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The Relationship Between Chest Computed Tomography Severity Scores and Demographic Features, Laboratory Parameters and Mortality in Patients with COVID-19

COVID-19'lu Hastaların Toraks Bilgisayarlı Tomografi Şiddet Skorları ile Demografik Özellikleri, Laboratuvar Parametreleri ve Mortaliteleri Arasındaki İlişki

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ABSTRACT

Aim: We aimed to investigate the relationship between chest computed tomography-severity score (CT-SS) and demographic and laboratory findings and mortality in Coronavirus disease-2019 (COVID-19) patients.

Materials and Methods: Our study was a single-center retrospective analysis of 162 patients (aged ≥18 years) with COVID-19. We included laboratory-confirmed COVID-19 patients between October 2020 and April 2021. Chest CT imagings, laboratory findings, and demographic data were collected at admission. CT-SS was calculated using a visual semi-quantitative scoring system (total score 0-25). We divided the patients into three subgroups based on chest CT-SS, as mild (0-7), moderate (8-17) and severe (>18).

Results: The mild group consisted of 91 patients (56.2%) with a median CT-SS value of 2 [interquartile range (IQR) 0-5], the moderate group consisted of 65 patients (40.1%) with a median CT-SS value of 11 (IQR 9-12), and the severe group was composed of 6 patients (3.7%) with a median CT-SS value of 19.5 (IQR 18-24). We found statistically significant relationships between high CT-SS and lymphocytopenia (p=0.001), increased C-reactive protein (p<0.001), procalcitonin (p<0.001), lactate dehydrogenase (p<0.001), serum creatinine (p<0.001), D-dimer (p<0.001), prolonged prothrombin time levels (p=0.006), history of chronic obstructive pulmonary disease (p=0.014), chronic renal disease (p=0.001), and cerebrovascular disease (p=0.029) in chi-square test. In addition, high CT-SS was statistically correlated with high mortality risk (p<0.001).

Conclusion: There was a relationship between high CT-SS and high mortality, inflammatory and anticoagulant laboratory markers, and some comorbidities in COVID-19 patients. Evaluation of CT-SSs and risk factors of demographic characteristics and laboratory findings provide useful prognostic information about the survival of COVID-19 patients.

Keywords: COVID-19, computed tomography, pneumonia, mortality

ÖZ

Amaç: Çalışmamızda Koronavirüs hastalığı-2019 (COVID-19) hastalarında toraks bilgisayarlı tomografi-şiddet skoru (BT-ŞS) ile demografik ve laboratuvar verileri ve ölüm oranları arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamız, COVID-19'lu 162 hastanın (≥18 yıl) tek merkezli retrospektif analiziydi. Ekim 2020 ile Nisan 2021 arasında laboratuvarca doğrulanmış COVID-19 hastaları çalışmaya dahil edildi. Başvuru sırasındaki toraks BT görüntülemeleri, laboratuvar bulguları ve demografik verileri toplandı. BT şiddet skoru, görsel bir yarı nicel puanlama sistemi kullanılarak hesaplandı (toplam skor 0-25). Hastalar toraks BT-ŞS'sine göre üç alt gruba ayrıldı; hafif (0-7), orta (8-17) ve şiddetli (>18).

Bulgular: Ortanca BT-ŞS değeri 2 [çeyrekler arası aralık (IQR) 0-5] olan 91 hasta hafif grubu (%56,2), ortanca BT-ŞS değeri 11 (IQR 9-12) olan 65 hasta (%40,1) orta grubu ve ortanca BT-ŞS değeri 19,5 (IQR 18-24) olan 6 hasta (%3,7) şiddetli grubu oluşturdu. Bu çalışmada, ki-kare testinde yüksek BT-ŞS ile lenfositopeni (p=0,001), artmış C-reaktif protein (p<0,001), prokalsitonin (p<0,001), laktat dehidrogenaz (p<0,001), serum kreatinin

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(p<0,001), D-dimer düzeyleri (p<0,001), uzamış protrombin zamanı düzeyleri (p=0,006), kronik obstrüktif akciğer hastalığı (p=0,014), kronik böbrek hastalığı (p=0,001) ve serebrovasküler hastalık (p=0,029) öyküsü arasında istatistiksel olarak anlamlı ilişkiler bulundu. Ayrıca yüksek BT-ŞS, yüksek mortalite riski ile istatistiksel olarak ilişkiliydi (p<0,001).

Sonuç: COVID-19 hastalarında yüksek toraks BT-ŞS ile yüksek mortalite, enflamatuvar ve antikoagülan laboratuvar belirteçleri ve bazı komorbiditeler arasında bir ilişki vardı. BT şiddet skorlarının, demografik özelliklerin ve laboratuvar bulgularının risk faktörlerinin değerlendirilmesi, COVID-19 hastalarının sağkalımı hakkında yararlı prognostik bilgiler sağlamaktadır.

Anahtar Kelimeler: COVID-19, bilgisayarlı tomografi, pnömoni, mortalite

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is an infectious disease caused by Severe acute respiratory syndrome-Coronavirus-2, which was firstly reported in Wuhan, China[1]. Most COVID-19 patients have a good prognosis and mild symptoms. However, in some patients, severe pneumonia, pulmonary edema, Acute respiratory distress syndrome (ARDS), multiple organ failure, and death were observed[2].

A specific viral nucleic acid test, real-time reverse transcriptase-polymerase chain reaction (RT-PCR) used for the diagnosis of COVID-19, was rapidly produced[3]. The RT-PCR test is standard for the diagnosis of COVID-19 but may give a false-negative result in some cases. False-negative RT-PCR results may depend on the early stages of the disease, possibly due to insufficient viral specimens in the sample or technical problems during nucleic acid extraction[4,5]. Based on past clinical information, chest computed tomography (CT) imaging can show abnormalities before RT-PCR testing. Currently, high-resolution CT has become one of the main screening methods for diagnosing and evaluating disease severity[6]. The typical chest CT findings in COVID-19 pneumonia are bilateral, peripheral, and basal predominant ground-glass opacities (GGOs) with or without consolidation and bronchovascular thickening[7].

In our study, the severity of lung involvement was visually scored according to the method proposed by Pan et al.[8]. We purposed to investigate the correlation between chest CT-severity score (SS) and age, gender, comorbidities, laboratory findings, and mortality in patients with COVID-19. As a result of our study, we aimed to detect high-risk COVID-19 patients who would require intensive treatment and might provide a risk stratification model for such patients.

MATERIALS AND METHODS

This study was approved by the Ethical Committee of Kanuni Training and Research Hospital and by the Ministry of Health of the Republic of Turkey and it was conducted according to the Declaration of Helsinki and Good Clinical Practice (date: 12.11.2020, no: 2020/68), and the requirement for informed consent was waived.

Study Population and Data Collection

Our study was a single-center retrospective analysis conducted on an original cohort of 162 patients with COVID-19, who underwent chest CT scans in the Radiology Department of Kanuni Training and Research Hospital between October 2020 and April 2021. We included only laboratory-confirmed patients determined by positive RT-PCR in samples acquired from oropharyngeal and nasopharyngeal sites in accordance with the World Health Organization interim guidelines. RT-PCR tests were repeated in patients with a high clinic and radiologic suspicion of COVID-19 when the initial PCR test was negative. We excluded the patients under 18 years of age or who had no chest CT scan.

We collected the data for retrospective analysis including demographic characteristics, comorbidities, laboratory findings, and chest CT imaging obtained at the time of admission. Chest CTs were performed on patients with fever, dry cough, respiratory distress, abnormal laboratory findings, and positive PCR test results. Chest CT scans of all patients were performed within 24 hours at the latest after admission to the hospital.

All patients underwent blood tests including complete blood count, kidney and liver function tests, troponin, D-dimer, prothrombin time (PT), and partial thromboplastin time (PTT), international normalized ratio (INR), C-reactive protein (CRP) and procalcitonin. We analyzed the laboratory results at the time of admission to the hospital.

CT Protocol

All patients underwent chest CT examinations on two multidetector CT scanners (16-slice Somatom Sensation; Siemens Healthineers or 128-slice GE Healthcare Computed Tomography Revolution EVO System). The non-contrast scans were performed with the following parameters: tube voltage=120 kV; tube current=70-280 automatic milliamperes; helical pitch=1.375; slice thickness=5 mm and interval=5 mm (128- slice GE Healthcare Computed Tomography Revolution EVO System) or tube voltage=130 kV; tube current=70-114 automatic milliamperes; helical pitch=1; slice thickness=5 mm and interval=5 mm (16- slice Somatom Sensation; Siemens

Healthineers). Images were reconstructed with a 1.25 mm slice thickness. All chest CT scans were assessed at a lung window of 1200 WW and -600 WL and a mediastinal window of 400 WW and 40 WL.

Image Analysis

A radiologist with more than 14 years of experience in chest CT imaging performed the CT image analysis in a standard clinical picture archiving and diagnostic system (PACS) workstation, blinded to the clinical data and laboratory indicators. The involvement of each pulmonary lobe was recorded and the 25 Point CT severity scores were calculated by using a semi-quantitative CT severity scoring system visually[8-10]. This scoring system depends on visual evaluation of pulmonary involvement based on the area in each of 5 lobes. Each lobe was scored from 0 to 5 as: 0, no involvement; 1, <5% involvement; 2, 25% involvement; 3, 26-49% involvement; 4, 50-75% involvement; 5, >75% involvement. Then, the total CT score was calculated by the sum of the CT scores of 5 lobes ranging from 0 (none) to 25 (maximum). Considering pulmonary involvement, we divided the COVID-19 patients into three subgroups based on the chest CT score, as mild (total severity score of less than 7), moderate (total severity score of 8-17) (Figure 1), or severe (18 and more), which was used by Saeed et al.[9].

Statistical Analysis

The study sample size was determined as 122 using the G-power program by taking impact size 0.30, α=0.05, power (1-β)=0.85 at a confidence level. A total of 162 were reached. Statistical analyses were performed by using IBM Statistical Package for the Social Sciences Statistics for Windows, version 25.0 (IBM Corp. Released 2017. Armonk, NY). Categorical variables were defined as frequency and percentage; continuous variables were defined as the mean±standard deviation or median [interquartile range (IQR)]. The conformity of the variables to the normal distribution was examined using the Kolmogorov-Smirnov. The Kruskal-Wallis and Mann-Whitney U tests were employed to compare the non-normally distributed variables according to the CT-SS groups. The chi-square test was used to determine the relationship between CT-SS groups and laboratory and demographic characteristics. The Fisher's test was used when the values displayed in the cells did not meet the assumptions of the chi-square test. The statistical significance level was accepted as 0.05 in the study.

RESULTS

Demographic Features

A total of 162 patients, including 69 male (42.6%) and 93 female (57.4%), were enrolled in the study. The mean age of total patients was 54.3±17.29 (ranging from 18 to 97) years. The most affected age group was the 61-70-year age group (37 patients; 22.8%) followed by the 51–60-year age group (35 patients; 21.6%), then the 41-50-year age group (28 patients; 17.3%) and the >70-year age group (26 patients; 16%).

The most common comorbidities were hypertension (HT) (77/162; 47.5%), diabetes mellitus (DM) (45/162; 27.8%), atherosclerotic heart disease (26/162; 16%), and congestive heart failure (16/162; 9.9%). Of the total 162 cases, 151 (93.2%) were discharged, and 11 (6.8%) died due to COVID-19 at hospital (Table 1).

Laboratory Parameters

In our study, most of the patients (109, 67.3%) had high CRP

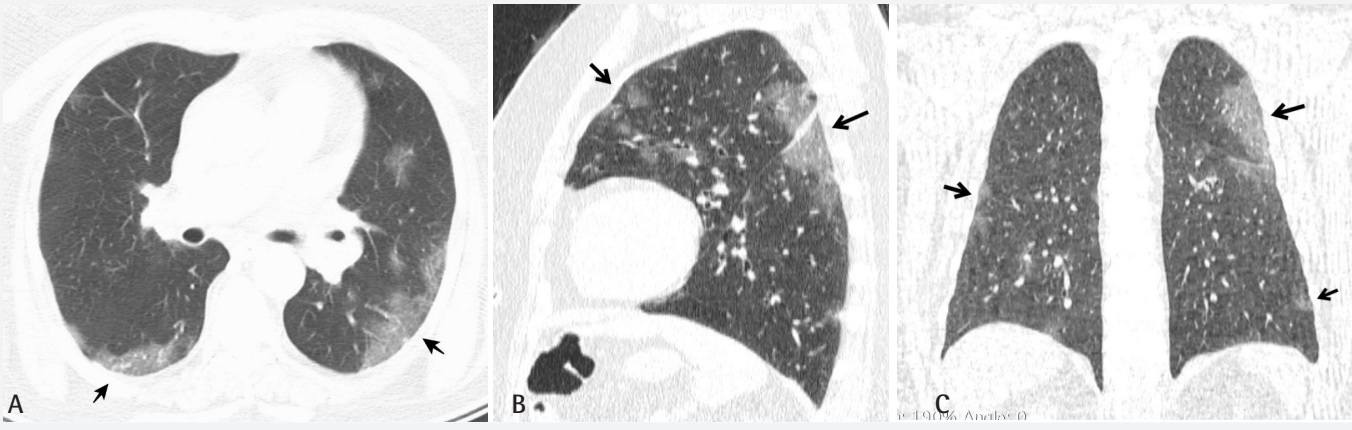

Figure 1. A 76-year-old woman with confirmed COVID-19 had a history of hypertension. Her CT-SS was calculated as 10 (moderate group) in CT that was performed at admission. She had got some abnormal laboratory findings (*). Axial (A), sagittal (B) and coronal (C) thin sections of unenhanced chest CT scans show bilateral multifocal rounded and peripheral ground-glass opacities (black arrows). She was discharged after 10 days of medical treatment in the service of the hospital (*elevated LDH, CRP values)

COVID-19: Coronavirus disease-2019, LDH: Lactate dehydrogenase, CRP: C-reactive protein, CT-SS: Computed tomography-severity score

values. Laboratory results showed elevated D-dimer in 42 (25.9%) patients, LDH levels in 62 (38.3%) patients, prolonged PT in 20 (12.3%) patients, PTT in 7 (4.3%) patients, increased INR in 14 (8.6%) patients, high troponin levels in 8 (4.9%) patients, lymphocytopenia in 15 (9.3%) patients, and anemia in 33 (20.4) patients (Table 1).

Chest CT Severity Scores

One hundred-twenty six (77.8%) COVID-19 confirmed cases had pneumonia and 36 (22.2%) COVID-19 confirmed cases had no pneumonia in their chest CT imaging at the time of admission. CT severity scores ranged from 0 to 24, with a mean value of 6.66±5.50 and a median value of 6 (IQR 1-11). The mild group (CT-SS of 0-7) consisted of 91 patients (56.2%), the moderate group (CT-SS of 8-17) consisted of 65 patients (40.1%) whereas the severe group (CT-SS of 18-25) was composed of 6 patients (3.7%). The median CT-SS value was 2 (IQR 0-5) for the mild group, 11 (IQR 9-12) for the moderate group, and 19.5 (IQR 18-24) for the severe group (Table 2).

Table 1. Demographic characteristics, comorbidities and laboratory findings of our study population at admission

Total patients=162	n (%)
Demographic information	
Age Mean±SD	54.3±17.29
Sex	
Female	93 (57.4%)
Male	69 (42.6%)
Comorbidities	
Hypertension	77 (47.5%)
Diabetes mellitus	45 (27.8%)
Atherosclerotic heart disease	26 (16%)
Congestive heart failure	16 (9.9%)
COPD	11 (6.8%)
Cerebrovascular disease	10 (6.2%)
Malignancy	8 (4.9%)
Chronic renal disease	7 (4.3%)
Chronic liver disease	3 (1.9%)
Laboratory findings	
Leukocytopenia <4000/mm^3	6 (3.7%)
Lymphocytopenia <800/mm^3	15 (9.3%)
Anemia Hgb <12 g/dL	33 (20.4%)
ALT >50 U/L	23 (14.2%)
AST >50 U/L	11 (6.8%)
Cr >1.1 mg/dL	6 (3.7%)
LDH >220 U/L	62 (8.3%)
CRP >5 mg/dL	109 (67.3%)
PT >12.6 sec	20 (12.3%)
PTT >48 sec	7 (4.3%)
INR >1.2	14 (8.6%)
Troponin >11 ng/L	8 (4.9%)
D-dimer >550 ng/mL	42 (25.9%)
Procalcitonin >0.5 ng/mL	4 (2.5%)

SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, Hgb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Cr: Serum creatinine, LDH: Lactate dehydrogenase, CRP: C-reactive protein, PT: Prothrombin time, PTT: Partial thromboplastin time, INR: International normalized ratio

Pathological involvement was most common in the inferior lobes, in the right lower lobe in 113 patients (69.8%) and in the left lower lobe in 114 patients (70.4%). The right upper lobe was involved in 97 patients (59.9%), the right middle lobe was involved in 99 patients (61.1%), left upper lobe was involved in 110 patients (67.9%). The frequency of each lobe involvement of the CT-SS groups is shown in Table 3.

Correlation between CT Severity Score and Age, Gender, Laboratory Findings, Comorbidities, and Mortality

Age and Gender

There were 91/162 patients with 56 females in the mild group, 65/162 patients with 35 females in the moderate group, and 6/162 patients with 2 females in the severe group. The mean age was 53.15±16.37 years in the mild group, 55.28±18.52 years in the moderate group, and 61.17±17.88 years in the severe group. There was no statistical difference between the groups in terms of age (p=0.463) (Table 4).

Our results showed no significant statistical difference between CT-SS groups and gender (p=0.302). Also, there was no statistical correlation between age and CT-SS in the Spearman's test [correlation coefficient (r)=0.101; p=0.200].

Laboratory Results

In the current study, we found statistically significant relationships between CT-SS and lymphocytopenia (p=0.001), increased CRP (p<0.001), procalcitonin (p<0.001), LDH (p<0.001), Cr (p<0.001), alanine aminotransferase (ALT) (p=0.017) and aspartate aminotransferase (AST) (p<0.001), troponin (p=0.028), D-dimer levels (p<0.001) and prolonged PT levels (p=0.006) in the chi-square test (Table 5). A statistically significant difference was found by comparing groups 1-3 with regard to high procalcitonin, D-dimer, Cr, AST levels, prolonged PT levels, and lymphocytopenia. Also, a statistically significant difference was found by comparing groups 1-2 in terms of high LDH, CRP and D-dimer levels in the Pearson chi-square or Fisher's tests.

Comorbidities

In the mild group; 45/91 (49.5%) patients had a history of HT, 26/91 (28.6%) had DM, 13/91 (14.3%) had atherosclerotic heart disease, and 7/91 (7.7%) had congestive heart failure.

In the moderate group; 27/65 (41.5%) patients had a history of HT, 17/65 (26.2%) had DM, 12/65 (18.5%) had atherosclerotic heart disease, 8/65 (12.5%) had congestive heart failure, 9/65 (12.3%) had Chronic obstructive pulmonary disease (COPD), and 8/65 (12.3%) patients had cerebrovascular disease.

In the severe group; 5/6 (83.3%) patients had a history of HT, 2/6 (33.3%) had DM, 1/6 (16.7%) had atherosclerotic heart disease, 2/6 (33.3%) had chronic renal disease, 1/6 (16.7%) had congestive heart failure, and 1/6 (16.7%) patient had malignities.

Statistically significant relationships were found between high CT score and history of COPD (p=0.014), chronic renal disease (p=0.001) and cerebrovascular disease (p=0.029) in the chi-square test (Table 6). A statistically significant difference was found when the groups 1-2 were compared in terms of the history of COPD (p=0.008) and cerebrovascular disease (p=0.016) and groups 1-3 in terms of the history of chronic renal disease (p=0.009) in the Fisher's test.

Mortality

In our study, a total of 151 (93.2%) patients are alive, and 11 (6.8%) patients died due to COVID-19. Among the mild group, 91 (100%) patients are alive, and 0 patient died. In the moderate group, 77 (87.7%) patients are alive, and 8 (12.3%) died. In the severe group, 3 (50%) patients are alive, and 3 (50%) died (Figure 2). In the current study, a statistically significant correlation was found between the high CT-SS and the high risk for mortality (p<0.001) in the chi-square test.

Table 2. Frequency of patients (n) and mean±standard deviation, median-IQR values of chest CT severity scores of each group

Severity subgroups	n	Mean	Standard deviation	Minimum	Maximum	Percentiles		
						50th (Median)	25th	75th
Mild group (CT-SS 0-7)	91	2.62[c]	2.59	0	7	2	0	5
Moderate group (CT-SS 8-17)	65	11.05[b]	2.32	8	16	11	9	12
Severe group (CT-SS >18)	6	20.50[a]	2.81	18	24	19.5	18	24
Total	162	6.66	5.50	0	24	1	6	11

[a,b,c] Values in column with different superscripts indicate significant difference (p<0.01).

CT-SS: Computed tomography-severity score, IQR: Interquartile range

Table 3. Frequency of each lobe involvement on chest CT imaging of CT-SS groups

					Total	p value
		Group 1 n=91 (%)	Group 2 n=65 (%)	Group 3 n=6 (%)	n=162	
Right upper lobe involvement	Present	26 (28.6)	65 (100)	6 (100)	97 (59.9)	<0.001
	Absent	65 (71.4)	0 (0)	0 (0)	65 (40.1)	
Right middle lobe involvement	Present	30 (33)	63 (96.9)	6 (100)	99 (61.1)	<0.001
	Absent	61 (67)	2 (3.1)	0 (0)	63 (38.9)	
Right lower lobe involvement	Present	42 (46.2)	65 (100)	6 (100)	113 (69.8)	<0.001
	Absent	49 (53.8)	0 (0)	0 (0)	49 (30.2)	
Left upper lobe involvement	Present	40 (44)	64 (98.5)	6 (100)	110 (67.9)	<0.001
	Absent	51 (56)	1 (1.5)	0 (0)	52 (32.1)	
Left lower lobe involvement	Present	43 (47.3)	65 (100)	6 (100)	114 (70.4)	<0.001
	Absent	48 (52.7)	0 (0)	0 (0)	48 (29.6)	

CT-SS: Computed tomography-severity score, IQR: Interquartile range

Table 4. Comparison of the CT-SS groups in terms of age

CT-SS groups	n	Mean	Standard deviation	Minimum	Maximum	95% confidence interval for mean		p value
						Lower bound	Upper bound	
Mild group	91	53.15	16.37	18	85	49.75	56.56	0.463
Moderate group	65	55.28	18.52	19	97	50.69	59.87	
Severe group	6	61.17	17.88	28	81	42.4	79.93	
Total	162	54.3	17.29	18	97	51.62	56.99	

CT-SS: Computed tomography-severity score

A statistically significant difference was found by comparing groups 1-2 and groups 1-3 in terms of mortality in the Fisher's test (p<0.001).

DISCUSSION

The purpose of this study was to investigate the relationship between chest CT-SS and age, gender, comorbidities, laboratory findings, and mortality in COVID-19 patients. We found a statistically significant relationship between high CT-SS and high mortality rate. Due to the high comorbidity rate in the study population and the two pregnant patients who died due to COVID-19, the mortality in our study is above the Turkey average.

Although RT-PCR is thought to be the gold standard for the diagnosis of COVID-19 infection, it was reported that chest CT was diagnostic in cases with false-negative RT-PCR results. Chest CT is not used only for diagnosis, but also for providing important information in monitoring disease progression and evaluating medical treatment efficacy[11]. Ai et al.[12] reported that the sensitivity of chest CT imaging in indicating COVID-19 infection was 97%, the specificity was 25% with RT-PCR results as the reference standard in 1014 patients. Aslan et al.[13] reported that the sensitivity and specificity of the initial CT scan were 90.4% and 64.2% respectively in the study of 250 patients, finally diagnosed with COVID-19.

Different chest CT scoring systems have been used in previous studies on COVID-19 patients. Chest CT-SS can be assessed using software that describes the percentage of lung volumes affected or a visual scoring for each lobe[14-16]. In some studies, the calculated chest CT severity score visually ranged from 0 to

Table 5. Comparison of CT-SS in terms of laboratory findings

		Group 1 n=91 (%)	Group 2 n=65 (%)	Group 3 n=6 (%)	Total n=162	p value
Leukocytopenia <4000/mm^3	Present	5 (5.5)	1 (1.5)	0 (0)	6 (3.7)	0.386
	Absent	86 (94.5)	64 (98.5)	6 (100)	156 (96.3)	
Lymphocytopenia <800/mm^3	Present	4 (4.4)	8 (12.3)	3 (50)	15 (9.3)	**0.001**
	Absent	87 (95.6)	57 (87.7)	3 (50)	147 (90.7)	
Anemia Hgb <12 g/dL	Present	13 (143)	17 (26.2)	3 (50)	33 (20.4)	**0.036**
	Absent	78 (85.7)	48 (73.8)	3 (50)	129 (79.6)	
ALT >50 U/L	Present	9 (9.9)	11 (16.9)	3 (50)	23 (14.2)	**0.017**
	Absent	82 (90.1)	54 (83.1)	3 (50)	139 (85.8)	
AST >50 U/L	Present	3 (3.3)	5 (7.7)	3 (50)	11 (6.8)	**<0.001**
	Absent	88 (96.7)	60 (92.3)	3 (50)	151 (93.2)	
Cr >1.1 mg/dL	Present	1 (1.1)	3 (4.6)	2 (33.3)	6 (3.7)	**<0.001**
	Absent	90 (98.9)	62 (95.4)	4 (66.7)	156 (96.3)	
LDH >220 U/L	Present	25 (27.5)	34 (52.3)	3 (50)	62 (38.3)	**0.006**
	Absent	66 (72.5)	31 (47.7)	3 (50)	100 (61.7)	
CRP >5 mg/dL	Present	48 (52.7)	56 (86.2)	5 (83.3)	109 (67.3)	**<0.001**
	Absent	43(47.3)	9 (13.8)	1 (16.7)	53 (32.7)	
PT >12.6 sec	Present	7 (7.7)	10 (15.4)	3 (50)	20 (12.3)	**0.006**
	Absent	84 (92.3)	55 (84.6)	3 (50)	142 (87.7)	
PTT >48 sec	Present	4 (4.4)	2 (3.1)	1 (16.7)	7 (4.3)	0.293
	Absent	87 (95.6)	63 (96.9)	5 (83.3)	155 (95.7)	
INR >1.2	Present	5 (5.5)	7 (10.8)	2 (33.3)	14 (8.6)	**0.046**
	Absent	86 (94.5)	58 (89.2)	4 (66.7)	148 (91.4)	
Troponin >11 ng/L	Present	1 (1.1)	6 (9.2)	1 (16.7)	8 (4.9)	**0.028**
	Absent	90 (98.9)	59 (90.8)	5 (83.3)	154 (95.1)	
D-dimer >550 ng/mL	Present	15 (16.5)	22 (33.8)	5 (83.3)	42 (25.9)	**<0.001**
	Absent	76 (83.5)	43 (66.2)	1 (16.7)	120 (74.1)	
Procalcitonin >0.5 ng/mL	Present	0 (0)	2 (3.1)	2 (33.3)	4 (2.5)	**<0.001**
	Absent	91 (100)	63 (96.9)	4 (66.7)	158 (97.5)	

CT-SS: Computed tomography-severity score, Hgb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Cr: Serum creatinine, LDH: Lactate dehydrogenase, CRP: C-reactive protein, PT: prothrombin time, PTT: Partial thromboplastin time, INR: International normalized ratio

Table 6. Comparison of CT-SS groups in terms of demographic data and comorbidities

		Group 1 (mild) n (%)	Group 2 (moderate) n (%)	Group 3 (severe) n (%)	Total	p value
Gender	Female	56 (61.5)	35 (53.8)	2 (33.3)	93 (57.4)	0.302
	Male	35 (38.5)	30 (46.2)	4 (66.7)	69 (42.6)	
Survival	Ex	0 (0)	8 (12.3)	3 (50)	11 (6.8)	**<0.001**
	Alive	91 (100)	57 (87.7)	3 (50)	151 (93.2)	
Hypertension	Present	45 (49.5)	27 (41.5)	5 (83.3)	77 (47.5)	0.125
	Absent	46 (50.5)	38 (58.5)	1 (16.7)	85 (52.5)	
Diabetes mellitus	Present	26 (28.6)	17 (26.2)	2 (33.3)	45 (27.8)	0.902
	Absent	65 (71.4)	48 (73.8)	4 (66.7)	117 (72.2)	
Atherosclerotic heart disease	Present	13 (14.3)	12 (18.5)	1 (16.7)	26 (16)	0.782
	Absent	78 (85.7)	53 (81.5)	5 (83.3)	136 (84)	
Congestive heart failure	Present	7 (7.7)	8 (12.3)	1 (16.7)	16 (9.9)	0.541
	Absent	84 (92.3)	57 (87.7)	5 (83.3)	146 (90.1)	
COPD	Present	2 (2.2)	9 (13.8)	0 (0)	11 (6.8)	**0.014**
	Absent	89 (97.8)	56 (86.2)	6 (100)	151 (93.2)	
Chronic renal disease	Present	1 (1.1)	4 (6.2)	2 (33.3)	7 (4.3)	**0.001**
	Absent	90 (98.9)	61 (93.8)	4 (66.7)	155 (95.7)	
Malignancy	Present	3 (3.3)	4 (6.2)	1 (16.7)	8 (4.9)	0.289
	Absent	88 (96.7)	61 (93.8)	5 (83.3)	154 (95.1)	
Chronic liver disease	Present	2 (2.2)	1 (1.5)	0 (0)	3 (1.9)	0.901
	Absent	89 (97.8)	64 (98.5)	6 (100)	159 (98.1)	
Cerebrovascular disease	Present	2 (2.2)	8 (12.3)	0 (0)	10 (6.2)	**0.029**
	Absent	89 (97.8)	57 (87.7)	6 (100)	152 (93.8)	

COPD: Chronic obstructive pulmonary disease, CT-SS: Computed tomography-severity score

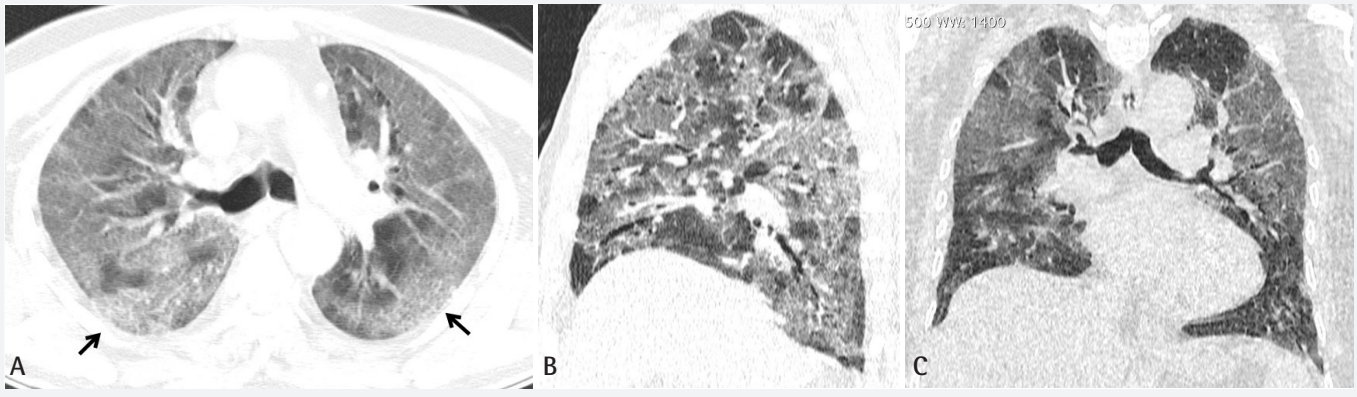

Figure 2. A 70-year-old man with confirmed COVID-19 had a history of prostate cancer and renal failure. His CT-SS was calculated as 24 (severe group) in CT that was performed at admission. He had got many abnormal laboratory findings (*). Axial (A), sagittal (B) and coronal (C) thin sections of unenhanced chest CT scans show bilateral extensive ground-glass opacities with interlobular and intralobular septal thickening (black arrows). The patient was transferred to the ICU on the same day of the CT scan and died 10 days after this scan (*lymphocytopenia, elevated AST, ALT, LDH, Cr, CRP, D-dimer, ferritin, procalcitonin, troponin, prolonged PT, INR values)

COVID-19: Coronavirus disease-2019, LDH: Lactate dehydrogenase, CRP: C-reactive protein, PT: Prothrombin time, CT-SS: Computed tomography-severity score, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Cr: Serum creatinine, LDH: Lactate dehydrogenase, INR: International normalized ratio, ICU: Intensive care unit

20[14-17]. We used the 25-point CT severity scoring system that was used in the literature[8-10].

Zhou et al.[18] reported that the total CT scores in COVID-19 patients who died were significantly higher than in those

who recovered. Francone et al.[10] reported that CT-SS was significantly higher in critical and severe patients than in mild ones. They reported that CT-SS ≥18 predicted a high patient mortality in COVID-19 patients. So, in the current study, the CT-SS ≥18 was accepted as the cut-off value between moderate and severe groups. We separated the patients into 3 groups as

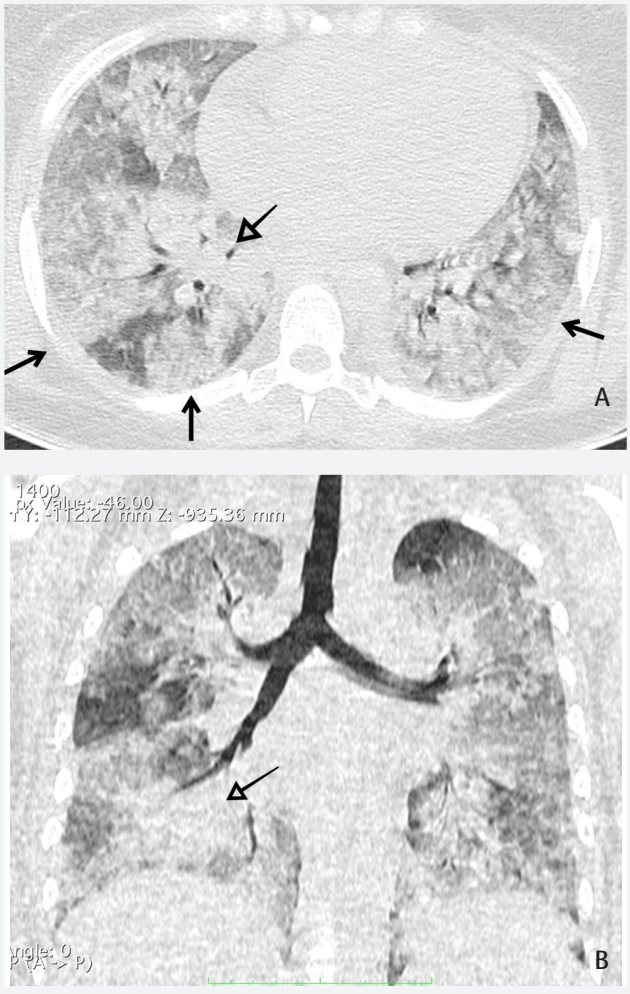

Figure 3. A 28-year-old patient with COVID-19 who was 29-week pregnant and taken to an emergency cesarean section. She died 17 days after this CT scan due to COVID-19 pneumonia, ARDS and septicemia. Her CT-SS was calculated as 24 (severe group) in CT. She had got many abnormal laboratory findings (*). Axial (a) and coronal (b) thin sections of unenhanced chest CT scans show extensive diffuse ground-glass opacities (black arrows) and few areas of consolidation with air bronchograms (empty arrows) and crazy-paving pattern giving a white lung appearance (*lymphocytopenia, elevated AST, ALT, LDH, Cr, CRP, D-dimer, ferritin, procalcitonin, troponin, prolonged PT, INR values)

COVID-19: Coronavirus disease-2019, LDH: Lactate dehydrogenase, CRP: C-reactive protein, PT: Prothrombin time, CT-SS: Computed tomography-severity score, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Cr: Serum creatinine, INR: International normalized ratio

in the recent study[9]. In our study, the mortality rates were 0% in the mild group, 12.3% in the moderate group, and 50% in the severe group. As a result, there was a statistically significant relationship between high CT-SS and high mortality in patients.

Increased levels of inflammatory biomarkers and infiltrating immune cells in lung lesions have been reported in patients with critical COVID-19. Cytokine storms can play a vital role in the increased disease severity of COVID-19 patients[19]. Francone et al.[10] reported statistically significant correlations between CT score and CRP and D-dimer levels. According to Saeed et al.[9], significant correlations were found between CT-SS and the male gender, with high inflammatory markers. They reported that CT-SS was found to be positively correlated with lymphopenia, increased serum CRP, D-dimer, and ferritin levels[9]. Zhang et al.[2] reported that chest CT score was found to be positively correlated with CRP, erythrocyte sedimentation rate, white blood cell count, procalcitonin, and abnormal coagulation function, and a negative association with lymphocyte count. In the current study, statistically significant correlations were found between CT score vs lymphocytopenia, high CRP, D-dimer, procalcitonin, LDH, Cr, ALT, AST, and troponin levels, and prolonged PT levels.

Different studies in the literature reported that older age, decreased lymphocytes, elevated CRP and D-dimer levels and comorbidities (cardiovascular and cerebrovascular diseases) were important high-risk factors that could lead to an increase in mortality in severe COVID-19 patients[20-22]. The male gender was most common in the severe group in the current study. However, the results showed no significant correlation between CT-SS and age and gender.

Several studies have reported that COVID-19 patients have a worse prognosis and severe clinical outcomes when multiple risk factors are present, particularly DM, HT, lung, and coronary artery disease[23,24]. Statistically significant correlations were found between CT score and chronic renal disease, COPD and cerebrovascular disease in the current study.

In addition, some special conditions such as pregnancy and malignancy are associated with the disease severity of COVID-19[25,26]. In our study, a 28-year-old woman in the severe group (CT-SS=24), who was 29-week pregnant and taken to emergency cesarean section, died due to COVID-19 pneumonia, ARDS, and septicemia (Figure 3).

Several recent studies have reported coagulation disorders, and liver and kidney dysfunctions in COVID-19 patients[20,27,28]. In our study, laboratory results showed also abnormal liver, kidney, and anticoagulation values. There were statistically significant correlations between CT-SS and high Cr, ALT and AST, D-dimer levels, and prolonged PT levels.

Study Limitations

Our study has some limitations. First, it is a retrospective study performed in a single center and a relatively limited cohort of patients was included in the study. Therefore, a multicenter study with a large sample size is needed for

further confirmation. Second, patients' CT-SSs were calculated by an experienced radiologist using a visual semi-quantitative CT severity scoring system. The accuracy of the study could be increased by two or more observers.

CONCLUSION

There was a relationship between high chest CT-SS and high mortality, inflammatory and anticoagulant laboratory markers, and some comorbidities (chronic renal disease, cerebrovascular disease, COPD) in COVID-19 patients. Chest CT-SS is a useful method for evaluating the severity and extent of COVID-19 pneumonia and it can provide clinicians with more detailed information about patients' prognosis and can be helpful for early intervention planning.

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Ethics

Ethics Committee Approval: This study was approved by the Ethical Committee of Trabzon Kanuni Training and Research Hospital and by the Minister of Health of the Republic of Turkey and it was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (date: 12.11.2020, no: 2020/68).

Informed Consent: The requirement for informed consent was waived.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.A., H.A.A.K., Design: B.A., Data Collection or Processing: B.A., H.A.A.K., Analysis or Interpretation: B.A., Literature Search: B.A., H.A.A.K., Writing: B.A.

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