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CORRELATION OF PATIENT FEATURES OF COVID-19, LABORATORY TESTS AND COMPUTED TOMOGRAPHY FINDINGS: SINGLE-CENTER RETROSPECTIVE STUDY

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Abstract

Aim: Computed Tomography (CT) findings, clinical and laboratory data are very important in the diagnosis and treatment process of Coronavirus Disease 2019 (COVID-19). In this study, the relationship between these findings was investigated.

Methods: 93 patients with positive Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) test for SARS-CoV-2 were included in the study. CT findings, laboratory tests, and the World Health Organization Clinical Progress Scale (WHO-CPS) were evaluated.

Results: Of the patients, 52 were male and 41 were female. The mean age was 46. The most common laboratory finding is high CRP levels (67.74%). GGO, consolidation, halo sign and air bronchogram were most frequent CT findings. The mean of CT score was 4.91. A statistically significant positive correlation was found between CT score and age, D-dimer, CRP, ferritin and fibrinogen. There was a significant negative correlation between CT score, lymphocyte count and oxygen saturation. There was no correlation between CT score and procalcitonin, gender and presence of comorbid disease. There was a moderate negative correlation between CT score and IL-6 blocker use and corticosteroid therapy, and a mild negative correlation between CT score and favipravir use. The correlation between CT score and immunosuppressant use was not significant. We also found a moderate positive correlation between WHO-CPS and CT scores.

Conclusions: The CT score is correlated with some laboratory and clinical markers, and we think that these findings indicate that CT is a very useful test in the diagnosis as well as in the follow-up.

Keywords: *COVID-19, CT, laboratory findings*

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Introduction

The new type of coronavirus (SARS-CoV-2), which can cause severe disease in humans, was officially identified on January 2020 and named coronavirus disease 2019 (COVID-19)[1]. COVID-19 can present as upper respiratory tract infection, pneumonia, encephalitis, pulmonary or systemic emboli formation, acute respiratory distress syndrome, respiratory failure, systemic inflammatory response or sepsis[2]. The gold standard method for the diagnosis is the polymerase chain reaction (PCR) test[3]. However, the PCR test may show negative results, especially in the early period[4]. In the diagnosis of COVID-19, computed tomography (CT) can be helpful, and show positive findings even before the onset of symptoms[5,6]. Clinical findings and laboratory data are also very important in the diagnosis and treatment process[7]. In this study, we investigated the correlation between laboratory data, clinical findings and CT findings of patients with COVID-19.

Materials and Methods

Patients

A total of 148 patients who were applied to our hospital, between March 2020 to June 2020, with the symptoms such as fever, fatigue, myalgia, cough, loss of taste and smell, and were suspected for COVID-19 included in this retrospective study. Because of negative real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2, 55 patients were excluded from the study. In addition, pediatric patients were not included into the study. Finally, we included 93 patients (41 female, 52 male) who had positive result of RT-PCR test for SARS-CoV-2. All the patients have thin-sectional non-contrast chest CT. This study approved by our institutional ethical committee and Ministry of Health COVID-19 Science Committee.

Image Acquisition and Chest CT Evaluation

Thin-sectional non contrast chest CT was performed with a 4-slice CT scanner (Asteion Super 4, Canon). To minimize motion artifacts, patients were scanned on single breath hold, on inspiratory phase in the supine position. The associated parameters were used: tube voltage, 120 kV; automatic tube current modulation, 100–250 mAs; slice thickness, 1.25 mm without interslice gap.

The major CT findings were based on the standard glossary for thoracic imaging reported by the Fleischner Society[8]. The evaluated CT features were ground glass opacity (GGO), consolidation, reticular pattern, halo and reversed halo signs, crazy paving, air bronchogram, vascular enlargement, subpleural line, mediastinal lymphadenopathy and pleural effusion that were defined for SARS-CoV-2 pneumonia by novel literature. Also bilaterality, peripheral or central involvement, multilobar distribution of the lesions were estimated. The outer one-third of the lung was accepted as peripheral, the remaining locations were accepted as central.

A semi-quantitative CT severity scoring system was used, described by Pan et al (1). Each of the five lung lobes were visually scored on a scale 0 to 5.

0 means no involvement.
1, less than 5% involvement.
2, 5%-25% involvement.
3, 26%-49% involvement.
4, 50%-75% involvement.
5 for more than 75% involvement.

The total score was the sum of the lobar scores and ranged 0 to 25. Image analysis was performed by two radiologists with 15- and 5-years' experience. Final scores were decided by common consensus.

Patient characteristics and laboratory data

We retrospectively collected the laboratory data including lymphocyte count, lymphocyte percentage, D-dimer, C-reactive protein (CRP), ferritin and procalcitonin levels. Also, the drugs which needed for the treatment: corticosteroid, IL-1 blocker, IL-6 blocker and favipravir were recorded. Patient characteristics were sex, age, presence of comorbid disease. Information about patient characteristics is given in the Table 1. We calculated the WHO Clinical Progression Scale (WHO-CPS)[9]. The scale provides a measure of illness severity across a range from 0 (not infected) to 10 (dead) with data elements that are rapidly obtainable from clinical records. The features and scores used in the scale are given in Table 2.

Statistical analysis

Patient findings are given as frequencies and percentages in categorical variables; mean ± standard deviation in numerical variables is given as minimum-maximum values. Correlation analysis was performed by Pearson Correlation Test. $p<0.05$ was considered significant in all comparisons. Analyzes were performed with SPSS 20.0.

Results

Of the 93 included patients with COVID-19, 52 (55.9%) were male and 41 (44.1%) were female, and the mean age was 46±16,77 (range 21-83) years old. All patients have symptoms like fever, cough and weakness, myalgia and 46 (49.5%) patients have comorbid disease and 7 (7.5%) of them have a history of immunosuppressant treatment.
The results of laboratory tests were often abnormal, the most frequent abnormalities were mildly decreased lymphocyte count, lymphocyte percentage and increased CRP, D-dimer, procalcitonin, fibrinogen levels (Table 3).

Table 1. Demographic data and patient characteristics

Parameters		n	%
Gender	Female	41	44,1
	Male	52	55,9
Intubation status	+	6	6,5
	-	87	93,5
Additional disease	+	47	50,5
	-	46	49,5
Immunsuppressive drug use	+	7	7,5
	-	86	92,5
IL-1 Blocker use	+	7	7,5
	-	86	92,5
IL-6 Blocker use	+	12	12,9
	-	81	87,1
Corticosteroid use	+	19	20,5
	-	74	79,5
Favipiravir use	+	62	66,7
	-	31	33,3

The most common laboratory finding is high CRP levels (n=63, 67.74%). Fibrinogen was high in 53 patient and 35 patient has high D-dimer levels (37.63%). 25 of 83 patients had high ferritin level (24.71%). Also 21 (22.58%) of 93 patients had lymphopenia and lymphocyte percentage was low in 37 patient (39.78%). The interval from onset symptoms to PCR test and chest CT scan was 4±3.2 (range 1-17) days.
Twenty patients had normal chest CT findings. GGO, consolidation, halo sign and air bronchogram were the most frequent CT findings, respectively (Table 4). The mean of CT score was 4.91 (range, 0-21) and CT score was compared with age, gender and laboratory findings. When the involvement patterns and frequencies were evaluated, it was found that bilateral lung involvement, multilobar and peripheral involvement were the most common (Table 5).
Statistically significant positive correlation were found between CT score vs age ($p<0.05$, $r=0.487$), D-dimer ($p<0.05$, $r=0.331$), CRP ($p<0.05$, $r=0.587$) (Graphic A), ferritin ($p<0.05$, $r=0.653$) (Graphic B) and fibrinogen ($p<0.05$, $r=0.592$) levels.

Table 2. WHO clinical progression scale[9]

Patient State		Descriptor	Score
Uninfected		Uninfected • no viral RNA detected	• 0
Ambulatory mild disease		Asymptomatic • viral RNA detected Symptomatic • independent • assistance needed	• 1 • 2 • 3
Hospitalized	moderate disease	• no oxygen therapy* • oxygen by mask or nasal prongs	• 4 • 5
Hospitalized	severe diseases	Hospitalized • oxygen by NIV or high flow • Intubation and mechanical ventilation, pO2/FiO2 ≥150 or SpO2/FiO2 ≥200 • Mechanical ventilation pO2/FIO2 <150 (SpO2/FiO2 <200) or vasopressors • Mechanical ventilation pO2/FIO2 <150 and vasopressors, dialysis, or ECMO • Dead	• 6 • 7 • 8 • 9 • 10

ECMO=extracorporeal membrane oxygenation. FiO2=fraction of inspired oxygen. NIV=non-invasive ventilation. pO2=partial pressure of oxygen. SpO2=oxygen saturation. *If hospitalised for isolation only, record status as for ambulatory patient.

Statistically significant negative correlation were found between CT scores vs. lymphocyte count and lymphocyte percentage ($p<0.05$, $r=-0.317$) (Graphic C) and oxygen saturation ($p<0.05$, $r=-0.606$).
There was no significant correlation between CT score and procalcitonin ($p > 0.05$, $r= - 0.033$) levels, confirming that this disease is transmitted by a virus.
No significant relationship was found between CT score vs. gender ($p > 0.05$, $r = 0.148$), presence of comorbid disease ($p > 0.05$, $r = - 0.097$).
IL-1 and IL-6 blockers were used for 7 (7.5%) and 12 (12.9%) patients, respectively. 19 (20.4%) patients have used corticosteroids and favipravir.

Table 3. Laboratory findings

Findings	n=93
Lymphocyte count ($10^3/\mu$lt), mean (SD)	1.391 (7.3)
Lymphocyte percentage (%)	23.6 (12.5)
CRP (mg/L), mean (SD)	45.9 (81.1)
Ferritin, mean (SD)	388.7 (811)
Procalcitonin (ng/ml), mean (SD)	1.3 (10.3)
D-dimer level (mg/L), mean (SD)	1.0 (1.8)
Fibrinogen (mg/dl), mean (SD)	418.5 (160.7)
Oxygen saturation (%),mean(SD)	94.9 (4.6)

When we looked for relationship between CT score and the required drugs for the treatment, statical analyses showed moderate negative correlation between usage of IL-6 blocker ($p<0.05$, $r=0.627$) and corticosteroid therapy ($p<0.05$, $r=0.496$). There was a mild negative correlation between CT score and use of favipravir ($p<0.05$, $r=0.378$).
The correlation between CT score and use of immunosuppressant was non-significant ($p > 0,05$, $r = -0,071$). We found a mild negative correlation between CT score and intubation ($p<0.05$, $r=0.388$), 6 (6.45%). Patients had needed intubation, 4 (4.30%) of them died because of COVID-19. Also, we found moderate positive correlation between the WHO-CPS score and CT score ($p<0.05$, $r = 0.571$) (Graphic D).

Table 4. CT features

Features	n(%)
Ground-glass opacity	68 (73.1)
Consolidation	38 (40.9)
Crazy paving	14 (15.1)
Reticular	19 (20.4)
Air bronchogram	32 (34.4)
Pleural thickening	13 (14.0)
Subpleural lines	10 (10.8)
Bronchiectasis	7 (7.5)
Halo sign	34 (36.6)
Vascular enlargement	24 (25.8)
Mediastinal lymphadenomegaly	9 (9.6%)
Pleural effusion	3 (3.2%)

Table 5. Involvement patterns of lung

	n (%)
Involvement of lungs	
• bilateral	63 (88.7)
• unilateral	8 (11.3)
Involvement of the lobes	
• multilobar	63 (88.7)
• unilobar	8 (11.3)
Distribution of pulmonary lesions	
• peripheral	28 (39.4)
• central	1 (1.40)
• peripheral and central	43 (60.6)

Discussion

COVID-19 pandemic started in 2019 and become most important public health-care problem in whole world since then. Most cases are asymptomatic but around 1-2% of COVID-19 infection could result with significant morbidity and even mortality. Though, well-known diffuse systemic involvement of different organs were reported, lung was the far most common involved organ in COVID-19 infection and mainly diagnosed by chest CT. The most common CT findings of COVID-19 were reported as GGOs with or without consolidation in significant number of studies[2]. With the current study we looked for whether there was correlation with patient characteristics', common laboratory values, and CT findings or not. We found the most frequent laboratory data is high CRP levels (67.74%) in accordance with the literature[10]. Bilateral multilobe involvement, peripheral (including peripheral and central) distribution and GGO appearance were the most common chest CT findings of COVID-19. These results are similar to the CT findings of COVID-19 reported in the literature[3].

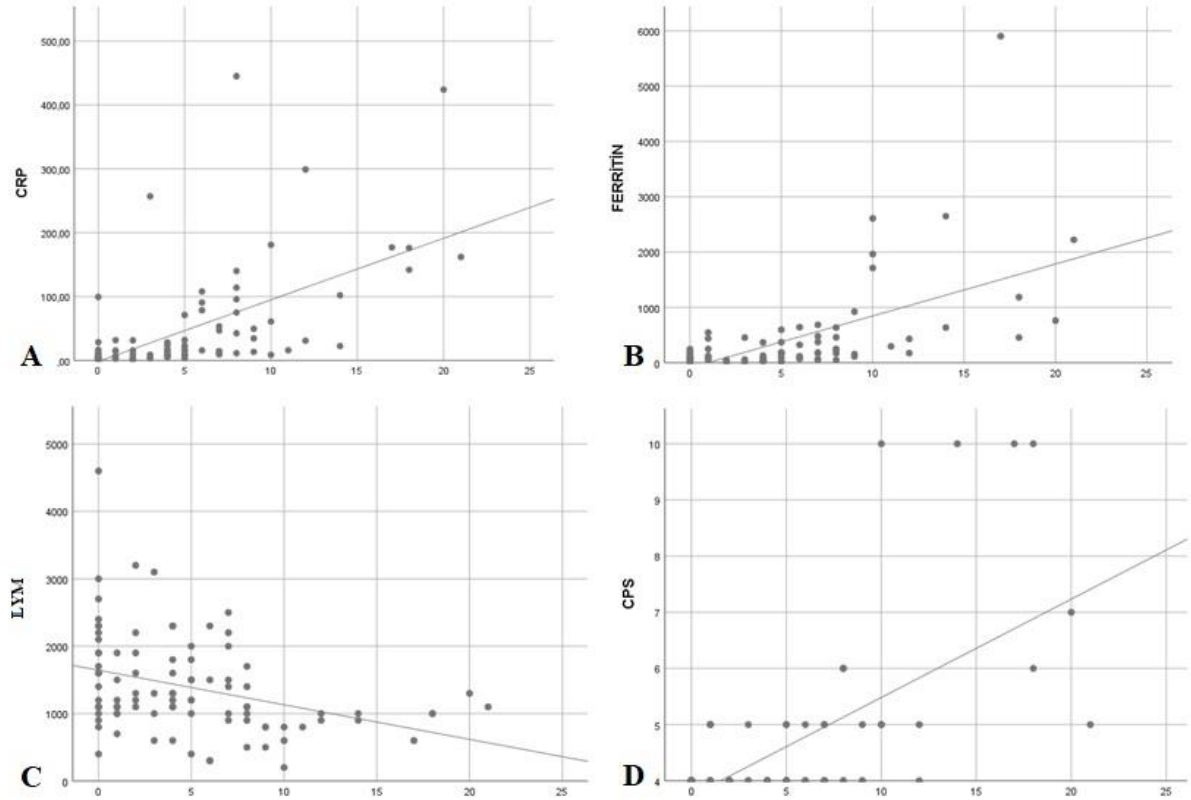

Figure 1. Correlation graphics
A Correlation between CT score and CRP
B Correlation between CT score and ferritin
C Correlation between CT score and lymphocyte count
D Correlation between CT score and WHO-CPS

In our study, a significant correlation was observed between the CT score vs age. This result is consistent with the presentation of the disease with more severe findings in the elderly and is correlated with the literature. No significant relationship was found between CT score and gender. It is already known that CT findings are detected at similar rates in both genders[11].

Statistically significant negative correlation were found between CT score vs. lymphocyte count and lymphocyte percentage and oxygen saturation. It has been showed that severe COVID-19 patients have significantly higher levels of CRP, and there is a relationship with high CRP levels and mortality. Beside increasing CRP, the lymphocyte count decreases with increasing disease severity. By being in correlation with CRP levels and lymphocyte counts, CT score may predict disease severity and be used as a tool for management of the treatment[12-14].

The limitations of our study are that it was single-centered and the number of cases was small, the number of patients using IL blockers was low, and the lack of optimization in laboratory data, since we did not know on which day of the disease the patients applied.

According to results of our study, a mild negative correlation detected between CT score and favipravir therapy. In the literature, there are studies advocating and not advocating that the treatment is effective[15]. However, no significant correlation was observed in our study, and the use of favipravir in the following periods became very controversial, especially in patients with mild signs, it was shown that it isn't effective for treatment[16].

In our study, it was determined that D-dimer levels and CT score were correlated. Similarly, in the studies of Zhu J et al., D-dimer and CRP levels were found to be correlated with the CT score[17]. Ferritin and fibrinogen levels are also a commonly used parameter to evaluate the severity of the disease. In our study, correlation was found between CT score and ferritin and fibrinogen level, and literature information supports our results[18,19]. In follow-up, the CT score may be useful in correlating infection severity.

Conclusion

The correlation of CT score with laboratory and clinical findings such as D-dimer, CRP, lymphocyte count and lymphocyte percentage, oxygen saturation and WHO-CPS highlights the importance of CT findings in the diagnosis as well as in the method. In order to better define this relationship, multicenter studies with a larger number of patients are required

Author contributions
All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval

This study was approved by the Institutional Investigation and Ethics Committee with the approval number of "99/05" -2020 and conducted at Cukurova University in Turkey

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