ORIGINAL RESEARCH

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Can PNI and CONUT Scores Predict One-year Survival Both in Older and Younger Hospitalized Patients with COVID-19?

Yelda Öztürk[1], Murat Özdede[2], Oğuz Abdullah Uyaroğlu[2], Merve Güner Oytun[1], Serdar Ceylan[1], Meltem Halil[1]

[1]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatric Medicine, Ankara, Turkey
[2]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of General Internal Medicine, Ankara, Turkey

Abstract

Objective: This study aimed to find out the prognostic effect of the prognostic nutritional index (PNI) and controlling nutritional status (CONUT) score for 1-year mortality prediction in older (≥65 years) and younger (<65 years) hospitalized Coronavirus disease-2019 (COVID-19) patients, separately.

Materials and Methods: This retrospective and the observational study included 368 patients who were admitted to a single tertiary care university hospital due to COVID-19 disease with positive severe acute respiratory syndrome-coronavirus-2 real-time reverse transcriptase-polymerase chain reaction test. Multivariable Cox regression analyses were performed to predict 1-year mortality prediction for the older and younger groups.

Results: Among 368 patients, 112 (30.4%) patients were 65 years and older. There were 45 (12.2%) deaths at the end of the 1-year follow-up. The 1-year mortality rate was higher in the older group (23.2% vs 7.4%). When all patients were analyzed (n=368), PNI [hazard ratio (HR)=0.924, 95% confidence interval (CI)=0.877-0.974, p=0.003] and CONUT (HR=1.423, 95% CI=1.194-1.696, p<0.001) scores were significantly associated with 1-year mortality in multivariable model. When older and younger groups were assessed separately; PNI and CONUT scores failed to estimate 1-year mortality in the older group. On the other hand, the independent estimating capacities of PNI (HR=0.899, 95% CI=0.836-0.966, p=0.004) and CONUT (HR=1.944, 95% CI=1.478-2.557, p<0.001) scores increased when the only younger group was taken into analysis.

Conclusion: PNI and CONUT scores as indicators of nutritional and immune status, predicted 1-year mortality in hospitalized COVID-19 patients. However, their prognostic effects in older patients with COVID-19 may be less prominent. Future, large sample studies are needed to provide data about geriatric COVID-19 patients.

Keywords: Geriatrics, nutritional assessment, COVID-19, PNI, CONUT

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection developed into a global pandemic after first seen in China in 2019. Age, male sex, and the existence of comorbidities are shown to be associated with severe Coronavirus disease-2019 (COVID-19), higher risk of hospitalization, and in-hospital mortality, so far (1-5). Both biological and immune function of humans' decrease gradually with the aging process; this immune aging process is called immunosenescence, contributing to the higher susceptibility to infections, autoimmune diseases, and infections. Immunosenescence causes a low-grade pro-inflammatory state with the increment of inflammatory mediators like IL-6, IL-1RA, TNF-α, IL-1, and C-reactive protein (CRP) called inflammaging. Inflammaging with other features of the immunosenescence may fasten the disease severity of COVID-19 in older adults (6). Regardless of age, the features of COVID-19, including inflammation, hypercatabolism, and increased energy expenditure, may predispose to malnutrition and muscle wasting. On the other hand, preexisting malnutrition and sarcopenia may worsen the disease progression and related complications. The social isolation and quarantine measures due to pandemics may cause changes in dietary habits, difficulties in accessing food, lack of physical activity, and worsening of

Address for Correspondence: Yelda Öztürk, Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatric Medicine, Ankara, Turkey
Phone: +90 533 615 12 86 **E-mail:** yeldaozturk67@gmail.com **ORCID:** orcid.org/0000-0003-3847-0967
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chronic disease. All these issues may contribute to the increment in malnutrition prevalence both before and after the COVID-19 disease (7-9).

The prognostic impact of new nutritional indices based on biochemical and clinical markers in the pandemic world has emerged. Prognostic nutritional index score (PNI) calculated using albumin and lymphocyte; controlling nutritional status score (CONUT) calculated by using albumin, lymphocyte and cholesterol are the major ones (10,11). As they are easy and practical to obtain data about the nutritional status of patients, they are widely used especially in oncology wards.

When the risks and difficulties in managing hospitalized patients with COVID-19 and the effect of nature of the disease on nutritional status itself were considered; we planned to investigate the long-term prognostic effects of PNI and CONUT scores on hospitalized patients with COVID-19, retrospectively. Therefore, we aimed to find out the effect of these indices to predict 1-year mortality both in older and younger patients with COVID-19.

Materials and Methods

Study population and data collection

This retrospective observational study was conducted in a single tertiary care university hospital and included patients with COVID-19 who were admitted to the hospital between June 01 2020 and December 31 2021. All included patients had positive SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) tests (Bioeksen R&D Technologies Ltd, Turkey) taken by a doctor from both combined oropharyngeal and nasopharyngeal samples. The patients who were pregnant and clinically suspected COVID-19 with negative RT-PCR tests were excluded. The data of patients about date of birth, sex, length of stay, comorbidities, medications, and pulmonary computed tomography (CT) findings were obtained from medical records. The laboratory values including white blood cells ($\times 10^3/\mu L$), neutrophils ($\times 10^3/\mu L$), lymphocyte ($\times 10^3/\mu L$), fasting plasma glucose (mg/dL), total cholesterol protein (mg/dL), albumin (g/dL), alanine aminotransferase (U/L), aspartate aminotransferase (U/L), creatinine (mg/dL), CRP (mg/dL), ferritin (µg/L), D-dimer (mg/L) and fibrinogen (mg/dL), taken within 24 hours of admission, were recorded.

Nutritional assessment

The nutritional status of patients was assessed by using PNI and CONUT. PNI score was calculated using the following formula: 10*serum albumin (g/dL) +0.005*total lymphocyte count (per mm^3). Whereas a score of >38 was considered normal nutritional status; scores of 35-38 and <35 were evaluated as moderate and severe malnutrition, respectively (10,12). CONUT score was calculated from serum albumin, total cholesterol, and lymphocyte count. Lymphocyte count was scored as 0, 1, 2, and 3 when it was ≥1.600, 1.200-1.599, 0.800-1.199, and <0.800, respectively. Serum albumin was scored as 0, 2, 4, 6 when it was ≥3.5, 3.0-3.49, 2.5-2.99, <2.5 g/dL, respectively. Serum cholesterol was scored as 0, 1, 2, and 3 when it was ≥180, 140-179, 100-139, and <100 mg/dL, respectively. Finally, the total CONUT score was classified as normal nutritional status, mild, moderate, and severe malnutrition when ıt was 0-1, 2-4, 5-8, and 9-12, respectively (11,12).

Follow-up and outcomes

All the study participants were followed from hospital admission to death or until 31 December 2021. Vital status and the date of death were obtained from the Turkish national death registry. The primary outcome of this study was all-cause mortality.

Ethics approval

The Local Ethics Committee of Hacettepe University approved the study (no: GO 21/818), and conducted according to the guidelines laid down in the Declaration of Helsinki.

Statistics

The variables were controlled by using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test) to determine whether or not they were normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed age. Medians and interquartile range (25-75 percentile) were used for the non-normally distributed and ordinal variables. Categorical variables were summarized in terms of counts and percentages. Whereas normally distributed variables were compared using independent samples t-test, non-normally distributed variables were compared using Mann-Whitney U test between groups. The chi-square test or Fisher's Exact test, where appropriate, was used to compare proportions between groups. The area under curve values were calculated based on the receiver operating characteristic (ROC) curves analysis to estimate predicting capacities of PNI and CONUT regarding mortality in both ≥65 years and <65 years groups and shown as figure. The unadjusted Cox model was used to assess the relationship between 1-year mortality and nutritional indices. Multivariable Cox regression models were also generated by adjusting for age, and gender. As PNI and CONUT scores were calculated by using albumin, cholesterol, and lymphocyte, these laboratory values were not put into models. The results were expressed as hazard ratios (HRs) and corresponding 95% confident intervals (CI). The proportional hazards assumption and model fit were assessed using residual (Schoenfeld and Martingale) analysis. All analyses were considered statistically significant when the p-value was <0.05 and was performed by the Statistical Package of Social Science 23.0 (SPSS Inc., Chicago, IL).

Results

Three-hundred and sixty-eight patients were enrolled in the study. The mean age of the participants at the time of hospital admission was 57.1±15.7 (range, 18-97) with a 46.7% male rate. The median follow-up time was 16.1 months. There were 45 (12.2%) deaths during the 1-year follow-up. The proportions of older patients (57.8%) and male sex (68.9%) were higher in the deceased group, whereas the rate of white blood cells, neutrophils, alanine aminotransferase, serum creatinine, CRP, ferritin, and D-dimer were higher; lymphocyte, total cholesterol, and albumin were lower in the deceased group. Nutritional status, defined by CONUT and PNI, was worst in the deceased group as well (Table 1). One hundred and twelve (30.4%) of the participants were placed in the geriatric (≥65 years) group. Older patients had longer length of stay, higher CRP and D-dimer, and lower albumin and total cholesterol level. Nutritional indices were worse in the geriatric group than younger group. The one-year mortality rate was higher in geriatric group as well (Table 2).

A comparison of the ROC curves is given in Figure 1. The univariable and multivariable (age and sex adjusted) cox models are given in Table 3 and Table 4, in detail. When all patients were analyzed (n=368), PNI (HR=0.924, 95% CI=0.877-0.974, p=0.003) and CONUT (HR=1.423, 95% CI=1.194-1.696, p<0.001) scores were significantly associated with 1-year mortality in a multivariable model. However, when we assessed the older and younger groups, separately in multivariable analysis; PNI and CONUT scores failed to estimate in geriatric group. On the other hand, the independent estimating capacities of PNI (HR=0.899, 95% CI=0.836-0.966, p=0.004) and CONUT (HR=1.944, 95% CI=1.478-2.557, p<0.00) scores for 1-year mortality increased when only younger group were taken into analysis.

Discussion

In the present study, both PNI and CONUT scores were independently associated with 1-year mortality in hospitalized patients with COVID-19. However, when the patients were divided into two groups according to their ages (≥65 years or <65 years of age), we showed that PNI and CONUT scores failed to estimate 1-year mortality risk in geriatric patients. This data was the major finding of our study. To the best of our knowledge, this was the first study investigating the estimating capacities of PNI and CONUT scores to predict 1-year mortality in older and younger hospitalized patients with COVID-19, separately.

PNI score, calculated using albumin and lymphocyte; CONUT score, calculated using albumin, lymphocyte, and cholesterol has gained popularity, especially in oncology and surgery wards as they are easy and practical tools. There are emerging studies supporting their use in clinical practice to predict prognosis, especially in mortality estimation (13-21). Recently, PNI and CONUT have been used in hospitalized patients with COVID-19 (8,22). Bengelloun et al. (23) assessed nutritional status using the CONUT index at hospital admission to predict COVID-19 related health outcomes in 2844 COVID-19 patients (mean age was 67.3±16.5). They found the CONUT index to be an independent indicator of mortality (in-hospital and 30-day mortality) and length of stay similar to us (23). Therefore, we showed that the independent prognostic ability of the CONUT score lasted at least 1-year, when all patients were included in the analysis. However, when older and younger patients were evaluated separately, CONUT score failed to predict 1-year mortality in the older group. Another retrospective observational study from China assessed 295 hospitalized COVID-19 patients and showed PNI and CONUT scores as a prognostic indicators for in-hospital mortality (24). Although this study was consistent with our results, the median age of participants was 58 years. Hu et al. (25) found the independent predictive value of PNI for the severity of COVID-19 and they suggested PNI score as a simple and effective predictor with different sex, age, and BMI for hospitalized patients with COVID-19. Although they presented the independent effect of PNI, the mean age in the study was 44 years [standard deviation (SD)=13.4] (25). Wei et al. (26) published a study in line with this data and showed PNI as an independent predictor of mortality for hospitalized COVID-19 patients. A study from Turkey investigated the estimating capacity of PNI for hospital mortality in COVID-19 patients with cardiovascular risk factors, and found it independently associated with mortality. The mean age of patients in the study was 55.4 years (SD=12.8) (27).

Although there are emerging studies about using PNI and CONUT scores in hospitalized COVID-19 patients, the data about the confounding factors, especially in older patients and comorbidities are missing. The first challenge is immune aging called immunosenescence and inflammaging as a result of cell senescence. The second one is the high prevalence of comorbidities with aging that may cause low-grade inflammation. Thirdly, the data about the frailty status of patients are important when managing hospitalized patients. As, frailty is a dynamic process at all ages, it should be evaluated in all conditions. However, the effect of frailty on hospitalized COVID-19 patients is controversial (28-30). In the light of these data with the enormous effect of virus, the nutritional indices should be interpreted cautiously, especially for COVID-19 patients. Albumin and lymphocyte counts are both used in the calculation of PNI and CONUT scores. Albumin is synthesized in the liver and is an indicator of nutritional status. However, the synthesis of albumin is reduced when systemic inflammation is present and its sensitivity as a nutritional marker decreases as it is a negative acute-phase reactant. Lymphocyte count is an indicator of the immune system and low lymphocyte level

Table 1. Characteristics of patients according to 1-year survival

Parameters	Total	Alive (1-year) (n=323)	Deceased (1-year) (n=45)	p-value
Age	57.1±15.7	55.5±15.1	68.5±15.2	<0.001
≥65 years	112 (30.4)	86 (26.6)	26 (57.8)	<0.001
Sex, male	172 (46.7)	141 (43.7)	31 (68.9)	0.001
Follow-up time, month	16.1 (13.1-17.4)	16.6 (14.9-17.5)	0.8 (0.5-1.7)	<0.001
Length of stay, day	6.0 (4.0-10.0)	6.0 (4.0-9.0)	18.0 (7.5-27.5)	<0.001
Comorbidities				
Diabetes mellitus	83 (25.4)	67 (23.4)	16 (39.0)	0.032
Hypertension	129 (39.4)	106 (37.1)	23 (56.1)	0.020
COPD	19 (5.8)	15 (5.2)	4 (9.8)	0.248
Coronary artery disease	53 (16.2)	40 (14.0)	13 (31.7)	0.004
Cerebrovascular disease	15 (4.6)	11 (3.8)	4 (9.8)	0.091
Malignancy	34 (10.4)	19 (6.6)	15 (36.6)	<0.001
Laboratory indices				
White blood cell, x10^3/uL	4.8 (3.2-6.1)	4.8 (3.2-6.0)	5.6 (3.5-8.2)	0.031
Neutrophils, x10^3/uL	2.9 (1.8-4.3)	2.9 (1.8-4.1)	3.7 (2.2-6.2)	0.009
Lymphocyte, x10^3/uL	1.0 (0.7-1.4)	1.0 (0.7-1.5)	0.8 (0.6-1.2)	0.020
Fasting plasma glucose, mg/dL	105 (90-131)	103 (90-126)	128 (96-167)	0.510
Total cholesterol, mg/dL	188 (146-227)	190 (152-230)	138 (106-165)	<0.001
Albumin, (g/dL)	3.9 (3.6-4.2)	4.0 (3.7-4.2)	3.6 (2.9-3.9)	<0.001
Alanine aminotransferase, U/L	24 (16-38)	24 (16-38)	22 (16-36)	0.685
Aspartate aminotransferase, U/L	31 (23-44)	30 (23-42)	38 (29-53)	0.005
Serum creatinine, mg/dL	0.86 (0.71-1.02)	0.84 (0.71-0.99)	0.96 (0.80-1.31)	0.002
C-reactive protein, mg/dL	2.2 (0.9-7.5)	1.8 (0.8-6.2)	7.6 (3.4-15.5)	<0.001
Ferritin, ng/mL	155 (64-365)	138.2 (56.5-315.5)	438.1 (124.7-941.6)	<0.001
D-dimer, mg/L	0.54 (0.32-0.90)	0.52 (0.32-0.85)	0.87 (0.50-2.30)	<0.001
Fibrinogen, mg/dL	405 (323-509)	405 (323-509)	416 (332-520)	0.475
CONUT score CONUT category Normal Mild Moderate Severe	2 (1-4) 75 (26.7) 163 (58.0) 39 (13.9) 4 (1.4)	2 (1-3) 75 (28.6) 153 (58.4) 32 (12.2) 2 (0.8)	4 (3-5) 0 (0) 10 (52.6) 7 (36.8) 2 (10.5)	<0.001 <0.001
PNI score PNI category Normal Moderate Severe	45.0 (41.3-48.5) 325 (88.3) 20 (5.4) 23 (6.3)	45.8 (41.9-49.0) 292 (90.4) 19 (5.9) 12 (3.7)	41.2 (36.1-44.3) 33 (73.3) 1 (2.2) 11 (24.4)	<0.001 <0.001
Abnormal CT imaging findings	274 (84)	238 (83.5)	36 (87.8)	0.482
COVID-19 pneumonia (n=327)	323 (98.8)	284 (99.3)	39 (95.1)	0.078

CONUT: Controlling nutritional status score, COPD: Chronic obstructive pulmonary disease, PNI: Prognostic nutritional index. Numbers were presented as means ± SD, medians (25th-75th percentiles), or frequencies n (%), as appropriate. SD: Standard deviation, CT: Computed tomography, COVID-19: Coronavirus disease-2019

was shown to be an independent risk factor for COVID-19 (31). Another parameter used in the calculation of CONUT score is cholesterol level and it is a nutritional indicator, too. A reduced level of cholesterol is associated with an impaired immune response (32). Not only being a nutritional indicator but also an immune-inflammatory index; both PNI and CONUT are valuable, especially in the COVID-19 pandemic area. However, the cut-off values of PNI and the CONUT scores need to be updated for COVID-19 patients and older adults, separately, evaluating the confounders and taking comprehensive geriatric assessment into consideration.

Table 2. Baseline characteristics of patients according to age categories

	Total	≥65 years (n=112)	<65 years (n=256)	p-value
Age	57.1±15.7	75.4±6.8	49.1±11.1	<0.001
Sex, male	172 (46.7)	51 (45.5)	121 (47.3)	0.760
Follow-up time	16.1 (13.1-17.4)	15.1 (12.0-16.7)	16.6 (14.0-17.6)	<0.001
Length of stay	6.0 (4.0-10.0)	9.0 (5.0-16.2)	5.0 (4.0-8.0)	<0.001
Comorbidities				
Diabetes mellitus	83 (25.4)	41 (42.7)	42 (18.2)	<0.001
Hypertension	129 (39.4)	67 (69.8)	62 (26.8)	<0.001
COPD	19 (5.8)	11 (11.5)	8 (3.5)	0.005
Coronary artery disease	53 (16.2)	35 (36.5)	11 (11.5)	<0.001
Cerebrovascular disease	15 (4.6)	10 (10.4)	5 (2.2)	0.001
Malignancy	34 (10.4)	11 (11.5)	23 (10)	0.685
Laboratory indices				
White blood cell, $\times10^3/\mu L$	4.8 (3.2-6.1)	4.7 (3.2-6.0)	4.9 (3.3-6.1)	0.864
Neutrophils, $x10^3/uL$	2.9 (1.8-4.3)	2.9 (1.9-4.6)	2.9 (1.8-4.2)	0.718
Lymphocyte, $x10^3/uL$	1.0 (0.7-1.4)	0.9 (0.7-1.3)	1.0 (0.7-1.5)	0.076
Fasting plasma glucose, mg/dL	105 (90-131)	118 (92-159)	101 (90-122)	0.007
Total cholesterol, mg/dL	188 (146-227)	173 (137-214)	190 (148-233)	0.018
Albumin, g/dL	3.9 (3.6-4.2)	3.7 (3.5-4.0)	4.0 (3.7-4.2)	<0.001
Alanine aminotransferase, U/L	24 (16-38)	21 (16-29)	25 (16-41)	0.014
Aspartate aminotransferase, U/L	31 (23-44)	31 (25-43)	31 (22-44)	0.353
Serum creatinine, mg/dL	0.86 (0.71-1.02)	0.95 (0.81-1.29)	0.82 (0.67-0.96)	<0.001
C-reactive protein, mg/dL	2.2 (0.9-7.5)	3.0 (1.2-9.1)	1.9 (0.8-6.3)	0.004
Ferritin, ng/mL	155 (64-365)	158 (71-367)	151 (59-359)	0.559
D-dimer, mg/L	0.54 (0.32-0.90)	0.81 (0.50-1.21)	0.45 (0.28-0.74)	<0.001
Fibrinogen, mg/dL	405 (323-509)	424 (349-527)	395 (311-497)	0.090
CONUT score CONUT category Normal Mild Moderate Severe	2 (1-4) 75 (26.7) 163 (58.0) 39 (13.9) 4 (1.4)	3(2-4) 12 (16.4) 45 (61.6) 14 (19.2) 2 (2.7)	2 (1-3) 63 (30.3) 118 (56.7) 25 (12.0) 2 (1.0)	 0.008 0.063
PNI score PNI category Normal Moderate Severe	45.0 (41.3-48.5) 325 (88.3) 20 (5.4) 23 (6.3)	42.9 (39.6-46.4) 93 (83) 8 (7.1) 11 (9.8)	46.2 (42.0-49.2) 232 (90.6) 12 (4.7) 12 (4.7)	<0.001 0.097
Abnormal CT imaging findings (n=324)	274 (84)	83 (87.4)	191 (82.7)	0.294
COVID-19 pneumonia (n=327)	323 (98.8)	95 (99)	228 (98.7)	0.753
Mortality rate 3-months 6-months 1-year	 35 (9.5) 38 (10.3) 45 (12.2)	 20 (17.9) 22 (19.6) 26 (23.2)	 15 (5.9) 16 (6.3) 19 (7.4)	 <0.001 <0.001 <0.001

CONUT: Controlling nutritional status score, COPD: Chronic obstructive pulmonary disease, PNI: Prognostic nutritional index. Numbers were presented as means ± SD, medians (25^{th}-75^{th} percentiles) or frequencies n (%), as appropriate. SD: Standard deviation, CT: Computed tomography, COVID-19: Coronavirus disease-2019

Study Limitations

This study has some limitations. First of all, it has a retrospective design so we could not perform comprehensive geriatric assessment including the functional, cognitive, and frailty status of patients. Therefore, malnutrition risk screening of patients by using short-form mini-nutritional assessment, nutritional

risk screening (NRS 2002) etc. was not available. Secondly, the number of older patients was low and the effect of comorbidities was not evaluated separately. On the other hand, we did not exclude patients who use lipid-lowering therapy, and it might affect the total cholesterol results also CONUT scores.

Conclusion

PNI and CONUT scores as indicators of nutritional and immune status, predicted 1-year mortality in hospitalized COVID-19 patients when all patients were analyzed. However, their prognostic effects in geriatric patients may be different especially for COVID-19 patients. Future and large sample size studies are needed to provide data about the use of these indices in geriatric COVID-19 patients adjusting for other confounders.

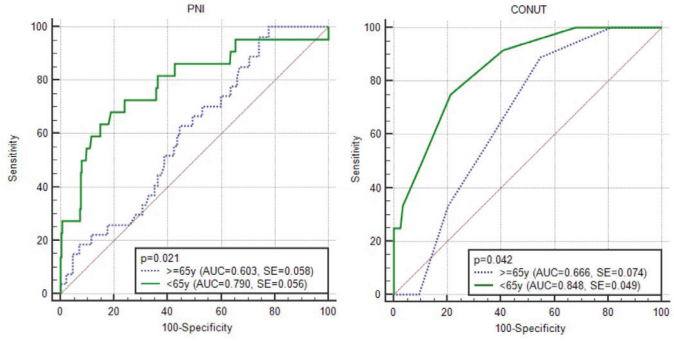

Figure 1. Comparisons of ROC curves for PNI and CONUT according to age categories

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index

Ethics

Ethics Committee Approval: The study protocol was approved by the Local Ethics Committee of Hacettepe University (Ankara, Turkey), and written informed consent was obtained from all participants (no: GO 21/818). All the procedures were in accordance with the ethical standards established by the 1964 Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants. All the procedures were in accordance with the ethical standards established by the 1964 Declaration of Helsinki.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Y.Ö., M.G.O., S.C., M.H., Design: Y.Ö., M.Ö., O.A.U., M.H., Data Collection or Processing: Y.Ö., M.Ö., O.A.U., M.G.O., S.C., M.H., Analysis or Interpretation: Y.Ö., M.G.O., S.C., M.H., Literature Search: Y.Ö., M.H., Writing: Y.Ö., M.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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Table 3. Univariable analysis of two malnutrition indices to predict mortality

Variables	All patients		≥65 years		<65 years	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.058 (1.036-1.081)	<0.001	1.088 (1.035-1.144)	0.001	1.052 (1.002-1.105)	0.043
Sex	2.657(1.413-4.995)	0.002	3.685 (1.548-8.773)	0.003	1.960 (0.772-4.979)	0.157
CONUT score	1.543 (1.304-1.826)	<0.001	1.147 (0.865-1.522)	0.340	1.948 (1.519-2.498)	<0.001
PNI score	0.890 (0.848-0.935)	<0.001	0.923 (0.859-0.991)	0.028	0.884 (0.823-0.950)	0.001

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index, CI: Confident interval, HR: Hazard ratio

Table 4. Multivariable analysis of two malnutrition indices to predict mortality

Variables	All patients (n=368)		≥65 years (n=112)		<65 years (n=256)	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Model 1						
Age	1.036 (1.001-1.072)	0.043	1.042 (0.958-1.134)	0.336	1.051 (0.981-1.126)	0.154
Sex	2.674 (0.870-8.220)	0.086	9.599 (1.142-80.720)	0.037	0.660 (0.128-3.391)	0.618
CONUT score	1.423 (1.194-1.696)	<0.001	-	-	1.944 (1.478-2.557)	<0.001
Model 2						
Age	1.052 (1.029-1.075)	<0.001	1.077 (1.030-1.127)	0.001	1.042 (0.990-1.097)	0.116
Sex	2.538 (1.340-4.808)	0.004	3.770 (1.572-9.039)	0.003	1.507 (0.579-3.920)	0.401
PNI score	0.924 (0.877-0.974)	0.003	0.955 (0.885-1.031)	0.236	0.899 (0.836-0.966)	0.004

CONUT: Controlling nutritional status score, PNI: Prognostic nutritional index, CI: Confident interval, HR: Hazard ratio, Model 1: Age, sex, CONUT, Model 2: Age, sex, PNI

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