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ORIGINAL PAPER

Effect of the prognostic nutritional index and systemic immune-inflammatory index in predicting short-term mortality in geriatric patients with SARS-CoV-2 infection

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ABSTRACT

Introduction and aim. We aimed to investigate whether systemic immune inflammatory index (SII) and prognostic nutritional index (PNI) were associated with short-term mortality in geriatric patients with SARS-CoV-2.

Material and methods. Our study was designed retrospectively. The data of patients that presented to a single center. The primary outcome of the study was the diagnostic value of SII and PNI in predicting 28-day mortality in geriatric patients with SARS-CoV-2 pneumonia.

Results. 272 geriatric patients with SARS-CoV-2 included. The median PNI was 42.5, and the median SII was 687.6 (430–1404.2). In univariant analysis, PNI and SII has a significant relationship with mortality ($p<0.001$ and $p=0.008$, Mann-Whitney U test). PNI had an area under the curve (AUC) value of 0.680, which was significantly higher than that of SII (AUC: 0.6). The odds ratio of PNI (>40.1) and SII (<1.267) for 30-day mortality were determined as 1.12 , and 1.

Conclusion. In conclusion, the blood tests used to calculate PNI and SII are routinely included in complete blood count and biochemistry tests that can be performed in every hospital. According to the results of the current study, the mortality group had significantly higher SII values and significantly lower.

Keywords. mortality, SARS-Cov-2 infection, PNI

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started in 2019 in Wuhan, China. It soon became a pandemic, resulting in the death of more than five million people. SARS-CoV-2 causes an inflammatory disease transmitted by droplets and progresses from clinically asymptomatic to acute respiratory syndrome in the lungs. It has a more mortal course in geriatric patients, associated with weakened immunity, poor nutrition, and comorbidities in this patient population.[1,2] The prognostic nutritional index (PNI), calculated using the lymphocyte count and serum albumin levels, is an indicator of nutrition and immunity.[3] Some studies have shown PNI to be a useful marker for predicting long-term outcomes in patients receiving chemotherapy.[4] The systemic immune inflammatory index (SII) is a new leukocyte-based inflammatory index developed in the last decade. It has been suggested that SII can be a prognos-

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tic determinant in patients.[5] SII has been reported to be associated with mortality in various cancers, including pancreatic, hepatocellular, lung, stomach, and esophageal cancers. SII was also found as mortality predictor in coronary artery disease.[6] Studies have been conducted in which SII was able to predict poor outcomes in patients with venous sinus thromboses.[3]

Patients infected with SARS-CoV-2 have increased inflammation, which affects blood parameters, such as lymphocyte, neutrophil, thrombocyte, and albumin values.

Aim

In this study, we aimed to investigate SII and PNI in terms of their possible association with short-term mortality in geriatric patients with SARS-CoV-2.

Material and methods

Study design and ethical approval

This study was designed retrospectively and conducted in a single center; at the emergency department of the University of Health Sciences Umraniye Training and Research Hospital. The data of patients that presented to our hospital between November 01, 2021, and March 01, 2022, and were confirmed to have SARS-CoV-2 based on a positive reverse transcription-polymerase chain reaction (RT-PCR) test were screened. Ethical approval was obtained from the local ethics committee on March 31, 2022 and number 119. All the stages of the study followed the tenets of the Declaration of Helsinki.

Study population

The patients included in our study were all aged over 65 years and presented to the emergency department with symptoms of SARS-CoV-2 (weakness, myalgia, cough, fever above 37.5 °C, shortness of breath, loss of taste and smell, diarrhea, sore throat, and nausea) and were admitted to the inpatient ward or intensive care unit. The RT-PCR test results of all the patients were positive. Outpatients and patients with missing data were excluded from the study.

Data collection

All the patients were brought to the emergency department via outpatient or emergency ambulance services. Patient data were obtained from the hospital computer-based data system. The patients' demographic data and blood parameters, including hemoglobin, whole blood cell count, neutrophil count, thrombocyte cunt, lymphocyte count, hematocrit, albumin, lactate, C-reactive protein, blood urea nitrogen (BUN), platelet, mean platelet volume, and plateletcrit values were recorded. In addition, 28-day all-cause mortality data were obtained from the hospital computer-based data system and the national mortality reporting system. SII was calculated using the following formula: platelets × neutrophils/lymphocytes, and PNI was calculated as follows: 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count. Lastly, the C-reactive protein/albumin ratio (CAR) and the BUN/albumin ratio (BAR) were determined.

Outcomes

The primary outcome of the study was the diagnostic value of SII and PNI in predicting 28-day mortality in geriatric patients with SARS-CoV-2 pneumonia.

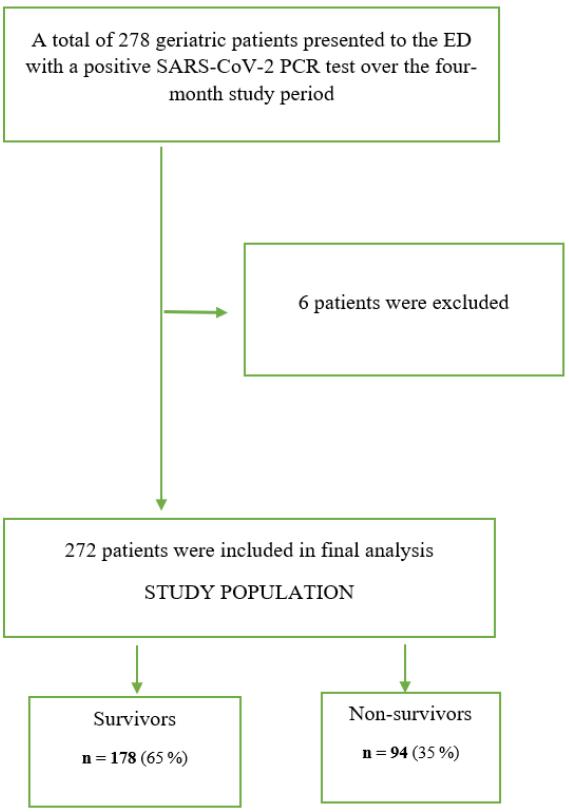

Fig. 1. A flow diagram of the study

Statistical analysis

Data were analyzed using Jamovi (Version 2.3.12.0; The Jamovi Project, 31 May 2022; R Core Team, 2022). The conformity of continuous variables to the normal distribution was examined using the Shapiro-Wilk test. Categorical variables were expressed as percentages, and continuous variables as median (interquartile range) values. The differences between the survivor and non-survivor groups were compared using the Mann–Whitney U test for non-normally distributed quantitative variables. A p value of <0.05 was considered statistically significant. The receiver operating characteristic (ROC) analysis was performed to determine the power of statistical mortality-related parameters in predicting mortality, and the results of this analysis were shown with area under the curve (AUC), cut-off, sensitivity, and specificity values, and 95% confidence intervals (CIs). Odds ratios (OR) were calculated by using two-by-two frequency tables of ratios. ORs were used to compare the ability of the pa-

rameters to predict mortality. A p value of <0.05 was considered statistically significant.

Results

A total of 278 geriatric patients presented to the emergency department of our hospital due to SARS-CoV-2. Of these patients, six were excluded using the study criteria (Figure 1).

As a result, 272 patients were included in the sample. The median (25^{th}–75^{th} percentile) age value was 77 (71–84) years, and 146 (53.7%) of the patients were female. Baseline characteristics of the enrolled patients and their comparison between the survivor and non-survivor groups are shown in Table 1, and the laboratory parameters of the enrolled patients and their comparison between the survivor and non-survivor groups are given in Table 2.

Table 1. Baseline characteristics of the enrolled patients and their comparison between the survivor and non-survivor groups

	Total (n=272)	Survivor (n=176)	Non–survivor (n=96)	p value
Age (years)	77 (71–84)	75 (70–82)	81.5 (74–87)	<0.001
Female	146 (53.7%)	100 (56.2%)	46 (48.9%)	0.312
Male	126 (46.3%)	78 (43.8%)	48 (51.1%)	
Comorbidities				
Hypertension	206 (75.7%)	135.0 (76.7%)	71 (74%)	0.614
Diabetes mellitus	109 (40.1%)	68.0 (38.6%)	41.0 (42.7%)	0.513
Malignancy	26 (9.6%)	16.0 (9.1%)	10.0 (10.4%)	0.722
Hypothyroidism	11 (4.0%)	7 (4%)	4.0 (4.2%)	0.940
Hyperthyroidism	3 (1.1%)	0 (0%)	3.0 (3.1%)	0.018
Hyperlipidemia	124 (45.6%)	75 (42.6%)	49 (51%)	0.182
Obesity	2 (0.7%)	0 (0%)	2.0 (2.1%)	0.055
Alzheimer's disease	23 (8.5%)	13 (7.4%)	10.0 (10.4%)	0.391
Epilepsy	17 (6.2%)	11 (6.2%)	6.0 (6.2%)	0.999
Chronic obstructive pulmonary disease	49 (18.0%)	31 (17.6%)	18.0 (18.8%)	0.816
Coronary heart disease	101 (37.1%)	63 (35.8%)	38.0 (39.6%)	0.537
Asthma	51 (18.8%)	33 (18.8%)	18.0 (18.8%)	0.999
Congestive heart failure	31 (11.4%)	17 (9.7%)	14.0 (14.6%)	0.222
Chronic kidney disease	23 (8.5%)	14 (8%)	9.0 (9.4%)	0.687

For the whole sample, the median neutrophil–to–lymphocyte ratio (NLR) was 3.8 (2.5–7.5), the median PNI was 42.5 (39.2–45.8), and the median SII was 687.6 (430.0–1404.2). Mortality occurred in 94 (35%) patients within 28 days. PNI, SII, NLR, CAR, and BAR has a significant relationship with mortality (p<0.001, p=0.008, p<0.001, p<0.001, and p<0.001, respectively). The ROC curve analysis revealed that a low PNI had potential predictive value in the prognosis of geriatric patients (Figure 2).

Figure 2 present the AUC values of PNI for short–term mortality according to the ROC analysis. PNI had an AUC value of 0.680 (95% CI: 1.07–1.18), which was significantly higher than that of SII (AUC: 0.600). The OR of PNI (>40.1) and SII (<1.267) for 30-day mortality were determined as 1.12 (95% CI: 1.07–1.18), and 1.0 (95% CI: 1–1), respectively.

Table 2. Laboratory parameters of the enrolled patients and their comparison between the survivor and non–survivor groups

Variables	Total n=272 (%, 25^{th}–75^{th} percentile)	Non-survivors n=94 (35%) (%, 25^{th}–75^{th} percentile)	Survivors n=178 (65%) (%, 25^{th}–75^{th} percentile)	p values
Lactate (mmol/L)	1.7 (1.3–2.1)	1.6 (1.2–2)	1.8 (1.3–2.2)	0.027
Albumin (g/dl)	36.7 (34.1–39.1)	37.5 (34.8–39.7)	35.2 (32.8–37.5)	<0.001
C–reactive protein (mg/dl)	5.1 (1.8–10)	4.0 (1.1–7.4)	8.5 (4.0–15.9)	<0.001
Blood urea nitrogen (mg/dl)	44.9 (34.2–71.2)	44.9 (34.2–63.7)	55.6 (38.5–88.8)	0.004
White blood cell count (10^3/µl)	6.5 (4.9–8.5)	6.2 (4.9–8.0)	7.4 (4.8–9.8)	0.029
Neutrophil count (10^3/µl)	4.6 (3.4–6.5)	4.3 (3.3–6.0)	5.4 (3.6–7.6)	0.004
Lymphocyte count (10^3/µl)	1.1 (0.8–1.6)	1.2 (0.8–1.7)	1.0 (0.7–1.3)	0.013
Hemoglobin (g/dl)	12.8 (11.4–13.8)	12.8 (11.6–13.8)	12.9 (11.1–13.7)	0.77
Hematocrit (%)	38.5 (34.9–41.5)	38.1 (35.5–41.5)	38.8 (34.2–42)	0.984
Platelet count (10^3/µl)	185 (149–245)	189.0 (152–247.8)	177.5 (148.2–211)	0.157
Mean platelet volume (fl)	9.8 (9–10.8)	9.8 (9–10.8)	10 (9.1–10.7)	0.591
Plateletcrit (%)	0.2 (0.1–0.2)	0.2 (0.2–0.2)	0.2 (0.1–0.2)	0.236
Platelet distribution width (%)	16.3 (16–16.6)	16.3 (16.0–16.5)	16.3 (16.1–16.6)	0.561
Neutrophil/lymphocyte ratio	3.8 (2.5–7.5)	3.3 (2.3–5.9)	5.5 (2.7–9.4)	<0.001
Platelet/lymphocyte ratio	164.9 (120.9–257.4)	157.3 (118.7–243.8)	189.0 (122.2–278.5)	0.092
C-reactive protein/albumin ratio	0.1 (0–0.3)	0.1 (0–0.2)	0.2 (0.1–0.4)	<0.001
Blood urea nitrogen/albumin ratio	1.3 (0.9–2.1)	1.1 (0.9–1.8)	1.6 (1.1–2.6)	<0.001
Prognostic nutritional index	42.5 (39.2–45.8)	40.3 (36.8–43.9)	43.6 (40.8–47.1)	<0.001
Systemic immune–inflammation index	687.6 (430–1404.2)	861.6 (492.8–1785.7)	667.0 (383.1–1200.7)	0.008

Table 3 present the accuracy of PNI and SII in predicting short term mortality in geriatric patients with SARS-CoV-2 infection.

Discussion

In this study, we evaluated the laboratory parameters of geriatric patients with SARS-CoV-2 at the time of their presentation to the emergency department. We investigated the predictive power of PNI and SII in short–term mortality. We determined that the PNI and SII values were associated with mortality (p<0.001 and p=0.008, respectively). An increase in the SII value and a decrease

in the PNI value were affected the results. The cut-off value was calculated as 40.1 for PNI and 1,267 for SII.

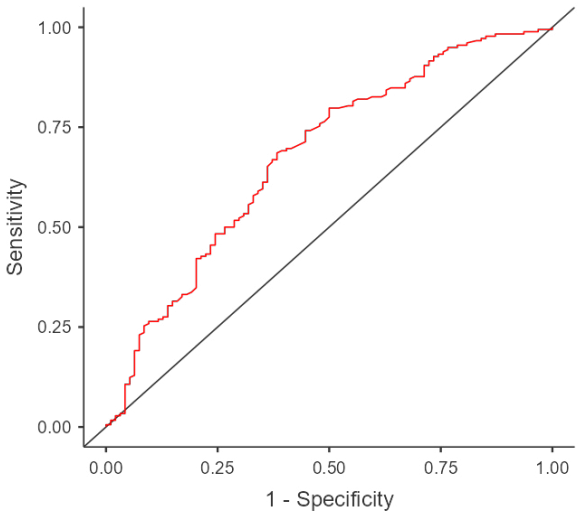

Fig. 2. ROC curve of the PNI in predicting in short term mortality of geriatric patients

Table 3. Accuracy of prognostic nutritional index and systemic immune-inflammation index in predicting short term mortality in geriatric patients with SARS-CoV-2 infection

	Prognostic nutritional index	Systemic immune-inflammation index
Sensitivity	50 %	37 %
Specificity	80 %	79 %
Accuracy	69 %	64 %
Prevalence	35 %	35 %
Positive Predictive Value	57 %	48 %
Negative Predictive Value	75 %	70 %
Positive Likelihood Ratio	2.47	1.74
Negative Likelihood Ratio	0.63	0.8
Area under the curve	0.68	0.6
95% confidence interval values	0.538–0.678	0.618–0.752
Cut-off	40.1	1,267

Due to the high levels of inflammatory markers in the elderly, their frailty increases, and defense against external stimuli and diseases decreases.[7] SARS-CoV-2 creates an inflammatory disease and affects older individuals to a greater extent, and as a result mortality is higher in the geriatric population.[8]

It has been shown that PNI can be used to predict the poor outcomes of various diseases.[9] Proinflammatory cytokines and albumin level affected by nutrition are used in the calculation of PNI. Studies have found that PNI predicts prognosis in patients with malignancies.[10] Matsuda et al. showed that PNI was significant in predicting the risk of postoperative complications (AUC=0.609, cut-off=50, p=0.008).[11] In another study aiming to predict the prognosis with PNI in patients diagnosed with COVID-19, Hu et al. evaluated 122 patients and associated a low PNI score with a poor prognosis (odd ratio: 0.797; p=0.03).[12] Ikeya et al. showed that PNI was a useful marker in predicting long–term outcomes in patients receiving chemotherapy (p=0.001).[3] Soeters et al. concluded that albumin was associated with inflammation, reporting a decrease in albumin mass and half–life in diseases causing inflammation, which was also associated with mortality.[13] Baldemir and Alagöz recommended starting nutritional support early in geriatric patients with chronic obstructive pulmonary disease considering that the albumin level was affected by nutritional status and reduced albumin was associated with mortality.[14] Since SARS-CoV-2 is an inflammatory disease, a decrease in the albumin level is expected. In our study, there was a positive correlation between low albumin and mortality (p<0.001). Similar to previous studies, there was a significant correlation between mortality and PNI in geriatric patients in our study (AUC=0.68, p<0.001, odds ratio: 1.12, 95% CI: 1.07–1.18). Inflammation that develops during the SARS-CoV-2 disease process coupled with inflammation observed in the elderly affect the parameters that constitute PNI. This can explain the significant relationship between PNI and mortality due to SARS-CoV-2 in geriatric patients.

Lymphopenia predicts clinical worsening in SARS-CoV-2 disease.[15, 16, 17, 18] NLR is calculated using lymphocyte values. Özdemir et al. showed that NLR could predict short–term mortality in their study with more than 2000 SARS–CoV–2 infected patients.[2] Yang et al. showed that NLR was associated with a poor prognosis in patients with SARS-CoV-2.[17] In our study, there was a significant relationship between NLR and mortality (p<0.001).

Platelet, neutrophil, and lymphocyte values change in SARS-CoV-2 disease according to the severity of inflammation.[18] SII is calculated using these values. Fois et al. showed a significant correlation between SII and mortality in patients with SARS-CoV-2 (p=0.039).[19] In our study, a high SII level was also associated with mortality (p<0.001), which is consistent with the literature.

Limitations of the study

There were some important limitations to our study. First, our number of patients was limited and the sample represented patients that presented to the hospital over a certain period. Second, during the COVID–19 pandemic, the virus underwent several mutations, and patient mortality and adverse outcomes varied according to the nature of the virus. Third, our study was single–centered, and therefore the data obtained from our study may differ from domestic and international data. Multicenter controlled randomized studies with a larger number of patients should be conducted.

Conclusion

In conclusion, the blood tests used to calculate PNI and SII are routinely included in complete blood count and biochemistry tests that can be performed in every hos-

pital. As a result, PNI and SII are easily accessible and easy to calculate. According to the results of the current study, the mortality group of geriatric SARS-CoV-2 infected patients had significantly higher SII values and significantly lower PNI values. Multicenter controlled randomized studies with a larger number of patients should be conducted to verify our results.

Declarations

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Author contributions

Conceptualization, A.Ö; Methodology, A.Ö., M.İ.; Software, S.E.; Validation, G.A.; Formal Analysis, A.Ö; Investigation, A.Ö.; Resources, A.Ö.; Data Curation, S.E.; Writing – Original Draft Preparation, H.A.; Writing – Review & Editing, A.Ö.; Visualization, S.E.; Supervision, S.E.

Conflicts of interest

The authors declare no competing interests.

Data availability

The datasets used and/or analyzed during the current study are open from the corresponding author on reasonable request.

Ethics approval

Study was approved by the institutional review board, and a waiver of authorization was given (Ethics Committee decision no. 119, date: 31/03/2022).

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