





Original Article



Scoring Pulmonary Fibrosis Following COVID-19 Pneumonia with Quantitative HRCT: Relationship with Clinical Parameters, Mean Platelet Volume and Lymphocyte/Monocyte Ratio

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Cite this article as: Değirmenci C, Şahin Kalkan G, Ertürk H, Ergün P. Scoring pulmonary fibrosis following COVID-19 pneumonia with quantitative HRCT: relationship with clinical parameters, mean platelet volume and lymphocyte/monocyte ratio. *Thorac Res Pract.* [Epub Ahead of Print]

Abstract

OBJECTIVE: Our study aims to quantify post-Coronavirus disease-2019 (COVID-19) pneumonia-related pulmonary fibrosis using high resolution computed tomography (HRCT) scoring and assess its correlation with clinical parameters, lymphocytes, mean platelet volume (MPV), and lymphocyte/monocyte ratio (LMR). Early detection and understanding of fibrosis progression in patient subsets are essential for enhancing post-COVID-19 patient outcomes.

MATERIAL AND METHODS: This retrospective, single-center study aims to quantify post-COVID-19 pneumonia pulmonary fibrosis using HRCT scoring and explore its associations with clinical parameters, lymphocytes, MPV, and LMR. From March 1, 2020, to December 31, 2021, HRCT reports of patients diagnosed with COVID-19 within 14 days of symptom onset were reviewed. Those with COVID-19 pneumonia were identified, and subsequent HRCTs performed 2 months or later post-infection were analyzed for fibrosis. Data on demographics, hospitalization details, and laboratory findings were collected. Fibrosis scores were determined using quantitative HRCT.

RESULTS: A total of 133 patients (60.2% male, mean age 57.3) were included. Of these patients, 50.4% were hospitalized. Quantitative HRCT analysis indicated average fibrosis of 2.7% (range: 0.9-28.7%). Lower lymphocyte counts correlated significantly with increased fibrosis ($P = 0.002$). No significant correlations were found between fibrosis development and hospitalization duration, age, or gender.

CONCLUSION: This study underscores the importance of monitoring lymphocyte counts in COVID-19 patients for early detection of pulmonary fibrosis. The findings suggest a need for screening and prompt diagnosis of fibrosis post-COVID-19, particularly in patients with lymphopenia. Further research using quantitative HRCT could enhance understanding and management of progressive interstitial lung diseases, especially in the context of future pandemics.

KEYWORDS: COVID-19, pulmonary fibrosis, quantitative HRCT, inflammation

Received: 19.07.2024

Revision Requested: 07.10.2024

Last Revision Received: 06.01.2025

Accepted: 13.01.2025

Epub: 23.01.2025

INTRODUCTION

There is currently insufficient evidence regarding the development of progressive irreversible pulmonary fibrosis characterized by widespread fibrotic involvement on high resolution computed tomography (HRCT), decreased quality of life, and increased mortality in patients who have recovered from Coronavirus disease-2019 (COVID-19) pneumonia in the long term. Early detection of pulmonary fibrosis, determining which patient groups are experiencing progression, and early initiation of treatment are crucial for improving the quality of life of patients in the post-COVID-19 period.

The most common initial tomographic findings are bilateral subpleural ground-glass opacities and consolidation in the lower zones when the radiological course of the disease is followed in the acute phase of COVID-19 pneumonia.¹ It

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often takes time for the tomographic images to improve in most patients. Ground-glass opacities may develop into consolidations approximately 4-14 days after the onset of symptoms, and after two weeks, the findings gradually disappear.¹ However, in some patients, even in early tomographies, fibrotic streaks and bronchiectasis may be examined.² There is little research on the progression of fibrosis in these patients during subsequent follow-ups, as well as on the clinical manifestations it causes and the treatments that should be applied. Additionally, there are limited studies on the use of quantitative HRCT, an objective scoring system, in the evaluation of fibrosis in progressive fibrotic interstitial lung diseases, when radiologists compare HRCT images for reporting.

It has been demonstrated in several studies that idiopathic pulmonary fibrosis (IPF) is associated with thrombotic events. In one study, patients with IPF showed higher mean platelet volume (MPV) values and lower platelet counts.³ Another study in patients with pulmonary fibrosis investigated the role of monocyte count and lymphocyte/monocyte ratio (LMR). A negative correlation was found between monocyte count and forced vital capacity, and in newly diagnosed IPF patients, an LMR <4.18 was significantly associated with shorter survival as an independent risk factor.⁴ In another study, a high monocyte count in IPF patients was associated with increased IPF progression, hospitalization, and mortality risks.⁵ However, the relationship of these parameters with fibrosis developing after COVID-19 has not been investigated.

MPV has also been associated with several diseases, excluding pulmonary. MPV has been suggested as an inflammatory marker in various inflammatory diseases, including rheumatoid arthritis,⁶ obesity,⁷ type 2 diabetes mellitus,⁸ infections.⁹

MPV is related to inflammation in the intensive care unit (ICU) population; in one study, elevated MPV levels in ICU patients should alert clinicians to worse outcomes.¹⁰ If we consider gastrointestinal diseases, red cell distribution width (RDW) and MPV values were found to be significantly higher in patients with hepatosteatosis.¹¹ RDW and MPV have been shown to be increased in subjects with irritable bowel syndrome, a condition that is associated with low-grade inflammation compared to the healthy population.¹² On the other hand, a MPV/lymphocyte ratio (MPVLR) level greater than 3.41% has 71% sensitivity and 51% specificity in predicting frailty in diabetic patients. MPVLR may be useful in predicting frailty in the type 2 diabetes population, study suggests.¹³

The aim of our study is to score pulmonary fibrosis developing after COVID-19 pneumonia using quantitative HRCT and to examine its relationship with clinical parameters, MPV, and LMR.

Main Points

- Our study examines the effects of the Coronavirus disease-2019 (COVID-19) pandemic.
- It is one of the rare studies that conducts a quantitative evaluation of post-COVID-19 fibrosis.
- In our study, the importance of the use of quantitative high resolution computed tomography were mentioned.

MATERIAL AND METHODS

This was a retrospective, single-center study. As our study was retrospective, no informed consent was obtained from patients. HRCT images taken within the first 14 days of patients diagnosed with COVID-19 in the hospital system were examined. Those with COVID-19 pneumonia (with or without ground-glass opacities, consolidations with or without air bronchograms) were identified, and among them, those who had HRCTs taken two months or later after COVID-19 infection were noted. Additionally, findings of fibrosis (honeycombing, traction bronchiectasis, interlobular septal thickening, reticular pattern) were recorded from follow-up HRCTs.¹⁴

The reason for setting the lower limit at two months is that in an immunocompetent individual, if there is less than 50% radiological improvement at two weeks despite effective treatment of pneumonia, or if there is no complete resolution at 4 weeks, delayed or unresolved pneumonia is considered.¹⁵ Therefore, individuals with persistent radiological findings associated with COVID-19 on HRCT for at least two months were included in the study. Most patients had HRCTs available at 6 or 8 months, and those eligible for were included in the study.

Determining a clear fibrosis value in IPF is difficult, similar to the challenges faced with emphysema.¹⁶ Various CT density thresholds have been proposed for evaluating the spectrum of interstitial lung diseases, including >-700 Hounsfield units (HU) and a range between -750 HU and -300 HU for specific detection of ground-glass opacities.^{17,18} Based on studies, an optimal range for post-COVID-19 fibrosis has been suggested to be between -250 and -500 HU.^{16,19}

In the follow-up of these patients, fibrosis scores were determined using quantitative HRCT. Patient age, gender, comorbidities, if any, length of hospital stay, duration of ICU, platelet count, MPV, and LMR were noted. Data analysis was conducted to examine correlations.

Inclusion criteria;

- Over 18 years of age,
- Patients who were diagnosed with COVID-19 and who were diagnosed with COVID-19 pneumonia during the active disease period at Ankara Atatürk Sanatorium Training and Research Hospital Hospital, who were COVID-19 polymerase chain reaction (PCR) positive, who were found to have COVID-19 pneumonia on HRCT imaging taken within the first 14 days, and who had follow-up HRCTs.

Patients excluded from the study;

- Those with diagnosed interstitial lung disease with fibrosis,
- Those with interstitial lung disease not associated with COVID-19 pneumonia,
- COVID-19 PCR (-) are those considered to have radiological COVID-19 disease.

Ethical approval of the study was obtained from the Ankara Atatürk Sanatorium Training and Research Hospital Clinical

Research Ethics Committee (project number: E-53610172-799, date: 09.08.2022).

Statistical Analysis

The data were evaluated using the IBM Statistical Package for the Social Sciences statistics 25.0. Descriptive statistics were provided as unit count (n), percentage (%), mean±standard deviation, and median (Q1-Q3) values. Pearson’s chi-square and Fisher’s exact test were used to evaluate categorical variables. A P value <0.05 was considered statistically significant. Multiple linear regression analysis was conducted to consider the effect of follow-up lymphocyte percentage and confounders.

RESULTS

Tomography data of patients were accessed within the specified dates (Table 1). Due to incomplete data, 65 patients were excluded from the study. Data analysis was conducted on a total of 133 patients (Figure 1). Of these, 60.2% (n = 80) were male, and 39.8% (n = 53) were female. Approximately half of the patients were hospitalized (50.4%, n = 67). The mean age of the patients was 57.3. The average length of hospital stay was 0 (0-65) days for ward admission and 0 (0-45) days for ICU admission. The initial lymphocyte count was 1.66 µL (0.2-4.26), platelet count was 252 µL (37-682), monocyte count was 6.75 µL ±2.62, MPV was 9.4 fL ±0.98, and LMR was 3.51 (0.2-11.67); while the follow-up lymphocyte count was 4.73 (0.5-19.83), follow-up platelet count was 274.03 µL ±80.66, follow-up monocyte count was 6.3 µL (0.8-12.3), MPV was 9.3 fL (7.4-12.3), and LMR was 4.73 (0.5-19.83). Quantitative HRCT analysis revealed an average of 2.7% (minimum: 0.9, maximum: 28.7) fibrosis development (Table 1). No significant relationship was found among hospitalization duration, age, gender, and fibrosis development (Table 2). Additionally,

no significant relationship was found between MPV and the development of fibrosis.

When a more detailed examination was conducted on the relationship between laboratory parameters and the development of fibrosis, it was found that patients with lower lymphocyte counts were more likely to develop pulmonary fibrosis. The statistical significance of this finding was quite strong (P = 0.002), suggesting a robust association between low lymphocyte levels and increased fibrosis (Table 2). However, no other laboratory parameter showed a statistically significant

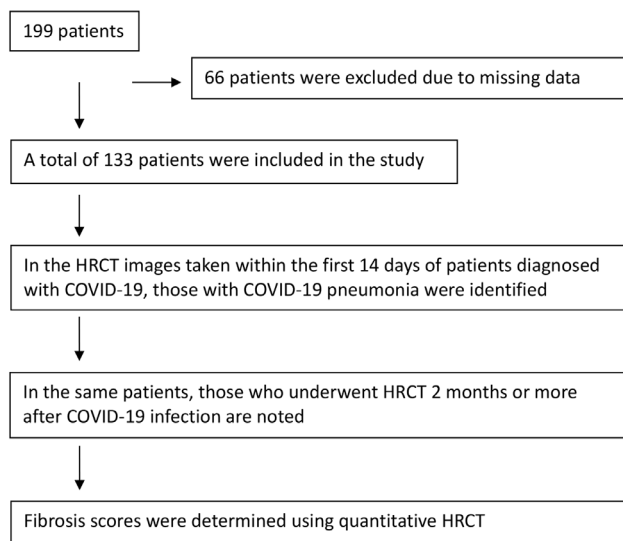


Figure 1. Selection of the study population

COVID-19: Coronavirus disease-2019, HRCT: high resolution computed tomography

Table 1. Laboratory parameters and fibrosis percentages

Variables	Descriptive statistics: n (%)*	
Clinical/laboratory/radiological features		
Gender, n = 133 (100%)	Male, n = 80 (60.2%)	
	Female, n = 53 (39.8%)	
Quantitative BT score -250 HU	99 (92-99.8)	
Quantitative BT score -500 HU	96.3 (63.3-98.6)	
Fibrosis %	2.7 (0.9-28.7)	
Hospitalization duration (day)	0 (0-65)	
	Initial values	Follow-up values
Lymphocyte (10³/µL)	1.66 (0.2-4.26)	2.49±0.99
Lymphocyte %	23.81±9.38	29.95±11.47
Monocytes (10³/µL)	0.48 (0.08-7)	0.53 (0.06-2.12)
Monocytes %	6.75±2.62	6.3 (0.8-12.3)
Platelet (10³/µL)	252 (37-682)	274.03±80.66
Mean platelet volume (fL)	9.4±0.98	9.3 (7.4-12.3)
Lymphocyte monocytes ratio	3.51 (0.2-11.67)	4.73 (0.5-17.63)
Lymphocyte % monocytes % ratio	3.49 (0.27-23)	4.73 (0.5-19.83)

*Mean±standard deviation is given for normally distributed variables, median (minimum-maximum) is given for non-normally distributed variables. HU: hounsfield unit, BT: bleeding time

Table 2. Correlation analysis between fibrosis development and the study parameters

Fibrosis %	Correlation coefficient	Fibrosis %	Hospitalization duration	Onset lymphocyte %	Onset lymphocyte	Onset monocytes %	Onset monocytes	Onset platelet	Onset MPV	ICU duration	Follow-up lymphocyte %	Follow-up lymphocyte	Follow-up monocytes %	Follow-up monocytes	Follow-up platelet	Follow-up MPV
1.00		1.00	0.015	0.086	-0.063	-0.006	-0.162	0.051	-0.081	0.132	-0.165	-0.264	0.017	-0.036	-0.065	-0.069
P		0.084	0.084	0.324	0.469	0.941	0.063	0.0557	0.352	0.129	0.058	0.002	0.843	0.677	0.459	0.428
n		133	133	133	133	133	133	133	133	133	133	133	133	133	133	133

ICU: intensive care unit, MPV: mean platelet volume

relationship with fibrosis development. This means that aside from lymphocyte counts, other measured values in the lab tests did not significantly affect the likelihood of the patients studied developing fibrosis. Furthermore, when considering the percentage of fibrosis development, no significant relationships were found with gender ($P = 0.207$) or hospitalization duration ($P = 0.151$) (Table 2). This suggests that neither the patient's gender nor the length of their hospital stay significantly influenced the extent of fibrosis development.

Box-Cox transformation was applied to the dependent variable, fibrosis %, to satisfy linear regression assumptions such as normality of residuals. Age, gender, and hospitalization duration variables, in addition to the follow-up lymphocyte %, were added to the model as confounders. The results of the model are provided in Table 3. According to the table, follow-up lymphocyte percentage still significantly affects fibrosis percentage after controlling for confounders ($P = 0.004$).

DISCUSSION

The effects of the COVID-19 pandemic continue worldwide, although the pandemic appears to be over, and we have not yet discovered other unknown side effects and long-term systemic effects. Pulmonary effects significantly affect human life and quality of life, and there is a need for new studies on diseases with pathogenesis and treatments that are not yet fully understood, such as fibrosis. In our study, we gathered valuable insights into the development of pulmonary fibrosis, a condition that significantly impacts long-term survival and quality of life. We observed that patients with a decrease in lymphocyte count, as measured by routine blood tests, experienced a notably higher rate of fibrosis progression. This finding has been instrumental in allowing us to monitor these patients more closely. When found in low numbers, lymphocytes, vital components of the immune system, may signal a weakened immune response, which could, in turn, accelerate the development of fibrosis. Our study highlights a clear link between low lymphocyte counts and increased fibrosis progression, underscoring the critical role of lymphocytes in understanding and managing this condition. These findings underscore the need for further research to understand the underlying mechanisms and to identify other potential factors that may influence fibrosis progression.

Humphries et al.²⁰ conducted a study examining the relationship between quantitative HRCT scores, pulmonary function tests, and the six-minute walk test in 141 patients diagnosed with IPF. It was shown that the measurement of lung fibrosis degree in quantitative HRCT is reliable and sensitive. A 3.4% increase in fibrosis score leads to a clinically significant decrease in patient performance. In our study, an average fibrosis development of 2.7% was detected, and without a pandemic period, a similar correlation could have been observed if these patients had undergone serial pulmonary function tests.

In a study on the quantitative HRCT detection of honeycombing areas in IPF, the honeycombing area measured by computer-aided methods showed a correlation with that estimated by expert radiologists and with parameters of pulmonary function tests. This study demonstrated that quantitative HRCT analysis

Table 3. Evaluation of the effect of follow-up lymphocyte percentage and confounders using multiple linear regression analysis

	β	SE (β)	Beta	t	P value	95% confidence interval for β	
						Lower bound	Upper bound
(Constant)	-0.499	0.467		-1.067	0.288	-1.423	0.426
Age	0.019	0.006	0.244	3.015	0.003	0.006	0.031
Gender	-0.163	0.162	-0.080	-1.004	0.317	-0.484	0.158
Hospitalization duration	0.025	0.009	0.226	2.813	0.006	0.007	0.042
Follow-up lymphocyte %	-0.021	0.007	-0.235	-2.898	0.004	-0.035	-0.007

F=7.622, $P < 0.001$, adjusted R^2 : 0.17.
SE: standard error

of honeycombing areas may be useful and reliable in patients with IPF.²¹

In another study evaluating mortality in IPF patients using quantitative HRCT, correlation with pulmonary function tests was examined, and it was emphasized that quantitative scoring of HRCT can provide accurate predictions for survival.²² Mortality data were not examined in our study because attributing the cause of death in patients with pulmonary fibrosis was not possible, as long-term follow-up was not performed.

In a study investigating the relationship between platelet count and MPV with IPF, it was found that MPV was higher in IPF patients and associated with both high and low platelet counts. This finding suggests that MPV could be used as an initial biomarker in IPF patients, but more comprehensive studies are needed.³ However, in our study, no relationship was found between MPV and platelet count, and fibrosis developing after COVID-19.

In a study by Yu et al.²³ aimed at predicting the development of fibrosis following COVID-19 pneumonia, it was shown that fibrosis was more likely to develop in patients with high inflammatory markers (interleukin-6) and severe clinical conditions. Predictors of pulmonary fibrosis, such as interstitial thickening, irregular interfaces, coarse reticular pattern, and parenchymal bands, were identified as emerging during the disease process. It was indicated that irregular interfaces and parenchymal bands could be used to predict the early onset of pulmonary fibrosis.

In a recent investigation into the relationship between various laboratory parameters and the development of fibrosis, researchers focused specifically on lymphocyte counts. Fibrosis, which is the excessive accumulation of extracellular matrix components leading to tissue scarring, can significantly impact organ function and is associated with various chronic diseases.²⁴ For example, increased monocyte-to-lymphocyte ratio (MLR) levels are reliable markers of disease activity in ulcerative colitis and have been linked to active inflammation in inflammatory bowel disease.²⁵

Numerous studies have demonstrated that lung cancer can develop from pulmonary fibrosis.²⁶⁻²⁸ Also, a multicenter retrospective study of 345 patients with IPF found that those receiving antifibrotic therapy had a significantly lower incidence and prevalence of lung cancer compared to those

not receiving treatment.²⁹ Additionally, lung cancer-related mortality was significantly lower in patients on antifibrotic therapy.²⁹ These findings suggest that antifibrotic therapy may be associated with a reduced risk of lung cancer development in IPF patients, potentially contributing to improved survival.

In a study of 113 patients with small cell lung cancer, survival was significantly longer in patients with MLR < 0.367 than in those with MLR ≥ 0.367 .³⁰ The development of fibrosis can also lead to malignancy in extrapulmonary organs, and studies have explored the role of MLR in predicting this. In particular, in gastrointestinal cancers, a high MLR predicts survival in gastric cancer and is associated with tumour response to neoadjuvant chemoradiotherapy in rectal cancer.³¹ In hepatocellular carcinoma, high MLR is associated with poor outcomes and shorter progression intervals.³² In gastrointestinal cancers, the majority of studies support that a high MLR indicates a poor prognosis, although there are few studies to the contrary.³³

The study found that patients with lower lymphocyte counts tended to exhibit a greater propensity for fibrosis development. Lymphocytes are a crucial component of the immune system, playing vital roles in immune response and inflammation regulation. Their reduction may indicate an impaired immune response, which can facilitate the fibrotic process.

This discovery may have important clinical implications, as it highlights the potential role of lymphocyte levels as a biomarker for fibrosis risk. Understanding this relationship could lead to improved monitoring and therapeutic strategies for patients at risk of fibrotic diseases, allowing for earlier intervention and potentially better outcomes. Further research is needed to explore the underlying mechanisms that connect lymphocyte counts with fibrosis development, which may involve complex interactions between the immune system and fibrogenic pathways.

One of the limitations of the study was the inclusion of a small number of patients and its single-center design. Also, the patient group included in the study was not homogeneous; the number of male and female patients was not equally distributed, and baseline comorbidities were not recorded. The only people excluded were those with a previous diagnosis of interstitial lung disease, which was an important part of our study. However, when considering the strengths of the study, its importance lies in being the first study in the literature on quantitative HRCT and post-COVID-19 pulmonary fibrosis.

CONCLUSION

In conclusion, the assessment of IPF using HRCT requires considerable expertise, and there may be differences in interpretation even between experienced radiologists. Screening and early detection of pulmonary fibrosis will allow early initiation of treatment, and slowing fibrosis can improve patients' quality of life. Considering the possibility of new outbreaks unrelated to COVID-19, the importance of the widespread use of quantitative HRCT, paired with an objective scoring system for the assessment of fibrosis in progressive fibrotic interstitial lung disease, is emphasised. We believe that our study is valuable in this regard and provides important data for future research.

Ethics

Ethics Committee Approval: Ethical approval of the study was obtained from Ankara Atatürk Sanatorium Training and Research Hospital Clinical Research Ethics Committee (project number: E-53610172-799, date: 09.08.2022).

Informed Consent: Written informed consent was obtained from all patients during the time they were hospitalized for their clinical data to be registered in the database and used anonymously for scientific purposes.

Acknowledgements

The authors thank patients for their participation in the study.

Presented in: This study was presented as an oral presentation at the 27th Annual International Congress of the Turkish Thoracic Society.

Footnotes

Authorship Contributions

Concept: C.D., P.E., G.Ş.K., H.E., Design: C.D., P.E., G.Ş.K., H.E., Data Collection or Processing: C.D., G.Ş.K., H.E., Analysis or Interpretation: C.D., P.E., G.Ş.K., H.E., Literature Search: C.D., P.E., G.Ş.K., H.E., Writing: C.D., P.E., G.Ş.K., H.E.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Türkaş H, Oğuzgülen İK. Post-COVID-19 pulmonary sequela: longterm follow up and management. *Tuberk Toraks*. 2020;68(4):419-429. [\[Crossref\]](#)
2. Fang Y, Zhou J, Ding X, Ling G, Yu S. Pulmonary fibrosis in critical ill patients recovered from COVID-19 pneumonia: Preliminary experience. *Am J Emerg Med*. 2020;38(10):2134-2138. [\[Crossref\]](#)
3. Steiropoulos P, Boglou P, Ntoliou P, et al. Platelet activation indices in patients with idiopathic pulmonary fibrosis. *European Respiratory Journal*. 2014;44(Suppl 58). [\[Crossref\]](#)
4. Bernardinello N, Grisostomi G, Coconcelli E, et al. The clinical relevance of lymphocyte to monocyte ratio in patients with Idiopathic Pulmonary Fibrosis (IPF). *Respir Med*. 2022;191:106686. [\[Crossref\]](#)
5. Kreute M, Lee JS, Tzouveleakis A, et al. Monocyte count as a prognostic biomarker in patients with idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2021;204(1):74-81. [\[Crossref\]](#)
6. Cakir L, Aktas G, Mercimek B, Enginyurt O, Kaya Y, Mercimek K. Are red cell distribution width and mean platelet volume associated with rheumatoid arthritis. *Biomed Res*. 2016;27(2):292-294. [\[Crossref\]](#)
7. Aktas G, Kocak MZ, Duman TT, Erkuş E, Atak BM. Mean platelet volume (MPV) as an inflammatory marker in type 2 diabetes mellitus and obesity. *Bali Med J*. 2018;7(3):650-653. [\[Crossref\]](#)
8. Cakir L, Aktas G, Enginyurt Ö, Çakir ŞA. Mean platelet volume increases in type 2 diabetes mellitus independent of HbA1c level. *Acta Medica Mediterranea*. 2014;30(2):425-428. [\[Crossref\]](#)
9. Aktas G, Çakiroğlu B, Şit M, et al. Mean platelet volume: a simple indicator of chronic prostatitis. *Acta Medica Mediterranea*. 2013;29:551-554. [\[Crossref\]](#)
10. Karagoz I, Aktas G, Yoldas H, et al. Association between hemogram parameters and survival of critically ill patients. *J Intensive Care Med*. 2019;34(6):511-513. [\[Crossref\]](#)
11. Aktas G, Alcelik A, Tekce BK et al. Mean platelet volume and red cell distribution width in hepatosteatosis. *National Journal of Medical Research*. 2013;3(3):264-266. [\[Crossref\]](#)
12. Aktas G, Alcelik A, Tekce BK, Tekelioglu V, Sit M, Savli H. Red cell distribution width and mean platelet volume in patients with irritable bowel syndrome. *Prz Gastroenterol*. 2014;9(3):160-163. [\[Crossref\]](#)
13. Bilgin S, Aktas G, Kahveci G, Atak BM, Kurtkulagi O, Duman TT. Does mean platelet volume/lymphocyte count ratio associate with frailty in type 2 diabetes mellitus? *Bratisl Lek Listy*. 2021;122(2):116-119. [\[Crossref\]](#)
14. Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between Chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. *AJR Am J Roentgenol*. 2020;214(5):1072-1077. [\[Crossref\]](#)
15. Raj A, Venugopal KPP, Musthafa S, Narayan KV. Characterising aetiologies and clinical-radiological factors of non-resolving pneumonia in a tertiary care centre. *Egypt J Bronchol*. 2024;18(1):61. [\[Crossref\]](#)
16. Chen A, Karwoski RA, Gierada DS, Bartholmai BJ, Koo CW. Quantitative CT analysis of diffuse lung disease. *Radiographics*. 2020;40(1):28-43. [\[Crossref\]](#)
17. Jacob J. Quantitative CT analysis in ILD and use of artificial intelligence on imaging of ILD. *ERS Monograph: Pulmonary Manifestations of Systemic Diseases*. 2019;86:27-43. [\[Crossref\]](#)
18. Shin KE, Chung MJ, Jung MP, Choe BK, Lee KS. Quantitative computed tomographic indexes in diffuse interstitial lung disease: correlation with physiologic tests and computed tomography visual scores. *J Comput Assist Tomogr*. 2011;35(2):266-271. [\[Crossref\]](#)
19. Hasan D, Imam H, Megally H, Makhlof H, Elkady R. The qualitative and quantitative high-resolution computed tomography in the evaluation of interstitial lung diseases. *Egypt J Radiol Nucl Med*. 2020;51(1):135. [\[Crossref\]](#)
20. Humphries SM, Swigris JJ, Brown KK, et al. Quantitative high-resolution computed tomography fibrosis score: performance characteristics in idiopathic pulmonary fibrosis. *Eur Respir J*. 2018;52(3):1801384. [\[Crossref\]](#)

21. Nakagawa H, Nagatani Y, Takahashi M, et al. Quantitative CT analysis of honeycombing area in idiopathic pulmonary fibrosis: correlations with pulmonary function tests. *Eur J Radiol.* 2016;85(1):125-130. [\[Crossref\]](#)
22. Torrisi SE, Palmucci S, Stefano A, et al. Assessment of survival in patients with idiopathic pulmonary fibrosis using quantitative HRCT indexes. *Multidiscip Respir Med.* 2018;13:43. [\[Crossref\]](#)
23. Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia. *Korean J Radiol.* 2020;21(6):746. [\[Crossref\]](#)
24. Antar SA, Ashour NA, Marawan ME, Al-Karmalawy AA. Fibrosis: types, effects, markers, mechanisms for disease progression, and its relation with oxidative stress, immunity, and inflammation. *Int J Mol Sci.* 2023;24(4):4004. [\[Crossref\]](#)
25. Cherfane CE, Gessel L, Cirillo D, Zimmerman MB, Polyak S. Monocytosis and a low lymphocyte to monocyte ratio are effective biomarkers of ulcerative colitis disease activity. *Inflamm Bowel Dis.* 2015;21(8):1769-1775. [\[Crossref\]](#)
26. Karampitsakos T, Tzilas V, Tringidou R, et al. Lung cancer in patients with idiopathic pulmonary fibrosis. *Pulm Pharmacol Ther.* 2017;45(1):10. [\[Crossref\]](#)
27. Tzouvelekis A, Gomatou G, Bouros E, Trigidou R, Tzilas V, Bouros D. Common pathogenic mechanisms between idiopathic pulmonary fibrosis and lung cancer. *Chest.* 2019;156(2):383-391. [\[Crossref\]](#)
28. Duan J, Zhong B, Fan Z, et al. DNA methylation in pulmonary fibrosis and lung cancer. *Expert Rev Respir Med.* 2022;16(5):519-528. [\[Crossref\]](#)
29. Naoi H, Suzuki Y, Mori K, et al. Impact of antifibrotic therapy on lung cancer development in idiopathic pulmonary fibrosis. *Thorax.* 2022;77(7):727-730. [\[Crossref\]](#)
30. Sakin A, Sahin S, Yasar N, et al. The relation between hemogram parameters and survival in extensive-stage small cell lung cancer. *Oncol Res Treat.* 2019;42(10):506-514. [\[Crossref\]](#)
31. Hamid HKS, Emile SH, Davis GN. Prognostic significance of lymphocyte-to-monocyte and platelet-to-lymphocyte ratio in rectal cancer: a systematic review, meta-analysis, and meta-regression. *Dis Colon Rectum.* 2022;65(2):178-187. [\[Crossref\]](#)
32. Wang Q, Qiao W, Liu B, et al. The monocyte to lymphocyte ratio not only at baseline but also at relapse predicts poor outcomes in patients with hepatocellular carcinoma receiving locoregional therapy. *BMC Gastroenterol.* 2022;22(1):98. [\[Crossref\]](#)
33. Balci BS, Aktas G. A comprehensive review of the role of hemogram derived inflammatory markers in gastrointestinal conditions. *Iran J Colorectal Res.* 2022;10(3):75-86. [\[Crossref\]](#)