# The Relationship of Covid19 Mortality and Prognostic Nutritional Index In Geriatric Population / *Geriatrik Popülasyonda Prognostik Nutrisyonel İndex ve Covid19 Mortalite İlişkisi*

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**Abstract:**

Introduction: We aimed to investigate the effect of Prognostic nutritional index (PNI) on prognosis and mortality among elderly patients with COVID-19 infection. Methods: 401 patients included in the study, all of them were over 65 years old. PNI was compared with laboratory and demographic data. Results: Analysis was made of 401 patients, comprising 181 (45%) females and median age of 75.8±7.7 years. Three hundred and two (75.4%) patients were in the recovered group. Mean PNI value was 41.9±5.9 in the recovered group and 36.9±7 in the exitus group ($p<0.001$). According to multivariate logistic regression analysis, advanced age, high maximum ferritin level, high maximum IL-6 level and PNI<40 were identified as independent risk factors predicting exitus in COVID-19 patients. Conclusion: Prognostic models which including PNI scoring system, have been found to be useful in assessing the progression of COVID-19 and enhancing patient monitoring. Since all the patients included in our study were in the geriatric age group, the data we obtained may guide the course of COVID-19 infection, especially in patients in this age group.

Keywords: Nutrition, mortality, SARS-COV-2, elderly, geriatrics

**Öz:**

Giriş: COVID-19 enfeksiyonu geçiren yaşlı hastalarda prognostik nutrisyonel indeksin (PNI) prognoz ve mortalite üzerindeki etkisini araştırmayı amaçladık. Gereç ve Yöntemler: Çalışmaya dahil edilen 401 hasta, tümü 65 yaş üstü idi. PNI laboratuvar ve demografik verilerle karşılaştırıldı. Bulgular: Değerlendirme 181'i (%45) kadın ve ortanca yaşı 75.8±7.7 yıl olan 401 hasta üzerinde yapıldı. Üç yüz iki (%75.4) hasta iyileşen gruptaydı. Ortalama PNI değeri iyileşen grupta 41.9±5.9, eksitus grubunda 36.9±7 idi ($p<0.001$). Çok değişkenli lojistik regresyon analizine göre, COVID-1+9 hastalarında ileri yaş, yüksek maksimum ferritin düzeyi, yüksek maksimum IL-6 düzeyi ve PNI<40 mortaliteyi öngörmede bağımsız risk faktörleri olarak belirlendi. Sonuç: PNI skorlama sistemini içeren prognostik modellerin COVID-19 progresyonunu değerlendirmede ve hasta takibini geliştirmede faydalı olduğu bulunmuştur. Çalışmamıza dahil edilen hastaların tamamı geriatrik yaş grubunda olduğundan elde ettiğimiz veriler özellikle bu yaş grubundaki hastalarda COVID-19 enfeksiyonunun seyrine kılavuz olabilir.

*Anahtar kelimeler: Beslenme, ölüm, SARS-COV-2, yaşlı, geriatri*

## 1.Introduction

In 30 December 2019, cases of atypical pneumonia of unkown etiology were reported in China. A new beta corona virus was identified that caused a new severe acute respiratory distress syndrome (ARDS) in January 2020(Cevik et al., 2020). The disease caused by this virus was named COVID-19. In the first year of the disease, there were more than 44 million cases and more than 1.1 million deaths(Mohamadian et al., 2021). The mortality rate was higher in the population 60 years or higher age, especially with comorbid hypertension, type 2 diabetes mellitus (DM) and coronary artery disease (CAD). The disease spreads by droplet or direct contact. Patients may present with various symptoms such as fatigue, fever, dry cough, myalgia, shortness of breath, nasal congestion, headache, sore throat, loss of taste and smell, vomiting and diarrhea. Patients usually develop dyspnea and/or hypoxemia 1 week after onset, then septic shock, ARDS, difficult-to-recover metabolic acidosis, and coagulation disorder in severe disease. Asymptomatic and mild cases are important in terms of spreading the disease to large populations. Bilateral ground-glass opacities are typical in thorax tomographic examination. Nucleic acid detection is an important method in laboratory diagnosis. Reverse transcription quantitative PCR (RT-qPCR) is a molecular biological diagnostic technology based on defining nucleic acid sequences and a nasopharyngeal and throat swab is taken as an example (Cevik et al., 2020).

It is now well-known that mortality increases with advancing age. It is also well known that success in preventing COVID-19 among these older age groups directly determines the mortality rate in countries. Early Chinese reports showed that the mortality rate may be 3 times higher in elderly patients, especially those over 80 years of age. In an Italian study, intensive care unit (ICU) mortality was 26%, while it was 36% over 65 years of age. As of 7 April 2020 in Italy, 83% of COVID-19-related deaths were reported in the age group over 70 years of age. In another study conducted in Korea, although the overall mortality rate was 0.9%, the mortality rate was found to be 9.3% in patients aged 80 years and above. Similar results have been reported from the USA (Cevik et al., 2020; Dhama et al., 2020).

Immunological and nutritional status of patients affect malignant tumor postoperative outcomes. Albumin concentrations are affected by nutrition, kidney and liver function. Lymphocyt counts reflect inflammatory and immune system activation. The prognostic nutritional index (PNI) is calculated by serum albumin level and peripheral lymphocyte count. It was first used in 1980 to evaluate the prognosis of patients undergoing gastrointestinal surgery. Other than this, it has also been used in the evaluation of prognosis in various malignancies, pulmonary embolism and cardiac diseases. The PNI is calculated at the input according to the following formula: PNI=10 x serum albumin (g/dL) + (0.005 x total lymphocyte count / mm) (Candeloro et al., 2020; Nozoe et al., 2010).

Complete blood count is easy and inexpensive. The measurement of various cells such as neutrophils, lymphocytes, monocytes, platelets is very informative. The ratios of these parameters to each other are thought to be used as inflammation indices to support the diagnosis and risk assessment in inflammatory diseases. The systemic inflammation index (SII) has also been shown to be useful in risk stratification in inflammatory diseases. It is calculated with platelet count x Neutrophil/Lymphocyte formula (Fois et al., 2020).

There is a few information about patients' nutritional and inflammatory status as potential prognostic factors for COVID-19 infection outcomes. We think that by using such factors in the management of COVID-19, it will facilitate the treatment of patients and have positive results on morbidity and mortality by providing prognostic prediction.

## 2.Materials and Methods

**2.1 Type of research:** A descriptive study

**2.2 Research place and time:** XXX City Hospital, 01.10.2020-31.12.2020

**2.3 Population, sample and sampling method** It was planned to retrospectively examine hospitalized COVID-19 patients records followed-up in the internal medicine service of XXX City Hospital. 401 patients whose nasopharyngeal/oropharyngeal swab samples were PCR positive and who had Covid 19 infection and with associated pneumonia were included in the study.

**2.4 Data collection tools** XXX City Hospital records were used for collecting data.

**2.5 Data collection** Age, gender, length of hospital stay, oxygen requirement, intensive care need and comorbid diseases of the patients were recorded. Serum complete blood count, ferritin, c reactive protein (CRP), procalcitonin, interleukin 6 (IL-6), d-dimer, albumin, lactate dehydrogenase (LDH), sedimentation values were obtained. The patients were divided into two groups, recovered and exitus. It was evaluated whether the differences of these groups were significant in terms of SII and PNI.

### 2.6 Ethical approval and informed consent

All procedures performed in this study were conducted in accordance with the ethical standards of the institutional and / or national research committee and the 1964 Declaration

of Helsinki and its subsequent amendments or comparable ethical standards. Study was approved by the Ethics Committee of XXX City Hospital,(31.03.2021, E1-21-1699)

### 2.7 Statictical analysis

Data coding and statistical analyzes were performed on the computer using the SPSS 22 software package program (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The conformity of the variables to the normal distribution was examined using the Shapiro-Wilk tests. Variables were expressed as mean ± standard deviation and median (minimum-maximum) values. Mann-Whitney U test was used to compare non-categorical parameters between groups. Chi-square test was used for categorical variables. The features of PNI evaluated in predicting exitus in COVID-19 patients were analyzed with the ROC curve at 95% confidence interval. Risk factors for exitus in COVID-19 patients determined by univariate logistic regression analysis. Backward LR method with multivariate analysis is used to identify independent risk factors. Cases with a p value below 0.05 were considered statistically significant.

## 3.Results

The mean age of 401 COVID-19 enrolled patients in the study was 75.8±7.7 years and 181 (45.1%) were women. While 302 (75.4%) patients were in the survived group, 99 (24.6%) patients were in the exitus group. Age, hospitalization time, oxygen need, intensive care requirement were higher in the group of ex ones. The number of patients with CAD, dementia and chronic renal failure (CRF) was higher in this group. Also mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelet volüme (MPV) values, neutrophil, creatinine, LDH, CRP, d-dimer, procalcitonin, maximum ferritin, IL-6 and maximum IL-6 levels were higher in patients in this group but albumin level and lymphocyte value were lower in the exitus group. While the mean PNI of the ex group was 36.9±7, it was 41.9±5.9 in the survived group and this difference was statistically significant ($p<0.001$). SII was higher in the exitus group, but the difference was not statistically significant ($p=181$). Demographic, clinical, additional diseases shown in Table 1, laboratory and treatment data about the patients are shown in Table 2.

**Table 1. Demographic, clinical characteristics of patients who were healed or died due to COVID-19 disease**

| | Total (n=401) | Survived (n=302, % 75.4) | Exitus (n=99, % 24.6) | p |
|---|---|---|---|---|
| Demographical data | | | | |
| Age (years) (Mean ± SD) | 75.8±7.7 | 75±7.4 | 78.2±8.1 | 0.001[m] |
| Female gender, n (%) | 181 (45.1) | 143 (47.4) | 38 (38.4) | 0.12[x] |
| Clinical data | | | | |
| Hospitalization time (days) (median)(min-max) | 11 (1-49) | 10 (1-49) | 15 (1-46) | 0.01[m] |
| Oxygen treatment need, n (%) | 264 (65.8) | 173 (57.3) | 91 (91.9) | <0.001[x] |
| Intensive care need, n (%) | 135 (33.7) | 57 (18.9) | 78 (78.8) | <0.001[x] |
| Comorbidity | | | | |

| | | | | |
|---|---|---|---|---|
| Hypertension, n (%) | 286 (71.3) | 211 (69.9) | 75 (75.8) | 0.261[x] |
| Diabetes Mellitus, n (%) | 160 (39.9) | 127 (42.1) | 33 (33.3) | 0.124[x] |
| COPD, n (%) | 93 (23.2) | 67 (22.2) | 26 (26.3) | 0.404[x] |
| CAD, n (%) | 153 (38.2) | 107 (35.4) | 46 (46.5) | 0.05[x] |
| Dementia, n (%) | 36 (9) | 21 (7) | 15 (15.2) | 0.013[x] |
| Hypothyroidism, n (%) | 25 (6.2) | 19 (6.3) | 6 (6.1) | 0.934[x] |
| CRF, n (%) | 41 (10.2) | 25 (8.3) | 16 (16.2) | 0.025[x] |

COPD: chronic obstructive pulmonary disease, CAD: coronary artery disease, CRF: chronic renal failure

**Table 2. Laboratory characterictics of patients who were healed or died due to COVID-19 disease**

| **Laboratory tests** | | | | |
|---|---|---|---|---|
| **Hemoglobin (unit) (median)(min-max)** | 12.6 (7.4-17.7) | 12.6 (7.4-17.4) | 12.5 (7.6-17.7) | 0.572[m] |
| **MCV (unit) (median)(min-max)** | 88.3 (8.5-938) | 88 (26-938) | 90.4 (8.5-118) | **0.045[m]** |
| **RDW (unit) (median)(min-max)** | 14.5 (1.4-88.5) | 14.4 (1.4-88.5) | 14.8 (12.3-26) | **0.007[m]** |
| **MPV (unit) (median)(min-max)** | 8.7 (6.5-12.4) | 8.6 (6.5-11.3) | 9 (6.8-12.4) | **0.002[m]** |
| **Platelet (unit) (median)(min-max)** | 213000 (220-1950000) | 217500 (32-1950000) | 206000 (220-1740000) | 0.058[m] |
| **WBC (unit) (median)(min-max)** | 6530 (5.3-23580) | 6510 (5.2-23580) | 6800 (710-22730) | 0.134[m] |
| **Lymphocyte (unit) (median)(min-max)** | 910 (110-8210) | 970 (110-8210) | 760 (230-2770) | **<0.001[m]** |
| **Neutrophil (unit) (median)(min-max)** | 4770 (4.5-65540) | 4695 (4.5-65540) | 5630 (71.2-21840) | **0.047 [m]** |
| **Monocyte (unit) (median)(min-max)** | 370 (50-2780) | 380 (50-2780) | 360 (50-1270) | 0.728[m] |
| **Eosinophil (unit) (median)(min-max)** | 20 (0-770) | 20 (0-770) | 10 (0-390) | 0.130[m] |
| **Creatinine (unit) (median)(min-max)** | 1 (0.4-12.5) | 0.9 (0.4-7.6) | 1.2 (0.4-12.5) | **<0.001[m]** |
| **Albumin (units) (median)(min-max)** | 3.6 (0.7-43) | 3.7 (2-42) | 3.5 (0.7-43) | **<0.001[m]** |
| **LDH (unit) (median)(min-max)** | 336 (3.9-1402) | 326 (3.9-920) | 370 (4.9-1402) | **0.03[m]** |
| **Phosphorus (unit) (median)(min-max)** | 3.2 (1-78) | 3.2 (1-78) | 3.1 (1.5-48) | 0.705[m] |
| **Sedimentation (unit) (median)(min-max)** | 40 (3-140) | 40 (3-140) | 41 (3-123) | 0.946[m] |
| **CRP (unit) (median)(min-max)** | 80 (0.5-409) | 68 (0.5-264) | 100 (3-409) | **<0.001[m]** |
| **D-dimer (unit) (median)(min-max)** | 1.1 (0.2-43) | 1.1 (0.2-43) | 1.3 (0.2-35) | **0.014[m]** |
| **Procalcitonin (unit) (median)(min-max)** | 0.1 (0.01-39) | 0.1 (0.01-39) | 0.2 (0.1-34) | **<0.001[m]** |
| **Ferritin (unit) (median)(min-max)** | 352 (9-12391) | 345.5 (9-12391) | 362 (23-6042) | 0.286[m] |
| **Maximum ferritin level (unit) (median)(min-max)** | 595 (24-65356) | 479 (24-20509) | 1409 (58-65356) | **<0.001[m]** |
| **Interleukin-6 (unit) (median)(min-max)** | 34 (0.1-1515) | 28.5 (0.1-1515) | 48 (8-1000) | **<0.001[m]** |
| **Maximum interleukin-6 level (unit) (median)(min-max)** | 40 (0.1-16003) | 30.9 (0.1-3442) | 87 (6.4-16003) | **<0.001[m]** |
| **PNI (Mean ± SD)** | 40.7±6.5 | 41.9±5.9 | 36.9±7 | **<0.001[m]** |
| **SII (Median)(min-max)** | 1091666.7 (1350.9-57977692.3) | 1071953.7 (1350.9-57977692.3) | 1175200 (2604.8-31989176.5) | 0.181[m] |
| **Medical Treatment** | | | | |
| **Steroid, n (%)** | 241 (60.1) | 168 (55.6) | 72 (72.7) | **0.001[x]** |

MCV: mean corpuscular volüme, RDW: red cell distribution width, MPV: mean platelet volüme, WBC: white blood cell, LDH: lactate dehydrogenase, CRP: c reactive protein, PNI: prognostic nutritional index, SII: systemic inflammation index, m: Mann Whitney U Test, x: Chi-square Test

In our study, ROC curves were produced with a 95% confidence interval regarding whether the PNI value is a predictor of exitus in COVID-19 patients and cut-off points were determined (table 3 and figure 1). Multivariate logistic regression analysis showed that advanced age (OR=1.064; 95% CI=1.027-1.102; p=0.001), high maximum ferritin level (OR=1; 95% CI=1-1; p<0.001), high maximum IL-6 level (OR=1.002; 95% CI=1-1.003; p=0.004) and PNI<40 (OR=3.019; 95% CI=1.752-5.202; p<0.001) predicted exitus in COVID-19 patients are independent risk factors (Table 3).

**Table 3. Best cut-off point for the PNI value that separates exitus group from survivors with 95% confidence according to the area under the ROC curve**

PNI: Prognostic Nutritional Index, AUC: Area Under the Curve, CI: Confidence Interval

| | **PNI** |
|---|---|
| **AUC** | 0.707 |
| **% 95 CI** | 0.645-0.77 |
| **p value** | <0.001 |
| **Cutoff point** | 40 |
| **Sensitivity** | 0.697 |
| **Specificity** | 0.642 |

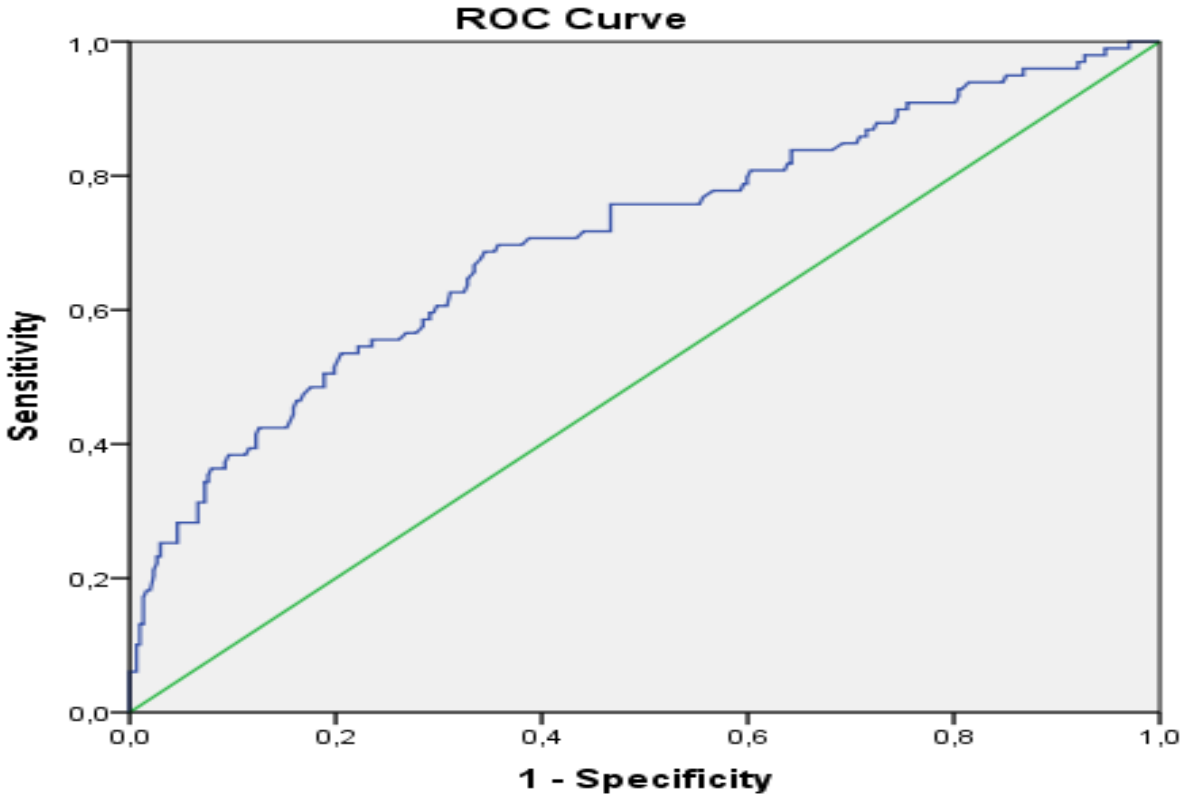

**Figure 1. ROC curve evaluating the effectiveness of the Prognostic Nutritional Index in predicting exitus in COVID-19 patients**

**Table 4. Determination of risk factors for death in patients with COVID-19 by univariate and multivariate logistic regression analysis**

| | Univariate | | | Multivariate | |
|---|---|---|---|---|---|
| | OR (% 95 CI) | p | | OR (% 95 CI) | p |
| **Age (year)** | 1.055 (1.024-1.086) | **<0.001** | **Age (year)** | 1.064 (1.027-1.102) | **0.001** |
| **CAD** | 0.632 (0.399-1.001) | 0.051 | | | |
| **Dementia** | 2.389 (1.179-4.841) | **0.016** | **Dementia** | 1.985 (0.865-4.555) | 0.106 |
| **CKD** | 2.136 (1.089-4.19) | **0.027** | **CKD** | 1.049 (0.438-2.511) | 0.915 |
| **MCV (unit)** | 0.995 (0.978-1.012) | 0.586 | | | |
| **RDW (unit)** | 1.019 (0.972-1.069) | 0.437 | | | |
| **MPV (unit)** | 1.432 (1.142-1.795) | **0.002** | **MPV (unit)** | 1.3 (0.996-1.697) | 0.054 |
| **Lymphocyte (unit)** | 0.999 (0.999-1) | **0.004** | **Lymphocyte (unit)** | 1 (0.999-1) | 0.98 |
| **Neutrophil (unit)** | 1 (1-1) | 0.077 | | | |
| **Albumin level (unit)** | 0.976 (0.905-1.052) | 0.525 | | | |
| **LDH (unit)** | 1.002 (0.905-1.052) | **0.014** | **LDH (unit)** | 1.001 (0.999-1.003) | 0.369 |
| **CRP (unit)** | 1.006 (1.003-1.01) | **<0.001** | **CRP (unit)** | 1.001 (0.997-1.006) | 0.515 |
| **D-dimer (unit)** | 1.032 (0.984-1.082) | 0.19 | | | |
| **Procalcitonin (unit)** | 1.018 (0.963-1.076) | 0.535 | | | |
| **Maximum ferritin (unit)** | 1 (1-1.001) | **<0.001** | **Maximum ferritin level (unit)** | 1 (1-1) | **0.001** |
| **Maximum IL-6 (unit)** | 1.002 (1.001-1.003) | **<0.001** | **Maximum IL-6 (unit)** | 1.002 (1-1.003) | **0.004** |
| **PNI<40** | 3.94 (2.425-6.403) | **<0.001** | **PNI<40** | 3.019 (1.752-5.202) | **<0.001** |

CAD: Coronary Artery Disease, CKD: Chronic Kidney Disease, MCV: Mean Corpuscular Volume, RDW: Red Cell Distribution Width, MPV: Mean Platelet Volume, WBC: White Blood Cell, LDH: Lactate dehydrogenase, CRP: C reactive protein, IL- 6: Interleukin 6, OR: Odds Ratio, CI: Confidence Interval

## 4.Discussion

This study was planned to evaluate its usefulness in predicting mortality with PNI and SII among geriatric COVID-19 patients. It has shown that PNI is an independent risk factor in severe COVID-19 disease in geriatric group patients. The cut-off value that can be used for COVID-19 risk assessment for PNI was <40 in our study. Similar results were found in another study involving 450 adult COVID-19 patients.(Wang et al., 2020) PNI can be used to predict

high-risk COVID-19 patients at an early stage. Contrary with other studies no relationship was found between SII and COVID-19 mortality. This may have been caused by the frequent occurrence of thrombocytopenia in the geriatric patient group.

In the study of Wang et al., mortality was 17.3% in 450 covid-19 patients, while it was 12% in 3988 covid-19 patients of Graselli et al. (Grasselli et al., 2020; Wang et al., 2020) Mortality was found to be 24.6% in 401 patients in our study, and this may be due to the inclusion of only patients over 65 years of age.

The increase in mortality in geriatric patients with increasing age and male gender was consistent with other studies in the literature. (Grasselli et al., 2020; Zhou et al., 2020) Covid-19 mortality increase with ckd and cad was consistent with previous studies (Albitar et al., 2020)

PNI is calculated according to lymphocyte and albumin values and provides objective information about the patient's inflammatory and nutritional status. There are studies showing the prognostic value of PNI associated with cancer and cardiovascular diseases.(Shirakabe et al., 2018; Y.-S. Xu et al., 2021)

Studies have shown that the risk of ARDS is significantly increased in patients with low albumin levels.(Thongprayoon et al., 2020) Studies with COVID-19 patients have also showed that the risk of ARDS is increased and associated with more adverse clinical outcomes.(Chen et al., 2021; Y. Xu et al., 2021) In a single-centered retrospective study, low albumin levels associated with long hospital stay and mortality.(Acharya et al., 2021) Furthermore, several studies have shown that low lymphocyte count is closely associated with COVID-19 disease progression.(Huang et al., 2020; Lagadinou et al., 2020) Lymphocyte migration to the infection area, lymphocyte depletion due to excessive immune activity and bone marrow suppression are considered to be possible causes of low lymphocyte count. In severe COVID-19 disease, increased IL-6 and IL-8 levels associated with cytokine storm syndrome have been found.(Li et al., 2020) In addition, T-cell activation and differentiation-related gene expression down-regulation has been shown to be another cause of lymphopenia in COVID-19 patients.(Ouyang et al., 2020) While low albumin level and lymphocyte count alone are associated with high mortality, PNI, the combination of these two values, can be used as an easily measurable, inexpensive and effective method in COVID-19 patients. The results of our study also showed that PNI can be used in geriatric COVID-19 patients.

The limitation of our study is, firstly, the lack of anthropometric measurement data due to the fact that the patients were in the isolation unit. Secondly, the study was single-centered.

## 5.Conclusion and Suggestions

The low PNI is associated with mortality and other outcomes of COVID-19 disease. This prognostic model is suitable for predicting severe disease and mortality. It can be a guide for which patients to follow more intensively in the treatment of COVID-19 patients.

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**Declarations**

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