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## Prediction of mortality in COVID-19 through combining CT severity score with NEWS, qSOFA, or peripheral perfusion index

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### ABSTRACT

**Introduction:** The assessment of disease severity and the prediction of clinical outcomes at early disease stages can contribute to decreased mortality in patients with Coronavirus disease 2019 (COVID-19). This study was conducted to develop and validate a multivariable risk prediction model for mortality with using a combination of computed tomography severity score (CT-SS), national early warning score (NEWS), and quick sequential (sepsis-related) organ failure assessment (qSOFA) in COVID-19 patients.

**Methods:** We retrospectively collected medical data from 655 adult COVID-19 patients admitted to our hospital between July and November 2020. Data on demographics, clinical characteristics, and laboratory and radiological findings measured as part of standard care at admission were used to calculate NEWS, qSOFA score, CT-SS, peripheral perfusion index (PPI) and shock index (SI). Logistic regression and Cox proportional hazard models were used to predict mortality, which was our primary outcome. The predictive accuracy of distinct scoring systems was evaluated by the receiver-operating characteristic (ROC) curve analysis.

**Results:** The median age was 50.0 years [333 males (50.8%), 322 females (49.2%)]. Higher NEWS and SI was associated with time-to-death within 90-days, whereas higher age, CT-SS and lower PPI were significantly associated with time-to-death within both 14 days and 90 days in the adjusted Cox regression model. The CT-SS predicted different mortality risk levels within each stratum of NEWS and qSOFA and improved the discrimination of mortality prediction models. Combining CT-SS with NEWS score yielded more accurate 14 days (DBA:  $-0.048$ ,  $p = 0.002$ ) and 90 days (DBA:  $-0.066$ ,  $p < 0.001$ ) mortality prediction.

**Conclusion:** Combining severity tools such as CT-SS, NEWS and qSOFA improves the accuracy of predicting mortality in patients with COVID-19. Inclusion of these tools in decision strategies might provide early detection of high-risk groups, avoid delayed medical attention, and improve patient outcomes.

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### 1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is associated with substantial morbidity and mortality [1]. Predicting undesirable outcomes is therefore crucial, even on admission to an emergency department (ED), as it enables clinicians to make informed decisions regarding patients at high risk. In this context, risk-stratification scores can improve clinical decision-making and lead to significantly reduced risks and better patient outcomes.

Pre-COVID-19, several mortality prediction tools such as The national early warning score (NEWS), quick sequential (sepsis-related) organ failure assessment (qSOFA) score, computed tomography severity score (CT-SS), peripheral perfusion index (PPI), and shock index (SI) were extensively studied for application in the context of distinct disease conditions including COVID-19 [2–6]. These risk-stratification tools use clinical, physiological, and radiologic parameters to some extent, and they are beneficial in identifying patients at a higher risk of mortality and with a worse prognosis [6,7]. Among the five instruments mentioned, NEWS and qSOFA are well-validated tools that have proven useful in ED settings. Both scores have performed well in predicting prognosis in pneumonia, both in the ED and in wards. Although NEWS

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requires seven physiologic variables to compute, the advantage of the qSOFA score is that the variables are clinical, making laboratory tests unnecessary [8].

The CT-SS is a semiquantitative scoring method previously validated in patients with acute respiratory distress syndrome [9,10]. However, there is scarce evidence demonstrating the importance of CT-SS as a prognostication tool in COVID-19 [11]. The present study aim to determine whether measuring CT-SS, in addition to an illness acuity tool such as NEWS and qSOFA and other hemodynamic indicators, improves the prognostication of COVID-19 patients admitted to the ED.

## 2. Material and methods

### 2.1. Study design and patient eligibility

In this retrospective cohort study, we enrolled 655 consecutive COVID-19 patients admitted to the ED and treated at Çanakkale Onsekiz Mart University (COMU) hospital. The medical records of patients who were positive for SARS-CoV-2 by reverse transcription polymerase chain reaction (RT-PCR) of nasal and pharyngeal swab samples from July 2020 to November were analyzed retrospectively. The inclusion criteria were as follows: [1] age  $\geq 18$  years; [2] SARS-CoV-2 in respiratory tract specimens, detected by RT-PCR; [3] high resolution computed tomography (HRCT) performed; and [4] no missing medical records. The exclusion criteria were defined as [1] patients receiving any empirical treatment other than the standard protocol determined by responsible authorities and [2] patients in whom CT scan not performed.

COMU hospital is a tertiary-care state hospital located in northwest Turkey. Since 23 March 2020, it has had 220 beds designated to COVID-19-only care, making it the primary treatment facility for SARS-CoV-2 infected patients in the Çanakkale region. Overall, the hospital received moderate-to severely ill COVID-19 patients from secondary hospitals throughout Çanakkale province.

The study was approved by the institutional review board of COMU medical center (Approval No: 2011-KAEK-27/2020-E.2000070224). The requirement for informed consent was waived because of the retrospective study design and rapid emergence of this infectious disease.

### 2.2. Real-time reverse transcription polymerase chain reaction

SARS-CoV-2 Real-time reverse transcription polymerase chain reaction (RT-PCR) tests were implemented using kits supplied by the Ministry of Health, Turkey. During the study period, two different kits were used for SARS-CoV-2 RNA detection. PCR tests were performed using Biospeedy SARS-CoV-2 Double Gene RT-qPCR (Bioeksan, Istanbul, Turkey) or Diagnostical HS SARS-CoV-2 Real-Time PCR (RTA Labs, Kocaeli, Turkey) kits according to the manufacturer's protocol. All PCR analysis was executed using Biorad CFX-96 Touch Real-Time PCR detection system (California, USA). Laboratory performance was evaluated with participation in the national external quality assessment program supplied by MOTAKK (EQA program for molecular diagnosis, Ankara, Turkey).

### 2.3. Clinical data assessment

Turkey has a government-financed universal health insurance system. All Turkish hospitals connect to the National Health Information System (NHIS), but each hospital runs private clinical record systems that integrate with the NHIS. We collected clinical and demographic data from the COMU Hospital Information and Management System (HIMS). Database access was granted by the management of the COMU medical center. The data obtained from the hospital's electronic database allowed us to analyze the following clinical and demographic variables: age, gender, vital and laboratory parameters, Glasgow coma scale (GCS) score, date presenting to the hospital, length of stay in the

hospital, variables related to mortality, medications used, accompanying diseases, discharge status, and disposition at discharge (home, hospital admission, intensive care unit admission, death). Laboratory work-up at admission included hemogram, liver and renal function tests, lactate dehydrogenase (LDH), serum C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).

### 2.4. Thin-section CT imaging and scoring

All patients underwent a dedicated CT scan in the radiology department of COMU medical center. Imaging was performed using a CT scanner (Asteion TSX-021B; Toshiba Corporation, Tokyo, Japan). The tube voltage was 120 kVp, and the tube current was set to 150 mAs. The images were analyzed by a single radiologist who had over ten years' experience in thoracic imaging. All volumetric chest CT were assessed at lung window of 1600 WW and 550 WL and mediastinal window of 400 WW and 40 WL using 2D coronal and sagittal planes for better assessment of the extent of the disease. The scans were first assessed as negative or positive for typical findings of COVID-19 pneumonia (bilateral, multilobe, posterior peripheral ground-glass opacities) as defined by the RSNA Consensus statement [12].

To quantify the extent of disease, a thin-section CT score was assigned on the basis of the area involved. A semiquantitative scoring system was used to quantitatively estimate the pulmonary involvement of all these abnormalities based on the area involved. CT severity score was calculated by assessing the degree of lobe involvement for each of the five lung lobes separately on a scale of 0–5, with 0 indicating no involvement, 1 indicating less than 5% involvement, 2 indicating 5–25% involvement, 3 indicating 26–49% involvement, 4 indicating 50–75% involvement, and 5 indicating more than 75% involvement. The sum of the five lobe scores ranged from 0 (no involvement) to 25 (maximum involvement), giving a total lung CT score.

### 2.5. Defining screening tools and outcome measures

The CT-SS is a widely used scoring tool initially developed for assessing the severity of lung involvement in acute respiratory distress syndrome on thin-section lung CT scans [10]. It is a validated scoring system to assess mortality in COVID-19 patients [11,13]. According to CT-SS, the overall lung score (out of 25) was classified as mild and severe, depending on the score range. We defined a score between 0 and 10 as a mild disease and between 11 and 25 as a severe disease.

Clinical acuity was measured by NEWS and qSOFA [6]. The NEWS (0–20, higher = worse) comprises seven physiological variables (respiratory rate, oxygen saturation, supplemental oxygen, temperature, systolic blood pressure, heart rate, and level of consciousness) that often integrate early warning systems to identify high-risk patients in acute care settings. The NEWS proved to be associated with ICU admission and death outside ICU [14,15]. The qSOFA score is based on blood pressure, respiratory rate, and the Glasgow Coma Scale and does not require laboratory parameters. Scores range from 0 to 3 (higher = worse), with 1 point for each of 3 criteria: [1] respiratory rate  $\geq 22$  breaths/min, [2] altered mental status, and [3] systolic blood pressure (SBP)  $\leq 100$  mmHg [16].

The SI was calculated according to the formula (SI) = heart rate / systolic blood pressure (BP). BP was measured using the oscillometric non-invasive technique in the supine position after 5 min of rest. The IntelliVue MX450 monitor system calculated the PPI as the ratio between the pulsatile component and the nonpulsatile component of the light reaching the light-sensitive cell of the pulse oximetry probe [4].

Time-to-death within 14 days and 90 days of ED admission were defined as the primary outcome of this study. The ED admission, discharge, or death dates up to 90 days were recorded. The survival status of the patients was determined using the national death certificate system (NDCS). The follow-up duration for deceased patients was determined as the time between ED admission and the time of death according to

the NDCS. For surviving patients, 01 March 2021 was used as the end-point for survival assessment.

## 2.6. Statistical analysis

Descriptive statistics were presented as median (interquartile range –IQR) for the non-normally distributed variables, whereas they were presented as number and percentage (%) for nominal variables. The significance of the difference between the groups in terms of the median values was analyzed using a Mann-Whitney *U* test. Categorical variables were evaluated using Pearson's chi-square test or Fisher's exact test. Receiver-operating characteristic (ROC) analysis was performed to identify a threshold value for SI and PPI, and threshold values of 1 and 1.5 were chosen for overall survival (OS) analyses. Multivariable Cox proportional hazard models were fitted to study the association between the distributions of risk factors among survival. The results of the analysis were presented in terms of the estimated hazard ratios (HR) with 95% confidence intervals (95% CI). ROC analysis was used to calculate the areas under the receiving operator curves (AUROC) with 95% confidence intervals for study parameters to predict 14- and 90-days mortality. The DeLong test was then used for a pairwise comparison of AUROCs [17]. All statistical analyses were conducted using SPSS

19.0 for Windows (IBM Corp., Armonk, NY, USA) and R software version 3.6.2. All *p*-values of less than 0.05 were considered to indicate statistical significance.

## 3. Results

A total of 655 patients aged 18 and over with a SARS-CoV-2 RT-PCR-positive test and for whom CT imaging was performed were included in the study between July and November 2020. The median age was 50 years [range: 35–65 years, 333 males (50.8%), 322 females (49.2%)]. Table 1 shows the clinical and demographic characteristics of all patients with regard to survival status. On follow-up after 90 days, 128 (19.5%) patients died (121 [18.4%] in the hospital and seven [1.1%] after discharge). The median length of hospital stay was 6.0 days (IQR = 1.0–9.0 days).

The cumulative incidence of 14- and 90-days mortality across several demographic and clinical parameters is presented in Table 2. The higher age, qSOFA, and CT-SS and the lower PPI were significantly associated with time-to-death within 14 days in the adjusted Cox regression model; the higher age, NEWS, SI, and CT-SS and the lower PPI were significantly associated with time-to-death within 90 days in the adjusted Cox regression model.

**Table 1**  
Baseline characteristics of patients admitted to emergency department according to survival status

Variables	All patients (n = 655)	Survivors (n = 527)	Deceased (n = 128)	P value
<b>Demographics</b>				
Age	50.0 (35.0–65.0)	45.0 (32.0–57.0)	76.0 (66.5–83.0)	<0.001
Gender/Male, n(%)	333 (50.8)	255 (48.4)	78 (60.9)	0.011
<b>Chronic disease, n(%)</b>				
None	312 (47.63)	293 (55.6)	19 (14.8)	<0.001
1	140 (21.37)	108 (20.5)	32 (25.0)	
2 or more	203 (30.99)	126 (23.9)	77 (60.2)	
<b>Vital signs at triage</b>				
Heart rate (/min)	87.0 (78–98)	86.0 (78.0–96.0)	90.0(81.0–110.0)	<0.001
Respiratory rate (/min)	18.0 (17–20)	18.0 (17.0–20.0)	22.0 (19.0–24.0)	<0.001
SBP (mm/Hg)	128.0 (120–139)	129.0 (120.0–139.0)	128.0 (111.0–140.0)	0.299
MAP (mm/Hg)	96.0 (88.8–103.3)	96.7 (90.7–103.7)	93.0 (83.0–103.0)	0.002
Temperature (°C)	36.5 (36.4–36.8)	36.5 (36.4–36.8)	36.6 (36.5–36.8)	0.068
<b>Complete Blood Count</b>				
WBC	6.2 (4.9–8.3)	5.7 (4.7–7.3)	9.3(6.9–13.3)	<0.001
Hemoglobin	13.5 (12.3–14.8)	13.7 (12.5–14.9)	12.6(10.8–13.9)	<0.001
Hematocrit	39.3 (35.9–42.6)	39.8 (36.5–43.0)	37.1(31.7–40.7)	<0.001
Platelet	202.0 (162.0–250.0)	201.0 (163.0–247.0)	202.5(153.3–256.3)	0.857
NLR	2.5 (1.6–5.2)	2.1 (1.4–3.4)	10.5 (5.4–20.9)	<0.001
MLR	0.4 (0.3–0.6)	0.3 (0.2–0.5)	0.6(0.4–1.0)	<0.001
<b>Biochemical measurements</b>				
Blood glucose	105 (92.5–128.0)	101.0 (91.9–117.0)	148.9 (114.9–206.0)	<0.001
Urea	28.8 (21.6–39.8)	26.5 (20.6–33.1)	56.7 (38.8–95.9)	<0.001
Creatinine	0.9 (0.7–1.1)	0.8 (0.7–1.0)	1.3 (1.0–1.7)	<0.001
Uric acid	4.7 (3.7–6.1)	4.4 (3.6–5.4)	6.8 (4.5–8.6)	<0.001
Ferritin	141.7 (52.0–364.5)	111.2 (44.0–232.9)	634.6 (336.1–1197.5)	<0.001
ALT	19.0 (12.5–30.3)	18.9 (12.6–27.8)	20.5 (12.8–36.0)	0.152
AST	23.6 (18.0–33.5)	21.7 (17.6–28.6)	36.2 (25.0–58.0)	<0.001
LDH	259.0(213.0–362.0)	236.0 (202.8–303.3)	383.0 (288.3–542.0)	<0.001
CRP	1.1 (0.3–5.8)	0.8 (0.2–2.4)	11.3 (6.9–18.5)	<0.001
Sedimentation	20.0(10.0–37.0)	16.0 (9.0–31.0)	42.5 (25.8–63.0)	<0.001
<b>Illness acuity assesment tools</b>				
NEWS	1.0 (0.0–4.0)	1.0 (0.0–2.0)	8.0 (5.0–11.0)	<0.001
<b>Quick SOFA, n(%)</b>				
Mild (0–1)	609 (92.9)	527 (100.0)	82 (67.2)	<0.001
Severe [2,3]	46 (7.1)	0 (0.0)	46 (32.8)	
Shock Index	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.7 (0.6–0.9)	0.001
PPI	1.9 (1.1–3.25)	2.3 (1.4–3.5)	0.8 (0.6–1.2)	<0.001
<b>CT Severity Score, n(%)</b>				
Mild (0–10)	516 (78.8)	491 (93.2)	25 (19.5)	<0.001
Severe [11–25]	139 (21.2)	36 (6.8)	103 (80.5)	

Data are presented as n (%) or median (IQR).

SBP: Systolic blood pressure, MAP: Mean arterial pressure, WBC: White blood count, NLR:Neutrophil-lymphocyte ratio, MLR: Monocyte-lymphocyte ratio, ALT: alanine aminotransferase,AST: Aspartate aminotransferase, CRP: C-reactive protein, NEWS: National Early Warning Score, SOFA: Sequential (Sepsis-Related) Organ Failure Assessment, PPI: peripheral perfusion index, CT: Computerised tomography.

**Table 2**  
Association between clinical risk scores and mortality in COVID-19 patients

	Time to death 14 days mortality					Time to death 90 days mortality				
	n died / n total (%)	Crude	Hazard ratio (95% CI)			n died / n total (%)	Crude	Hazard ratio (95% CI)		
			p	Adjusted	p			p	Adjusted	p
<b>Age</b>										
18–64 (years old)	5/472 (1.05%)	Reference	<0.001	Reference	0.001	22/480 (4.58%)	Reference	<0.001	Reference	<0.001
≥65 (years old)	83/183 (45.35%)	16.590 (9.510–28.939)		3.24 (1.64–6.40)		103/175 (58.86%)	18.26 (11.50–28.99)		3.61 (2.04–6.40)	
<b>Gender</b>										
Female	40/322 (12.42%)	Reference	0.493	Reference	0.582	50/322 (15.53%)	Reference	0.034	Reference	0.522
Male	48/333 (14.41%)	1.15 (0.761–1.762)		0.89 (0.57–1.37)		75/333 (22.52%)	1.472 (1.03–2.11)		1.13 (0.77–1.66)	
<b>NEWS</b>										
0–6 points	26/554 (4.69%)	Reference	<0.001	Reference	0.098	40/554 (7.22%)	Reference	<0.001	Reference	0.012
≥7 points	62/101 (61.39%)	19.39 (12.23–30.74)		1.70 (0.91–3.18)		85/101 (84.16%)	22.90 (15.57–33.66)		1.99 (1.16–3.41)	
<b>Quick SOFA</b>										
0–1 points	52/609 (8.54%)	Reference	<0.001	Reference	0.039	80/609 (13.14%)	Reference	<0.001	Reference	0.128
2–3 points	36/46 (78.26%)	17.61 (11.44–27.13)		1.76 (1.03–3.01)		45/46 (97.83%)	19.65 (13.41–28.80)		1.44 (0.90–2.29)	
<b>Shock Index</b>										
<1	69/618 (11.17%)	Reference	<0.001	Reference	0.107	102/608 (16.78%)	Reference	<0.001	Reference	0.040
≥1	19/37 (51.35%)	6.22 (3.74–10.34)		1.57 (0.91–2.73)		23/37 (62.16%)	5.67 (3.60–8.92)		1.67 (1.02–2.73)	
<b>PPI</b>										
<1.5	11/381 (2.89%)	13.06 (6.93–24.60)	<0.001	3.47 (1.73–6.94)	<0.001	16/381 (%13.6)	13.22 (7.80–22.40)	<0.001	4.607 (2.60–8.17)	<0.001
≥1.5	75/234 (32.05%)	Reference		Reference		102/234 (%86.4)	Reference		Reference	
<b>CT Severity</b>										
0–10 points	14/516 (2.71%)	Reference	<0.001	Reference	<0.001	24/516 (%19.2)	Reference	<0.001	Reference	<0.001
11–25 points	74/139 (53.24%)	26.35 (14.86–46.72)		6.17 (2.98–12.78)		101/139 (%80.8)	26.34 (16.79–41.31)		6.63 (3.60–12.21)	

NEWS: National Early Warning Score, SOFA: Sequential (Sepsis-Related) Organ Failure Assessment, PPI: peripheral perfusion index, CT: Computerised tomography, CI: confidence interval.

Mortality in hospitalized COVID-19 patients according to levels of NEWS/qSOFA and CT-SS is demonstrated in Table 3. Survival over 90 days varied significantly within NEWS subgroups depending on CT-SS. Classifying patients by CT-SS score significantly improved the 90-days prediction of mortality across the subgroups of NEWS (Fig. 1A). Patients with a NEWS score ≥ 7 and CT-SS over 11 had the highest hazard ratio. Similar improvement in 90-days mortality prediction was also observed in qSOFA subgroups (Table 3 and Fig. 1B).

The impact of CT-SS on the discriminating accuracy of different mortality models is analyzed in Table 4. First, we designed a base model including age, gender, PPI, and SI to identify patients at high risk of mortality. Pairwise analysis demonstrated that after adjusting the base model with CT-SS, significantly higher accuracy was observed in predicting both 14-days (DBA:−0.031,  $p = 0.002$ ) and 90-days

mortality (DBA:−0.036,  $p < 0.001$ ). The NEWS score showed a significant capacity to predict 14-days and 90-days mortality (AUROC: 0.908 and 0.907, respectively). Combining CT-SS with NEWS score yielded more accurate 14-days and 90-days mortality prediction (AUROC: 0.955 and 0.972 respectively) (Fig. 2A). The combining of CT-SS with base model+NEWS score significantly increased the accuracy of identifying patients at high risk for 14-days and 90-days mortality. A similar ROC analysis was performed using qSOFA-based prognostic models (Table 4 and Fig. 2B).

#### 4. Discussion

The use of baseline clinical observations and metabolic profiles of patients as a predictor of mortality is widely recognized. It allows patients

**Table 3**  
Mortality in COVID-19 patients according to levels of NEWS and Quick SOFA in association with CT-SS

	Time to death within 90 days			
	N died / N total (%)	Crude model	P value	Adjusted model <sup>a</sup>
<b>NEWS   CT Severity score<sup>a</sup></b>				
NEWS 0–6   CT Severity 0–10	9/494 (1.8)	Reference		Reference
NEWS 0–6   CT Severity 11–25	31/60 (51.67)	39.88 (18.93–84.03)	<0.001	18.061 (8.09–40.31)
NEWS ≥7   CT Severity 0–10	15/22 (68.18)	64.29 (27.82–148.61)	<0.001	25.091 (9.87–63.79)
NEWS ≥7   CT Severity 11–25	70/79 (88.60)	116.76 (57.42–244.0)	<0.001	67.96 (29.85–154.74)
<b>Quick SOFA/ CT Severity score<sup>a</sup></b>				
Quick SOFA 0–1   CT Severity 0–10	15/507 (2.95)	Reference		Reference
Quick SOFA 0–1   CT Severity 11–25	65/102 (63.72)	33.24 (18.90–58.47)	<0.001	12.88 (6.93–23.95)
Quick SOFA 2–3   CT Severity 0–10	9/9 (100)	101.15 (42.08–243.13)	<0.001	17.07 (6.84–42.62)
Quick SOFA 2–3   CT Severity 11–25	36/37 (97.30)	101.74 (52.99–195.34)	<0.001	45.97 (20.06–105.33)

NEWS: National Early Warning Score, SOFA: Sequential (Sepsis-Related) Organ Failure Assessment, CT-SS: Computerised tomography severity score, CI: confidence interval.

<sup>a</sup> The adjusted model included age and gender.



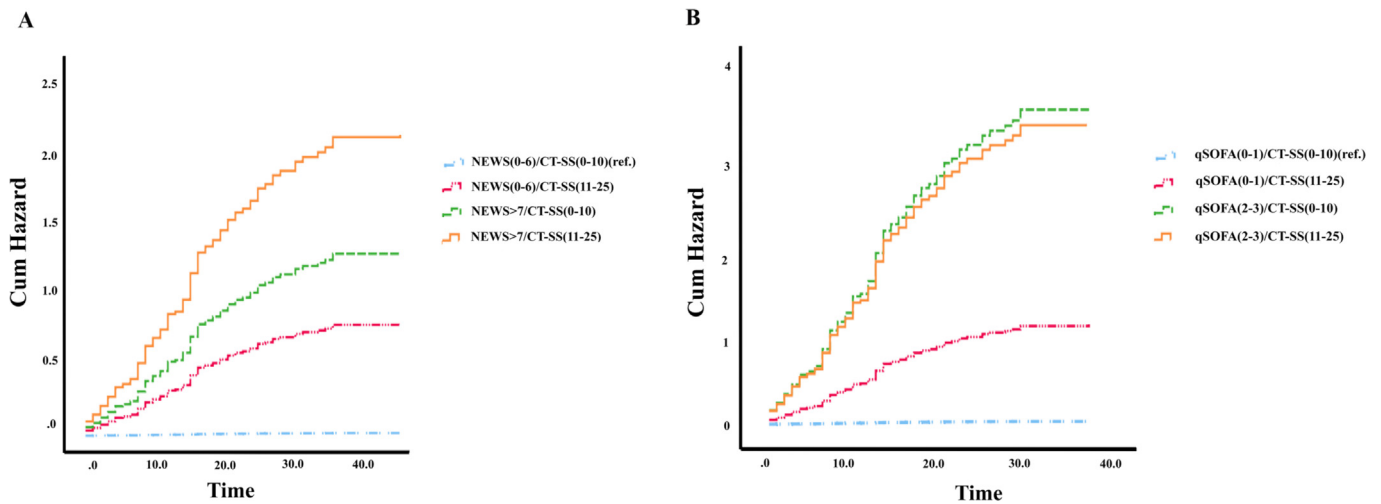


Fig. 1. Predicted cumulative hazard (Cum Hazard) function of 90-day mortality for (A) NEWS with CT-SS subgroups and (B) qSOFA with CT-SS subgroups.

**Table 4**  
Effect of CT severity score on the discrimination accuracy of mortality models

Prognostic model		Area under the ROC curve (95% CI)		Area under the ROC curve (95% CI)		Pairwise Analysis 95% CI			
		Without CT severity score	With CT severity score	DBA	SE	Lower	Upper	Z statistic	p
Base Model = Age, gender, PPI and SI	14 days-mortality	0.938 (0.912–0.963)	0.968 (0.956–0.981)	-0.031	0.139	-0.050	-0.012	-3.147	0.002
	90 days-mortality	0.951 (0.931–0.972)	0.987 (0.981–0.993)	-0.036	0.117	-0.053	-0.018	-4.022	<0.001
NEWS	14 days-mortality	0.908 (0.871–0.944)	0.955 (0.940–0.970)	-0.048	0.162	-0.078	-0.017	-3.080	0.002
	90 days-mortality	0.907 (0.871–0.943)	0.972 (0.962–0.983)	-0.066	0.154	-0.096	-0.035	-4.203	<0.001
Base model + NEWS	14 days-mortality	0.963 (0.949–0.977)	0.973 (0.962–0.984)	-0.010	0.112	-0.018	-0.002	-2.451	0.014
	90 days-mortality	0.977 (0.966–0.988)	0.991 (0.986–0.996)	-0.014	0.091	-0.022	-0.006	-3.437	0.001
Quick-SOFA	14 days-mortality	0.829 (0.779–0.879)	0.949 (0.927–0.971)	-0.120	0.191	-0.165	-0.076	-5.288	<0.001
	90 days-mortality	0.835 (0.793–0.876)	0.967 (0.950–0.984)	-0.132	0.172	-0.170	-0.095	-6.902	<0.001
Base Model + Quick-SOFA	14 days-mortality	0.961 (0.947–0.975)	0.972 (0.961–0.984)	-0.011	0.114	-0.019	-0.003	-2.652	0.008
	90 days-mortality	0.977 (0.966–0.987)	0.991 (0.986–0.996)	-0.014	0.089	-0.022	-0.007	-3.695	<0.001

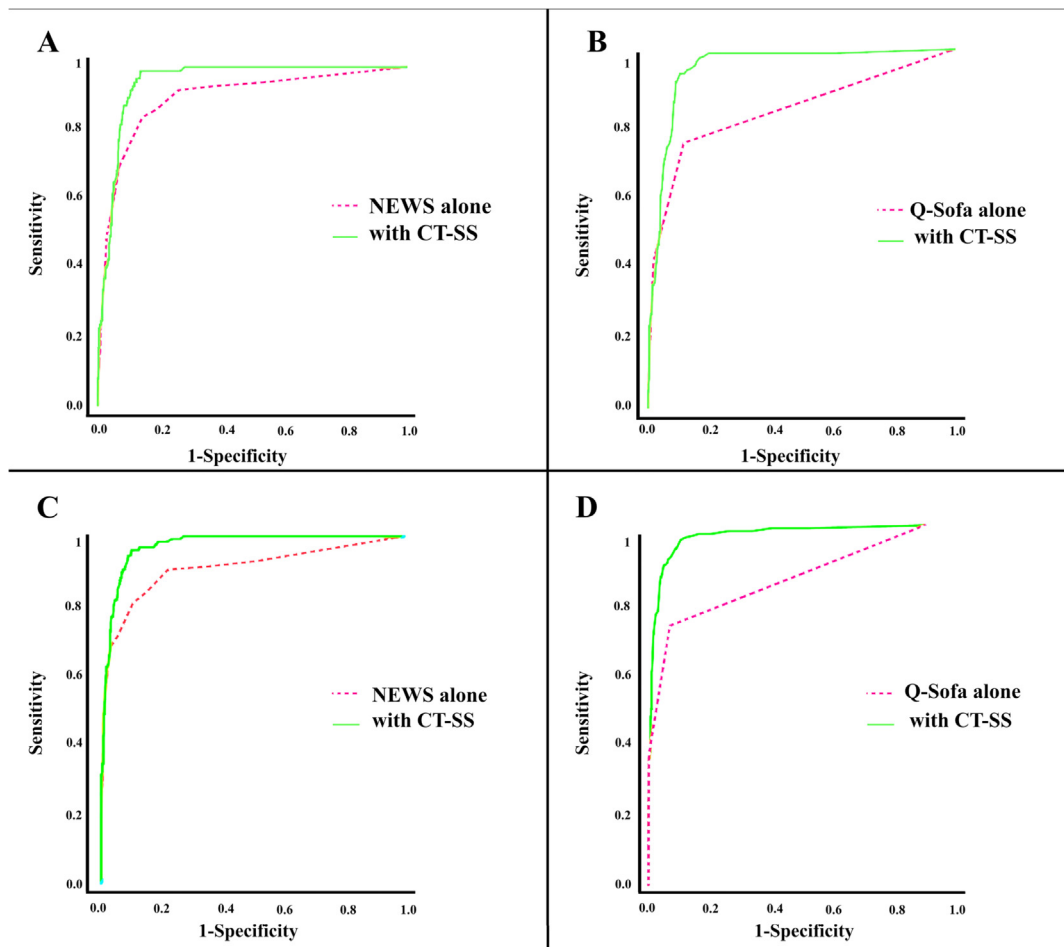
NEWS: National Early Warning Score, SOFA: Sequential (Sepsis-Related) Organ Failure Assessment, CT-SS: Computerised tomography severity score, CI: confidence interval, SI: shock index, DBA: difference between areas, SE: standart error, ROC: reciever operating characteristic.

to be stratified into risk categories, and specific interventions and levels of care can be offered where appropriate. The present study aimed to evaluate whether distinct rapid-risk-stratification tools, either alone or combined, could predict short- and long-term death in SARS-CoV-2-infected patients admitted to the ED of a designated COVID-19-only care facility. We demonstrated that NEWS, CT-SS, and lower PPI were significantly related to time-to-death within 14 days and 90 days, whereas qSOFA was only associated with time-to-death within 14 days in adjusted Cox regression models. Furthermore, predictive models incorporating CT-SS were more precise than those that did not consider tomographic findings. The results of the present study therefore underline the importance of adding a validated imaging tool to commonly used risk-stratification scores when estimating the probability of progression to severe or critical state in COVID-19.

Given the importance of early recognition, early treatment, and appropriate risk stratification, an imperative mission for emergency care physicians is to screen patients with a high mortality risk from severely ill COVID-19 patients [18,19]. Unfortunately, limited time and resources due to the rapidly evolving COVID-19 pandemic make this task even more difficult. For this reason, it is not surprising to see a growing number of studies focusing on simple and convenient prediction tools that can help emergency care physicians to more rapidly and effectively recognize patients at high risk of mortality. Although NEWS, the Charlson comorbidity index (CCI), SOFA, qSOFA, complete blood cell count

differentials, and CT-SS are the most studied risk-stratification tools in this context, they have several shortcomings that cause concern in practical applications, especially when they are used as the single tool for mortality prediction in severely ill COVID-19 patients [5,7,21]. Thus, timely identification of those with an increased risk of mortality is still difficult and relies on the adequate evaluation of a broad spectrum of demographic, clinical, and metabolic variables, which explains the diversity of results in different studies [22,23]. Hence, we studied the combined performance of distinct clinical and radiologic risk-stratification tools and analyzed the impact of CT-SS on the discriminating accuracy of different mortality models to determine an efficient risk-stratifying tool for COVID-19 patients.

In addition to being an important diagnostic tool in COVID-19, this study highlights the importance of CT-SS as a significant prognostication tool in patients with COVID-19. In this context, we retrospectively utilized a semiquantitative approach for all COVID-19 patients, based on the approach of Zhou et al. [24], to score the degree of lung involvement using a thin-section lung CT scan in acute respiratory distress syndrome patients. Our results showed that mortality rates were significantly elevated in patients with higher CT-SS even after adjustment for both demographic and clinical parameters. Similar results were documented by Abbasi et al. [11] and Yilmaz et al. [2], who found that death rates were significantly elevated in COVID-19 patients with elevated CT-SS.



**Fig. 2.** Time-dependent receiver-operating characteristic curves (ROC) for the prediction of mortality for different groups of variables. Panels A and B show ROC curves for predicting 14-days mortality using crude NEWS and qSOFA, and those in panels C and D show 90-days mortality using crude NEWS and qSOFA, with and without adjusting for CT-SS.

Early warning systems have been developed and broadly used in clinical practice for early recognition of clinical deterioration [25,26]. The NEWS was introduced and endorsed by the Royal College of Physicians in 2012 and is reported to have better performance than other EWs in recognizing patients at risk of ICU admission and mortality [27]. The qSOFA is a simple, rapid and practical version of SOFA and is intended for non-ICU patients. Although the overall performance of qSOFA is slightly lower than that of SOFA, it is still accepted as a useful adjunctive risk-scoring system at initial admission in patients with COVID-19 [19,28,29]. Previous studies suggested that NEWS and qSOFA have a substantial potential to foresee mortality in COVID-19 patients [5,7,18,29,30]. Our study found that non-survivor COVID-19 patients had significantly higher NEWS and qSOFA scores than the survivors. Nevertheless, based on the AUROC analysis, NEWS has been shown to have superior predictive performance than qSOFA, as shown in Table 4. The low predictive accuracy of qSOFA compared to NEWS in COVID-19 clinical outcomes may be due to the presence of many “silent hypoxemia” cases in severely ill COVID-19 patients and the low percentage of hypotension and altered mental status in this cohort. Patients with silent hypoxemia seem to breathe properly, but oxygen saturation is usually decreased when evaluated through a pulse oximetry device [31].

Based on the restricted performance of the formerly validated and commonly utilized risk-stratification scores mentioned here, we also investigated whether predictive analytics could be improved by using multiple logistic regression models. To do so, we evaluated the

predictive significance of distinct disease acuity tools and hemodynamic screening tools such as PPI and SI and confirmed the ability of the CT-SS to recognize different levels of mortality risk within the NEWS and qSOFA strata. Our results showed that the addition of CT-SS to an illness acuity tool significantly improves the prognostication of COVID-19 patients admitted to the ED. Adding CT-SS to NEWS (AUROC: 0.955 for 14 days and 0.972 for 90 days) and qSOFA (AUROC: 0.949 for 14 days and 0.967 for 90 days) yielded more accurate mortality predictions. The higher CT-SS levels were significantly associated with time-to-death within 14 and 90 days, even after adjusting for age, sex, PPI, and SI. Although, to the best of our knowledge, this is the first study to evaluate the effectiveness of CT-SS combined with NEWS, qSOFA, and PPI for the prediction of mortality in COVID-19 populations, Aliberti et al. [6] recently suggested that combining tools such as NEWS, qSOFA, and PRO-AGE may help stratify the risk of mortality from COVID-19. Similarly, a recent paper by Bellos et al. [32], in which chest CT findings were combined with clinical and laboratory data to create multivariate predictive models, demonstrated that CT-SS was positively correlated with markers of COVID-19 severity including SOFA and APACHE II.

This study explored the combined predictive value of five existing risk-stratification scores in COVID-19 patients, but it is not without limitations. First, all SpO<sub>2</sub> data recorded from the electronic patient files were the first record of the patient when they arrived at the ED. Due to the retrospective nature of the study, we cannot confirm with certainty that the oxygen saturation measurements do not include patients' oxygen supply. Second, this study was confined to a single

center and may have been affected by selection bias. Third, although our hospital is the only tertiary-care hospital in this region, the results may not be generalizable for all the patients in the region because it is not the only hospital admitting COVID-19 patients. Fourth, we measured NEWS at the time of admission only, but evaluating NEWS at regular intervals during the hospital stay would be beneficial.

In conclusion, all five severity scoring systems have the potential to be used as tools for predicting mortality in COVID-19 patients. Furthermore, combining severity tools such as CT-SS, NEWS, and qSOFA may help stratify the risk of death from COVID-19. Hence, the inclusion of these tools in decision strategies could provide early detection of high-risk groups, avoid delayed medical attention, and improve clinical outcomes in COVID-19 patients.

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