Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1180896
J Health Sci Med 2022; 5(6): 1682-1687

Does radiographic evaluation pulmonary edema score predict intensive care admission in COVID-19 patients presenting to the emergency department? A retrospective single-center observational study

Hilal Sipahioğlu[1], Ali Yeşiltepe[2], Mine Altınkaya Çavuş[1], Ayşe Kırış[2], Ahmet Savranlar[3]

[1]Kayseri City Training and Research Hospital, Department of Critical Care, Kayseri, Turkey
[2]Kayseri City Training and Research Hospital, Department of Internal Medicine, Kayseri, Turkey
[3]Kayseri City Training and Research Hospital, Department of Radiology, Kayseri, Turkey

Cite this article as: Sipahioğlu H, Yeşiltepe A, Altınkaya Çavuş M, Kırış A, Savranlar A. Does radiographic evaluation pulmonary edema score predict intensive care admission in COVID-19 patients presenting to the emergency department? A retrospective single-center observational study. J Health Sci Med 2022; 5(6): 1682-1687.

ABSTRACT

Aim: COVID-19 disease can progress from pneumonia to acute respiratory distress syndrome (ARDS). Performing computed tomography on all patients is expensive and exposes them to high radiation. The simple and reproducible Radiographic Evaluation Pulmonary Edema (RALE) score, used in ARDS and acute pulmonary edema in the emergency department, can predict the severity of the disease in COVID-19 patients.

Material and Method: In our study, a total of 221 COVID-19 patients we followed up between July-November, 2021 were evaluated retrospectively. The patients were divided into two as Intensive care hospitalization and no intensive care hospitalization.

Results: Ninety-five (43%) patients were admitted to the intensive care unit. The mean age (p<.001), white blood cell count (WBC) (p=.001), neutrophil count (p<.001), RALE score, and the number of hospitalization days of the patients admitted to the intensive care unit were higher (p<.001). These findings were positively correlated with the RALE score (p<.001). Age (p<.001), RALE score (p=.022), WBC (p=.029), and neutrophil count (p=.004) were independent risk factors in the multivariate analysis of factors affecting intensive care admission. RALE score cut-off value in predicting intensive care unit admission was ≥10.5. In the analysis with an Area Under the Curve value of 0.716, the application of this threshold resulted in a sensitivity of 67.4% and a specificity of 69.8%.

Conclusion: In conclusion, performing chest computed tomography in all patients admitted to the emergency department with COVID-19 disease increases the cost and exposure to radiation. The simple and recalculated RALE score can be used to predict intensive care admission in COVID-19 pneumonia.

Keywords: COVID-19, RALE, intensive care unit, emergency department

INTRODUCTION

At the end of 2019, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus was first observed in China. This new coronavirus has caused a highly contagious disease called Coronavirus Disease 19 (COVID-19). It can progress from lung infection to acute respiratory distress syndrome (ARDS)(1, 2). The genetic sequencing of SARS-CoV-2, real-time reverse transcription-polymerase chain reaction (RT-PCR) of viral nucleic acid is the gold standard for the diagnosis(1). However, this serological examination has limitations due to its high number of false negatives and delayed diagnosis. Especially in the emergency room, to be able to quickly evaluate the radiological thoracic involvement of patients with suspected COVID-19, the computed tomography (CT) findings are focused on first, which are more sensitive and specific rather than chest CXR. CT has been used as the primary diagnostic method for COVID-19 in China (3, 4). In addition, it should be kept in mind that CT scanning during the pandemic is not suitable as a primary imaging method, given the excessive radiation exposure and the mandatory disinfection procedures that must be performed. Most Italian hospitals use CXR as a primary

Corresponding Author: Hilal Sipahioğlu, hilalgul1983@gmail.com
Received: 27.09.2022 **Accepted:** 15.10.2022

method with portable X-ray units, which reduce the mobility of patients and minimize the risk of cross-infection (4-7). Previously, it was determined that there was a relationship between RALE scoring and oxygenation of patients with ARDS and disease severity. In a study, the high RALE score calculated by chest X-ray of patients admitted to the emergency room due to COVID-19 predicted admission to the intensive care unit (ICU) (8). RALE score, which may be associated with an increased risk of ICU admission, can be used as a quantitative measure of the COVID-19 pneumonia severity in emergency cases, as it is a simple and reproducible measure. It can help identify the highest-risk patients and allow timely initiation of currently available treatments against COVID-19 (9).

The primary aim of our study was to demonstrate that the RALE score calculated according to the safe and inexpensive CXR can predict ICU admission in patients with COVID-19. We suggested that the use of computed tomography, which is expensive and causes radiation exposure, can be reduced by evaluating the power of the RALE score in predicting ICU admissions.

MATERIAL AND METHOD

The study was conducted with the permission of the Non-invasive Clinical Education Planning Board of 3rd step Training and Research Hospital in Kayseri (Date: 17.06.2021 Decision No: 414). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The present study retrospectively evaluated COVID-19 patients who applied to the emergency department and who were hospitalized between July 01 and November 01, 2021.

Patients with RT-PCR positive results, who had chest x-rays in the emergency room or on the first day of hospitalization, were included in the study. Patients with lung/other malignancy, heart failure, acute/chronic renal failure, acute/chronic liver failure were excluded. A score of 0-4 was assigned to each lung depending on the extent of involvement by consolidation (0 = no involvement; 1 = <25%; 2 = 25-50%; 3 = 50-75%; 4 = >75% involvement). The scores for each lung were summed to produce the final RALE score.

In addition to viral pneumonia, patients' demographic data (age, BMI, gender), comorbidities, RALE scores, intensive care unit admissions, total hospitalization days, laboratory parameters (first-day C-reactive protein (CRP), procalcitonin, white blood cell (WBC), neutrophils, lymphocyte, platelet, ferritin, fibrinogen), acute pathologies in the lung (pneumothorax, pleural effusion, pulmonary embolism) were recorded.

All CXRs were obtained as digital radiographs in the isolation wards of our emergency department in the same portable X-ray unit (C50 Digital X-Ray system, Philips, Nederland). CXRs were generated in the rear-front or front-rear projection. All images were recorded in the hospital patient registry program. A chest radiologist and an intensive care specialist did the retrospective examination of each CXR. Thorax tomography was performed in all patients. In PCR-positive patients, radiographic findings (with thorax tomography), including pneumonia and consolidation, ground-glass opacities (GGO), pulmonary nodules, and reticular-nodular opacities, were diagnosed according to the Fleischer Society glossary of terms (10). CXRs were evaluated for the presence of distribution in the infiltration (mostly peripheral/perihilar, unilateral/bilateral, inferior/superior/diffuse). Other pulmonary pathological thoracic images were also evaluated (cardiomegaly, hilar vascular congestion, pleural effusion, pneumothorax). A severity scoring was applied to measure the extent of COVID-19 pulmonary involvement RALE. Following RALE indications, each CXR was assigned with a score ranging from 0 to 48. 0 points were given in the absence of any pathological findings and 48 points in the complete pathological involvement of the lung parenchyma. A score of 0-4 was assigned to each lung depending on the extent of involvement by consolidation (0 = no involvement; 1 = <25%; 2 = 25-50%; 3 = 50-75%; 4 = >75% involvement). The scores for each lung were summed to produce the final RALE score.

The RALE score, which was calculated by two people from the study team, was recorded with the common opinion of the two.

The patients were divided into two groups: intensive care hospitalization and no intensive care hospitalization. The demographic and clinical characteristics of the patients were compared between these two groups. The relationship between the RALE score and the independent risk factors predicting admission to the intensive care unit was determined.

Statistical Analysis

Statistical analysis of the data obtained in the study was performed using statistical package for social sciences (SPSS) version 22.0 software. Continuous variables were expressed as median value and interquartile range (IQR). On the other hand, categorical variables were presented as numbers (n) and percentages (%). The continuous variables were compared using analysis of variance (ANOVA) or Mann-Whitney U test (Kolmogorov–Smirnov test) according to whether the data were suitable for normal distribution. ROC

analysis was performed to determine the cut-off value for the RALE score. The correlation between the RALE score and the factors determining admission to the intensive care unit was examined using Spearman's correlations.

A forward-step binary logistic regression analysis was performed to determine the independent factors predicting admission to the ICU. The variables were determined as p-value <0.1 in univariate analysis, and the results were presented with the odds ratio (OR) and Confidence interval (CI).

RESULTS

For the study, the files of 300 patients who were hospitalized were evaluated retrospectively. Among all patients, 19 were excluded due to acute renal failure, 25 for chronic renal failure, 11 for cirrhosis, 14 for malignancy, and 10 for heart failure.

Of the 221 patients included in the study, 95 (43%) were admitted to the ICU. The patients were evaluated in two groups according to their admission to the ICU. The demographic and clinical characteristics of the patients in the two groups are compared in **Table 1**.

Table 1. Demographic and clinical characteristics according to patients' admission to the intensive care unit

Variables	General (n:221)	Intensive care hospitalization (n:95)	No intensive care hospitalization (n:126)	P value
Age, year	62 (53-72	71 (62-82)	60 (49.75-63)	<.001
Body mass index	28 (25-32)	28.5 (22-36,5)	28 (26-32)	.555
Female/male	117/104 (53/4)	43/51 (45/55)	73/53 (42/58)	.087
Diabetes mellitus	119 (54)	38 (40)	81 (64)	<.001
Hypertension	111 (50)	48 (51)	63 (50)	.938
Chronic obstructive pulmonary disease	46 (21)	18 (19)	28 (20)	.682
Coronary artery disease	40 (18)	24 (25)	16 (13)	.529
Cerebrovascular disease	11 (5)	7 (7)	4 (3)	.157
Distribution				.684
Peripheral	179 (81)	76 (80)	103 (82)	
Perihilar	4 (2)	1 (1)	3 (2)	
Basal predominance	31 (14)	15 (16)	16 (13)	
Superior predominance	5 (2)	2 (2)	3 (2)	
Diffuse	2 (1)	1 (1)	1 (1)	
Lung involvement				.686
Unilateral	8 (4)	4 (3)	4 (3)	
Bilateral	213 (96)	91 (96)	122 (97)	
Pulmonary embolism	5 (2)	4 (3)	1 (1)	.09
Pneumothorax	1 (1)	1 (1)	0 (0)	.385
Pleural effusion	8 (3)	8 (8)	0 (0)	.001
Mechanical				<.001
Ventilation(MV)support	46 (21)	46 (48)	0 (0)	
Invasive MV support	34 (15)	34 (36)	0 (0)	
Noninvasive MV support	28 (13)	28 (29)	0 (0)	
Reservoir mask	69 (31)	55 (57)	14 (11)	<.001
Nasal oxygen	173 (78)	47 (49)	126 (100)	<.001
White blood cell count, $\times10^3$/L,	8.48 (5.9-12.9)	10.8 (7.4-14.2)	6.85 (5.25-9.72)	.001
Lymphocyte count, $\times10^3$/L	1.09 (0.62-1.74)	0.71 (0.49-1.2)	1.3 (0.89-1.95)	.740
Neutrophil count, $\times10^3$/L	5 (3.38-9.93)	8.87 (5.84-12.46)	3.65 (2.95-5.41)	<.001
Platelets, $\times10^3$/L, (median)	234 (178-297)	235 (163-293)	231 (187.25-310.25)	.541
C-reactive protein, mg/L	49.5 (15.75-110	91 (49.2-143)	28.5 (8.97-66.52)	<.001
Procalcitonin, ng/ml	0.13 (0.07-0.54)	0.3 (0.11-1.07)	0.09 (0.05-0.21)	.230
Serum ferritin, ng/ml	355 (160-794)	567 (267.5-1226)	208 (111-554.5)	.012
Serum fibrinojen, ng/ml	5410 (4510-6500)	5505 (4460-6767.5)	5360 (4520-6380)	.707
Hospital stay, day	11 (7-17)	15 (9-23)	9 (7-13)	<.001
RALE score	10 (6.5-16)	14 (9-20)	8 (6-12)	<.001

The median age of patients hospitalized in the intensive care unit was 71 years (62-82), and of patients not hospitalized in the intensive care unit was 57 (50-64) (p <.001).

WBC (10.8[7.4-14.2] vs. 6.85[5.25-9.72]x103/L) and neutrophil (8.8 [5.8-12.46] vs. 3.65[2.95-5.41] x103/L) counts were higher in ICU hospitalized patients compared to the other group (p=.001). CRP (91[49.2-143] vs. 28.5[8.97-66.52] mg/L, p=.001) and ferritin (567[267.5-1226] vs. 208[111-554.5] ng/ml, p=.012) levels were higher ICU patients.

At the same time, total duration of hospital stay (15 [9-23] vs. 9[7-13] days p<.001) and RALE scores (14 [9-20] vs. 8[6-12] p<.001) were higher in those admitted to the ICU.

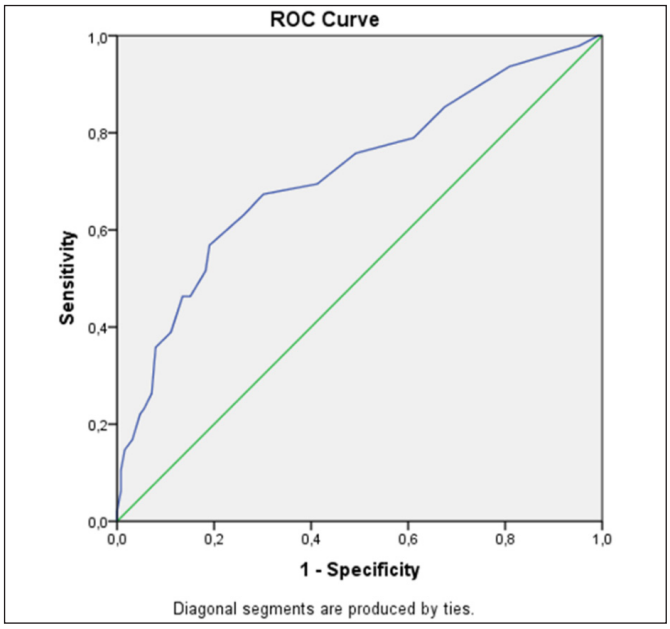
WBC, neutrophil, CRP, number of days of hospitalization, and RALE score, which was higher in patients admitted to the ICU, showed a positive correlation (**Table 2**). As the RALE score increased, CRP and number of hospitalization days increased.

Age (p<.001), RALE score (p=.022), WBC (p=.029), and neutrophil count (p=.004) were independent risk factors in the multivariate analysis of factors affecting intensive care admission (**Table 3**).

Table 3. Multivariate analysis of factors affecting intensive care admission

	p	OR	95% C.I.for EXP(B)	
			Lower	Upper
Age	<.001	1.085	1.046	1.125
RALE	.022	1.114	1.015	1.222
WBC	.029	1.141	1.013	1.285
Neutrophil	.004	1.239	1.072	1.433
CRP	.412	1.004	.998	1.013
Hospital stay	.075	1.051	.995	1.111

ROC analysis for the RALE score was performed to evaluate its success in predicting admissions to the intensive care unit. RALE score cut-off value in predicting intensive care unit admission was ≥10.5. In the analysis with an AUC value of 0.716, the application of this threshold resulted in a sensitivity of 67.4% and a specificity of 69.8%. The ROC curve showing the diagnostic performance in predicting ICU admission is presented in a graph (**Figure 1**).



Risk Factor	AUC (%95)	Cut Off	Sensitivity	Specificity
RALE	0.716	10.5	67.4	69.8

Figure 1. ROC curve RALE score

DISCUSSION

This study evaluated the parameters used to predict ICU admission in COVID-19 pneumonia and revealed that the RALE score was associated with these parameters. In the study, the RALE score was calculated by evaluating the chest x-rays taken in the emergency room of 221 patients who applied with the symptoms of COVID-19 and had positive PCR test results. The patients were divided into two groups according to their intensive care hospitalization status. Patients admitted to the intensive care unit were determined to be older and had higher white blood cell and neutrophil counts, CRP levels, number of hospitalization days, and RALE scores. When the correlation of these parameters indicating admission to the intensive care unit was examined, all parameters showed a positive correlation with the RALE score. Patients with a high RALE score in the beginning also had higher hospitalization days. RALE score cut-off value in predicting intensive care unit admission was ≥10.5. In the analysis with an AUC value of 0.716, the application of this threshold resulted in a sensitivity of 67.4% and a specificity of 69.8%. In recent studies, COVID-19 chest computed tomography examination has been discussed, and its sensitivity has been reported as 98% (11-13).

Table 2. Correlation of RALE score and factors affecting intensive care admission

	RALE		CRP		Hospital stay		WBC		Neutrophil	
	r	p	r	p	r	p	r	p	r	p
RALE	1	NS	0.572	<0.001	0.331	<0.001	0.144	0.032	0.343	<0.001
WBC	0.144	0.032	0.170	0.011	0.000	0.997	1	NS	0.413	<0.001
Neutrophil	0.343	<0.001	0.473	<0.001	0.124	0.066	0.413	<0.001	1	NS
CRP	0.572	<0.001	1	NS	0.184	0.006	0.170	0.011	0.473	<0.001
Hospital stay	0.331	<0.001	0.184	0.006	1	NS	0.000	0.997	0.124	0.066

Although CXR has less sensitivity than CT, it is less expensive and contains less radiation.

Due to the pandemic experienced worldwide, rapid determination of the radiological diagnosis of patients with suspected COVID-19 infection is vital for the most efficient operation of the emergency department. While CXR is the primary imaging tool, the typical features of COVID-19 pneumonia are defined by chest CT in selected cases (5, 6). Many recent studies have reported that CXR does not have the diagnostic power of CT but has a crucial role as a primary examination in managing the pandemic (5, 13, 14). Although CT has a high sensitivity (approximately 97–98%) in detecting typical characteristics of COVID-19 pneumonia, it has low specificity (13-15). RALE score higher than 15 is associated with an increased risk of admission to the intensive care unit. It is stated that the RALE score can be used in an emergency (8).

In a study, advanced age, comorbidities, RALE score, and biomarkers of systemic hyperinflammation (i.e., Lymphopenia below 0.9 x 103/L, high LDH, and high D-dimer) were determined as predictors of early death in COVID-19 pneumonia (16). In our study, age, WBC, neutrophils, CRP, and the number of days of hospitalization affected the number of days of COVID-19 pneumonia. A very recently published study indicated that inflammatory markers and RALE scores were correlated in COVID-19 patients (17).

In the initial patient evaluation in the emergency department, the RALE score seems like a simple tool to predict clinical outcomes quite early.

There are multiple potential applications for the RALE score for both patient care and clinical research in patients with ARDS. RALE scores can be used to clinically identify patients at the highest risk of mortality, leading to earlier detection and intervention of high-risked patients with ARDS. It has been stated that a similar approach can be used for the therapeutic risk classification of ARDS patients (9). In this study, we have statistically demonstrated that the RALE score predicts the severity of COVID-19 pneumonia and the indication for hospitalization in the intensive care unit.

Both computed axial tomography and ultrasound have been used to evaluate the presence and distribution of pulmonary edema (18). However, none are as practical as RALE scoring for daily assessment. Sensusiati et al.(19). stated that there was a strong correlation between the risk of death in hospitalized COVID-19 patients and the RALE score and that the RALE score could be used as a predictor of mortality in COVID-19 patients. Considering that hospitalization in the intensive care unit for COVID-19 disease determines the risk of mortality, the factors affecting the hospitalization of the patients to the intensive care unit also affect mortality.

In our study, admission to the intensive care unit was affected independently by age, WBC, neutrophil, CRP, and RALE scores. However, since the sensitivity specificity of the RALE score is not very high, its use may be more limited.

The retrospective nature of the study and the inability to detect mortality results can be considered among the limitations of our study. Our other limitations are that we could not compare the patients with non-COVID-19 patient groups, and could not examine the effect of comorbidity conditions on the RALE score.

CONCLUSION

It suggests that the simple and recalculated RALE score can be used to show the severity and prognosis of COVID-19 pneumonia in the first place..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was conducted with the permission of the Non-invasive Clinical Education Planning Board of 3rd step Training and Research Hospital in Kayseri. (Date: 17.06.2021 Decision No: 414).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020; 470-3.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.
3. Yang W, Sirajuddin A, Zhang X, et al. The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). Eur Radiol 2020; 30: 4874-82.
4. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. AJR Am J Roentgenol 2020; 214: 1287-94.
5. Giovagnoni A. Facing the COVID-19 emergency: we can and we do. Radiol Med 2020; 125: 337-8.

6. Neri E, Miele V, Coppola F, Grassi R. Use of CT and artificial intelligence in suspected or COVID-19 positive patients: statement of the Italian Society of Medical and Interventional Radiology. Radiol Med 2020; 125: 505-8.
7. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. American College of Radiology. March 11, 2020.
8. Cozzi D, Albanesi M, Cavigli E, et al. Chest X-ray in new coronavirus disease 2019 (COVID-19) infection: findings and correlation with clinical outcome. Radiol Med 2020; 125: 730-7.
9. Warren MA, Zhao Z, Koyama T, et al. Severity scoring of lung oedema on the chest radiograph is associated with clinical outcomes in ARDS. Thorax 2018; 73: 840-6.
10. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008; 246: 697-722.
11. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical coronavirus disease 2019 (COVID-19) pneumonia: relationship to negative RT-PCR testing. Radiology 2020; 296: E41-E5.
12. Huang P, Liu T, Huang L, et al. Use of Chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology 2020; 295: 22-3.
13. Fang Y, Zhang H, Xie J, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology 2020; 296: E115-E7.
14. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020; 296: E32-E40.
15. Choi H, Qi X, Yoon SH, et al. Extension of coronavirus disease 2019 on chest CT and Implications for chest radiographic ınterpretation. Radiol Cardiothorac Imaging 2020; 2: e200107.
16. Ciceri F, Castagna A, Rovere-Querini P, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol 2020; 217: 108509.
17. Marques P, Fernandez-Presa L, Carretero A, et al. The radiographic assessment of lung edema score of lung edema severity correlates with inflammatory parameters in patients with coronavirus disease 2019-Potential new admission biomarkers to predict coronavirus disease 2019 worsening. Front Med 2022; 9: 871714.
18. Bellani G, Rouby JJ, Constantin JM, Pesenti A. Looking closer at acute respiratory distress syndrome: the role of advanced imaging techniques. Curr Opin Crit Care 2017; 23: 30-7.
19. Sensusiati AD, Amin M, Nasronudin N, et al. Age, neutrophil lymphocyte ratio, and radiographic assessment of the quantity of lung edema (RALE) score to predict in-hospital mortality in COVID-19 patients: a retrospective study. F1000Res 2020; 9: 1286.