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Chest CT Score in COVID-19 Patients: The Relationship Between Neutrophil-Lymphocyte Ratio, Monocyte, Lactate Dehydrogenase, Albumin And Ferritin

COVİD-19 Hastalarında Toraks BT Skoru: Nötrofil-Lenfosit Oranı, Monosit, Laktat Dehidrojenaz, Albümin ve Ferritin Arasındaki İlişki

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ABSTRACT

Objective: *Various laboratory and vital parameters can be used in the diagnosis and assessment of the severity of COVID-19 infection .*

Methods: *The chest computed tomography (CT) scores, lymphopenia, neutrophil/lymphocyte ratio, neutrophil, lymphocyte, lactate dehydrogenase, albumin, C-reactive protein, white blood cells, platelets, basophil, eosinophil, monocytes, procalcitonin, D-dimer, ferritin, ages, genders, hospitalization units, oxygen-free fingertip saturations in room air, additional diseases and symptoms of 693 patients diagnosed with COVID-19 were recorded. The parameters of the patients were compared according to the severity of the chest CT score.*

Results: *As a result of this study neutrophil/lymphocyte ratio was found to be significantly higher in the severe group when compared to the moderate group and the mild group. As chest CT score increased, lactate dehydrogenase level was higher at a statistically significant level in the severe group than in the mild group. When the practical effectiveness of using hematological and biochemical parameters to differentiate patients with severe CT scores from non-severe patients based on the chest CT score of the patients was examined by using the ROC Analysis, it was found that the neutrophil/lymphocyte ratio value had the strongest predictive ability (AUC, 0.787, SD=0.057, P<0.001, 95% CI 0.682-0.683). neutrophil/lymphocyte ratio was found to have 68.2% sensitivity and 68.3% specificity when the cut-off value was set at 5.58*

Conclusion: *Close clinical and laboratory follow-up can be started by examining neutrophil/lymphocyte ratio, lymphocyte, lactate dehydrogenase, albumin, monocyte and ferritin, predicting that the lung involvement of COVID-19 has increased and early treatment can be started in healthcare centers where chest CT scan is not possible or to avoid frequent CT scans*

ÖZET

Amaç: *COVID-19 enfeksiyonunun tanısında ve ağırlığının değerlendirilmesinde çeşitli laboratuvar ve vital parametreler kullanılabilir.*

Yöntemler: *COVID-19 tanısı konulan 693 hastaya ait toraks bilgisayarlı tomografi (BT) skoru, nötrofil/lenfosit oranı, nötrofil, lenfosit, laktat dehidrogenaz, albümin, C-reaktif protein, beyaz kan hücreleri, trombosit, bazofil, eozinofil, monosit, prokalsitonin, D-dimer, ferritin değeri, yaş, cinsiyet, yatış birimi, oda havasında oksijensiz parmak ucu satürasyonu, ek hastalıklar ve semptomlar kaydedildi. Hastaların kaydedilen parametreleri toraks BT skorunun ağırlığına göre karşılaştırıldı.*

Bulgular: *Bu çalışma sonucunda BT skoru ağır olan grupta nötrofil/lenfosit oranı orta ve hafif gruba göre anlamlı derecede yüksek bulundu. Laktat dehidrogenaz düzeyi, şiddetli grupta hafif gruba göre istatistiksel olarak anlamlı düzeyde daha yüksekti. Hastaların Toraks BT skorlarına göre ağır BT skoru olan hastaları ağır olmayan hastalardan ayırt etmek için hematolojik ve biyokimyasal parametrelerin kullanılmasının pratik etkinliği ROC Analizi kullanılarak incelendiğinde, nötrofil/lenfosit oranı değerinin ağır grupta yüksek olduğu görüldü. En güçlü tahmin yeteneği (AUC, 0.787, SD=0.057, P<0.001, %95 CI 0.682-0.683). Nötrofil/lenfosit oranının cut-off değeri 5,58 olarak ayarlandığında %68,2 duyarlılığa ve %68,3 özgüllüğe sahip olduğu görüldü.*

Sonuç: *Nötrofil/lenfosit oranı, lenfosit, laktat dehidrogenaz, albümin, monosit ve ferritin değeri incelenerek COVID-19' un akciğer tutulumunun arttığı öngörülerek yakın klinik ve laboratuvar takibine başlanabilir ve sağlık merkezlerinde erken tedaviye başlanabilir. Bu laboratuvar testleri toraks BT taramasının mümkün olmadığı yerlerde veya sık BT taramalarından kaçınmak için kullanılabilir.*

Keywords:
Neutrophil-lymphocyte ratio
Chest CT score
COVID-19

Anahtar Kelimeler:
Nötrofil-lenfosit oranı
Toraks BT skoru
COVID-19

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INTRODUCTION

In 2019, a group of patients with pneumonia of uncertain forms were admitted to China. In the detailed examination, the cases were diagnosed with corona virus disease 2019 (COVID-19) (1).

The disease has various clinical forms. Although COVID-19 infection manifests with mild symptoms and a good prognosis, It is known that COVID-19 causes multiple organ damage in its patients. In the respiratory system, it can cause pneumonia and subsequent respiratory failure (2). Successful treatment of the disease and prevention of secondary infection in cases of Covid-19 are very important in reducing complications and mortality. Accordingly, it is very important to specify the factors related to the severity of the disease and to use them in clinical practice (3,4).

Computed tomography (CT) has an important place in the diagnosis of COVID-19. The severity of the disease can also be determined with CT (5).

Various laboratory and vital parameters, including leukopenia, lymphopenia, neutrophil/lymphocyte ratio (NLR) elevation, D-dimer and ferritin elevation, and low albumin can be used in the diagnosis and assessment of the severity of COVID-19 infection (6-8). Increased NLR is very popular in evaluating the severity of CT involvement in COVID-19 (9).

The purpose of the present study was to determine the relationship of chest CT score with other laboratory and clinical parameters. The secondary purpose was to find a cutoff value for the laboratory parameters that would determine the severity of the chest CT score.

METHODS

This retrospective study was conducted in Mardin Training and Research Hospital. The study was approved by the Ethics Committee of Mardin Artuklu University, Non-Interventional Research Ethics Committee, and was started in February 2022 (E-76272411-900-44449). The chest CT scores, ages, genders, hospitalization units, oxygen-free fingertip saturations in room air, additional diseases, symptoms, and laboratory data were obtained simultaneously with chest CT of 693 patients who were diagnosed with COVID-19 pneumonia between 10 July 2021 and 10 April 2022 were recorded. The parameters of the patients were compared according to the severity of the chest CT score. The comorbidities under evaluation were diabetes mellitus (DM), hypertension (HT), chronic kidney disease (CKD), congestive heart failure (CHF), and other additional diseases. Symptoms under consideration were cough, fever, dyspnea, sputum, chest pain, wheezing, and loss of taste and smell. Laboratory parameters under evaluation NLR, neutrophil, lymphocyte, lactate dehydrogenase (LDH), albumin, C-reactive protein (CRP), white blood cells (WBC), platelets, basophil, eosinophil, monocytes, procalcitonin, D-dimer, and ferritin.

Patient selection

The inclusion criteria for the study were a diagnosis of COVID-19 pneumonia using Reverse-Transcriptase Polymerase Chain Reaction (RT-PCR) and chest CT, being hospitalized because of COVID-19 pneumonia, study time of chest CT, and blood parameters less than 24 hours.

Exclusion criteria were being under 18 years of age, and having more than 24 hours between blood parameters evaluation and chest CT imaging. Other chronic respiratory diseases that would deepen respiratory failure (e.g. chronic obstructive pulmonary disease, asthma).

Computed tomography procedure

All CT scans were performed using a 16-slice multi-detector CT scanner (MX16, Philips Medical System, Koninklijke, The Netherlands). The patients were placed on the table in the supine position in the center of the table and hands up. The procedure was performed in the deep inspiration of the patients. Chest CT examination included the region from the apex of the lung to the costophrenic sinuses. The section thickness was taken at 2.5 mm. The reconstruction interval was taken equal to the slice thickness. Appropriate window settings were used to evaluate the lung parenchyma and mediastinal structures when the images were transferred to the film. Window settings: Lungs: Width (WW): 900-1500, Level (WL): -600 (-500, -800) Mediastinum (soft tissue): Width (WW): 300-500, Level (WL): 50 (40-60).

Image interpretation

All CT images were analyzed by using the corporate database system (Oracle database V1.10.43.134). The images were evaluated by two radiologist with 5 (M.F.) and 4 years (Y.G.) of experience. When these two radiologists disagreed, a third radiologist was included in the evaluations. The final decision in the dispute was made by the third radiologist (E.Ö.) with 16 years of experience. The chest CT scoring method is used to determine the severity of CT involvement in COVID-19 pneumonia. A total of five lung lobes are evaluated, with the involvement of each lobe evaluated separately. The total score gives us the chest CT score. Classification of scores is as follows: “0” no involvement (0%), “1” minimal involvement (1–25%), “2” mild involvement (26–50%), “3” moderate involvement (51%–75%), and “4” severe involvement (76–100%). Patients were grouped as mild (0-5 points), moderate (6-10), and severe (11-20) according to their radiological scores (4,10).

Statistics

The “SPSS for Windows Version 21” program was used for statistical analysis. Whether the numerical measurements provided the assumption of normal distribution in the study group was tested with the Shapiro-Wilk test. The descriptive statistics of the parametric numerical data were calculated as mean ± standard deviation and median (minimum-maximum) of the non-parametric ones. The One-way ANOVA test was used when the assumptions were met, and the Kruskal-Wallis H test was used when the assumptions were not met in the comparisons of the numerical measurements of the groups. The limit of significance was taken as $p<0.05$. For differential diagnosis, the practical effect of using hematological and biochemical parameters was examined by using the ROC Analysis. The effectiveness of the values in predicting the differential diagnosis was calculated by using the analysis of the ROC curve and calculations of the area under the curve (AUC). The cut-off values of the strongest

predictive parameters with the highest specificity and sensitivity were determined and recorded according to the Youden Index.

RESULTS

A total of 693 patients were included in the present study. According to the chest CT scores, the patients were grouped as mild (0-5 points), moderate (6-10 points), and severe (11-20 points). It was found in the comparison between the groups that the mean age of the mild group was 73.8 ±24.74, the mean age of the middle group was 74.1 ±12.36, and the mean age of the severe group was 67.1 ±19.98 (Table 1). There were no statistically significant differences between the groups. When the gender distribution of the groups was evaluated, the female/male ratio was found to be 154/66 in the mild group, 132/99 in the moderate group, and 132/110 in the severe group (Table 1). No statistically significant differences were detected between the groups in this respect. The demographic data and clinical characteristics of the patients are shown in Table 1, and the comparison of chest CT severity scores with the laboratory parameters and saturation is given in detail in Table 2.

No statistically significant differences were detected between the patients' chest CT scores and age, gender, and comorbidities. When the symptoms of the patients were compared with the chest CT scores, although no statistically significant differences were detected between cough, fever, sputum, chest pain, wheezing, loss of taste and smell, and the grade of the chest CT scores, statistically significant increases were detected in the dyspnea as the chest CT score increased (Table 1).

When the patients' chest CT severity degree was compared with the laboratory parameters and saturation, it was found that NLR was found to be significantly higher in the severe group when compared to the moderate group and the mild group ($p<0.05$). The lymphocyte level was found to be lower at a statistically significant level in the severe group than in the mild group ($p<0.05$). As chest CT score increased, LDH level was higher at a statistically significant level in the severe group than in the mild group ($p<0.05$). Albumin levels were found to be lower in the severe group at a statistically significant level than in the mild group ($p<0.05$). Monocyte levels were found to be lower in the severe group at a statistically significant level when compared to the moderate and mild groups ($p<0.05$). Ferritin level was higher in the severe group at a statistically significant level when compared to the moderate and mild groups. Fingertip saturation in room air was statistically significant between all groups ($p<0.05$). As the CT score increased, the saturation of the fingertip was also statistically lower (Table 2).

When the practical effectiveness of using hematological and biochemical parameters to differentiate patients with severe CT scores from non-severe patients based on the chest CT score of the patients was examined by using the ROC Analysis, it was found that the NLR value had the strongest predictive ability (AUC, 0.787, SD=0.057, $P<0.001$, 95% CI 0.682-0.683). NLR was found to have 68.2% sensitivity and 68.3% specificity when the cut-off value was set at 5.58 (Figure 1, Table 3).

Table 1: The demographic and clinical characteristics of the study population.

Parameter	CT severity (n)		P value
Age (Mean ±SD)	Mild (220)	73.8 ±24.74	
	Moderate (231)	74.1 ±12.36	0.2
	Severe (242)	67.1 ±19.98	
Gender (Female/ Male)	Mild (220)	154/66	
	Moderate (231)	132/99	0.5
	Severe (242)	132/110	
Hospitalization unit (Intensive care/Ward)	Mild (220)	0/220	
	Moderate (231)	66/165	0.001*
	Severe (242)	154/88	
COMORBIDITIES			
Comorbidity (Yes/No)	Mild (220)	121/99	
	Moderate (231)	176/55	0.3
	Severe (242)	143/99	
DM (Yes/No)	Mild (220)	88/132	
	Moderate (231)	66/165	0.7
	Severe (242)	88/154	
HT (Yes/No)	Mild (220)	110/110	
	Moderate (231)	121/110	0.1
	Severe (242)	66/176	
CKD (Yes/No)	Mild (220)	0/220	
	Moderate (231)	22/209	0.3
	Severe (242)	22/220	
CHF (Yes/No)	Mild (220)	22/198	
	Moderate (231)	66/176	0.4
	Severe (242)	33/209	
SYMPTOMS			
Cough (Yes/No)	Mild (220)	143/77	
	Moderate (231)	110/121	0.09
	Severe (242)	77/165	
Fever (Yes/No)	Mild (220)	121/99	
	Moderate (231)	66/165	0.1
	Severe (242)	77/165	
Dyspnea (Yes/No)	Mild (220)	33/187	
	Moderate (231)	132/99	0.001*
	Severe (242)	231/11	
Sputum (Yes/No)	Mild (220)	66/154	
	Moderate (231)	55/176	0.6
	Severe (242)	88/154	
Chest pain (Yes/No)	Mild (220)	55/165	
	Moderate (231)	33/198	0.5
	Severe (242)	66/176	
Wheezing (Yes/No)	Mild (220)	77/143	
	Moderate (231)	99/132	0.6
	Severe (232)	111/121	
Loss of taste/smell (Yes/No)	Mild (220)	88/132	
	Moderate (231)	66/165	0.1
	Severe (242)	33/209	

CT: Computed tomography, SD: Standard deviation, DM: Diabetes mellitus, HT: Hypertension, CKD: Chronic kidney disease, CHF: Congestive heart failure.
P<0.05 was considered statistically significant.

Table 2: Comparison of CT severity scores with laboratory parameters and saturation.

Parameter	CT severity (n)	Mean ±SD	P value
NLR	Mild (220)	5.02 ±3.18	0.001*
	Moderate (231)	5.70 ±4.47	
	Severe (242)	13.98 ±13.29	
Neutrophil	Mild (220)	5.98 ±2.14	0.2
	Moderate (231)	5.75 ±3.28	
	Severe (242)	7.28 ±3.47	
Lymphocyte	Mild (220)	1.42 ±0.63	0.02*
	Moderate (231)	1.21 ±0.74	
	Severe (242)	0.85 ±0.55	
LDH	Mild (220)	280.85 ±101.38	0.01*
	Moderate (231)	361.71 ±144.17	
	Severe (242)	412.5 ±167.60	
Albumin	Mild (220)	3.7 ±0.5	0.009*
	Moderate (231)	3.8 ±0.5	
	Severe (242)	3.3 ±0.5	
CRP	Mild (220)	65.72 ±80.03	0.09
	Moderate (231)	76.18 ±51.74	
	Severe (242)	114.78 ±91.27	
WBC	Mild (220)	8.09 ±2.57	0.7
	Moderate (231)	8.27 ±4.60	
	Severe (242)	8.89 ±3.39	
Platelets	Mild (220)	222.25 ±81.79	0.4
	Moderate (231)	232.19 ±76.24	
	Severe (242)	262.59 ±142.86	
Basophil	Mild (220)	0.021 ±0.01	0.8
	Moderate (231)	0.024 ±0.02	
	Severe (242)	0.021 ±0.01	
Eosinophil	Mild (220)	0.03 ±0.05	0.3
	Moderate (231)	0.03 ±0.05	
	Severe (242)	0.01 ±0.03	
Monocyte	Mild (220)	0.67 ±0.29	0.004*
	Moderate (221)	0.58 ±0.28	
	Severe (242)	0.38 ±0.27	
Procalcitonin	Mild (220)	0.13 ±0.12	0.3
	Moderate (231)	2.41 ±6.14	
	Severe (242)	2.21 ±6.37	
D-dimer	Mild (220)	999.98 ±977.07	0.7
	Moderate (231)	1269.71 ±1717.98	
	Severe (242)	1161.54 ±827.155	
Ferritin	Mild (220)	240.31 ±212.82	0.002*
	Moderate (231)	295.78 ±176.34	
	Severe (242)	556.78 ±424.31	
Fingertip saturation at room air	Mild (220)	90.2 ±3.65	0.001*
	Moderate (231)	86.38 ±4.92	
	Severe (242)	78.95 ±5.59	

CT: Computed tomography, SD: Standard deviation, NLR: Neutrophil/lymphocyte ratio, LDH: Lactate dehydrogenase, CRP: C-reactive protein, WBC: White blood cells.
P<0.05 was considered statistically significant.

Table 3: Area under the curve for NLR, LDH, ferritin.

	AUC (95% CI)	Cut-off according to Youden's Index	P	Sensitivity %	Specificity %
LDH	0.683 (0.526-0.841)	350.50	<0.05	0.727	0.756
NLR	0.787 (0.675-0.898)	5.58	<0.001	0.682	0.683
Ferritin	0.740 (0.610-0.870)	355.30	<0.05	0.591	0.805

AUC: Area under the curve, NLR: Neutrophil/lymphocyte ratio, LDH: Lactate dehydrogenase

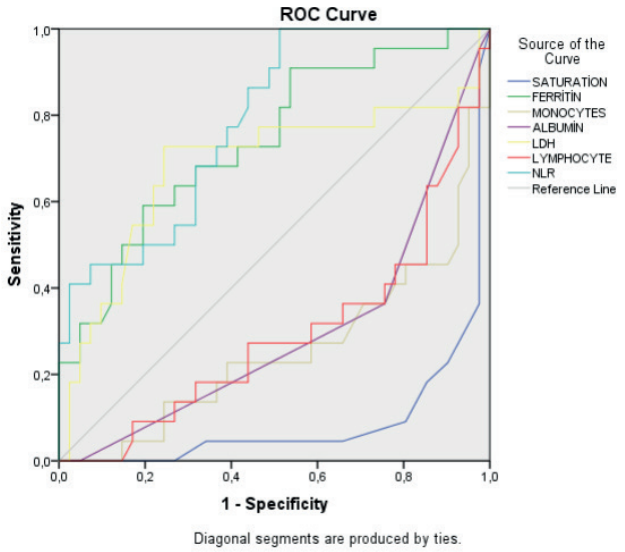

Figure 1: Roc analysis of NLR, LDH, ferritin, saturation, monocytes, albumin, lymphocyte.

DISCUSSION

COVID-19 pneumonia is a big problem for the entire world. The present study investigated the parameters that might be related to the grade of chest CT score in patients hospitalized in our tertiary hospital because of COVID-19 pneumonia. The hospital unit of the patients, dyspnea symptoms, NLR values, lymphocyte, LDH, albumin, monocytes, ferritin levels, and fingertip saturation in room air were found to be statistically significantly related to the grade of chest CT scores. It was also found that the most important indicator of severe lung involvement because of COVID-19 was high NLR scores.

After viruses enter the body, they stimulate CD8 + T lymphocytes, which are part of the defense system. As a result of the stimulation of CD8+ T lymphocytes, a large number of neutrophils are released. Excessive neutrophil secretion causes a cytokine storm. Another effect of viruses is the decreased amount of lymphocytes. NLR values increase in viral infections as neutrophil levels increase and lymphocyte levels decrease (11). In studies conducted, it has been stated that an NLR value above 19.94 may be determinant for poor prognosis and death. Therefore, it has been suggested to use NLR as a biomarker (6,12).

In their study, Man et al. associated the elevated NLR levels with the severity of chest CT involvement. When the NLR value was below 5.04, they found the CT score below 3 with a 94% probability (13). Zhang et al. In another study on NLR in COVID-19, it was stated that the severity of the disease increased as the NLR rate increased in COVID-19 pneumonias. A statistically significant difference was found in the NLR rate between the severe, moderate and mild groups, CT correlated positively with severity scores (14). Similar to all these studies, in our study the NLR was significantly higher in the severe group than in the other groups. NLR was found to be the most important factor determining the severity of CT involvement in the present study. NLT had a sensitivity of 68% in detecting severe CT scores above 5.58. We think that NLR is an important biomarker to determine the degree of pulmonary involvement in COVID-19.

In the present study, the lymphocyte level of the patients was found to be lower at statistically significant levels in the severe group when compared to the mild group in the chest CT scores. Lymphopenia indicates that the immune system is damaged in patients with high CT scores. Lymphopenia may show increased involvement because of COVID-19 (15). In other studies conducted on CT involvement and laboratory parameters in COVID-19, it was reported that lymphopenia was present in the severe group as CT involvement increased (16-18).

In their study conducted on the severity of chest CT involvement and laboratory findings in COVID-19, Li et al. found the mean age of severe and critical patients with high chest CT involvement to be higher and reported that the severity of COVID-19 pneumonia was independent of gender. In the same study, the chest CT score of severely critical patients was reported to be high (16). In the present study, similar to this study, no differences were detected between the groups in gender distribution, and patients hospitalized in the ıntensive care units were statistically significantly more in the group with severe chest CT scores. Unlike this study, no significant correlation was found between the chest CT score and the age of the patients in the present study.

COVID-19 can affect very different systems and cause very different symptoms (19). In the study that was conducted by Li et al. on the severity of the disease in chest CT involvement and laboratory findings, it was reported that as the chest CT examination increased, the symptoms of dyspnea and chest pain increased (20). In the present study, the chest CT score-related symptoms were compared and it was found that dyspnea increased at significant levels as the chest CT scores increased. Other symptoms were not significantly related to the chest CT scores in the present study. Increased dyspnea may be an important marker for the clinician to determine the

increased lung involvement of COVID-19 pneumonia.

Studies conducted on COVID-19 CT involvement reported significant relationships between increased chest CT involvement and LDH elevation (21,22). Similarly, in the present study, LDH levels and chest CT scores were higher in the severe group at a statistically significant level than in the mild group. In the present study, LDH elevation was found to be statistically significant in the ROC test performed to determine the severe group with chest CT scores.

Studies are reporting that there is a negative correlation between monocyte levels and chest CT involvement (23). Similarly, in the present study, it was also found that as the chest CT score increased, the monocyte level decreased statistically. Chest CT score was lower in the severe group at a statistically significant level when compared to the other groups.

Ferritin plays a role in macrophage activation as an important part of innate immunity. The ferritin levels in the blood increase in many viral and bacterial infections. High serum ferritin levels were reported in those with high chest CT scores (24). In our study, we found that ferritin levels were statistically significantly higher in the severe group than in the other groups.

In the study that was conducted by Salvatore et al., fingertip saturation was found to be significantly lower in the group with high chest CT uptake and high mortality (25). In the present study, it was found that fingertip saturation was significantly lower in the group with high CT scores.

It was reported in their study that the neutrophil percentage, CRP and D-dimer levels had a positive correlation with the severity of CT involvement (24,26). In the present study, although CRP and neutrophil levels increased more in the group with high chest CT scores, no statistically significant differences were detected between the groups. Contrary to these studies, no significant relationships were detected in the present study between D-dimer level and chest CT scores.

Limitations

The limitation of the present study is that it had a retrospective design, included only hospitalized patients, and was single-centered. Only patients with CT examinations and simultaneous laboratory parameters to establish further associations between laboratory and CT features were included in it. Possible selection bias. There were no patients under the age of 18 in the study. Current findings cannot be stated for the pediatric age group.

CONCLUSION

Close clinical and laboratory follow-up can be started by examining NLR, lymphocyte, LDH, albumin, monocyte, ferritin, and fingertip saturation values, predicting that the lung involvement of COVID-19 has increased and early treatment can be started in healthcare centers where chest CT scan is not possible or to avoid frequent CT scans. NLR, lymphocyte, LDH, albumin, monocyte, ferritin, and fingertip saturation can be used as important indicators in the follow-up of patients rather than D-dimer, CRP, and neutrophil values.

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