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The modified systemic inflammation score is a predictor of ICU admission of COVID-19 patients

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ABSTRACT

Objective: To evaluate the effect of the modified systemic inflammation score (mSIS) on prognosis in patients diagnosed with COVID-19.

Methods: In this retrospective cross-sectional study, 181 patients were selected and divided into two groups: patients with and without admission to the intensive care unit (ICU). An albumin level of ≥4.0 g/dL and lymphocyte-to-monocyte ratio (LMR) of ≥3.4 was scored 0, an albumin level of <4.0 g/dL or LMR of <3.4 was scored 1, and an albumin level of <4.0 g/dL and LMR of <3.4 was scored 2.

Results: A total of 242 COVID-19 positive patients were initially included in this study. Of these patients, 61 were excluded and 181 patients remained. Among the 181 participants, 94 (51.9%) were female, and the median age was 61 (51, 75) years. The mSIS scale ranged from 0 to 2. After analysis, the median score was 0 (0, 0) in the non-ICU group and 2 (0, 2) in the ICU group (P<0.001). The median white blood cell, lymphocyte counts, and albumin levels were lower in the ICU group (P<0.001, P<0.001, and P<0.001, respectively). In logistic regression analysis lymphocytopenia (OR=5.158, 95% CI=1.249-21.304, P=0.023), hypoalbuminemia (OR=49.921, 95% CI=1.843-1 352.114, P=0.020), AST elevation (OR=3.939, 95% CI=1.017-15.261, P=0.047), and mSIS=2 (OR=5.853, 95% CI=1.338-25.604, P=0.019) were identified as independent predictors of ICU admission.

Conclusion: The mSIS can be used as an independent parameter for establishing the intensive care needs of patients with COVID-19.

KEYWORDS: Modified systemic inflammation score; COVID-19; Intensive care; Biomarker; Comorbidity

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic affected the whole world[1]. Since the beginning of the pandemic, the disease has manifested itself with various symptoms[2]. To establish disease prognosis, various biomarkers, including C-reactive protein (CRP), D-dimer, white blood cell count (WBC), lactate dehydrogenase, and platelet count, are evaluated[3]. The modified systemic inflammation score (mSIS) was first established to perform risk assessments for patients with cancer scheduled for surgery[4,5], which is a scoring system based on the lymphocyte-to-monocyte ratio (LMR) and serum albumin level that evaluates systemic inflammatory response

Significance

During the COVID-19 pandemic, many scoring systems have been investigated to determine the prognosis of the disease. In this study, it has been determined that the modified systemic inflammation score, which is mainly used in cancer patients, can be used as an independent parameter in determining ICU administration in COVID-19 patients.

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and nutritional level in patients[5]. However, this scoring system has not been well-investigated for other diseases or diagnoses other than malignancy. Few study so far have examined lymphocyte count and LMR in combination with albumin in patients with COVID-19[6,7]. Hence, this study aims to evaluate the effect of the mSIS on COVID-19 prognosis in patients diagnosed with COVID-19.

2. Patients and methods

2.1. Study setting

In this retrospective cross-sectional study, a total of 181 patients who were admitted to the emergency department of a tertiary care hospital and diagnosed with COVID-19 between December 1, 2020, and February 1, 2021, were included for analysis.

2.2. Ethical approval

This study was initiated after obtaining approval from the Karabük University ethics committee (approval number: 2022/875) and was conducted in accordance with the Declaration of Helsinki. All the data used in this study were anonymized before being subjected to statistical analysis and reporting.

2.3. Inclusion criteria exclusion criteria

The inclusion criteria were patients who were 18 years old and above had a positive real-time polymerase chain reaction test for COVID-19 and had one or more comorbidities before being diagnosed with COVID-19. The comorbidities included hypertension, diabetes mellitus, hypothyroidism, chronic obstructive pulmonary disease, hyperlipidemia, asthma, coronary artery disease, malignancy, cerebrovascular diseases, arrhythmias, heart failure, chronic renal failure, and use of immunosuppressant therapy. We added only patients with comorbidities because mSIS was developed for patients with comorbidities. Patients who were aged <18 years, tested negative for COVID-19, were pregnant, had missing records in the hospital information system, and had no comorbidities were excluded from the study.

2.4. Data collection

The patients were divided into two groups: those who did and those who did not require admission to the ICU. The demographics of the patients, such as age, sex, comorbidities, as well as WBC, lymphocyte, monocyte, and platelet counts and hemoglobin, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, and CRP levels were recorded. LMR was calculated as the ratio of the total lymphocyte count to the total monocyte count using the recorded values. The mSIS of each patient was calculated using the LMR and albumin values obtained. The mSIS scale ranged from 0 to 2. An albumin level of ≥4.0 g/dL and LMR of ≥3.4 was scored 0, an albumin level of <4.0 g/dL or LMR of <3.4 was scored 1, and an albumin level of <4.0 g/dL and LMR of <3.4 was scored 2. An increased mSIS score is associated with poor outcomes. The calculated mSIS values were compared with the outcomes of the patients

2.5. Primary outcome

The primary outcome was the correlation between the mSIS and need for admission to the ICU in patients with COVID-19 and comorbidities.

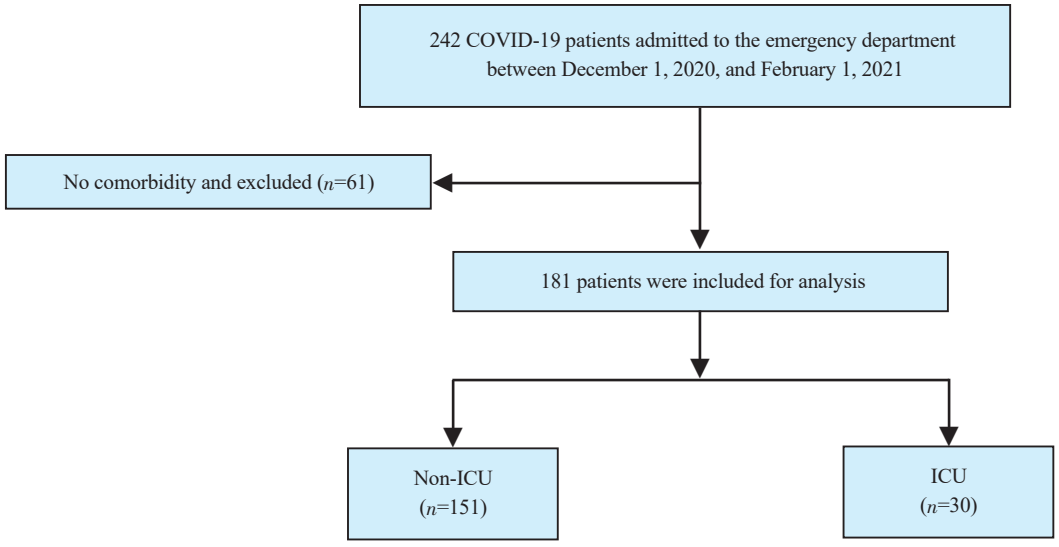

Figure 1. The study flowchart.

2.6. Statistical analysis

BM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses. Numerical and normally distributed data are expressed as mean±standard deviation, while ordinal and non-normally distributed data are expressed as median and first and third quartiles (Q1, Q3). Categorical variables are presented as frequency distributions and percentages (%). The normality of the data was tested using the Kolmogorov-Smirnov test. Quantitative data were compared using Mann-Whitney *U* test for non-normally distributed data, while qualitative data were compared using Chi-square test. To identify independent variables that can be used for evaluating patients' need for admission to the ICU, a logistic regression analysis was performed. A *P*-value <0.05 at a 95% confidence interval was considered statistically significant.

Table 1. Demographics and comorbidities.

Variables	*n*=181
Age, years, median, Q1, Q3	61 (51, 75)
Sex, *n*, %	
Female	94 (51.9%)
Male	87 (48.1%)
Comorbidity, *n*, %	
Chronic obstructive pulmonary disease	4 (2.2%)
Hypertension	111 (64.1%)
Diabetes mellitus	53 (29.3%)
Hypothyroidism	26 (14.4%)
Hyperlipidemia	51 (28.2%)
Asthma	25 (13.8%)
Coronary artery disease	37 (20.4%)
Malignancy	6 (3.3%)
Cerebrovascular disease	11 (6.1%)
Arrhythmias	18 (9.9%)
Heart failure	15 (8.3%)
Chronic renal failure	7 (3.9%)
Immunosuppression diseases	6 (3.4%)

3. Results

A total of 242 patients who were admitted to the emergency department of a tertiary care hospital and tested positive for COVID-19 between December 1, 2020, and February 1, 2021, were initially included in this study. Of these patients, 61 were excluded because they did not have any comorbidity (Figure 1). The study was initiated with the remaining 181 patients. Of these patients, 94 (51.9%) were female, with a median age of 61 (51, 75) years. The median number of comorbidities that all the patients had was 2 (1, 3). Of all the comorbidities encountered in the participants, the most common were hypertension, with 111 patients (64.1%), and the second most common was diabetes mellitus, with 53 patients (29.3%) (Table 1).

Among the 181 patients, 151 did not need admission to the ICU, and the median age was 59.0 (51.0, 71.0) years; 30 patients required intensive care and the median age was 74.0 (62.5, 83.0) years. The median age of patients needing admission to the ICU was higher than that of patients not needing it (*P*<0.001). In terms of sex, among the total number of female patients (94, 51.9%), 83 (45.8%) did not need admission to the ICU, while 11 (6%) needed it. Of the remaining male patients (87, 48.1%), 68 (37.5%) did not need admission to the ICU, while 19 (10.5%) needed it. There was no significant difference in terms of sex distribution across the two groups. When the mSIS of the patients were determined, the median score was 0 (0, 0) in the group of patients not needing admission to the intensive care unit and 2 (0, 2) in the group of patients needing it. The mSIS of the patients needing admission to the ICU was significantly higher than those of patients not needing it (*P*<0.001) (Table 2).

When the laboratory data of the patients were evaluated, the median WBC count was 5 810.0×10^6/L (4 670.0×10^6/L, 7 550.0×10^6/L) in the group of patients not needing admission to the ICU and 7 825.0×10^6/L (5 460.0×10^6/L, 11 537.5×10^6/L) in the group of patients needing

Table 2. Demographics, laboratory values, and mSIS of patients with and without admission to the intensive care unit.

Variables	Non-ICU (*n*=151)	ICU (*n*=30)	U/χ^2	*P*
Age, years, median, Q1, Q3	59.0 (51.0, 71.0)	74.0 (62.5, 83.0)	1 186.0^U	<0.001*
Sex, *n*, %				
Female	83 (45.8%)	11 (6.0%)	3.4^C	0.075
Male	68 (37.5%)	19 (10.5%)		
Number of comorbidities, median, Q1, Q3	2 (1, 3)	2 (2, 3)	2 247.0^U	0.943
WBC, ×10^6/L, median, Q1, Q3	5 810.0 (4 670.0, 7 550.0)	7 825.0 (5 460.0, 11 537.5)	1 307.5^U	<0.001*
Monocyte, ×10^6/L, median, Q1, Q3	440 (330, 600)	365 (225, 645)	1 847.5^U	0.136
Lymphocyte, ×10^6/L, median, Q1, Q3	1 490.0 (1 140.0, 1 930.0)	785.0 (457.5, 1 075.0)	853.5^U	<0.001*
Hemoglobin, g/dL, median, Q1, Q3	13.5 (12.4, 14.6)	12.4 (11.1, 13.8)	1 539.0^U	0.006*
Platelet, ×10^6/L, median, Q1, Q3	207 000 (163 000, 254 000)	191 000 (152 750, 281 500)	2 137.5^U	0.627
Creatinine, mg/dL, median, Q1, Q3	0.83 (0.69, 1.00)	0.96 (0.74, 1.59)	1 586.5^U	0.010*
AST, U/L, median, Q1, Q3	28 (21, 37)	44 (32, 73)	1 094.0^U	<0.001*
ALT, U/L, median, Q1, Q3	22 (16, 33)	29 (19, 66)	1 571.0^U	0.008*
Albumin, g/dL, median, Q1, Q3	4.4 (4.1, 4.7)	3.7 (3.4, 4.1)	837.0^U	<0.001*
CRP, mg/L, median, Q1, Q3	16.5 (8.0, 44.6)	85.5 (39.0, 131.1)	812.5^U	<0.001*
mSIS, median, Q1, Q3	0 (0, 0)	2 (0, 2)	1 001.0^U	<0.001*

^{U}Mann-Whitney *U* test; ^{C}Chi-squre test; WBC: white blood cell; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; mSIS: modified systemic inflammation score. *Significant at α=0.05.

Table 3. Multivariate logistic regression of significant risk factors of intensive care unit admission.

Variables	Beta coefficient	Standard error	Wald statistic	*P*	Odds ratio (*95% CI*)
Age, years	0.043	0.023	3.326	0.068	1.044 (0.997-1.093)
WBC, ×10^6/L					
4 000-11 000	Reference	-	-	-	-
Below	−2.399	1.624	2.181	0.140	0.091 (0.004-2.192)
Above	1.157	0.891	1.689	0.194	3.182 (0.555-18.235)
Lymphocyte, ×10^6/L					
800-4 000	Reference	-	-	-	-
Below	1.641	0.724	5.140	0.023*	5.158 (1.249-21.304)
Above	1.919	1.619	1.405	0.236	6.812 (0.285-162.554)
Hemoglobin, g/dL					
11-16	Reference	-	-	-	-
Above	−0.408	0.801	0.260	0.610	0.665 (0.138-3.194)
Creatinine, mg/dL					
0.5-1.3	Reference	-	-	-	-
Above	0.928	0.735	1.593	0.207	2.530 (0.599-10.691)
AST, U/L					
5-34	Reference	-	-	-	-
Above	1.371	0.691	3.936	0.047*	3.939 (1.017-15.261)
ALT, U/L					
10-49	Reference	-	-	-	-
Above	0.904	0.721	1.570	0.210	2.469 (0.601-10.145)
Albumin, g/dL					
3.2-4.8	Reference	-	-	-	-
Below	3.910	1.683	5.397	0.020*	49.921 (1.843-1 352.114)
Above	−0.301	1.217	0.061	0.804	0.740 (0.068-8.030)
CRP, mg/L	−0.001	0.004	0.036	0.849	0.999 (0.992-1.007)
mSIS					
Score=0	Reference	-	-	-	-
Score=1	−1.332	1.510	0.779	0.378	0.264 (0.014-5.087)
Score=2	1.767	0.753	5.507	0.019*	5.853 (1.338-25.604)

WBC: white blood cell; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; mSIS: modified systemic inflammation score. *Significant at α=0.05.

it, revealing a significant difference between the groups (*P*<0.001). The median lymphocyte count was 1 490.0×10^6/L (1 140.0×10^6/L, 1 930.0×10^6/L) in the group of patients not needing admission to the ICU, while it was 785.0×10^6/L (457.5×10^6/L, 1 075.0×10^6/L) in the group of patients needing it, revealing a significant difference between the groups (*P*<0.001). Similarly, the median CRP level was 16.5 (8.0, 44.6) mg/L in the group of patients not needing admission to the ICU, while it was 85.45 (39.0, 131.1) mg/L in the group of patients needing it (*P*<0.001). The median creatinine, AST, and ALT levels were lower in the group of patients not needing admission to the ICU than in the group of patients needing it (*P*=0.010, *P*<0.001, and *P*=0.008, respectively). The median hemoglobin and albumin levels were higher in the group of patients not needing admission to the ICU than in the group of patients needing it (*P*=0.006 and *P*<0.001, respectively) (Table 2).

Based on logistic regression analysis, lymphocytopenia (*OR*=5.158, 95% *CI*=1.249-21.304, *P*=0.023), hypoalbuminemia (*OR*=49.921, 95% *CI*=1.843-1 352.114, *P*=0.020), AST elevation (*OR*=3.939, 95% *CI*=1.017-15.261, *P*=0.047), and mSIS=2 (*OR*=5.853, 95% *CI*=1.338-25.604, *P*=0.019) were identified as independent predictors of ICU admission (Table 3).

4. Discussion

Some parameters have been used to assess the severity of COVID-19. A study by Shang *et al*. on clinical parameters that are indicative of the severity of COVID-19 found that albumin levels were significantly lower in the severely affected group[8]. Another study that included patients with COVID-19 also reported that the albumin level and lymphocyte count were significantly lower in the severely affected patient group[9]. Similarly, according to Liang *et al*., it was found that a low lymphocyte count and the incidence of comorbidities were associated with severe illness among COVID-19 patients[10]. In addition, Rozga *et al*. found that albumin levels could show the prognosis of the disease and nutritional findings in patients with chronic diseases[11]. However, in a study where Acharya *et al*. evaluated the association between albumin level and hospital admission in patients with COVID-19, the authors found that albumin level did not affect COVID-19-related hospital admissions[12]. Furthermore, many studies found that a high CRP level was associated with critical illness in patients with COVID-19[13-15]. In the study, we found that CRP level was significantly higher in the group of patients needing admission to the ICU than in the group of patients not needing it.

The mSIS system that we used in this study is a combination of those used in the studies and few studies so far have used the mSIS system for bacterial or viral infections as well as COVID-19. In this study, we found that the mSIS was higher in patients with COVID-19 who needed admission to the ICU than in those who did not. This scoring system can be used as an independent parameter for establishing the intensive care needs of patients with COVID-19. Conducting on patients with comorbidities is one of the limitations of this study. Thus, further studies that investigate the usefulness of the mSIS system in patients without comorbidities are needed. Besides, this was a retrospective study on a relatively small group of patients; thus, prospective studies with a larger sample size are needed.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

DAM and HM: developed the concept of the study, performed literature search, and data acquisition. DAM and ŞEA: designed the study and performed data analysis. All authors contributed to the definition of intellectual content, conducted the study and prepared, edited and reviewed the manuscript.

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