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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(2):399-404

Assessing the relationship between CO-RADS scores and hemogram parameters in COVID-19

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Received 19 January 2025; Accepted 12 February 2025
Available online 31 May 2025 with doi: 10.5455/medscience.2025.01.015

Abstract

The Coronavirus disease 2019 (COVID-19) Reporting and Data System (CO-RADS) is a standardized Computed Tomography (CT) assessment tool for COVID-19 pneumonia. However, its correlation with hematological parameters needs further investigation. This study aimed to evaluate the relationship between CO-RADS scores and hemogram parameters in COVID-19 patients and assess their potential role in predicting disease severity. This retrospective study included 6,703 Polymerase Chain Reaction (PCR)-confirmed COVID-19 patients who presented to the emergency department between March 15 and June 15, 2020. Patients were classified according to CO-RADS scoring [1-5], and their demographic data, hemogram parameters, and CT findings were analyzed. The relationship between CO-RADS scores and laboratory parameters was evaluated, and ROC analysis was performed to determine cut-off values for predicting severe disease (CO-RADS 4-5). The mean age of patients was 56.8±17.2 years, and 48% were female. Analysis revealed significant correlations between CO-RADS scores and various hemogram parameters. Higher CO-RADS scores correlated with elevated white blood cell (WBC), neutrophils, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR), while lymphocytes decreased ($p<0.001$). ROC analysis identified NLR as the strongest predictor of severe involvement (AUC: 0.862, 95% CI: 0.844-0.880), with a cut-off value of 4.32 yielding 82.4% sensitivity and 76.8% specificity. PLR (cut-off: 245) also showed significant predictive value (AUC: 0.816), while MLR and lymphocyte count demonstrated lower predictive values (AUC: 0.712 and 0.742, respectively). The CO-RADS scoring system is strongly correlated with inflammatory markers and can serve as a reliable tool for assessing COVID-19 severity. The established cut-off values for NLR and PLR could be valuable in predicting severe disease, potentially aiding in clinical decision-making and patient triage. These findings suggest that integrating CO-RADS scoring with hemogram parameters might improve the assessment of COVID-19 severity in clinical practice.

Keywords: COVID-19, CO-RADS, computed tomography, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, disease severity

Introduction

Coronavirus disease 2019 (COVID-19) is an infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that emerged in Wuhan, China, in December 2019 and quickly became a global health threat [1]. Rapid and reliable diagnostic methods are needed for early diagnosis and to control the spread of the disease. Reverse Transcriptase Polymerase Chain Reaction (PCR-RT), which is currently considered the gold standard for diagnosing COVID-19, has varying sensitivities depending on symptom duration and sample type [2]. Furthermore, the test can detect high viral loads and a negative test result does not exclude disease [2,3]. Computed Tomography (CT) is a time-saving and non-invasive imaging modality that is widely used in the diagnosis of COVID-19. CT has been shown to be highly sensitive in diagnosing COVID-19 and effective for monitoring disease progression [4]. However, due to differences

CITATION
Bulut B, Genc M, Akkan Oz M, et al. Assessing the relationship between CO-RADS scores and hemogram parameters in COVID-19. Med Science. 2025;14(2):399-404.

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DOI: 10.5455/medscience.2025.01.015

in interpretation between radiologists and centres, a standardised reporting system was needed. For this purpose, the COVID-19 Reporting and Data System (CO-RADS) was created by the Dutch Radiological Society and a 5-point scoring system (CO-RADS 1 to 5) was defined for the evaluation of CT images [5].

The cause of death in COVID-19 is usually Acute Respiratory Distress Syndrome (ARDS) caused by SARS-CoV-2 [3,6,7]. In the early stages of ARDS, a cytokine storm occurs due to uncontrolled increase in the release of cytokines, and sepsis develops as a result of this uncontrolled release [5-9]. It has been reported that acute phase reactants such as C-reactive protein (CRP) and hemogram parameters are affected at the onset of this cytokine storm [8-11]. It has been discussed that the diagnosis of COVID-19 can be made using inflammatory markers and even hemogram parameters [11-13]. It is obvious that an effective laboratory test is needed to reliably diagnose a disease that is threatening the whole world.

In this study, we aimed to evaluate the use of the CO-RADS classification system and its correlation with laboratory parameters in patients diagnosed with COVID-19. Our study will contribute to the literature by demonstrating the role of CO-RADS scoring in predicting disease severity and its correlation with laboratory parameters.

Material and Methods

Study Design and Participants

This study was conducted between 15 March 2020 and 15 June 2020 at Ankara Yenimahalle Training and Research Hospital Emergency Department COVID-19 Outpatient Clinic. It consisted of patients over 18 years of age who came to Ankara Yenimahalle Training and Research Hospital Emergency Department COVID-19 Outpatient Clinic and were diagnosed with COVID 19 by PCR-RT. Approval was obtained from the Ethics Committee of the Dr. Abdurrahman Yurtaslan Oncology Health Practice and Research Centre of the Health Sciences University (ethics committee no: 2020-07/704, desicion date: 08.07.2020). Demographic data, chronic diseases, hemogram parameters and CT imaging findings were collected retrospectively and each case was studied separately. Patients were divided into four groups based on their age: 18-44, 45-59, 60-74, 75 years and older. For patients who presented to the COVID-19 Emergency Department (ED), full body physical examination and requesting of hemogram and biochemical parameters were performed routinely in our hospital. If deemed appropriate by the attending physicians depending on the clinical condition and the results of the physical examination, chest CT imaging was requested. CT images were interpreted by the radiologist and classified according to the CO-RADS.

CO-RADS classification is as follows:

- CO-RADS 1 represents a very low suspicion of COVID-19-related lung lesions, either due to a normal CT scan or findings with an uncertain infectious origin;
- CO-RADS 2 refers to lung CT findings that point to infections other than COVID-19, including conditions like bronchopneumonia, lobar pneumonia, bronchitis, infectious bronchiolitis, or pulmonary abscess;
- CO-RADS 3 indicates uncertain CT findings for COVID-19 lung involvement, which could also be observed in other viral pneumonias or non-infectious causes;
- CO-RADS 4 signifies a strong likelihood of COVID-19-related lung involvement, based on characteristic CT findings, though there may be some similarities with other forms of (viral); pneumonia;
- CO-RADS 5 signifies a very high probability of COVID-19-related lung lesion, supported by characteristic CT findings.

Patients with a CT finding of CO-RADS 4-5 were considered to be severe cases.

Patients were considered eligible for inclusion in our study if they were over 18 years old, underwent chest CT, had a hemogram performed upon admission to the ED, were diagnosed with COVID-19 through PCR-RT, and had complete datasets. Conversely, patients under 18 years old, those not diagnosed by PCR-RT, those who did not undergo chest CT, or those with incomplete data for any studied parameter were excluded from the study. The study was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was not required due to the retrospective nature of the study.

Statistical Analysis

Data analysis was performed using IBM SPSS 27.0 (Armonk, NY: IBM Corp.). In addition to descriptive statistical methods (frequency, percentage, mean, standard deviation, median, IQR), chi-square test (χ^2) was used to compare qualitative data. The Bonferroni correction was applied in cases where there was a difference in multiple comparisons. Conformity of the data to a normal distribution was assessed using the Kolmogorov-Smirnow test, skewness-kurtosis and graphical methods (histogram, Q-Q plot, StemandLeaf, boxplot). Independent samples t-test and one-way ANOVA test were used to compare quantitative data with normal distribution, and Mann-Whitney U test was used to compare data with non-normal distribution. Relationships between variables were assessed using Spearman's rho correlation test. The level of statistical significance was accepted as α=0.05.

Results

Of the 25,462 patients who presented to our COVID-19 ED within the specified time frame, 8,612 patients were excluded from our study because of lack of chest CT imaging, 2,461 for lack of hemogram results, 1,024 because they were repeat presentations and 6,662 for other reasons. A total of 6,703 patients were included in the study (Figure 1). The mean age of the patients included in the study was 56.8±17.2 years and

DOI: 10.5455/medscience.2025.01.015

3,218 (48%) of them were female. Analysing the distribution of patients by age group, the most common age group was 18-44 years, representing 32% (2144) of the enrolled patients. CO-RADS classification of one third of the patients was CO-RADS 3. The CO-RADS distribution of the patients according to demographic data and age groups is shown in Table 1.

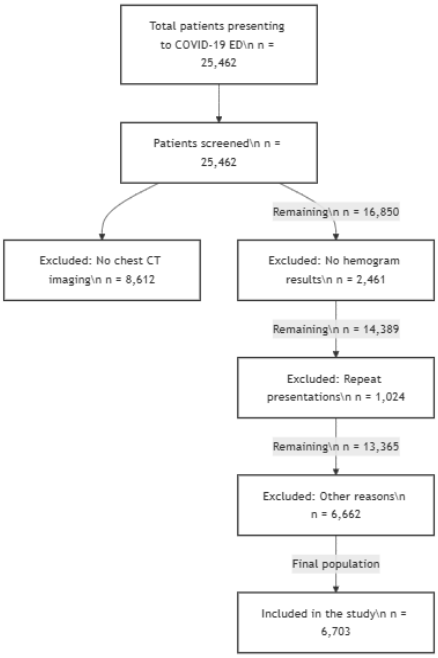

Figure 1. Patient flow chart

Table 1. CO-RADS distribution according to age groups and demographic data

Variables	Total n (%)	CO-RADS 1 n (%)	CO-RADS 2 n (%)	CO-RADS 3 n (%)	CO-RADS 4 n (%)	CO-RADS 5 n (%)	P value*
Gender							
Male, n (%)	3485 (52.0)	486 (13.9)	731 (21.0)	1115 (32.0)	696 (20.0)	457 (13.1)	0.124
Female, n (%)	3218 (48.0)	452 (14.0)	676 (21.0)	1061 (33.0)	612 (19.0)	417 (13.0)	
Age, (Mean±SD)	56.8±17.2						
Distribution of imaging findings according to age groups (y)							
18-44 y (young adult)	2144 (32.0)	386 (18.0)	365 (17.0)	815 (38.0)	386 (18.0)	192 (9.0)	
45-59 y (middle age)	2078 (31.0)	270 (13.0)	457 (22.0)	665 (32.0)	457 (22.0)	229 (11.0)	
60-74 y (old age)	1742 (26.0)	191 (11.0)	296 (17.0)	522 (30.0)	383 (22.0)	350 (20.0)	**0.008***
≥75 y (geriatric)	739 (11.0)	59 (8.0)	96 (13.0)	230 (31.0)	206 (28.0)	148 (20.0)	
Total	6703 (100)	906 (13.5)	1214 (18.1)	2232 (33.3)	1432 (21.4)	919 (13.7)	

CO-RADS: COVID-19 reporting and data system, SD: standard deviation, y: year, n: number; Data represented as mean±standard deviation, median and 25th–75th percentiles or n (%), *p-value<0.05

When laboratory parameters were evaluated in relation to CO-RADS scores, we found that white blood cell (WBC), neutrophil, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR) increased and lymphocyte values decreased in high CO-RADS scores (p: <0.001). Laboratory parameters of patients in relation to their CO-RADS score are shown in Table 2.

DOI: 10.5455/medscience.2025.01.015

Table 2. Laboratory parameters in relation to CO-RADS scores

Variables	CO-RADS 1	CO-RADS 2	CO-RADS 3	CO-RADS 4	CO-RADS 5	p-value*
WBC	6.8±1.9	7.4±2.2	8.1±2.6	8.6±2.8	9.2±3.1	**<0.001**
Neutrophils	4.2±1.4	5.1±1.6	6.2±1.9	7.0±2.1	7.8±2.4	**<0.001**
Lymphocytes	1.9±0.5	1.6±0.4	1.2±0.4	0.9±0.3	0.7±0.3	**<0.001**
Monocytes	0.51±0.16	0.53±0.17	0.55±0.18	0.56±0.19	0.58±0.20	**0.042**
Platelets	238±52	242±54	235±56	232±58	228±60	0.086
MPV	10.1±0.9	10.4±1.0	10.7±1.1	11.0±1.2	11.2±1.3	**0.032**
RDW-CV	13.1±1.1	13.4±1.2	13.8±1.3	14.3±1.4	14.8±1.5	**0.015**
NLR	2.2±0.8	3.2±1.2	5.2±2.1	7.8±3.1	11.1±4.2	**<0.001**
PLR	125.3±42.6	151.3±52.4	195.8±72.6	257.8±92.4	385.7±112.3	**<0.001**
MLR	0.27±0.10	0.33±0.13	0.46±0.18	0.62±0.24	0.83±0.32	**0.028**
MPV/Plt	0.042±0.009	0.043±0.010	0.046±0.011	0.047±0.012	0.049±0.013	**0.045**

CO-RADS: COVID-19 reporting and data system, WBC: white blood cell, MPV: mean platelet volume, RDW-CV: red cell distribution width- coefficient of variation, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, MPV/Plt: mean platelet volume-to-platelet ratio; Data represented as mean±standard deviation, median and 25th–75th percentiles or n (%), *p-value<0.05

According to the results of the receiver operating characteristic (ROC) analysis of the statistically significant parameters, NLR was found to have the highest predictive value for severe involvement (CO-RADS 4-5) (AUC: 0.862, 95% CI: 0.844-0.880). When the cut-off for NLR was set at 4.32, severe involvement could be predicted with 82.4% sensitivity and 76.8% specificity. The PLR (cut-off: 245) also had a significant predictive value (AUC: 0.816). MLR and lymphocyte count had a lower predictive value (AUC: 0.712 and 0.742, respectively) (Table 3).

Table 3. Analysis of the area under the ROC curve for severe involvement (CO-RADS 4-5)

	AUC	95% CI	Cut-off	Sensitivity	Specificity	+PV	-PV	p value*
NLR	0.862	0.844-0.880	>4.32	82.4	76.8	80.3	98.5	<0.001
PLR	0.816	0.798-0.834	>245.0	76.2	74.5	85.9	98.8	<0.001
MLR	0.712	0.692-0.732	>0.48	68.4	65.7	73.6	99.1	<0.001
Lymphocyte count	0.742	0.722-0.762	>1.1	70.6	71.2	44.2	97.9	0.488

ROC: receiver operating characteristic, AUC: area under the curve, CI: confidence interval, PPV: positive predictive value; NPV: negative predictive value, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio; Data represented as mean±standard deviation, median and 25th–75th percentiles or n (%), *p-value<0.05

Discussion

Imaging modalities play an significant role in the early diagnosis of COVID-19 and the assessment of disease severity. The CO-RADS is a 5-point scoring system developed by the Dutch Radiological Society to standardise CT assessment of COVID-19 pneumonia and facilitate reporting [14]. CT is known to have a high performance in detecting COVID-19 infection [14,15]. In our study, in which we evaluated the use of the CO-RADS classification system in 6,703 patients diagnosed with COVID-19 and the relationship of this system with laboratory parameters, we found that WBC, neutrophil, NLR, PLR and MLR increased and lymphocyte values decreased in high CO-RADS scores.

In our study, we observed a positive correlation between CO-RADS score and age and inflammatory markers, and a negative correlation with lymphocyte count. De Smet et al. highlighted that there was a strong correlation between CT findings and clinical severity and that CT was a valuable tool in predicting disease severity [16]. Similarly, Bellini et al. showed that the

DOI: 10.5455/medscience.2025.01.015

CO-RADS scoring system has a high reliability in the diagnosis and follow-up of the disease [17].

Inflammatory markers and lymphocyte count are important parameters in assessing the severity of COVID-19 infection [8-11]. In our study, lower lymphocyte counts and higher inflammatory markers were found in patients with positive CT findings. In the study conducted by Fan et al, it was highlighted that lymphopenia and high levels of LDH were important markers to show the severity of the disease in patients with COVID-19 [18]. In addition, in our study, CT-positive patients were of older age and male gender was predominant. This finding is compatible with the results of the study conducted by Schalekamp et al. in the emergency department [19].

Lessmann et al. reported that CO-RADS scoring with artificial intelligence-assisted evaluation showed high performance in the diagnosis of COVID-19 [20]. Fujioka et al. also showed that CO-RADS is a reliable tool in the assessment of COVID-19 pneumonia and that interobserver consistency is high [21]. Similar to the literature, according to the ROC analysis results of our study, the sensitivity and specificity of CT were found to be 90.5% and 25%, respectively.

Interpreting radiological and laboratory findings together in COVID-19 infection is of great importance in determining the severity of the disease. In our study, the strong positive correlation between CO-RADS score and inflammatory markers and the negative correlation with lymphocyte count showed that imaging findings were compatible with laboratory parameters. In the study conducted by Lieveld et al. in the emergency department, it was emphasised that the CO-RADS score was an effective method to evaluate the gravity of the disease and that it to contributes to clinical decision making [22]. Similarly, Hermans et al. reported that CO-RADS is a reliable triage tool in the assessment of patients with possibly infected with COVID-19 [23].

The NLR, PLR, MLR and lymphocyte cut-off values obtained in our study provide a valuable guide for risk assessment and patient triage. The study by Yang et al. reveals that integration of such cut-off values into clinical practice leads to improvements in patient management [24]. The use of inflammatory markers in the management of COVID-19 may not only improve individual patient management, but also the overall capacity of healthcare systems. Integration of markers such as NLR, PLR and MLR into routine clinical practice may provide more accurate prediction of prognosis and optimisation of treatment processes [25]. Future validation of these markers in different populations will be an important contribution to the literature [26].

This study makes several unique contributions to the literature. First, with a large sample size of 6,703 patients, it represents one of the most comprehensive investigations examining the relationship between CO-RADS scoring and hemogram parameters. The cut-off values determined in our study -4.32 for NLR and 245 for PLR - demonstrate higher accuracy rates compared to previously reported values in the literature. Furthermore, this study is among the first to thoroughly examine the relationship between CO-RADS scoring and MLR values, adding a novel dimension to existing knowledge. Another distinctive aspect of our research is its provision of practical cut-off values that can be utilized for COVID-19 patient triage in emergency department settings. These values offer clinicians concrete and reliable guidance in patient management, particularly during periods when healthcare systems are under intense pressure, such as during a pandemic. The cut-off values we established enable more efficient use of hospital resources and allow for more objective risk stratification. Additionally, our study's integration of radiological findings with multiple hematological parameters provides a more comprehensive approach to disease severity assessment than previous studies, which typically focused on individual markers. This multi-parameter approach enhances the practical utility of our findings in clinical decision-making processes.

The strengths of our study include the large number of patients, confirmation of diagnoses by PCR-RT and detailed analyses with CO-RADS and hemogram parameters; however, the study includes a few limitations. First, the study was conducted using single-center data and the results may not be generalizable to the whole population; second, some clinical data could not be fully evaluated due to the retrospective design. Finally, the absence of long-term patient follow-up data prevented the evaluation of long-term complications.

Conclusion

In conclusion, the CO-RADS scoring system provides a reliable and practical diagnostic tool for evaluating patients with COVID-19. The positive correlation of the CO-RADS score with inflammatory markers and the negative correlation with lymphocyte count show that imaging findings are compatible with laboratory parameters. This finding suggests that the CO-RADS scoring system is an objective tool that can be used to predict the severity of COVID-19 infections. These findings should be validated in larger, multicenter, prospective studies, including AI-based automation of CO-RADS assessment.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Approval was obtained from the Ethics Committee of the Dr. Abdurrahman Yurtaslan Oncology Health Practice and Research Centre of the Health Sciences University (ethics committee no: 2020-07/704, desicion date: 08.07.2020).

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