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Determinants of prognosis in geriatric patients followed in respiratory ICU; either infection or malnutrition

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Abstract

Severity of illness, age, malnutrition, and infection are the important factors determining intensive care unit (ICU) survival.

The aim of the study is to determine the relations between Geriatric Nutritional Risk Index (GNRI), C-reactive protein/albumin (CAR), and prognosis-mortality of geriatric patients (age of ≥65 years) admitted to intensive care unit.

The study with 10/15/2020, 697 approval date, and number retrospectively registered. Between January 1, 2018 and December 31, 2019, 413 geriatric patients admitted to ICU. The patients were divided into three groups according to their age.

The age group, gender, Charlson comorbidity index, intensive care scores (Acute Physiology And Chronic Health Evaluation II and Sequential Organ Failure Assessment), the infection markers (white blood cell, procalcitonin, CAR levels), malnutrition tools for each patient (body mass index, Nutrition Risk in Critically ill score, and GNRI scores) were analyzed retrospectively. Also length of stay (LOS) ICU, length of stay hospital, and 30-day mortality were recorded.

Geriatric patients number of 403 was included in the study. Forty-nine (12.3%) patients had a history of malignancy, 272 (67.5%) patients had Chronic Obstructive Pulmonary Disease comorbidity. There was no difference in mortality between age groups.

In patients with mortality, body mass index, had being Chronic Obstructive Pulmonary Disease history, GNRI, length of stay hospital, and albumin were significantly lower; malignancy comorbidity rate, inotrope use, modified Nutrition Risk in Critically ill score, mechanical ventilation duration, LOS ICU, Sequential Organ Failure Assessment, Acute Physiology And Chronic Health Evaluation II, Charlson comorbidity index, C-reactive protein, procalcitonin, and CAR were significantly higher.

Both malnutrition and infection affect mortality in geriatric patients in intensive care. The GNRI is better than CAR at predicting mortality.

Abbreviations: APACHE II = Acute Physiology And Chronic Health Evaluation II, BMI = body mass index, CAR = CRP/albumin ratio, CCI = Charlson comorbidity index, COPD = Chronic Obstructive Pulmonary Disease, CRP = C-reactive protein, GNRI = Geriatric Nutritional Risk Index, ICU = intensive care unit, LOS H = length of stay hospital, LOS ICU = length of stay ICU, mNUTRIC score = modified Nutrition Risk in Critically ill score, MV = mechanical ventilation, NUTRIC score = Nutrition Risk in Critically ill score, SOFA = Sequential Organ Failure Assessment.

Keywords: CAR, geriatric patients, GNRI, ICU, infection, nutrition

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All the authors mentioned in the manuscript have agreed for authorship, read, and approved the manuscript, and given consent for submission and subsequent publication of the manuscript. The manuscript in part or in full has not been submitted or published anywhere.

The study was carried out with the permission of the Medical Specialization Training Board of Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital (approval date and number: 10/15/2020, 697).

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

The authors declare that this study complies with the Declaration of Helsinki.

The authors have no conflicts of interest to disclose.

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

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1. Introduction

Nowadays with the increase in average life expectancy and decrease in birth rates, the elderly population in the society increases and also the rate of geriatric patients in intensive care units is increasing day by day. It is reported that the number of persons aged 60 or over is expected to more than twice by 2050 compared to 2017.[1] In our country, the rate of elderly people was 5.3% in 2000.[2]

Severity of illness, age, malnutrition, and infection are the important factors determining intensive care unit (ICU) survival. There are many comorbidities that increase the mortality rate in the geriatric population.[3] Additionally, the incidence of sepsis increases with age, the ages over than 80 is associated with extremely high mortality rates.[4]

C-reactive protein (CRP) is an acute phase reactant and indicates inflammation due to infection. Albumin is an indicator of malnutrition and the ratio of CRP/albumin (CAR) has recently been evaluated as a prognostic marker for mortality in sepsis.[5,6] Elderly patients are vulnerable to infection, and nutritional condition is very important predictive factor.

While elderly patients hospitalized in intensive care are treated for primary disease, malnutrition may be overlooked. In evaluating the nutritional status of patients, all clinical findings should be taken into consideration; both anthropometric methods and screening tools should be used. The Geriatric Nutritional Risk Index (GNRI) is a tool to determine the nutritional status of elderly people based on their albumin level, current weight, and ideal weight.[7]

Although it is known that malnutrition and infection adversely affect the prognosis of geriatric patients [8], it has not been reported which one has more effect. In this study, we aimed to determine the possible relations between GNRI, CAR, and prognosis-mortality of geriatric patients admitted to intensive care unit.

2. Materials and methods

The study was designed retrospectively and initiated after approval from the Medical Specialization Training Board of Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital (approval date and number: 15/10/2020, 697). Between January 1, 2018 and December 31, 2019; consecutive 561 patients admitted to respiratory ICU. Four hundred thirteen of them were geriatric patients (age of ≥65 years). Patients with hyponatremia (135 mmol/L), hypernatremia (145 mmol/L), severe liver disease, and severe kidney failure (creatinine clearance < 15 mL/min) were excluded from the study to rule out albumin changes not related to malnutrition (n: 7). Also the patients had missing data (n: 3) were excluded from the study (Fig. 1). The number of patients were 403 included in the study.

The patients were divided into three groups according to their age; 65 to 74 early elderly, 75 to 84 advanced elderly, and 85 and over very advanced elderly.

The age group, gender, Charlson comorbidity index (CCI), Intensive care scores (Acute Physiology And Chronic Health Evaluation II [APACHE II] and Sequential Organ Failure Assessment [SOFA]), the infection markers (white blood cell, procalcitonin, CAR levels), malnutrition tools for each patient (body mass index [BMI], Nutrition Risk in Critically ill score [NUTRIC], and GNRI scores) were analyzed retrospectively.

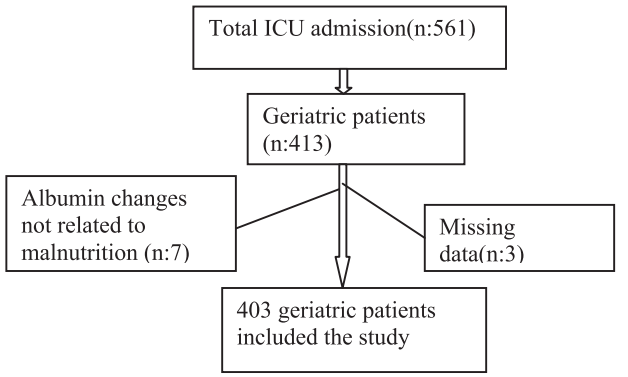

Figure 1. Flow diagram.

Also length of stay (LOS) ICU, length of stay hospital (LOS H), and 30-day mortality were recorded.

We calculated GNRI values according to Bouillanne et al[9]; GNRI = 1.489 × serum albumin level (g/L) + 41.7 × (actual bodyweight/ideal bodyweight).

If the actual body weight is higher than ideal bodyweight, the ratio (actual bodyweight/ideal bodyweight) is taken as 1.

We evaluate GNRI values as severe risk (GNRI < 82), moderate risk (GNRI 82–92), low risk (GNRI 92–98), and no risk (GNRI > 98).

2.1. Statistical analysis

Data analyses were performed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL). Whether the distribution of continuous variables was normal or not was determined by Kolmogorov Smirnov test. Levene test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as mean ± standard deviation and median (minimum value–maximum value) or categorical data were described as number of cases (%). Categorical variables were compared using Pearson's chi-square test or fisher's exact test. Statistical analysis differences in not normally distributed variables between two independent groups were compared by Mann–Whitney *U* test. It was evaluated degrees of relation between variables with point biserial correlation and spearman correlation analysis. First of all it was used one variable multinominal logistic regression with risk factors that is thought to be related with mortality. Variables with a p value below 0.25 in univariate logistic regression analysis were included in multivariate logistic regression analysis. Whether every independent variables were significant on model was analyzed with Wald statistic. It was evaluated with Nagelkerke R^2 how much independent variable explained dependent variable. Besides, it was evaluated model adaptation of estimates with Hosmer and Lemosow model adaptation test. ROC curve analysis was used to determine the cut-off points for mortality. It was accepted *P*-value < .05 as significant level on all statistical analysis.

3. Results

Geriatric patients number of 403 was included the study. The males were 229 (56.8%), female were 174 (43.2) of them. Forty-nine (12.3%) patients had a history of malignancy, 272 (67.5%)

Table 1

Continuous and categorical variables due to mortality.

n: 403	Mortality (+) (n: 186)		Mortality (−) (n: 217)		P
Age (yr)	78.42 ± 8.09	79 (30.55)	76.96 ± 8.10	77 (13.18)	.068
65–74	65 (34.9%)	96 (4.2%)			
75–84	68 (36.6%)	70 (32.3%)			
85 and over	53 (28.5%)	51 (23.5%)			
Sex, male %	114 (61.3%)	115 (53.0%)			.094
BMI	25.73 ± 5.98	24.45 (6.4)	26.78 ± 6.30	26.1 (8.55)	.029
COPD	107 (57.5%)	165 (76.0%)			<.001
Malignancy	33 (18.0%)	16 (7.4%)			.001
Pneumonia	53 (28.5%)	46 (2.2%)			.090
Sepsis	89 (47.8%)	56 (25.8%)			<.001
MV use	140 (75.3%)	40 (18.4%)			<.001
Intrope use	96 (51.6%)	13 (6.0%)			<.001
GNRI	81.32 ± 8.80	81.90 (10.93)	87.13 ± 9.24	87.86 (11.91)	<.001
No risk	4 (2.2%)	2 (9.2%)			
Low risk	16 (8.6%)	56 (25.8%)			
Moderate risk	67 (36.0%)	83 (38.2%)			
Severe risk	99 (53.2%)	58 (26.7%)			
Nutric score	6.70 ± 1.43	7 (2)	5.24 ± 1.29	5 (2)	<.001
MV duration (d)	5.01 ± 7.12	2 (5)	1.20 ± 4.74	0 (0)	<.001
LOS ICU (d)	7.28 ± 7.48	4 (8)	4.52 ± 5.66	3 (3)	<.001
LOS H (d)	15.41 ± 11.90	12 (17)	20.09 ± 14.96	15 (14)	<.001
Albumin (g/dL)	2.74 ± 0.55	2.8 (0.7)	3.13 ± 0.55	3.2 (0.7)	<.001
SOFA	7.56 ± 2.75	7 (5)	4.75 ± 1.22	4 (1)	<.001
APACHE II	26.25 ± 8.44	25 (13)	19.87 ± 5.19	19 (7)	<.001
CCI	7.44 ± 2.08	7 (3)	6.10 ± 1.47	6 (2)	<.001
WBC ($\times 10^3$/mL)	12.81 ± 7.08	12 (7.48)	11.91 ± 6.68	10.8 (6.1)	.133
CRP (mg/L)	65.16 ± 95.42	18.45 (84.23)	41.16 ± 71.81	10.5 (42.18)	<.001
Procalcitonin (ng/mL)	5.21 ± 13.35	0.4 (3.02)	2.28 ± 14.07	0.14 (0.48)	<.001
CAR	27.15 ± 43.41	6.60 (30.55)	14.92 ± 27.28	3.24 (13.18)	<.001

Continuous variables are expressed as either the mean ± standard deviation (SD) or the mean ± SD, and the median (IQR), and categorical variables are expressed as either frequency or percentage. Continuous variables were compared with the Mann Whitney *U* test, and categorical variables were compared using Pearson's chi-square test or fisher exact test. CAR = CRP/albumin ratio; CCI = Charlson comorbidity index; CRP = C-reactive protein; GNRI = Geriatric Nutritional Risk Index; ICU = intensive care unit; LOS H = length of stay hospital; MV = mechanical ventilation; NUTRIC score = Nutrition Risk in Critically ill score; SOFA = Sequential Organ Failure Assessment; WBC = white blood cell.

patients had Chronic Obstructive Pulmonary Disease (COPD) comorbidity. Mean GNRI score was 84.45 ± 9.48 and modified Nutrition Risk in Critically ill score (mNUTRIC score) was 5.9 ± 1.54. The intensive care severity scores of these patients were mean of APACHE II score 22.81 ± 7.58, mean of SOFA score 6.05 ± 2.5. The average of CAR of all patients was 20.57 ± 36.12.

There was no difference in mortality between age groups. There is no statistically significant difference in age, gender, and white blood cell count between those with and without mortality in geriatric ICU patients. In patients with mortality, BMI, had being COPD history, GNRI, LOS H, and albumin were significantly lower than those without mortality. Malignancy comorbidity rate, inotrope use, mNUTRIC score, mechanical ventilation (MV) duration, LOS ICU, SOFA, APACHE II, CCI, CRP, procalcitonin, and CAR were significantly higher in those with mortality than those without mortality (Table 1 and Fig. 2).

According to the correlation table results, there is a low statistically significant negative correlation between GNRI and intrope use, MV duration, LOS H, and LOS H. As GNRI decreases, intrope use, MV duration, LOS H, and LOS ICU increase. There is a low statistically significant correlation in the same direction between the mNUTRIC score and intrope use, MV duration, and LOS ICU. As the mNUTRIC score increases, intrope use, MV duration, and LOS ICU increase. There is no statistically significant relation between the mNUTRIC score and LOS H (Table 2).

There is a low statistically significant correlation between CAR and intrope use and MV duration in the same direction. As CAR increases, the duration of receiving introp support and MV increases. There is no statistically significant relation between CAR and LOS ICU or LOS H. There is a low statistically significant correlation between procalcitonin and intrope use, MV duration, and LOS ICU. As procalcitonin increases, intrope use, MV duration, and LOS ICU increase. There is no statistically significant relation between white blood cell and the prognostic parameters (Table 2).

There is a statistically significant correlation between ICU severity scores (APACHE II, SOFA) and intrope use, MV duration, and LOS H in the same direction (Table 2).

To determine the factors affecting mortality, firstly, single variables logistic regression analysis was applied (Univariate Analyze). Variables with $P < .25$ in univariate logistic regression analysis were included in multivariate logistic regression analysis. The backward LR method was used for multivariate logistic regression analysis. The results of Step 11, which is the last step of the analysis, are given in the table. According to the results, it was understood that CAR, SOFA, CCI, procalcitonin, length of hospital stay, MV, and COPD affect mortality. The increase in CAR, SOFA and CCI, procalcitonin and decrease in hospital stay and MV, and not having COPD increase mortality (Table 3).

A ROC curve analysis was applied in order to provide a cut-off value for the success of GNRI and CAR values in predicting

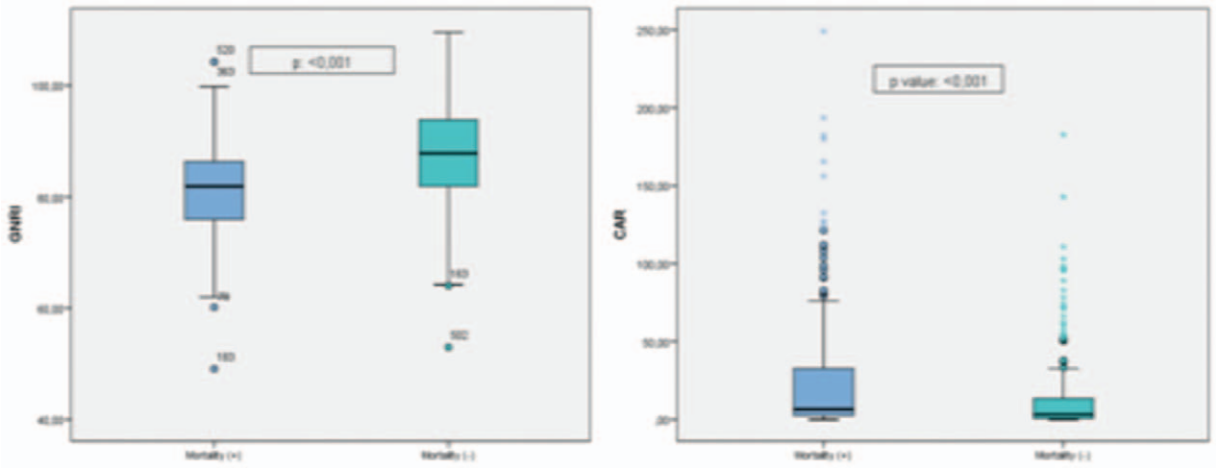

Figure 2. GNRI and CAR distribution according to mortality. GNRI = Geriatric Nutritional Risk Index.

mortality. It is observed that GNRI can differentiate in determining the mortality risk, that is, it can classify the patients correctly at a rate of 68.9% (medium level). In order to answer the question of which value should be taken as the cut-off value for this test, each sensitivity and specificity values given as a result of the analysis were examined and the optimum point was chosen. While the sensitivity value was 71% and the specificity value was 61.3%, the cut-off value was found to be 85.79. As a result, the risk of mortality was higher in cases with GNRI 85.79 and below (Fig. 3).

It shows that CAR can differentiate in determining the risk of mortality in cases, that is, it can classify patients correctly at a rate of 61.6% (moderate). In order to answer the question of which value should be taken as the cut-off value for this test, each sensitivity and specificity values given as a result of the analysis were examined and the optimum point was chosen. While the sensitivity value was 69.9% and the specificity value was 49.8%, the cut-off value was found to be 3.13. As a result, the risk of mortality was higher in cases with CAR 3.13 and above (Fig. 3).

In geriatric patients hospitalized in the intensive care unit, sepsis was most common in patients with malignancy comorbidity, followed by pneumonia, and least in those with both COPD and malignancy comorbidity, and this was statistically significant (Table 4).

4. Discussion

This study showed that while age and gender do not affect, both malnutrition and infection affect mortality in geriatric patients treated in respiratory intensive care. However, low GNRI significantly increases inotrope use, MV duration, LOS H, and LOS ICU, while high CAR levels only increase inotrope use and MV duration significantly and also at predicting mortality GNRI is better than CAR.

Table 2

Correlation between nutrition and infection parameters.

		İnotrop Desteği	Mv Süresi	Yb Yatış Süresi	Hastane Yatış Süresi
GNRI	*r*	−0.264	−0.232	−0.146	−0.142
	P	<.001	<.001	<.001	<.001
Nutric score	*r*	0.334	0.420	0.132	−0.036
	P	<.001	<.001	.008	.473
CAR	*r*	0.141	0.111	0.022	0.050
	P	.005	.026	.659	.312
CCI	*r*	0.257	0.160	0.034	−0.059
	P	<.001	.001	.497	.234
APACHE II	*r*	0.257	0.379	0.119	−0.009
	P	<.001	<.001	.017	.849
SOFA	*r*	0.412	0.508	0.117	−0.087
	P	<.001	<.001	.019	.082
WBC	*r*	0.014	0.074	0.047	0.037
	P	.783	.138	.343	.457
Procalcitonin	*r*	0.233	0.273	0.166	0.046
	P	<.001	<.001	.001	.356

CAR = CRP/albumin ratio; CCI = Charlson comorbidity index; CRP = C-reactive protein; GNRI = Geriatric Nutritional Risk Index; NUTRIC score = Nutrition Risk in Critically ill score; SOFA = Sequential Organ Failure Assessment; WBC = white blood cell.

Table 3

Logistic regression analysis for mortality.

	Univariate analyze					Multivariate analyze (backward LR Step 8)				
	Wald	OR	%95 CI		P	Wald	OR	%95 CI		P
Age	3.258	1.023	0.998	1.048	.071					
Sex, male %	2.801	0.712	0.478	1.060	.094					
BMI	2.843	0.972	0.941	1.005	.092	2.720	0.960	0.915	1.008	.099
GNRI	34.363	0.931	0.909	0.954	<.001					
Nutric score	73.451	2.157	1.809	2.571	<.001					
CAR	10.429	1.010	1.004	1.016	.001	4.391	1.009	1.001	1.017	.036
SOFA	84.042	2.161	1.833	2.548	<.001	27.887	1.711	1.402	2.088	<.001
APACHE II	57.663	1.151	1.110	1.194	<.001					
CCI	43.001	1.544	1.356	1.758	<.001	11.674	1.406	1.156	1.710	.001
WBC	1.672	0.196	0.990	1.050	.196					
Procalcitonin	3.650	1.021	0.999	1.042	.056					
CRP	7.699	1.004	1.001	1.006	.006	4.179	0.982	0.965	0.999	.041
LOS H	10.894	0.973	0.958	0.989	.001	16.922	0.950	0.927	0.974	<.001
MV use	113.577	13.467	8.348	21.725	<.001	42.849	8.463	4.465	16.042	<.001
COPD	15.324	0.427	0.279	0.654	<.001	7.235	0.432	0.235	0.796	.007
Malignancy	9.895	2.764	1.467	5.207	.002					
Pneumonia	2.861	1.481	0.940	2.336	.091					
Sepsis	20.627	2.638	1.736	4.009	<.001					

Multinominal Logistic Regression Nagelkerke $R^2 = 0.620$ (Hosmer ve Lemeshow $P > .05$). BMI = body mass index; CAR = CRP/albumin ratio; CCI = Charlson comorbidity index; COPD = Chronic Obstructive Pulmonary Disease; CRP = C-reactive protein; GNRI = Geriatric Nutritional Risk Index; LOS H = length of stay hospital; MV = mechanical ventilation; NUTRIC score = Nutrition Risk in Critically ill score; OR = odds ratio; SOFA = Sequential Organ Failure Assessment; WBC = white blood cell.

Some studies have found that chronological age has an impact on morbidity and mortality, some have suggested that biological age and some other factors are effective.[10,11] Brunner-Zeigler et al[12] determined that mortality increases with age, but the physiological condition of the patients is more effective on mortality. Contrary we evaluate that age do not affect the mortality in geriatric patients in ICU.

The CAR affect as a predictor of mortality is controversial. It has been stated that the CAR is more effective in predicting mortality compared to albumin and CRP alone.[13] In a study by Cirik et al[14] evaluating the clinical benefit of the CAR in predicting 30-day mortality in critically ill patients, it was revealed that the CAR was independently associated with 30-day mortality but APACHE II and CCI predicted mortality more than CAR. Although it was shown in a study that increased CAR was associated with increased mortality in intensive care patients, it was concluded that its sensitivity and specificity were not sufficient to predict mortality.[15]

Oh et al[6] found that CAR in admission was an important predictor of mortality in geriatric patients. Similarly, in our study, procalcitonin, CRP, and CAR, which are predictors of sepsis, were found to be significantly higher in patients with mortality. The CAR affects inotrop use and MV duration but did not affect LOS ICU and LOS H while GNRI affects both of them.

Malnutrition is common in geriatric patients, with significant effects on morbidity and mortality.[16] Sepsis creates life-threatening organ dysfunction secondary to infection.[17] In a study conducted with geriatric patients, mortality increased significantly in patients with GNRI < 92, and they found that CRP levels were related to low GNRI.[18]

Some studies have reported that low BMI and albumin levels are poor prognostic factors in determining mortality[3,19] but in our study, we found that BMI, GNRI, and albumin levels were significantly lower in patients with mortality. Some studies support our findings that they suggested low GNRI levels due to malnutrition suppressed the protein synthesis and a catabolic process began.[20,21] The nutritional status of geriatric patients is evaluated with scores such as GNRI and mNUTRIC. In this

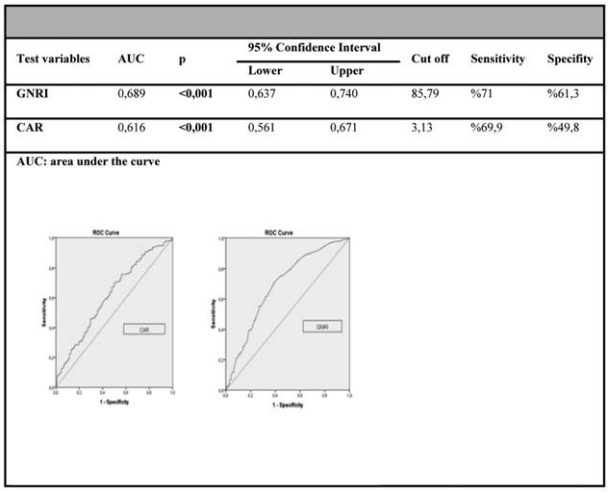

Figure 3. ROC curve analysis for GNRI and CAR. GNRI = Geriatric Nutritional Risk Index.

Table 4

The frequency of sepsis in geriatric patients in ICU.

	COPD (n: 252) n (%)	Malignancy (n: 31) n (%)	COPD + Malignancy (n: 18) n (%)	Pneumonia (n: 99) n (%)
Procalcitonin ≥ 0.5 ng/mL (SEPSIS)	78 (31.0%)	18 (58.1%)	5 (27.8%)	42 (42.4%)
P			.009	

COPD = Chronic Obstructive Pulmonary Disease; ICU = intensive care unit.

study, we determined that low GNRI and high mNUTRIC scores have a significant effect on mortality.

In this study we also found that had being malignancy history rather than COPD, and high CCI, APACHE II, SOFA scores were significantly increase mortality similar to Kao et al.[22] They suggested that CCI and SOFA scores were correlated with mortality.

This study has several limitations to be considered. It has a retrospective design, and conducted at a single center. The sample size was relatively small.

5. Conclusion

Both malnutrition and infection affect mortality in geriatric patients in intensive care. However, low GNRI increases inotrope use, MV duration, LOS H, and ICU, while high CAR levels only increase inotrope use and MV duration significantly and also at predicting mortality GNRI is better than CAR.

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Visualization: Mustafa Ozgur Cirik.
Writing – original draft: Guler Eraslan Doganay.
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