- **Elif Bombacı,**
- **Kemal Tolga Saraçoğlu,**
- **Ömer Aydıner,**
- **Fulya Ciyiltepe,**
- **Ayten Saraçoğlu,**
- **Ebru Dülger İliş,**
- **Recep Demirhan**

Elif Bombacı, Kemal Tolga Saraçoğlu, Fulya Ciyiltepe
University of Health Sciences Turkey, Kartal Dr. Lütfi
Kırdar City Hospital, Clinic of Anesthesiology and
Reanimation, Division of Intensive Care, İstanbul,
Turkey

Ömer Aydıner, Ebru Dülger İliş,
University of Health Sciences Turkey, Kartal Dr. Lütfi
Kırdar City Hospital, Clinic of Radiology, İstanbul,
Turkey

Ayten Saraçoğlu,
Marmara University Pendik Training and Research
Hospital, Clinic of Anesthesiology and Reanimation,
Division of Intensive Care, İstanbul, Turkey

Recep Demirhan
University of Health Sciences Turkey, Kartal Dr.
Lütfi Kırdar City Hospital, Clinic of Thoracic Surgery,
İstanbul, Turkey

Elif Bombacı MD (✉),
University of Health Sciences Turkey, Kartal Dr. Lütfi
Kırdar City Hospital, Clinic of Anesthesiology and
Reanimation, Division of Intensive Care, İstanbul,
Turkey

E-mail   : bombaciel@yahoo.com
Phone   : +90 216 441 39 00
ORCID ID : orcid.org/0000-0002-9153-140X

The Predictive Value of Thoracic Computed Tomography on the Mortality of Critically Ill COVID-19 Patients

Bilgisayarlı Toraks Tomografisinin Kritik COVID-19 Hastalarının Mortalitesi Üzerine Tahmin Değeri

ABSTRACT *Objective:* Although thoracic computed tomography (T-CT) has high sensitivity in the diagnosis of coronavirus disease-2019 (COVID-19), a specific involvement type or region for COVID-19 has not yet been identified in images consistent with viral pneumonia. This study determined the relationship between the degree of involvement in T-CT and mortality in patients with COVID-19.

Materials and Methods: One hundred and fifteen COVID-19 patients admitted to our intensive care unit were included in this study. Obtained T-CTs were evaluated according to the T-CT severity scoring system. Patients were divided into two groups as the mortality and the survival group. The two groups were compared in terms of age and gender, the presence and localization of abnormal T-CT findings and total CT score.

Results: The total CT score was significantly higher in the mortality group than in the survival group (10.88±5.67 vs 8.53±4.89, p=0.048). Bilateral involvement in the T-CT scan was found to be significantly higher in the mortality group.

Conclusion: Total CT scoring has predictive value in determining the survival of patients with a critical COVID-19. Bilateral involvement in the T-CT scans performed in the early period of disease and a total CT score of ≥10 may be indicative of mortality in COVID-19 patients.

Keywords: COVID-19, thoracic computed tomography, mortality, intensive care

ÖZ *Amaç:* Toraks bilgisayarlı tomografisi (T-BT) koronavirüs hastalığı-2019 (COVID-19) tanısında yüksek duyarlılığa sahip olmasına rağmen viral pnömoni ile uyumlu görüntülerde COVID-19 için spesifik bir tutulum tipi veya bölgesi henüz belirlenmemiştir. Bu çalışmada, COVID-19 hastalarında T-BT'de tutulum derecesi ile mortalite arasındaki ilişkinin belirlenmesi amaçlandı.

Gereç ve Yöntem: Bu çalışmaya yoğun bakım ünitesine yatırılan 115 COVID-19 hastası dahil edildi. Elde edilen T-BT'ler, T-BT şiddet skorlama sistemine göre değerlendirildi. Hastalar mortalite ve sağkalım grubu olarak iki gruba ayrıldılar. İki grup yaş ve cinsiyet, anormal T-BT bulgularının varlığı ve lokalizasyonu ve toplam BT skoru açısından karşılaştırıldı.

Bulgular: Toplam BT skoru, mortalite grubunda sağ kalım grubuna göre anlamlı derecede daha yüksekti (10,88±5,67'ye karşı 8,53±4,89, p=0,048). T-BT taramasında bilateral tutulum mortalite grubunda anlamlı olarak daha yüksek bulundu.

Sonuç: Toplam BT skorunun kritik COVID-19 hastalarında sağ kalımı belirlemede prediktif değeri vardır. Hastalığın erken döneminde yapılan T-BT taramalarında bilateral tutulum ve toplam BT skorunun ≥10 olması COVID-19 hastalarında mortalite göstergesi olabilir.

Anahtar Kelimeler: COVID-19, bilgisayarlı toraks tomografisi, mortalite, yoğun bakım

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), also known as coronavirus disease-2019 (COVID-19), originated in December 2019 in Wuhan, China. It has ever since rapidly spread worldwide, causing morbidity and mortality in its way. In March 2020, the World Health Organization designated the COVID-19 outbreak as a pandemic. SARS-CoV-2 primarily targets the respiratory system leading to clinical presentation of patients presenting clinical symptoms ranging from being asymptomatic to severe disease, leading to multi-organ dysfunction and death. In a recent study, patients developing severe disease symptoms often required invasive mechanical ventilation which lead to mortality of 40.8% (1). It is therefore imperative for everyone to diagnose the disease early on which helps in determining the level of care or interventions that could possibly lead to better survival rates. The lung is known to be the first organ affected by the virus in the COVID-19. In the guidelines and recommendations all over the world, if there is clinical and radiological suspicion in diagnosis, individuals with negative polymerase chain reaction (PCR) test have been accepted as COVID-19 cases according to lung computed tomography (CT) findings. In case that direct chest radiography is insufficient for diagnosis or exclusion of COVID-19, non-contrast thoracic CT (T-CT) is frequently used as an imaging method (2). However, in CT scans consistent with viral pneumonia, a specific involvement type or region for COVID-19 has not yet been identified. Despite high sensitivity in the diagnosis of COVID-19 in the screening population, the T-CT images of COVID-19 pneumonia are thought to be non-specific (3). We hypothesized that the type, localization, and intensity of involvement in the lung T-CT of the patients with confirmed COVID-19 has predictive value in determining the survival of critically ill patients in the intensive care unit (ICU). The study aimed to determine the predictive value of the total CT scoring on mortality of patients with a critical COVID-19.

Materials and Methods

Study Design and Population

This study was planned based on retrospective data analysis. The study was approved by the Ethical Review Board of the Kartal Dr. Lütfi Kırdar City Hospital (decision no: 2020/514/180/1, date: 26.06.2020). The records of the critically ill patients, who were admitted to the ICU with a diagnosis of COVID-19 between March 22 and May 22, 2020, were evaluated in the hospital's electronic patient record system. The data of the first 115 patients, whose COVID-19 diagnosis was confirmed with a positive PCR test and for whom T-CT was performed, was taken into analysis. T-CT imaging and PCR swab sampling of all patients were performed during their initial admission to the hospital's emergency department. Patients with lung malignancies, history of lung surgery, tuberculosis, sarcoidosis and similar lung diseases were excluded from the study. Data on age, gender, the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, degree of hypoxemia [PaO_2/FiO_2 (P/F) ratio], predicted mortality rates, length of intubation, length of ICU stay, length of hospital stay and the presence of mortality in the ICU were recorded. Each type of involvement on CT was scored according to the involvement rate for each lung lobe. The total score was calculated separately for each patient. Radiological evaluation was conducted independently by two expert radiologists, each being unaware of the other findings.

Radiological Analysis

All CT examinations to screen for SARS-CoV-2 pneumonia were performed with three scanners (Philips ingenuity with 128 sections and Toshiba Alexion with 16 sections) without the use of contrast agents. The main scanning protocol was as follows: Tubevoltage, 120 kVp; tube current modulation, 120 mA-380 mA; detector configuration, 64×0.625 mm or 16×0.625 mm; rotation time, 0.5-0.7 s; slice thickness, 5 mm; and pitch, 0.984. All images were examined in both lungs [width, 1200 Hounsfield units (HU); level, -700 HU] and mediastinal (width, 350 HU; level, 40 HU) settings. The two radiologists with 10-20 years of experience, without clinical informations, examined the chest images CT independently and scored CT findings. İf there was diffent result, they decided by consensus. Images from CT were examined for the presence and distribution of the following abnormalities described for COVID-19, according to a standardized protocol: (a) baseline ground-glass opacities (GGO), (b) nodules (c) linear compaction (d) crazy paving; (e) consolidations; (f) architectural distortions or traction bronchiectasis; (g) pleural effusion; (h) lymphadenopathy; (i) air bronchogram; (j) tree-in-bud sign; (k) white lung (4). The general anatomic distribution (subsegmental, segmental, lobar) zonal predominance (upper, middle, lower lung; central, middle, or peripheral location), and extent (focal,

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multifocal and diffuse) of lesions were also recorded. The predominant patterns of abnormalities on the high-resolution CT were divided into consolidation, GGOs network structure, and mixed patterns. A mixedpattern can be described as the presence of crazypaving and airbronchogram. Each of the five lungs lobes were interpreted for the degree of involvement.

The total score CT (4) is determined by scoring the percentage of each of the five lobes affected:

0: None
1: <5% involvement
2: 5-25% involvement (Figure 1)
3: 26-49% involvement
4: 50-75% involvement (Figure 2)
5: >75% participation (Figure 3)

The total score CT is the sum of the individual lobar scores and can range from 0 to 25 (maximum). For comparison, patients were divided into two groups: the mortality group and the survival group. The two groups were compared in terms of age and sex distribution, duration of intubation, ICU stay and hospitalisation, presence and distribution of abnormal CT findings, and total score CT.

Statistical Analysis

The SPSS 26.0 program was used for statistical analysis. The values of mean, standard deviation, median lowest, highest, frequency, and ratio were used in the descriptive statistics of the study data. The distribution of variables was analyzed with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to assess quantitative independent data while the qualitative-quantitative independent data was analyzed with the chi-square and Fisher's Exact tests.

Statistical significance was set at a p-value <0.05. The relation of T-CT involvement types and total CT score with mortality was evaluated using Spearman's rank correlation.

Results

Baseline Characteristics

Gender distribution was as follows: 30.4% (n=35) female and 69.6% (n=80) male with the mean age of 66.20±13.84 years (range; 21 to 94 years). The mean age was comparable in both male (65.36±12.57 years) and female (68.11±16.43 years) groups. Some of the patients had severe respiratory failure at presentation and were directly admitted to the ICU. On the other hand, most of the patients were receiving
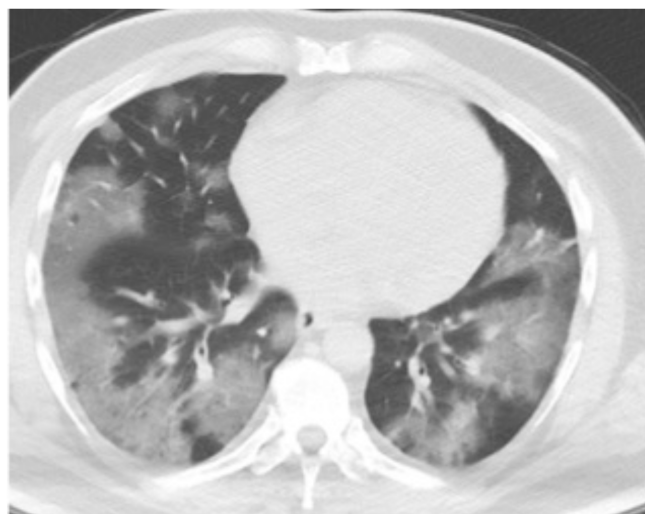

Figure 2. The percentage of lung involvement is approximately 50-75% by visual assessment
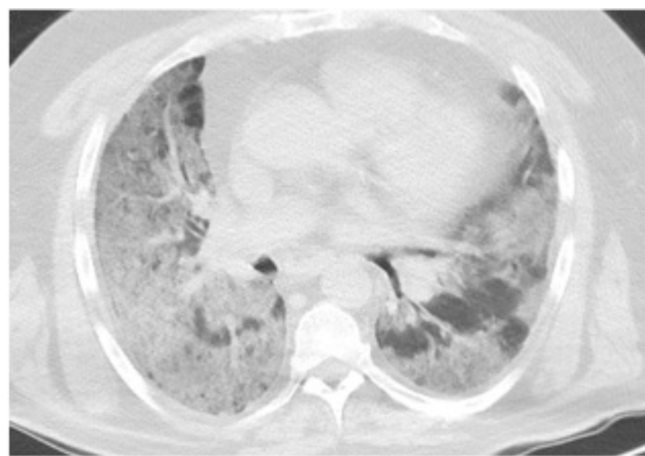

Figure 3. The percentage of lung involvement is approximately >75% involvement by visual assessment

Figure 1. The percentage of lung involvement is approximately 25% by visual assessment

treatment at pandemic clinics, they had to be admitted to the ICU since their condition worsened within 3 to 7 days. In the majority of the patients (101 patients, 87.8%), bilateral involvement was detected. Ninety eight (85.2%) of the 115 patients had multilobar involvement, 92 (80.0%) had peripheral subpleural distribution, and 89 (77.4%) had GGO. While the rate of consolidation was 59.1% (68 patients), the rate of pleural effusion and crazy paving pattern was low [33.9% (39 patients) and 22.6% (26 patients), respectively]. Eighty five (73.9%) of the 115 patients died. The percentage of male patients was higher in the mortality group compared to the survival group (p<0.05) (Table 1). When we compared the data of patients who died with the data of those who survived, the mean age was similar (p>0.05) between the patient groups. Lengh of intubation was significantly shorter and lengh of hospital stay was significantly longer in the survival group compared to the mortality group. APACHE-II scores, predicted mortality rates, and P/F rates were similar between the two groups (Table 2). Additionally, the patients with pleural effusion had a longer intubation time (8.49±7.50 vs 5.33±6.23 day, p=0.009).

Comparison of Imaging Findings Between Mortality and Survival Groups

In the comparison of T-CT findings between the two groups, bilateral involvement was found to be significantly higher in the mortality group (p<0.05), while there was no statistically significant difference between the groups in terms of the rates of multilobar involvement, peripheral subpleural distribution, GGO, crazy paving pattern, consolidation and pleural effusion (p>0.05) (Table 1). However, the total CT score was significantly higher in the mortality group than in the survival group (10.88±5.67 vs 8.53±4.89, p=0.048). Analyzing the age distribution according to the involvement types detected in T-CTs, the mean age of the patients with crazy paving pattern and pleural effusion was found to be significantly higher than that of the patients without such involvement (p=0.015 and p=0.000, respectively) (Table 3). Because some of the CT findings were more common in the given age groups, the mortality, and the survival groups were into 3 age groups (≤50, 51-70, and ≥71 years). The data were re-compared statistically according to these age groups. While the rate of bilateral involvement was found to be significantly higher in the 51-70 age group of the mortality group (p<0.05), there was no statistically significant difference between the groups in term of the other comparison parameters (p>0.05) (Table 4).

When we compared the rate of mortality in terms of the total CT score, we found that the higher the T-CT score was, the greater the mortality rate became. There was a statistically significant positive correlation between the total CT score and mortality (p<0.05). The risk of death significantly increased with the increase of CT score value using an estimated cut-off of ≥5.5. The value of the area under the curve for the total score was 0.617 (95% confidence interval: 0.502-0.733) (Figure 4).

Discussion

The main findings of this study are that the total CT scoring has predictive value in determining the survival of
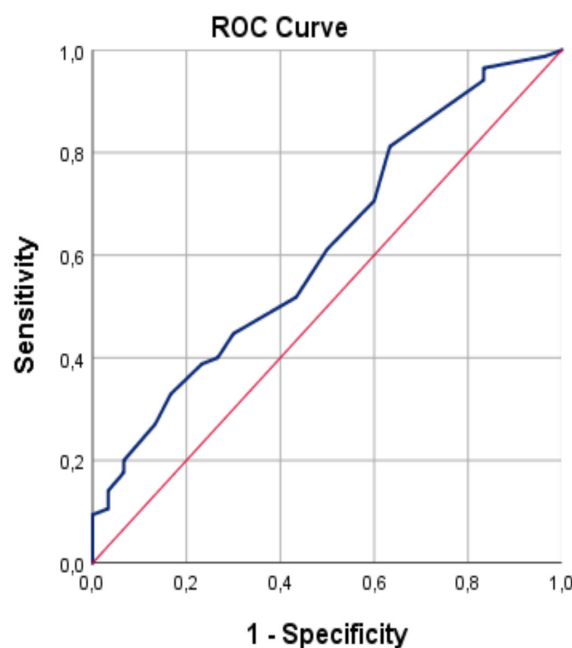
Area Under the Curve

Test Result Variable(s): Total score

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,617	,059	,057	,502	,733

The test result variable(s): Total score has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figure 4. Correlation of total CT score and mortality
CT: Computed tomography, ROC: receiver operating characteristic

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Table 1. Comparison of the two groups for gender and T-CT findings

		Survival n (%)	Mortality n (%)	p
Gender	F	14 (46.7%)	21 (24.7%)	0.025x^2
	M	16 (53.3%)	64 (75.3%)	
Bilateral involvement	(-)	8 (26.7%)	6 (7.1%)	0.005x^2
	(+)	22 (73.3%)	79 (92.9%)	
Multilobar involvement	(-)	7 (23.3%)	10 (11.8%)	0.125x^2
	(+)	23 (76.7%)	75 (88.2%)	
Peripheral subpleural distribution	(-)	8 (26.7%)	15 (17.6%)	0.288x^2
	(+)	22 (73.3%)	70 (82.4%)	
Ground glass opacity	(-)	10 (33.3%)	16 (18.8%)	0.102x^2
	(+)	20 (66.7%)	69 (81.2%)	
Crazy paving pattern	(-)	25 (83.3%)	64 (75.3%)	0.365x^2
	(+)	5 (16.7%)	21 (24.7%)	
Consalidation	(-)	15 (50.0%)	32 (37.6%)	0.237x^2
	(+)	15 (50.0%)	53 (62.4%)	
Pleural effusion	(-)	20 (66.7%)	56 (65.9%)	0.938x^2
	(+)	10 (33.3%)	29 (34.1%)	

F: Female, M: male, (+): present, (-): absent, T-CT: thoracic computed tomography, x^2chi-square test

Table 2. Comparison of the two groups for age, total T-CT score, lengh of intubation, ICU stay, hospital stay, APACHE-II scores, predicted mortality rates and PaO_2/FiO_2 ratio

	Survival Mean ± SD	Mortality Mean ± SD	p
Total T-CT score	8.53±4.89	10.88±5.67	0.048^m
Age (year)	62.50±18.46	67.51±11.65	0.379^m
Lengh of intubation (day)	6.13±8.69	7.87±6.51	0.005^m
Lengh of ICU stay (day)	11.10±7.75	8.49±6.31	0.101^m
Lengh of hospital stay (day)	17.43±7.06	10.29±7.03	0.000^m
APACHE-II score	25.43±6.25	28.69±9.42	0.233^m
Predicted mortality rates (%)	53.26±19.68	59.36±21.53	0.175^u
P/F ratio	149.54±68.10	130.17±64.88	0.167^u

P/F ratio: PaO_2/FiO_2 ratio, ^{m}Mann-Whitney U test, ^{u}unparied t-test, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SD: standard deviation, T-CT: thoracic computed tomography, ICU: intensive care unit

patients with a critical COVID-19 and a total CT score of ≥10 may be indicative of mortality in patients with COVID-19. Besides the T-CT score, bilateral involvement detected on a single scan may be considered as an indicator for the prediction of the risk for mortality. T-CT can be a diagnostic method for patients with suspected COVID-19 especially when PCR test is negative or PCR tests are not available. At the end of sequential PCR test and low-dose CT scan in 610 patients who presented to the emergency department with the suspicion of COVID-19, the sensitivity and specificity of CT for COVID-19 were found to be 86% (150/174) and 99% (408/411), respectively (5). Studies conducted with a low number of patients that were published at the onset of the pandemic reported that COVID-19 pneumonia produces a T-CT pattern resembling organizing pneumonia, peripheral GGOs, and nodular or mass-like GGOs that are mostly bilateral and multilobar. These publications drew attention to the fact that GGOs are especially located in peripheral,

Table 3. Distribution of gender, T-CT findings and mortality by age

		Age (year)			p
		Range	Median	Mean ± SD	
Gender	F	24.0-89.0	72.00	68.11±16.43	0.181[m]
	M	21.0-92.0	65.50	65.36±12.57	
Bilateral involvement	(-)	24.0-89.0	66.00	61.64±18.93	0.538[m]
	(+)	21.0-92.0	67.00	66.23±12.98	
Multilobar involvement	(-)	24.0-89.0	73.00	66.00±19.25	0.463[m]
	(+)	21.0-92.0	66.00	66.23±12.81	
Peripheral subpleural distribution	(-)	27.0-86.0	64.00	63.09±13.84	0.108[m]
	(+)	21.0-92.0	68.50	66.98±13.81	
Ground glass opacity	(-)	27.0-92.0	70.50	66.27±12.72	0.332[m]
	(+)	21.0-89.0	66.00	65.60±14.17	
Crazy paving pattern	(-)	21.0-92.0	66.00	64.36±14.31	0.015[m]
	(+)	55.0-88.0	72.00	72.50±10.01	
Consolidation	(-)	24.0-92.0	69.00	67.04±14.99	0.353[m]
	(+)	21.0-89.0	65.50	65.62±13.07	
Pleural effusion	(-)	21.0-87.0	65.0	62.58±14.07	0.000[m]
	(+)	56.0-92.0	73.00	73.26±10.33	
Mortality	(-)	21.0-92.0	66.00	62.50±18.46	0.379[m]
	(+)	39.0-89.0	67.00	67.51±11.65	

F: Female, M: male, (+): present, (-): absent, [m]Mann-Whitney U test, T-CT: thoracic computed tomography, SD: standard deviation

Table 4. Distribution of T-CT findings and mortality by different age groups

		≤50 years			51-70 years			≥71 years		
		Mortality (n)			Mortality (n)			Mortality (n)		
		(-)	(+)	p	(-)	(+)	p	(-)	(+)	p
Bilateral involvement	(-)	2	2	1.000[F]	3	2	0.044[F]	3	2	0.123[F]
	(+)	-	6		8	44		9	29	
Multilobar involvement	(-)	2	2	1.000[F]	2	2	0.164[F]	3	6	0.692[F]
	(+)	5	6		9	44		9	25	
Peripheral subpleural distribution	(-)	3	1	0.282[F]	3	10	0.700[F]	2	4	1.000[F]
	(+)	4	7		8	36		10	27	
Ground glass opacity	(-)	1	1	1.000[F]	4	10	0.435[F]	6	7	0.136[F]
	(+)	6	7		7	36		6	24	
Crazy paving pattern	(-)	7	8	-	8	36	1.000[F]	9	20	0.719[F]
	(+)	-	-		2	11		3	11	
Consolidation	(-)	4	3	0.619[F]	4	16	0.728[F]	7	14	0.509[F]
	(+)	3	5		6	31		5	17	
Pleural effusion	(-)	1	1	-	7	32	1.000[F]	9	16	1.000[F]
	(+)	-	-		3	15		6	12	

(+): Present, (-): absent, [F]Fisher's Exact test, T-CT: thoracic computed tomography

posterior or lower lung zones (6-8). However, these T-CT findings are not specific for COVID-19 pneumonia and may vary during the disease (8-11). Later on, in comprehensive meta-analyses conducted the frequency of association of vascular enlargement, interlobular septal thickening, and GGO findings with COVID-19 in the presence of bilateral and multilobar involvement was emphasized (11,12). In fact, T-CT involvement may not be observed in the first days when the symptoms first appear. Wang et al. (9) discovered as a result of the evaluation of repeated T-CT scans in patients with COVID-19 that the T-CT score progressed rapidly from the onset of the disease and peaked up on days 6-11. In their retrospective study conducted on 51 patients with COVID-19, Song et al. (10) reported that the findings of consolidation were more prominent in T-CTs taken on day 4 of symptom onset or later compared to T-CTs obtained within the first 4 days. Therefore, Song et al. (10) concluded that the signs of consolidation signify the disease progression and can be used as a guiding tool for proper treatment protocols or interventions.

The T-CT scans of the patients evaluated in our study were obtained at admission, and the rates of consolidation in the evaluated T-CTs were lower than the other types of involvement, which is consistent with the definition for the early stage of the disease. It was reported in a comprehensive review published in 2021 that although GGOs and vasodilation are common CT changes, severe disease is mostly associated with CT findings such as interlobular septal thickening, traction bronchiectasis, reticulation, pleural effusion, consolidation, and lymphadenopathy (11). Also, these differences are closely associated with involvement at different stages of the disease (13). However, as T-CTs were not repeated during the ICU stay of our patients, it was not possible to follow up how this rate changed in later stages of the disease. Nevertheless, according to our results, the rate of bilateral involvement was higher in the early T-CTs of the patients that died. Wang et al. (9) findings stating that patients with unilateral involvement were discharged within one month of treatment support our results. We believe that since repeating T-CT scanning especially for patients with COVID-19 treated at ICUs would be impractical and financially troublesome, the T-CT scoring obtained at admission to the ICU as in our study is valuable. The total CT scoring system was previously used to define and grade idiopathic pulmonary fibrosis, and it has also been used in T-CT examinations of patients with COVID-

19 as well as to define the pulmonary complications of the SARS-CoV virus in the SARS pandemic (4,14). In their retrospective study investigating the determinants of fatality in COVID-19 patients, Li et al. (15) reported that in T-CT scans obtained within the first week of symptom onset, the total severity score and the number of lung lobes affected were significantly higher in patients who died. In addition, the involvement of more than 5 lobes was reported to be associated with serious disease in a comprehensive review published later (11). Li et al. (15) revealed that a total severity score of ≥15 on T-CTs taken within the first week from the onset of the symptoms is a determinant for mortality. Also, in another study, a CT score of ≥18 was associated with mortality (16). Our findings are consistent with Li et al. (15) study. In this study, we also found that the rate of bilateral involvement was significantly higher in the patients who died. On the other hand, our results revealed that GGO, crazy paving pattern, consolidation, and pleural effusion, and age distribution did not differ significantly between the mortality and survival groups, contrary to Li et al. (15) where these rates and the average age were significantly higher in the mortality group. However, different from our study, all patients requiring intensive care follow-up in Li et al. (15) were in critical condition and CTs consisted of CTs taken within the first week of follow-up. The CT images were not obtained at different time points, but during admission to the hospital. In our study, it was determined that the intubation time was significantly longer and the hospital stay was significantly shorter in the mortality group than in the survival group. Similarly, as it is expected, the duration of intubation was also longer in patients with bilateral involvement compared to the others. When CT scanning is performed on every patient or every critically ill patient, who requires follow-up in the ICU, it can give clues about the course of the disease and prevent delayed intubation. In our study, we concluded that patients who deteriorate rapidly and have invasive mechanical ventilation requirements in the early period can be determined by T-CT scoring at the admission phase and aggressive treatment can be started when as soon as necessary. We found the total CT score cut-off value for the prediction of mortality to be 5.5. As different studies reported various cut-off values, it seems to be impossible to mention an agreed value (15,16). This may be a result of the differences in T-CT scoring. What is important is that every institution reveals its T-CT scoring and cut-off value. In this way, it may be possible to predict the mortality risk in

patients with T-CT scores above a given value and to organize close monitoring and even ICU follow-up in the early period. Our findings reveal that although there is no universally accepted cut-off value, total CT score is a useful criterion in determining the prognosis of COVID-19 patients with pulmonary involvement. There are several limitations of this study. The first is that it is a retrospective study. The second limitation is the ignorance of the co-morbidity situations of the groups. Because the number of young patients with low co-morbidity was low, they were not suitable for statistical evaluation. Therefore, patients with younger age and low co-morbidity could be compared with the other patients. The third limitation is that the relationship between T-CT score and ICU admission was not investigated. The strength of the study, on the other hand, is that it includes 115 well-documented patients whose findings were evaluated by two experienced radiologists.

Conclusion

Bilateral involvement in T-CT scans performed in the early period and a total CT score of ≥10 may be indicative of mortality in COVID-19 patients. We believe that in patients with COVID-19 pneumonia, performing T-CT imaging at first admission to the hospital and calculating the T-CT score may help to predict the progression of the cases and decrease mortality by interning these patients in ICU in the early period of disease and providing them close monitoring and early aggressive therapy. We concluded that thoracic CT is a valuable tool for diagnosis and risk stratification of COVID-19 patients both in the emergency department and ICU.

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