded as the optimal cutoff value. Then, logistic regression analysis of these cutoff values was performed.

3 | RESULTS

A total of 117 patients, 60 women (51.3%) and 57 men (48.7%), were included in the study. The mean age of the patients was 61.2 ± 13.3; the mean dialysis duration was 56.1 ± 42.2 months. Hypertension (HT) in 95.7%, coronary artery disease (CAD) in 76.9%, diabetes mellitus (DM) in 52.9%, congestive heart failure (CHF) in 21.4%, and chronic obstructive pulmonary disease in 19.7% of patients were present. Cough (70%), myalgia (70%), shortness of breath (60.7%), and fever (33.3%) were the most common symptoms; 101 patients (86.3%) had chest CT abnormality; 109 patients received favipiravir, 97 patients low molecular weight heparin (LMWH), 75 patients corticosteroid, 22 patients hydroxychloroquine, nine patients immune plasma, two patients tocilizumab, and 104 patients antibiotic treatment for bacterial pneumonia or other bacterial infections, While 31 (26.5%) patients were admitted to ICU, 29 (24.7%) patients died. High-flow (HF) oxygen therapy was applied to 16 patients, noninvasive mechanical ventilation (NIMV) to 12 patients, and 27 patients

TABLE 1 Demographic and laboratory data of the patients

Values	Mean ± SD (%)	Min–max
Age (year)	61.2 ± 13.3	31–92
Gender (F/M)	60/57 (51.3%)	
Dialysis duration (month)	56.1 ± 42.2	2–264
HT (±)	112/5 (95.7%)	
DM (±)	62/55 (52.9%)	
CAD (±)	90/27 (76.9%)	
CHF (±)	25/92 (21.4%)	
COPD (±)	23/94 (19.7%)	
Shortness of breath (±)	71/46 (60.7%)	
Fever (±)	39/78 (33.3%)	
Cough (±)	82/35 (70%)	
Myalgia (±)	82/35 (70%)	
CT abnormalities (±)	101/14 (86.3%)	
ICU need (±)	31/86 (26.5%)	
Exitus (±)	29/88 (24.7%)	
COVID-GRAM Score	148.6 ± 39.2	10–281
COVID-GRAM Risk of CI	50.3 ± 27.8	2–99.8
Medium/high	52/65 (44.4%)	
qCSI	4.9 ± 4.5	0–12
qCSI Risk of CI	27.3 ± 21.7	4–57
Low/low–inter/inter–high/high	49/23/20/25 (%41.9/19.6/17.1/21.4)	
pH	7.33 ± 0.1	7.05–7.54
Lactate (mmol/L)	2.54 ± 2.2	0.7–17
SO_2 (%)	89.5 ± 6.7	65–98
WBC (10^3/μl)	6.9 ± 4	1.89–22.9
Neutrophil (10^3/μl)	5.3 ± 3.8	1.3–21.7
Lymphocyte (10^3/μl)	0.93 ± 0.54	0.08–3.57
Hemoglobin (g/dl)	11.4 ± 2.3	6.3–17.2
Platelet (10^3/μl)	181.1 ± 59.9	58–344
MPV (fl)	11 ± 1.1	8.5–13.7
SII	1381.9 ± 1405.4	141–7102.1
NLR	7.5 ± 7	0.86–41.63
CRP (mg/L)	91.3 ± 87	2.7–350
LDH (U/L)	380.2 ± 289.6	127–2472
AST (U/L)	45.3 ± 64.4	7–461
ALT (U/L)	29.9 ± 34.8	7–252
Total bilirubin (mg/dl)	0.5 ± 0.4	0.2–2.8
CK (U/L)	182.3 ± 289.8	18–2064
Uric acid (mg/dl)	5.6 ± 1.8	2.3–12
Albumin (g/L)	35.6 ± 5.1	21–47
Total protein (g/L)	62.2 ± 6.8	46–80
PCT (ng/ml)	6.8 ± 18.1	0.24–98
Ferritin (ng/ml)	1358 ± 1182.9	158.8–8251.8
D-Dimer (ng/ml)	4.1 ± 6.2	0.35–34.9
INR	1.28 ± 0.8	0.9–6.7
CAR	5.7 ± 10	0.08–41

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CAD, coronary artery disease; CAR, CRP to albumin ratio; CHF, congestive heart failure; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HT, hypertension; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonine; qCSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index; WBC, white blood cell.

TABLE 2 Comparison of demographic and laboratory data of patients with and without ICU need

	ICU (−) (*n* = 86)	ICU (+) (*n* = 31)	*p*
Age (year)	59.8 ± 12.4	65 ± 14.9	0.105
Gender (F/M)	45/41	15/16	0.707
Dialysis duration (month)	59.4 ± 45	47.1 ± 32.4	0.199
HT (±)	82/4	30/1	NA
DM (±)	34/52	21/10	**0.007**
CAD (±)	65/21	25/6	0.566
CHF (±)	16/70	9/22	0.225
COPD (±)	17/69	6/25	0.960
CD ≥2	68/18	30/1	**0.022**
CT abnormalities (±)	70/14	31/0	**0.011**
Shortness of breath (±)	41/45	30/1	**<0.001**
Fever (±)	30/56	9/22	0.553
Cough (±)	64/22	18/13	0.088
Myalgia (±)	58/28	24/7	0.298
Exitus (±)	4/82	25/6	**<0.001**
COVID-GRAM	135.2 ± 32.1	185.8 ± 32.8	**<0.001**
COVID-GRAM %	40.3 ± 23.7	78 ± 17.9	**<0.001**
qCSI	3.4 ± 3.8	9.3 ± 3.1	**<0.001**
qCSI %	20.1 ± 19.6	47.2 ± 32.4	**<0.001**
pH	7.34 ± 0.1	7.31 ± 0.1	0.234
Lactate (mmol/L)	2.4 ± 2.4	2.8 ± 1.7	**0.043**
SO_2 (%)	91.4 ± 4.9	84.4 ± 7.9	**<0.001**
WBC (10^3/μl)	5.9 ± 1.8	9.3 ± 5.3	**0.001**
Neutrophil (10^3/μl)	4.3 ± 2.6	7.9 ± 4.9	**<0.001**
Lymphocyte (10^3/μl)	0.96 ± 0.5	0.84 ± 0.6	0.057
Hemoglobin (g/dl)	11.4 ± 2.2	11.3 ± 2.8	0.492
Platelet (10^3/μl)	178.5 ± 58.3	187.7 ± 64.3	0.521
MPV (fl)	10.8 ± 1.1	11.4 ± 1	**0.023**
SII	1077.9 ± 1196.1	2163.7 ± 1612.6	
NLR	5.9 ± 5.6	11.6 ± 8.7	**<0.001**
CRP (mg/L)	66.4 ± 70.1	155.4 ± 94.6	**<0.001**
BUN (mg/dl)	58.4 ± 28.9	68.9 ± 31	0.185
Creatinine (mg/dl)	7.6 ± 5	6.6 ± 2.3	0.470
Calcium (mg/dl)	8.8 ± 0.8	8.6 ± 0.9	0.201
Phosphorus (mg/dl)	4.9 ± 1.8	6 ± 2.5	0.051
LDH (U/L)	305.2 ± 130.4	575.7 ± 460.2	**<0.001**
AST (U/L)	36 ± 60.2	70 ± 70.2	**0.001**
ALT (U/L)	25 ± 19.9	43.1 ± 57.2	0.378
Total bilirubin (mg/dl)	0.42 ± 0.3	0.72 ± 0.6	**0.032**
CK (U/L)	116.4 ± 129.9	359.7 ± 463.1	**0.004**
Uric acid (mg/dl)	5.3 ± 1.7	6.2 ± 1.9	0.135
Albumin (g/L)	36.7 ± 5.1	32.9 ± 4.1	**<0.001**
Total protein (g/L)	63.5 ± 6.5	59 ± 6.8	**0.013**
PCT (ng/ml)	1.58 ± 1.3	13.9 ± 26.5	**0.028**
Ferritin (ng/ml)	1060.1 ± 600.2	2031.6 ± 1785.4	**0.001**
D-Dimer (ng/ml)	2.5 ± 2.5	8.18 ± 9.8	**0.002**

TABLE 2 (Continued)

	ICU (−) (*n* = 86)	ICU (+) (*n* = 31)	*p*
INR	1.12 ± 0.2	1.61 ± 1.2	**0.001**
CAR	5.26 ± 10.9	6.7 ± 7.3	**<0.001**

Note: Statistically significant values are presented in bold.
Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CAD, coronary artery disease; CAR, CRP to albumin ratio; CHF, congestive heart failure; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HT, hypertension; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonine; qCSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index; WBC, white blood cell.

TABLE 3 Comparison of survivor and nonsurvivors

	Survivor (*n* = 88)	Nonsurvivor (*n* = 29)	*p*
Age (year)	59.4 ± 12.1	66.8 ± 15.3	**0.017**
Gender (F/M)	47/41	13/16	0.423
Dialysis duration (month)	57.1 ± 44.9	53.1 ± 33.1	0.912
HT (±)	84/4	28/1	NA
DM (±)	36/52	19/10	**0.021**
CAD (±)	65/23	25/4	0.171
CHF (±)	14/74	11/18	**0.012**
COPD (±)	18/70	5/24	0.706
CD ≥2	70/18	28/1	**0.040**
CT abnormalities (±)	73/13	28/1	0.084
ICU need (±)	6/82	25/4	**<0.001**
High flow (±)	2/86	14/15	**<0.001**
NIMV (±)	1/87	11/18	**<0.001**
MV (±)	3/85	24/5	**<0.001**
Shortness of Breath (±)	42/46	29/0	**<0.001**
Fever (±)	32/56	7/22	0.226
Cough (±)	64/24	18/11	0.277
Myalgia (±)	61/27	21/8	0.752
COVID-GRAM	134.7 ± 30.4	190.8 ± 32.4	**<0.001**
COVID-GRAM %	40.1 ± 22.9	81.1 ± 16.1	**<0.001**
qCSI	3.33 ± 3.8	9.72 ± 2.5	**<0.001**
qCSI %	20 ± 19.5	49.2 ± 9.8	**<0.001**
pH	7.34 ± 0.1	7.30 ± 0.1	0.182
Lactate (mmol/L)	2 ± 0.1	3.7 ± 3.2	**<0.001**
SO_2 (%)	91.7 ± 4.8	83.2 ± 7.5	**<0.001**
WBC (10^3/μl)	6.01 ± 3.1	9.2 ± 5.3	**0.002**
Neutrophil (10^3/μl)	4.4 ± 2.8	7.8 ± 4.9	**<0.001**
Lymphocyte (10^3/μl)	0.96 ± 0.5	0.82 ± 0.5	0.083
Hemoglobin (g/dl)	11.1 ± 2.1	12.2 ± 2.8	0.142
Platelet (10^3/μl)	181.9 ± 59.3	178.5 ± 62.6	0.661
MPV (fl)	10.8 ± 1	11.7 ± 1	**0.001**
NLR	6 ± 5.6	11.7 ± 9.1	**<0.001**
SII	1129.9 ± 1200.2	2138 ± 1706.6	**0.001**
PLR	241.9 ± 194.6	276.1 ± 170.5	0.208
CRP (mg/L)	74.2 ± 78.5	144.5 ± 92.2	**0.001**
BUN (mg/dl)	60.3 ± 29.2	64.5 ± 31.6	0.728
Creatinine (mg/dl)	7.6 ± 4.9	6.6 ± 2.2	0.494

(Continues)

TABLE 3 (Continued)

	Survivor ($n = 88$)	Nonsurvivor ($n = 29$)	p
Calcium (mg/dl)	8.7 ± 0.8	8.7 ± 0.9	0.659
Phosphorus (mg/dl)	4.9 ± 1.7	6.2 ± 2.7	0.069
LDH (U/L)	301.4 ± 117	628.5 ± 481.5	**<0.001**
AST (U/L)	28.6 ± 23.1	98.8 ± 111.4	**<0.001**
ALT (U/L)	23.7 ± 17.6	50.3 ± 61.2	0.177
Total bilirubin (mg/dl)	0.4 ± 0.2	0.84 ± 0.7	**0.001**
CK (U/L)	125.1 ± 144.8	382.6 ± 495.4	**0.013**
Uric acid (mg/dl)	5.4 ± 1.7	6.2 ± 2	0.096
Albumin (g/L)	36.5 ± 4.6	33.1 ± 5.8	**0.004**
Total Protein (g/L)	63.2 ± 6.1	59.1 ± 8	**0.048**
PCT (ng/ml)	1.72 ± 1.5	17.2 ± 29.5	**0.012**
Ferritin (ng/ml)	1083.8 ± 637.7	2112.2 ± 1864.9	**0.002**
D-Dimer (ng/ml)	2.82 ± 2.7	8.39 ± 10.9	0.100
INR	1.1 ± 0.2	1.7 ± 1.4	**0.001**
CAR	5.7 ± 11	5.6 ± 6	**0.005**

Note: Statistically significant values are presented in bold.

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CAD, coronary artery disease; CAR, CRP to albumin ratio; CHF, congestive heart failure; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HT, hypertension; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonine; qCSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index; WBC, white blood cell.

TABLE 4 Comparison of medium and high risk patients according to COVID-GRAM risk scoring

COVID-GRAM	Medium risk ($n = 52$)	High risk ($n = 65$)	p
Age (year)	56.3 ± 11.6	65.1 ± 13.4	**<0.001**
Gender (F/M)	28/24	32/33	0.620
Dialysis duration (month)	64.3 ± 50	49.5 ± 33.8	0.112
HT (±)	49/3	63/2	0.654
DM (±)	12/40	43/22	**<0.001**
CAD (±)	36/16	54/11	0.077
CHF (±)	4/48	21/44	**0.001**
COPD (±)	7/45	16/49	0.131CD
CD ≥2	37/15	61/4	**0.001**
ICU need (±)	1/51	30/35	**<0.001**
CT abnormalities (±)	38/13	63/1	**<0.001**
Exitus (±)	1/51	28/37	**<0.001**
High flow (±)	0/52	16/49	**<0.001**
NIMV (±)	0/52	12/53	**0.001**
MV (±)	1/51	26/39	**<0.001**
Shortness of breath (±)	17/35	54/11	**<0.001**
Fever (±)	17/35	22/43	0.895
Cough (±)	36/16	46/19	0.857
Myalgia (±)	37/15	45/20	0.821
qCSI	1.67 ± 2.67	7.51 ± 3.9	**<0.001**
qCSI %	11 ± 12.6	40.3 ± 18.4	**<0.001**
SII	798.4 ± 686.1	1787.4 ± ±1624.5	**<0.001**
pH	7.35 ± 0.06	7.31 ± 0.1	0.395

TABLE 4 (Continued)

COVID-GRAM	Medium risk ($n = 52$)	High risk ($n = 65$)	p
Lactate (mmol/L)	1.7 ± 0.7	2.9 ± 2.5	**0.001**
SO_2 (%)	93.1 ± 3.5	86.8 ± 7.2	**<0.001**
WBC (10^3/μl)	5.3 ± 2.5	7.9 ± 4.5	**0.001**
Neutrophil (10^3/μl)	3.6 ± 2	6.5 ± 4.2	**<0.001**
Lymphocyte (10^3/μl)	0.98 ± 0.4	0.87 ± 0.6	**0.024**
Hemoglobin (g/dl)	11.2 ± 2.1	11.5 ± 2.5	0.729
Platelet (10^3/μl)	176.6 ± 57.4	184.2 ± 61.8	0.587
MPV (fl)	10.8 ± 1	11.1 ± 1.1	0.210
NLR	4.46 ± 4	9.52 ± 7.9	**<0.001**
PLR	224.5 ± 217.8	269.5 ± 162.7	**0.052**
CRP (mg/L)	56.8 ± 54.7	115.8 ± 97.2	**0.003**
BUN (mg/dl)	60 ± 29.3	62.2 ± 30.2	0.996
Creatinine (mg/dl)	8.4 ± 6	6.6 ± 2.5	**0.032**
Calcium (mg/dl)	8.9 ± 0.8	8.6 ± 0.8	0.097
Phosphorus (mg/dl)	4.9 ± 16	5.4 ± 2.3	0.645
LDH (U/L)	255 ± 75	471.5 ± 349.4	**<0.001**
AST (U/L)	25.5 ± 75	60.2 ± 81.7	**0.009**
ALT (U/L)	22.4 ± 15	35.8 ± 43.8	0.329
Total bilirubin (mg/dl)	0.36 ± 0.2	0.61 ± 0.5	**0.003**
CK (U/L)	89.3 ± 75.2	261.7 ± 364.9	**0.004**
Uric acid (mg/dl)	5.5 ± 1.7	5.7 ± 1.9	0.861
Albumin (g/L)	36.9 ± 4.2	34.7 ± 5.5	0.056
Total protein (g/L)	62.8 ± 5.7	61.8 ± 7.6	0.864
PCT (ng/ml)	1.37 ± 1.1	10.2 ± 22.5	**0.022**
Ferritin (ng/ml)	988.4 ± 587	1648.5 ± 1435.4	**0.006**
D-Dimer (ng/ml)	2 ± 2.1	5.7 ± 7.6	**0.002**
INR	1.1 ± 0.2	1.4 ± 0.9	**<0.001**
CAR	4.4 ± 9.8	6.5 ± 10.1	**0.010**

Note: Statistically significant values are presented in bold.

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CAD, coronary artery disease; CAR, CRP to albumin ratio; CHF, congestive heart failure; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HT, hypertension; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonine; qCSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index; WBC, white blood cell.

developed the need for invasive mechanical ventilation (MV); 14 of 16 patients who underwent HF, 11 of 12 patients who underwent NIMV, and 24 of 27 patients who were intubated, died ($p < 0.001$). The demographic and laboratory data of the patients are presented in Table 1.

The need for ICU was found to be significantly higher in patients with DM ($p = 0.007$); there was no difference in terms of other comorbid diseases. The need for ICU was also higher in patients with complaints of shortness of breath at admission ($p < 0.001$) and patients with abnormal chest CT ($p = 0.011$). COVID-GRAM, qCSI, and SII values were found to be significantly higher in patients who needed ICU. The comparison of patients who need and do not need to be transferred to the ICU is given in Table 2.

The mortality rate in our patient cohort was 24.7%. Nonsurvival patients were older ($p = 0.017$). DM and CHF were the most common comorbid conditions in nonsurvival patients ($p = 0.021$, $p = 0.012$). The complaint of all 29 nonsurvival patients at the time of admission was shortness of breath. COVID-GRAM, qCSI, and SII values were found to be significantly higher in nonsurvival patients. Comparison of the patients is given in Table 3.

The rate of DM and CHF was found to be significantly higher in COVID-GRAM high-risk group patients. The need for ICU and chest CT abnormality were higher in patients in the high-risk group. In addition, the need for HF, NIMV, and MV was significantly higher in these patients. Patients in the high-risk group have significantly higher lactate, WBC, neutrophil, NLR, PLR, CRP, LDH, AST,

TABLE 5 Comparison of patients by qCSI

	Low ($n = 49$)	Low–intermediate ($n = 23$)	Intermediate–high ($n = 20$)	High ($n = 25$)	p
Age (year)	60 ± 12.9	58.7 ± 12	66.7 ± 13.6	65.4 ± 13.1	**0.036**
Gender (F/M)	55.7 ± 36.2	64.1 ± 64.7	49.6 ± 32.8	54.7 ± 34.7	0.943
Dialysis duration (month)	29/20	9/14	9/11	13/12	0.407
HT (±)	48/1	19/4	20/0	25/0	**0.006**
DM (±)	19/30	10/13	10/10	16/9	0.220
CAD (±)	32/17	2073	16/4	22/3	0.076
CHF (±)	7/42	4/19	5/15	9/16	0.170
COPD (±)	10/39	2/21	6/14	5/20	0.373
CD ≥2	38/11	17/6	19/1	24/1	0.054
CT abnormalities (±)	38/10	20/3	18/1	25/0	0.130
Exitus (±)	0/49	4/19	9/11	16/9	**<0.001**
ICU need (±)	1/48	5/18	9/11	16/9	**<0.001**
High flow (±)	0/49	3/20	6/14	7/18	**0.001**
NIMV (±)	0/49	4/19	5/15	3/22	**0.009**
MV (±)	0/49	3/20	7/13	17/8	**<0.001**
Shortness of breath (±)	17/32	12/11	17/3	25/0	**<0.001**
Fever (±)	16/33	9/14	5/15	9/16	0.786
Cough (±)	35/14	18/5	13/7	16/9	0.691
Myalgia (±)	34/15	20/3	10/10	18/7	0.071
COVID-GRAM	123.2 ± 20.2	148.6 ± 50	181.1 ± 35.1	172.4 ± 23.6	**<0.001**
COVID-GRAM %	29.7 ± 17.1	50.1 ± 28.7	74.6 ± 20.7	71.3 ± 15.6	**<0.001**
SII	866.4 ± 763.4	1639.9 ± 1757.6	1804.1 ± 1344.7	1749.3 ± 1731.1	**0.008**
pH	7.34 ± 0.1	7.35 ± 0.1	7.34 ± 0.07	7.29 ± 0.1	0.194
Lactate (mmol/L)	1.83 ± 0.7	2.54 ± 1.4	2.4 ± 0.9	3.46 ± 3.6	0.144
SO_2 (%)	94.2 ± 2.1	91.2 ± 1.8	88.9 ± 4.4	79.7 ± 6.1	**<0.001**
WBC (10^3/μl)	5.6 ± 2.8	6.8 ± 3.3	9.1 ± 4.3	7.6 ± 5.3	**0.017**
Neutrophil (10^3/μl)	3.8 ± 2.4	5.5 ± 3.3	7.2 ± 3.5	6.4 ± 5.2	**0.001**
Lymphocyte (10^3/μl)	1.03 ± 0.6	0.76 ± 0.3	1.02 ± 0.7	0.82 ± 0.4	0.219
Hemoglobin (g/dl)	11.2 ± 1.9	11.5 ± 2.9	11.8 ± 1.9	11.3 ± 2.8	0.727
Platelet (10^3/μl)	179.3 ± 54.1	172.6 ± 63.6	198.8 ± 70.9	179.5 ± 59.3	0.730
MPV (fl)	10.9 ± 1	11 ± 1.3	11.3 ± 1.1	11.1 ± 1.1	0.709
NLR	4.9 ± 4.6	8.7 ± 7	8.7 ± 5.6	9.9 ± 9.9	**0.001**
PLR	235.3 ± 220.6	263.9 ± 174.4	252.3 ± 146.5	263.3 ± 165.6	0.780
CRP (mg/L)	67.9 ± 67.3	73.3 ± 91.2	152.3 ± 106.1	114.9 ± 88.3	**0.018**
BUN (mg/dl)	54 ± 27.6	71.7 ± 29.4	68.1 ± 35.9	62.3 ± 29.1	0.149
Creatinine (mg/dl)	6.8 ± 2.7	9.5 ± 8.3	8.1 ± 3.7	6.2 ± 1.6	0.137
Calcium (mg/dl)	8.8 ± 0.9	8.8 ± 0.9	8.7 ± 0.7	8.4 ± 0.8	0.215
Phosphorus (mg/dl)	5.1 ± 2	5.1 ± 1.3	5.2 ± 2.7	5.3 ± 2.4	0.894
LDH (U/L)	271.1 ± 94.2	362.4 ± 175.6	671.7 ± 678.3	437.6 ± 173.4	**<0.001**
AST (U/L)	26.6 ± 13.3	31.9 ± 20.8	68.7 ± 84.1	77 ± 106.2	0.135
ALT (U/L)	23.3 ± 16.2	25.4 ± 19.3	53.3 ± 76.4	34.1 ± 36.2	0.888
Total bilirubin (mg/dl)	0.38 ± 0.2	0.64 ± 0.6	0.63 ± 0.6	0.54 ± 0.4	0.066
CK (U/L)	104.3 ± 100.5	122.9 ± 176.6	413.6 ± 657.7	278.1 ± 274.4	**0.027**
Uric acid (mg/dl)	4.9 ± 1.5	6 ± 1.6	6.6 ± 1.6	5.8 ± 2.2	**0.041**
Albumin (g/L)	36.9 ± 4.8	36.1 ± 4.9	34.6 ± 5.9	33.6 ± 4.9	**0.029**
Total protein (g/L)	63.7 ± 5.9	62.1 ± 6.9	59.9 ± 8.2	61.1 ± 7.4	0.457

TABLE 5 (Continued)

	Low ($n = 49$)	Low–intermediate ($n = 23$)	Intermediate–high ($n = 20$)	High ($n = 25$)	p
PCT (ng/ml)	1.59 ± 1.8	1.84 ± 1.1	17.6 ± 35.8	11.3 ± 21.7	0.058
Ferritin (ng/ml)	1125.5 ± 697.5	950.7 ± 676.6	1480.4 ± 464.6	2003.9 ± 1947.7	**0.035**
D-Dimer (ng/ml)	2.03 ± 1.6	5.2 ± 5.6	7.5 ± 10.9	5.1 ± 7.6	0.112
INR	1.06 ± 0.01	1.29 ± 0.5	1.54 ± 0.7	1.44 ± 1.3	**0.008**
CAR	4 ± 9.3	7.8 ± 13.6	7.2 ± 9.2	5.7 ± 7.9	**0.039**

Note: Statistically significant values are presented in bold.

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; CAD, coronary artery disease; CAR, CRP to albumin ratio; CHF, congestive heart failure; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HT, hypertension; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PCT, procalcitonine; qCSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index; WBC, white blood cell.

TABLE 6 ROC analysis results for the value of scoring systems in predicting ICU need

		95% CI				
Need for ICU	AUC	Lower	Upper	Cutoff	Sensitivity–specificity	p
CG score	0.885	0.824–0.946		157	81%–77%	<0.001
CG risk of CI	0.883	0.821–0.945		60	81%–77%	<0.001
qCSI score	0.859	0.780–0.938		6.5	82%–78%	<0.001
qCSI risk of CI	0.839	0.757–0.920		37	82%–78%	<0.001
SII	0.752	0.644–0.861		1145	68%–67%	<0.001

Abbreviations: CG, COVID-GRAM; CI, critical illness; CSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index.

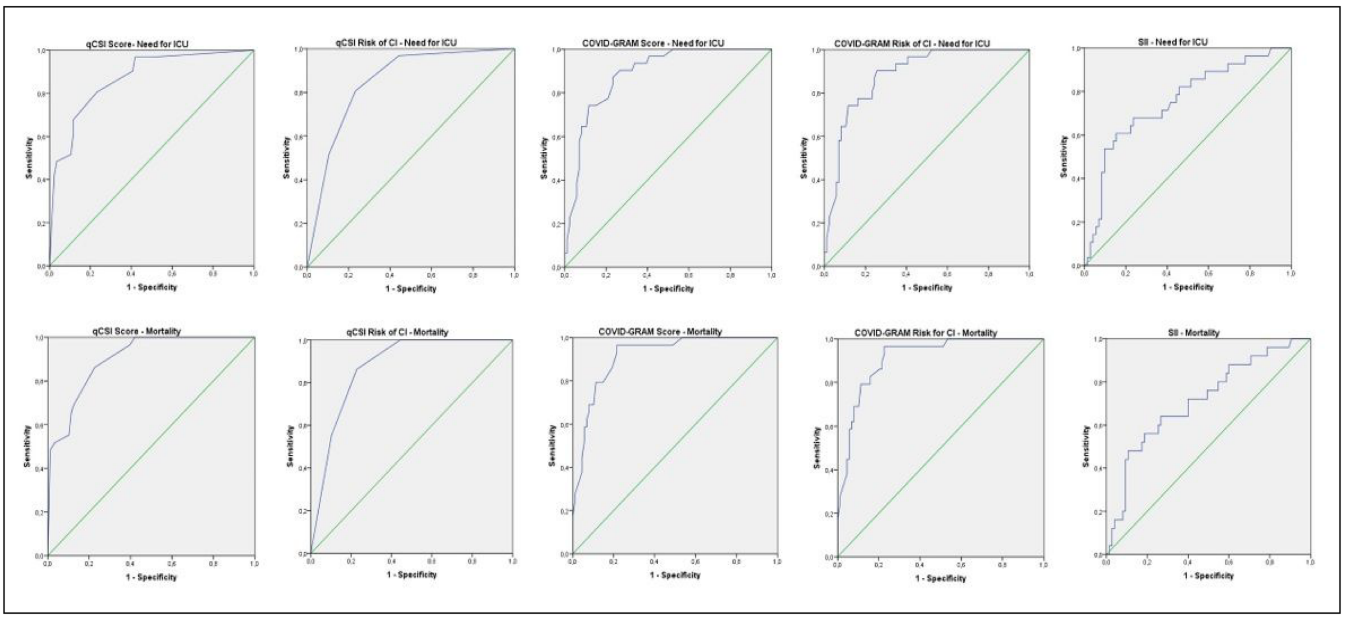

FIGURE 1 Receiver operating system (ROC) curves of risk scores for intensive care unit (ICU) need and mortality [Color figure can be viewed at wileyonlinelibrary.com]

total bilirubin, CK, procalcitonin, ferritin, D-Dimer, INR, and CRP/albumin values, and lower SO_2 levels. The qCSI and SII values of high-risk patients were found to be significantly higher ($p < 0.001$). Comparison of medium- and high-risk patients are given in Table 4.

The patients were divided into four groups according to the qCSI score: low, low–intermediate, intermediate–high, and high. The patients in intermediate–high and high were older. While 25 of the 45 patients in these two groups died, only four of the 72 patients in the other groups died ($p < 0.001$). As the risk increased, significantly higher WBC, neutrophil, NLR, CRP, LDH, CK, ferritin, INR, and CRP/albumin levels were detected in the patients. COVID-GRAM and SII risk scores were significantly higher. Comparative data of these four groups are given in Table 5.

TABLE 7 ROC analysis results for the value of scoring systems in predicting mortality

		95% CI				
Mortality	AUC	Lower	Upper	Cutoff	Sensitivity–specificity	*p*
CG score	0.927	0.879–0.976		157	92%–80%	<0.001
CG risk of CI	0.924	0.874–0.974		60	92%–79%	<0.001
qCSI score	0.899	0.838–0.961		6.5	81%–77%	<0.001
qCSI risk of CI	0.869	0.801–0.938		37	81%–77%	<0.001
SII	0.714	0.596–0.832		1145	64%–64%	<0.001

Abbreviations: CG, COVID-GRAM; CI, critical illness; CSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index.

TABLE 8 Logistic regression analysis for cutoff values and ICU need

			95% CI				
Need for ICU	r^2	βi	Lower	Upper	O.R.	Wald	*p*
CG score ≥157	0.250	2.687	5.265	41.007	14.693	26.336	<0.001
CG risk of CI ≥60	0.240	2.621	4.949	38.202	13.750	25.274	<0.001
qCSI score ≥6.5	0.240	2.621	4.949	38.202	13.750	25.274	<0.001
qCSI risk of CI ≥37	0.240	2.621	4.949	38.202	13.750	25.274	<0.001
SII ≥1145	0.094	1.440	1.662	10.725	4.222	9.170	0.002

Abbreviations: CG, COVID-GRAM; CI, critical illness; CSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index.

TABLE 9 Logistic regression analysis for cutoff values and mortality

			95% CI				
Mortality	r^2	βi	Lower	Upper	O.R.	Wald	*p*
CG score ≥157	0.328	3.518	9.162	123.979	33.704	28.018	<0.001
CG risk of CI ≥60	0.318	3.449	8.590	115.313	31.474	27.104	<0.001
qCSI score ≥ 6.5	0.279	3.056	6.613	68.283	21.250	26.335	<0.001
qCSI risk of CI ≥37	0.279	3.056	6.613	68.283	21.250	26.335	<0.001
SII ≥1145	0.058	1.151	1.231	8.115	3.116	5.720	0.017

Abbreviations: CG, COVID-GRAM; CI, critical illness; CSI, quick COVID-19 Severity Index; SII, systemic immune-inflammation index.

ROC analysis was performed for the diagnostic decision-making features of qCSI, COVID-GRAM, and SII in predicting ICU need. Area under the curve (AUC) was 0.859 (95% CI, 0.780–0.938) for the qCSI score, 0.885 (95% CI, 0.824–0.946) for the COVID-GRAM score, and 0.752 (95% CI, 0.644–0.861) for the SII score ($p < 0.001$). The cutoff value was 6.5 for the qCSI score, 157 for the COVID-GRAM score, and 1145 for the SII score. The values and results of the ROC analysis made for the ICU need are given in Table 6 and Figure 1.

ROC analysis was performed for the diagnostic decision-making features of qCSI, COVID-GRAM, and SII in predicting mortality. AUC was 0.899 (95% CI, 0.838–0.961) for the qCSI score, 0.927 (95% CI, 0.879–0.976) for the COVID-GRAM score, and 0.714 (95% CI, 0.596–0.832) for the SII score ($p < 0.001$). The cutoff value for ICU need was 6.5 for the qCSI score, 157 for the COVID-GRAM score, and 1145 for the SII score. The cutoff value for mortality was 6.5 for the qCSI score, 157 for the COVID-GRAM score, and 1145 for the SII score. ROC analysis curves and results for mortality are given in Table 7 and Figure 1. Logistic regression analysis was performed with these cutoff values for both ICU need and mortality. It was determined that when the qCSI is over 6.5, the need for ICU increased 13.8 times and mortality increased 21.3 times. When the COVID-GRAM score is >157, the ICU need increased 14.7 times and the mortality increased 33.7 times. We found that the need for ICU increased 4.2 times and mortality increased 3.1 times when the SII score was >1145 (Tables 8 and 9).

4 | DISCUSSION

Despite all global efforts, the COVID-19 outbreak has not yet been fully controlled, and single-day confirmed cases are on the rise. Although vaccines developed against the disease, which does not have an effective treatment, have started to be applied, it is still too early to comment on its effectiveness. Mortality is very high in

severe diseases.[12] In order to reduce mortality and control the disease, it is important to recognize the serious disease at an early stage and to identify patients who may develop a serious disease. It is possible to distinguish patients who may develop serious diseases, allowing mortality to be prevented by using laboratory data at the time of hospitalization. HD patients have a high risk of COVID 19 infection due to both the CKD itself and its existing comorbidities.[13,14]

In this study involving 117 patients, the most common symptoms at the time of admission to hospital were cough, myalgia fever, and shortness of breath. Fever is the most common symptom in studies conducted with the general population.[15,16] In HD patients, fever was not a common symptom due to the decreased inflammatory response. In our study, in accordance with the literature, fever was less observed compared with the other symptoms.[17]

In this study, conducted with 117 HD patients diagnosed with COVID-19, 26.5% of them were transferred to the ICU. The mortality rate of our study cohort was 24.7%. Nonsurvivors were significantly elder than survivors. Elderly patients with CKD have higher mortality than younger patients. This is because elderly patients have more comorbid diseases, delayed diagnosis due to mild symptoms due to decreased immune response, and atypical imaging findings.[18,19] HT, CAD, and DM were the most common comorbid diseases, compatible with the literature.[20,21]

Severe hypoxia and respiratory distress are characteristic of COVID-19, which may end with septic shock and end-stage organ failure.[22–24] Acute hypoxia is the main determinant of disease severity and progression. Therefore, the evaluation of respiratory functions is very important in terms of risk scoring. COVID-GRAM, qCSI, and SIIT scores were found to be significantly higher in patients who were in need of ICU and who died.

COVID-GRAM, developed by Liang et al., was created to predict development of severe disease in hospitalized COVID-19 patients.[8] Previous studies have shown that variables such as age, number of comorbid diseases, and cancer disease in this test increase the mortality in COVID-19.[25,26] In the study of Liang et al., the performance of this risk score was satisfactory with accuracy based on AUCs in both the development and validation cohorts of 0.88. In our study, the AUC for ICU need was 0.883 (95% CI 0.821–0.945) and AUC 0.924 (95% CI 0.874–0.974) for mortality. This test, which can be easily calculated by the clinician with the web-based calculator developed for the general population, can be used to predict the risk of developing a critical illness in hospitalized HD patients.

Severe respiratory failure may develop in COVID-19 patients within 24 h after hospitalization. The qCSI is a test calculated with data easily accessible at the bedside. The probability of developing severe respiratory failure in patients scoring 3 or less is around 4%. As the index score increases, the risk of developing respiratory failure rises.[11] The qCSI is an easy-to-apply tool for planning intensive care and hospital admissions. AUC of qCSI was 0.899 (95% CI 0.780–0.938) for intensive care need and 0.899 (95% CI 0.838–0.961) for mortality in our study cohort. Rodriguez-Nava et al. had found AUC of qCSI was 0.781 for mortality and 0.761 for ICU needs in 313 COVID-19 patients.[27] In the study of Haimovich et al., AUC of qCSI for critical respiratory disease (defined as oxygenation flow rate> 10 L/min, high-flow oxygenation, noninvasive ventilation, invasive ventilation, or death) was 0.81.[11] AUCs of qCSI were higher in our HD patient population. In light of these data, we think that this test, which can be easily applied at the bedside, can predict serious disease development in HD patients.

Hematological parameters such as lymphopenia, increased neutrophil count, and leukocytosis increased NLR, and thrombocytopenia are the most common findings observed and are positively correlated with disease severity.[28–30] In our study, NLR and neutrophil counts were found to be significantly higher in patients with high risk for critical illness according to qCSI compared to other groups ($p < 0.001$). Parameters previously determined and correlated with disease severity are also compatible with this risk score.

SII including neutrophil, platelet, and lymphocyte counts, which shows the balance between the immune system of the host and the inflammatory state, is a prognostic marker in patients with sepsis.[31] It is also used as a poor prognosis indicator for small cell lung, hepatocellular, colorectal, and gastric cancers.[32–35] In the study of Usul et al., in which they examined 282 patients, SII was found to be higher in COVID-19 patients compared to healthy controls, and it was suggested that it plays a diagnostic role for SARS-CoV-2 infection.[36] In the study of Fois et al., AUC of SII for mortality was found 0.628 for mortality.[10] In our study, AUC of SII was 0.752 for ICU need and 0.714 for mortality. Therefore, SII can be used to predict mortality and ICU need for hospitalized COVID-19 HD patients.

We found the qCSI was over 6.5, the need for ICU increased 13.8 times, and mortality increased 21.3 times. When the COVID-GRAM score is >157, the ICU need increased 14.7 times and the mortality increased 33.7 times. We found that the need for ICU increased 4.2 times and mortality increased 3.1 times when the SII score was >1145.

Although vaccines developed against SARS-CoV-2 are met with great hope all over the world, time is needed for the vaccination of all individuals and the development of social immunity, and the virus continues to spread in this period. Therefore, it is important to identify patients who may develop critical illness at the time of diagnosis to reduce mortality. Patients in the high-risk group for COVID-19, such as HD patients, should be evaluated in terms of ICU need and mortality at admission to hospital with easily accessible tests.

In our study, it has been shown that COVID-GRAM, qCSI, and SII can also be used in HD patients. Although it has been shown in the literature that these tests can be used separately in the general population to identify patients who may develop critical diseases, there are no studies conducted in HD patients. Risk scoring tests have advantages and disadvantages compared to each other. While COVID-GRAM also evaluates comorbid diseases, qCSI can be calculated with less information. Our study is the first study in the literature that examined three tests together and conducted in a special population such as HD patients.

As for any retrospective study, some limitations are worth considering. Our sample size is limited and therefore the global accuracy of our ROC curve estimation could be reduced, still keeping a good reliability in ROC curve comparison. The data are entirely from a single center in Turkey, which could potentially limit the generalizability of the risk scores in other areas of the world.

As a result, we think that these tests, which can be easily calculated from simple laboratory parameters measured on admission to the hospital, at the bedside, could be used to estimate the risk of developing critical illnesses among COVID-19 HD patients. Risk scores can help identify patients who are and are not likely to develop critical illness, thus supporting appropriate treatment and optimizing the use of medical sources. Identifying critically ill patients during their hospitalization can enable the rapid implementation of effective treatments. The Ministry of Health in our country recommends LMWH, high-dose glucocorticoid, tocilizumab, and anakinra treatments in the early period for critically ill patients. Estimating the risk of critical illnesses could help to reduce the mortality in HD patients.

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