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RESEARCH ARTICLE

Radiologic severity index can be used to predict mortality risk in patients with COVID-19

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ABSTRACT

Radiologic severity index can be used to predict mortality risk in patients with COVID-19

Introduction: Pneumonia is a common symptom of coronavirus disease-2019 (COVID-19), and this study aimed to determine how analyzing initial thoracic computerized-tomography (CT) scans using semi-quantitative methods could be used to predict the outcomes for hospitalized patients.

Materials and Methods: This study looked at previously collected data from adult patients who were hospitalized with a positive test for severe acute respiratory syndrome coronavirus-2 and had CT scans of their thorax at the time of presentation. The CT scans were evaluated for the extent of lung involvement using a semi-quantitative scoring system ranging from 0 to 72. The researchers then analyzed whether CT score could be used to predict outcomes.

Results: The study included 124 patients, 55 being females, with a mean age of 46.13 years and an average duration of hospitalization of 11.69 days. Twelve patients (9.6%) died within an average of 17.2 days. The non-surviving patients were significantly older, had more underlying health conditions, and higher CT scores than the surviving patients. After taking age and comorbidities into account, each increase in CT score was associated with a 1.048 increase in the risk of mortality. CT score had a good ability to predict mortality, with an area under the curve of 0.857 and a sensitivity of 75% and specificity of 85.7% at a cut-off point of 25.5.

Conclusion: Radiologic severity index, which is calculated using a semi-quantitative CT scoring system, can be used to predict the mortality of COVID-19 patients at the time of their initial hospitalization.

Key words: COVID-19; death; pneumonia; CT scan

ÖZ

Radyolojik ağırlık indeksi COVID-19 hastalarında mortalite riskini tahmin etmek için kullanılabilir

Giriş: Pnömoni, koronavirüs hastalığı-2019'un (COVID-19) yaygın bir semptomudur. Bu çalışmanın amacı, yarı kantitatif yöntemler kullanılarak yapılan ilk toraks bilgisayarlı tomografi (BT) taramalarının, hastaneye yatan COVID-19 hastalarının sonuçlarını tahmin etmede nasıl bir rol oynayabileceğini belirlemektir.

Materyal ve Metod: Bu çalışma, şiddetli akut solunum sendromu koronavirüs-2 testi pozitif olan ve başvuru anında toraks BT taraması yapılan yetişkin hastaların verileriyle yapılmıştır. Bilgisayarlı tomografi taramaları, akciğer tutulumunun kapsamını değerlendirmek için 0 ile 72 arasında değişen yarı niceliksel bir puanlama sistemi kullanılarak incelenmiştir. Araştırmacılar, BT puanının, hastaların sonuçlarını tahmin etmek için kullanılıp kullanılmayacağını analiz etmiştir.

Bulgular: Çalışmaya, ortalama yaşı 46.13 yıl ve ortalama hastanede kalış süresi 11.69 gün olan 55'i kadın, toplam 124 hasta dahil edildi. On iki hasta (%9.6) ortalama 17.2 gün içinde hayatını kaybetmiştir. Hayatta kalmayan hastalar, hayatta kalan hastalara göre önemli ölçüde daha yaşlı, daha fazla altta yatan hastalığı olan ve daha yüksek BT puanlarına sahipti. Yaş ve eşlik eden hastalıklar göz önünde bulundurulduğunda, BT puanındaki her bir artışın ölüm riskini 1.048 kat arttırdığı tespit edilmiştir. Bilgisayarlı tomografi skoru, 0.857 eğri altındaki alan ve 25.5 kesme noktasında %75 duyarlılık ve %85.7 özgüllük ile mortaliteyi tahmin etme konusunda yüksek bir doğruluğa sahipti.

Sonuç: Yarı kantitatif BT skorlama sistemi kullanılarak hesaplanan radyolojik ağırlık indeksi, COVID-19 hastalarının hastaneye ilk başvurularındaki mortaliteyi tahmin etmek için etkili bir şekilde kullanılabilir.

Anahtar kelimeler: COVID-19; ölüm; zatürre; CT taraması

INTRODUCTION

The world experienced a major pandemic of coronavirus disease-2019 (COVID-19) in the early 21st century. COVID-19 is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and is different from other historical pandemics because it spread rapidly across the world due to globalization and improvements in transportation (1). As a result, it could not be possible to contain the virus, and healthcare systems were overwhelmed by the increasing number of cases, even though most cases were either asymptomatic or mild and case fatality rate was low (especially in younger people) (2-4).

The symptoms and severity of COVID-19 can vary greatly, from no symptoms to fatal multi-organ failure (5,6). Symptoms usually appear 4-5 days after exposure and often include fever, fatigue, and dry cough (7). The most common severe manifestation of the disease is pneumonia, which can rapidly progress to acute respiratory distress syndrome and death (8,9). Many COVID-19 patients have undergone computerized-tomography (CT) scans of their thorax at the time

of initial evaluation, and the extent of lung involvement shown on these scans has been found to predict mortality (10,11). In this study, it was aimed to determine whether the radiologic severity index (RSI), calculated using the initial thoracic CT scans, could predict mortality in hospitalized COVID-19 patients.

MATERIALS and METHODS

This retrospective study was conducted at four hospitals in three cities in Türkiye between March and May 2020. The inclusion criteria for the patients were being over 18 years old, having a positive test for SARS-CoV-2 in a nasopharyngeal swab polymerase chain reaction (PCR) test, having CT scans of the lungs, having baseline laboratory tests at the time of presentation, and being hospitalized for at least one day. Patients with severe or critical diseases other than COVID-19, typical CT findings on the lungs but a negative PCR test for SARS-CoV-2, and those who were not hospitalized were excluded from the study. Clinical characteristics, medical histories, clinical symptoms, and progress of COVID-19 for the patients were obtained using a standardized form from the

patients and hospital records. All laboratory tests were performed on the first or second day of hospital admission.

Computer Tomography Scans

The CT scans of the patients were performed on different scanners in different hospitals. The images were obtained with mediastinal and parenchymal window settings while the patients were in a supine position holding their breath at the moment of inspiration.

Radiologic Scoring of Lung Involvement

All CT scans were non-enhanced and performed within 24 hours of admission. They were independently and blindly reviewed by one radiologist and one pulmonologist with at least three years of experience. The severity of lung involvement was scored using a semi-quantitative tool that has been used in the past to score H7N9 influenza and parainfluenza virus-associated lung infections, as described in detail in a study by Sheshadri et al. (12). This tool was chosen because it is practical and has been shown to predict mortality in viral infections, which have similar transmission and lung involvement to COVID-19. Before reviewing the CT scans, the participating radiologists and pulmonologists were required to read the details of the scoring tool from the reference study and come to an agreement with the study coordinator (12). According to the Fleischner society guidelines, pulmonary infiltrates that obscure the margins of vessels and airway walls were described as consolidation and infiltrates that do not obscure vessels and bronchi were considered ground glass opacities (13). The lungs were divided into three zones on each side: Upper (above the carina), middle (below the carina and above the inferior pulmonary vein), and lower (below the inferior pulmonary vein). The predominant lesion and extent of involvement were determined, and the corresponding scores were

multiplied in each lung zone. The sum of the scores for the total six zones was taken as the final CT score (Table 1).

Ethics: The study received approval from the Local Ethics Committee (27.04.2020, no-8) and the administration of each participating hospital and was conducted in accordance with the Helsinki Declaration.

Statistical Analysis

Continuous variables were reported as mean \pm standard deviation, and categorical variables were reported as numbers and percentages. The skewness of continuous variables was tested, and Mann-Whitney U test and chi-square test were used for comparisons of continuous and categorical variables, respectively. Spearman test was used for bivariate correlation analysis, and Cox regression analysis was performed to determine the unadjusted and adjusted hazard ratios. Receiver operator characteristic analysis was plotted to find the optimal cut-off point for the CT score that had the best sensitivity and specificity for detecting mortality. Kaplan-Meier survival analysis was then performed based on the cut-off point for the CT score. A p-value less than 0.05 was considered statistically significant. The analyses were performed with the use IBM SPSS version 20 (Armonk, NY) for Windows.

RESULTS

There were 350 patients admitted to hospitals with a provisional diagnosis of COVID-19, and 124 of these patients met the inclusion criteria (166 patients were excluded due to a negative PCR test and 60 patients did not have a thoracic CT scan on admission) and were analyzed. Mean age of the patients was 46.13 years and 44.3% were female. At least one comorbidity was present in 41.9% of the patients, with hypertension and diabetes mellitus being the most common. Clinical characteristics and baseline

Table 1. Scoring algorithm for radiologic severity index

Predominant radiologic pattern in lung zone	Pattern score	Extent of volumetric radiologic involvement	Volumetric score
Normal lung	1	0% (normal)	0
Ground glass opacities	2	1-24%	1
Consolidation	3	25-49%	2
		50-74%	3
		75-100%	4

RSI scores are calculated by multiplying the predominant pattern for each lung zone by the extent of volumetric radiologic involvement for that zone. The sum of scores from all six zones can give final RSI ranging from 0-72.

laboratory data are shown in Tables 2 and 3. Mean values of the CT score, C-reactive protein, ferritin, fibrinogen, lactate dehydrogenase, and Troponin T were above the upper limit of normal, while the averages of other parameters were within normal ranges. Mean duration of hospitalization was 11.69 days, 31.4% of the patients required oxygen supplementation, and 16.9% of the patients were admitted to the intensive care unit (ICU).

Twelve patients died from COVID-19 within an average follow-up period of 17.2 days. Oxygen support was required for all of these patients, and 11 of them were admitted to the ICU. Non-surviving patients were older and more frequently had comorbidities and had higher CT scores, lower renal function, elevated transaminases, higher inflammatory markers, higher cardiac troponins, and lower lymphocyte counts compared to survivors (as shown in Tables 2 and 3).

In bivariate analysis, age ($r = 0.329$, $p < 0.001$), the presence of comorbidities ($r = 0.385$, $p < 0.001$), and CT score were significantly correlated with mortality, with the highest correlation coefficient being with CT score ($r = 0.516$, $p < 0.001$) (Table 4). In Cox regression analysis, the hazard ratio for mortality increased by 1.058 ($p = 0.001$) and 1.048 ($p = 0.011$) per one unit increase in CT score in unadjusted and adjusted models, respectively (Table 5). A ROC curve analysis of the CT score for predicting mortality showed an area under the curve of 0.857 (0.744-0.970, $p < 0.001$), and a cut-off value of 25.5 for the CT score had 75% sensitivity and 85.7% specificity for mortality (Figure 1A). When the study cohort was divided into two groups based on a cut-off value of 25.5 for the CT score, Kaplan-Meier survival analysis showed a significantly lower survival curve, particularly during early follow-up, in patients with higher CT scores (log-rank "Mantel-Cox"; survival estimates 36.12 ± 3.37 vs. 30.64 ± 8.2 , $p = 0.001$) (Figure 1B).

Table 2. Initial clinical characteristics and hospitalization details at the start of treatment

Variable	All patients (n= 124)	Survivors (n= 112)	non-survivors (n= 12)	p
Age	46.13 ± 17	44.29 ± 16.2	63.3 ± 16.5	0.002
Sex (M/F)	69/55	61/51	8/4	0.419
Overall coexisting disorders	52/124 (41.9%)	40/112 (35.7%)	12/12 (100%)	<0.001
Diabetes mellitus	22/124 (17.7%)	16/112 (14.2%)	6/12 (50%)	0.002
Hypertension	24/124 (19.3%)	17/112 (15.1%)	7/12 (58.3%)	0.000
Coronary heart disease	3/124 (2.4%)	2/112 (1.7%)	1/12 (8.3%)	0.161
Heart failure	1/124 (0.8%)	1/112 (0.9%)	0/12 (0%)	0.742
Asthma	6/124 (4.8%)	6/112 (5.3%)	0/12 (0%)	0.411
COPD	6/124 (4.8%)	3/112 (2.6%)	3/12 (25%)	0.001
Cancer	1/124 (0.8%)	1/112 (0.9%)	0/12 (0%)	0.742
CVA	2/124 (1.6%)	1/112 (0.9%)	1/12 (8.3%)	0.052
Alzheimer disease	1/124 (0.8%)	1/112 (0.9%)	0/12 (0%)	0.742
Seizures	1/124 (0.8%)	0/112 (0%)	1/12 (8.3%)	0.002
CKD	2/124 (1.6%)	1/112 (0.9%)	1/12 (8.3%)	0.052
Psychiatric disease	5/124 (4%)	4/112 (3.5%)	1/12 (8.3%)	0.425
GERD	1/124 (0.8%)	1/112 (0.9%)	0/12 (0%)	0.742
Hypothyroidism	1/124 (0.8%)	1/112 (0.9%)	0/12 (0%)	0.742
Data of hospitalization				
Duration of hospitalization (days)	11.69 ± 8.5	11.1 ± 6.3	17.2 ± 19.6	0.024
ICU administration	21/124 (16.9%)	10/112 (8.9%)	11/12 (91.6%)	<0.001
Oxygen support	39/124 (31.4%)	27/112 (24.1%)	12/12 (100%)	<0.001

COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, CKD: Chronic kidney disease, GERD: Gastroesophageal reflux disease, ICU: Intensive care unit.

Table 3. Initial laboratory and radiologic values taken at the beginning of treatment

Laboratory parameters	All patients (n= 124)	Survivors (n= 112)	non-survivors (n= 12)	p
Glucose	127 ± 66	124 ± 61.9	167 ± 98.3	0.205
Urea	30.3 ± 14	28.6 ± 11.5	47.7 ± 24.5	<0.001
Creatinine	0.85 ± 0.27	0.83 ± 0.25	1.1 ± 0.4	0.001
Albumin	4.15 ± 0.54	4.2 ± 0.53	3.6 ± 0.35	0.001
Sodium	137 ± 4.3	137.1 ± 4.3	136.2 ± 4.8	0.569
Potassium	4.06 ± 0.41	4.0 ± 0.4	4.17 ± 0.5	0.512
LDH	290 ± 187	264.7 ± 112.8	569 ± 455	<0.001
AST	40.1 ± 83.9	30.9 ± 16	132 ± 268	<0.001
ALT	40.8 ± 95.7	31.7 ± 22.2	133.1 ± 308	0.001
ALP	74.8 ± 47.3	70 ± 19	105 ± 125	0.087
GGT	35.5 ± 30.3	34 ± 29	46 ± 35	0.342
Triglyceride	149.1 ± 77	148.3 ± 79	163 ± 17.1	0.263
Cholesterol	158.6 ± 45.3	156 ± 44	216 ± 12.4	0.001
Fibrinogen	342.6 ± 195	343 ± 205	334 ± 78	0.866
Ferritin	469.6 ± 764	343 ± 503	2212 ± 1488	<0.001
Procalcitonin	0.085 ± 0.34	0.045 ± 0.048	0.53 ± 1.18	<0.001
Troponin	40.6 ± 275	5.3 ± 12.4	465 ± 935	<0.001
C-reactive protein	30.2 ± 45.6	25.3 ± 39.5	79.2 ± 71	<0.001
Hemoglobin	13.8 ± 1.7	13.8 ± 1.67	13.4 ± 2.1	0.515
Leukocytes	6335 ± 2412	6144 ± 2214	8255 ± 3467	0.005
Neutrophils	4224 ± 2119	3975 ± 1753	6738 ± 3588	0.000
Lymphocytes	1540 ± 757	1592 ± 746	1016 ± 689	0.022
Platelets	215532 ± 71193	212981 ± 64649	241272 ± 120635	0.210
CT score	15.45 ± 15.5	12.8 ± 12	39.8 ± 22	0.000

LDH: Lactate dehydrogenase, AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma glutamyltransferase, CT: Computed tomography.

Table 4. An analysis of the relation between clinical characteristics, mortality, and CT scores at the time of hospital admission using bivariate correlation

Variable	Mortality		CT score	
	r	p	r	p
Age	0.329	<0.001	0.402	<0.001
Gender	0.073	0.423	0.107	0.238
Comorbidities	0.385	<0.001	0.310	<0.001
CT score	0.516	<0.001	na	na

CT: Computed tomography.

Table 5. An analysis using Cox regression to predict mortality based on CT scores at the time of initial admission, with both unadjusted and adjusted models

Variable	Hazard ratio	95% CI	p
Unadjusted			
CT score	1.058	1.023-1.093	0.001
Adjusted according to age and the presence of overall coexisting disorders			
CT score	1.048	1.011-1.088	0.011

CT: Computed tomography, CI: Confidence interval.

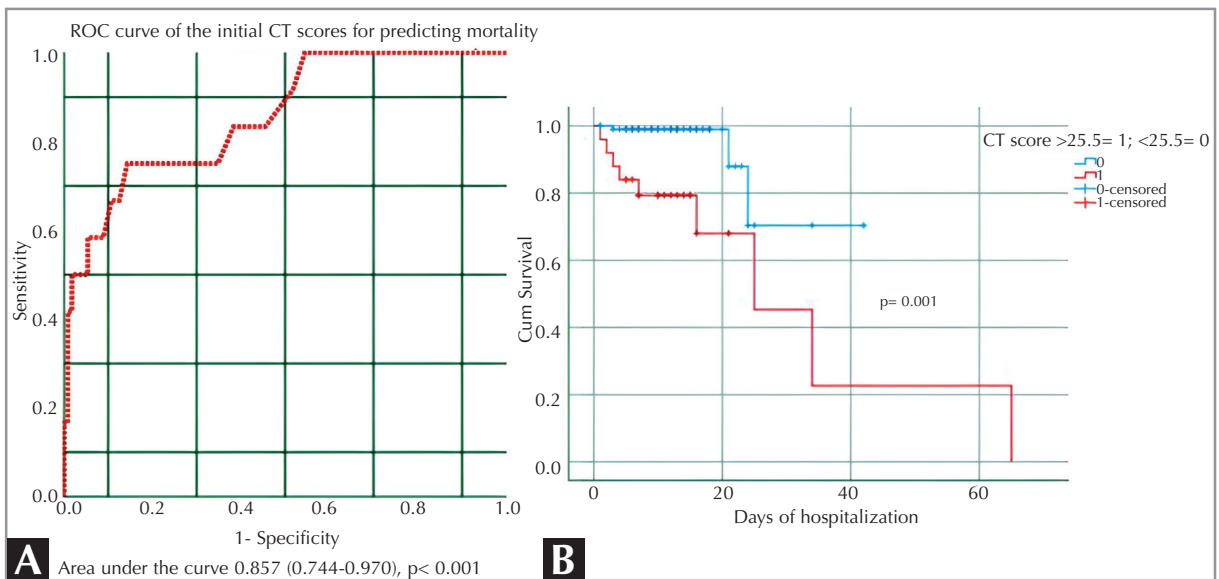


Figure 1. A. An analysis using receiver operating characteristic (ROC) curves to predict mortality based on initial CT scores. **B.** Estimations of survival using Kaplan-Meier analysis, with a CT score cutoff of 25.5.

DISCUSSION

Risk stratification is an important aspect of personalized medicine, but during a pandemic, it has a greater significance beyond individual patient needs. In this study, we retrospectively analyzed the outcomes of hospitalized COVID-19 patients based on their radiologic severity index, as determined by semi-quantitative analysis of initial thoracic CT scans. We found that this simple score of pneumonic infiltration was able to accurately distinguish between survivors and non-survivors (9.6%) with 75% sensitivity and 85.7% specificity. Assessing the extent of lung involvement, along with clinical features and laboratory parameters, is essential for making a clinical judgment for a patient with pneumonia. However, a quantitative analysis of lung infiltrations can provide additional help in making decisions when rapid judgment is necessary. Therefore, the results of this study may be useful for objectively assessing the severity and mortality risk of COVID-19 patients at presentation.

Several recent studies have explored the relation between radiologic severity of viral pneumonia, as determined by thoracic CT scans, and mortality in COVID-19 and other viral diseases (14,15). One study found that a radiologic severity index was significantly predictive of mortality in patients with H7N9 influenza pneumonia, with an area under the curve of 0.833 and an optimal cut-off of 21 (16).

Another study using the same methods in patients with parainfluenza virus-associated pneumonia found that each one-point increase in the radiologic severity index from baseline was associated with an increased hazard of mortality, although baseline CT scores were not predictive of death (12). Tabatabaei et al. used a slightly different scoring system based on the five pulmonary lobes in a case-control study of COVID-19 patients (30 who died and 60 who survived) and found that only the CT score was a significant predictor of mortality among multiple CT features on multivariate analysis (17). A retrospective analysis of initial CT scans of COVID-19 patients in Italy found that visual or software quantification of the extent of CT lung abnormality was a predictor of intensive care unit admission or death (18). In a single-center study of 697 COVID-19 patients, analysis of initial chest X-rays using artificial intelligence showed that the radiologic score, expressed as a percentage of lung involvement, was predictive of mortality and ICU admission (19). While the methodologies for radiologic scoring vary, the evidence suggests that the radiologic severity index may be a useful predictor of outcomes in COVID-19 patients (20).

There are a few limitations to this study. The study investigates using a semi-quantitative radiologic scoring system to predict mortality in COVID-19 patients. This is a timely topic with potential clinical impact as it may help identify high-risk patients based on early radiologic findings. Although using the radiological

severity index in this context is relatively novel, the small sample size (n= 124) and the retrospective design limit the generalizability of the findings. Additionally, including patients from only three centers in Türkiye could limit the study's external validity. Also, the subjective nature of radiologic scoring poses a risk of bias despite efforts to standardize scoring among radiologists and pulmonologists. The study does not account for potential confounders beyond age and comorbidities, such as different treatments received by patients or evolving SARS-CoV-2 variants (21).

CONCLUSION

In summary, this study found that the radiologic severity index, as assessed by semi-quantitative analysis of initial thoracic CT scans, can predict mortality in hospitalized COVID-19 patients. This finding is consistent with previous research on the use of CT scans to predict outcomes in other viral pneumonias. However, other factors such as age, comorbidities, clinical features, and laboratory parameters also play a role in determining the outcome of COVID-19 and should be considered in risk stratification. The use of artificial intelligence in clinical medicine may be helpful in quickly and accurately integrating all data points (22).

Ethical Committee Approval: This study was approved by Harran University Faculty of Medicine Clinical Research Committee (Decision no: 8 Date: 27.04.2020).

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: TS, ES

Analysis/Interpretation: MK, BÇ, KA, AP

Data acquisition: ŞG, MÖ, MT

Writing: BYK, TE

Clinical Revision: AŞ, FE

Final Approval: EK, TS

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