

# The relationship between acute physiology and chronic health evaluation-II, sequential organ failure assessment, Charlson comorbidity index and nutritional scores and length of intensive care unit stay of patients hospitalized in the intensive care unit due to chronic obstructive pulmonary disease

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## ABSTRACT

**Aim:** It is known that disease severity and nutritional status are determinants of prognosis in patients hospitalized in the intensive care unit (ICU). Different scoring systems are used to evaluate the nutritional status and disease severity of intensive care patients. It will be very useful in clinical practice to determine the intensive care scores that are in harmony with the nutritional parameters and affect the length of stay in the ICU in patients hospitalized with the diagnosis of chronic obstructive pulmonary disease (COPD). It was aimed to determine the relationship between acute physiology and chronic health evaluation-II (Apache-II), sequential organ failure assessment (SOFA), and Charlson comorbidity index (CCI) with nutritional scores in intensive care patients with a diagnosis of COPD. Also, it was aimed to determine the scoring systems that affect the length of stay in the ICU.

**Material and Method:** Nutritional risk score-2002 (NRS-2002), prognostic nutritional index (PNI), modified nutritional risk in critically ill (mNutric) score, albumin, Apache-II, SOFA and CCI values and intensive care unit length of stay of the patients hospitalized in the intensive care unit due to COPD were recorded. The scoring systems that affect the length of stay in the ICU and the relationship between nutritional scores and Apache-II, SOFA and CCI was analyzed using statistical methods.

**Results:** A significant correlation was found between only CCI and all nutritional scores. Only the CCI value was found to be significantly higher in those found to be at high risk compared to all nutritional scoring systems. CCI cut-off value determined according to nutritional scoring was determined as 4.5 according to PNI and albumin, and 5.5 according to mNutric score and NRS-2002. It was determined that CCI affects the length of stay in the intensive care unit.

**Conclusion:** CCI is a scoring system that is compatible with nutritional parameters and affects the length of stay in the intensive care unit. Therefore, we think that CCI can be used to predict prognosis and nutritional risk in patients with COPD in the intensive care unit and to predict the length of stay in the intensive care unit. In terms of malnutrition risk, a cut-off value of  $\geq 6$  can be used for CCI.

**Keywords:** Charlson comorbidity index, chronic obstructive pulmonary disease, COPD, intensive care, nutritional scores

## INTRODUCTION

Intensive care units (ICU) are high-tech special treatment units developed for close follow-up, rapid intervention, and treatment of acute disease (1). Prolongation of intensive care stays not only affects morbidity and mortality but also brings with it an increase in cost (2). It is known that disease severity and nutritional status are

determinants of prognosis in patients hospitalized in the ICU. Different scoring systems are used to evaluate the nutritional status and disease severity of intensive care patients. While the nutritional risk score-2002 (NRS-2002), modified nutritional risk in critically ill (mNutric) score, and albumin are used to evaluate the nutritional status of patients, recently the prognostic nutritional index (PNI) has been evaluated as a prognostic risk

score based on albumin and lymphocyte (3-6). Acute physiology and chronic health evaluation-II (Apache-II), sequential organ failure assessment score (SOFA) evaluates patients in terms of acute physiology, disease severity, and organ failure, while Charlson comorbidity index (CCI) evaluates patients in terms of comorbidity (7-10,11). However, there is no definite consensus on which scoring system should be used to determine the risk tendency in intensive care patients.

Patients with a diagnosis of chronic obstructive pulmonary disease (COPD) often have to stay in intensive care, especially during acute exacerbations. Malnutrition is a common condition in these patients (12). Malnutrition, on the other hand, affects the length of stay in the hospital and ICU and is a determinant in prognosis and mortality (12-14). Therefore, it will be very useful in clinical practice to determine the intensive care scores that are in harmony with the nutritional parameters and affect the length of stay in the intensive care unit in patients hospitalized with the diagnosis of COPD.

In this study, it was aimed to determine the relationship between NRS-2002, m Nutric score, PNI, and albumin, which shows the nutritional status of patients hospitalized in the intensive care unit with chronic obstructive pulmonary diagnosis, and Apache-II, sequential organ failure assessment, and Charlson comorbidity index (CCI). In addition, it is aimed to determine the scoring systems that affect the length of stay in the intensive care unit..

## MATERIAL AND METHOD

The study was initiated with the approval of the Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 11.01.2022, number: 2012-KAEK-15/2451). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The data of patients admitted to the intensive care unit with COPD between January 2018 and November 2018 were scanned retrospectively from patient files. Demographic data such as age, gender, body mass index, length of stay in intensive care, whether the patient received invasive mechanical ventilator support during admission to the intensive care unit, lymphocyte count, albumin value, Apache-II, SOFA, CCI, NRS- 2002, PNI, and mNutric Score values were recorded from patient files. Nutric score calculation is based on patient's age, Apache-II score, SOFA score, number of co-morbidities, Interleukin-6(IL-6), and the length of hospital stay before admission to the intensive care unit (15). In our study, the modified Nutric score (mNutric score) calculated without

taking into account IL-6 was used. PNI was calculated from the formula  $10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{lymphocyte count/mm}^3$  (16). The nutritional risk status of the patients was determined as follows:  $\text{PNI} \geq 45$ ; (low risk),  $\text{PNI} < 45$ ; (High Risk),  $\text{Albumin} \geq 35 \text{ g/L}$  (Low Risk),  $\text{Albumin} < 35 \text{ g/L}$  (High Risk),  $\text{NRS-2002} \leq 4$ ; (Low Risk),  $\text{NRS-2002} > 4$ ; (High Risk),  $\text{Nutric score} \leq 4$ ; (Low Risk),  $\text{Nutric score} > 4$ ; (High Risk) (15-18).

Those who were admitted to the intensive care unit for a reason other than COPD, those with a diagnosis of malignancy, those under the age of 18, those who were hospitalized in the intensive care unit for less than 24 hours, and those who lacked the necessary tests for the study were excluded from the study.

## Statistical Analyses

Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables was normal or not was determined by the Kolmogorov Smirnov test. Levene test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as  $\text{mean} \pm \text{SD}$  for normal distributions, and median (interquartile range) for skewed distributions. Categorical data were described as the number of cases (%). Statistical analysis differences in not normally distributed variables between two independent groups were compared by the Mann Whitney U test. Categorical variables were compared using Pearson's chi-square test or fisher's exact test. Univariate and multivariate linear regression analyzes were performed to determine the factors affecting the length of stay in the intensive care unit. It was evaluated degrees of the relationship between variables with Spearman correlation analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the cutoff value of the charlson comorbidity index associated with the risk of PNI, albumin, NRS-2002, mNutric score. It was accepted  $p$ -value  $< 0.05$  as a significant level on all statistical analyses.

## RESULTS

A total of 216 patients admitted to the intensive care unit for COPD were identified. 11 patients were excluded because their data were missing. Data from a total of 205 patients hospitalized in the intensive care unit due to COPD were analyzed. The demographic data of the patients, intensive care scores and the proportion of patients receiving invasive mechanical ventilator support are given in **Table 1**.

The risk distribution of the patients according to nutritional scores and Apache-II, SOFA, Charlson comorbidity scores of the patients are shown in **Table 2**.

**Table 1:** The demographic data of the patients, length of intensive care stay and the proportion of patients receiving mechanical ventilator support

		All patients (n:205)	
		±SD	Median (Q <sub>1</sub> -Q <sub>3</sub> )
Age, year		70.80±11.56	
Gender, n(%)	Male	125 (61.0%)	
	Female	80 (39.0%)	
BMI		24.8 (7.6)	
Intensive care stay, days		3 (4)	
MV support, n(%)	No	134 (65.4%)	
	Yes	71 (34.6%)	

Continuous variables were expressed as either the mean±standard deviation (SD) and median (interquartile range). Categorical variables were expressed as either frequency (percentage). BMI: body mass index, MV: mechanical ventilation,

**Table 2.** The risk distribution of the patients according to nutritional scores and Apache-II, SOFA, charlson comorbidity scores of the patients

		All Patients
<b>PNI</b>		
High-risk		180 (87.8%)
Low-risk		25 (12.2%)
<b>ALBUMIN</b>		
High-risk		133 (64.9%)
Low-risk		72 (35.1%)
<b>NRS -2002</b>		
High-risk		112 (54.6%)
Low-risk		93 (45.4%)
<b>mNUTRIC SCORE</b>		
High-risk		134 (65.4%)
Low-risk		71 (34.6%)
	±SD	Med (IQR)
APACHE-II	21.08±6.23	20(8)
CCI	5.70±1.95	6(3)
SOFA	6.17±1.84	6(2)

Continuous variables were expressed as either the mean±standard deviation (SD) and median (interquartile range). Categorical variables were expressed as either frequency (percentage). APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson comorbidity index, SOFA: Sequential Organ Failure Assessment Score, PNI: prognostic nutritional index, NRS-2002: nutritional risk score-2002, mNUTRIC: modified nutritional risk in critically ill

There is a statistically significant negative correlation between PNI and the Charlson comorbidity index (r:-0.332 p:<0.001). There is a statistically significant negative correlation between PNI and SOFA (r:-0.174 p:0.013) (Table 3). There is a statistically significant negative correlation between albumin and Apache-II (r:-0.186 p:0.008) and Charlson comorbidity index (r:-0.338 p:<0.001) (Table 3). There is a statistically significant negative correlation between albumin and SOFA (r:-0.273 p:<0.001) (Table 3).

There is a statistically significant positive correlation between NRS-2002 and Apache-II (r:0.189 p:0.007) and the Charlson comorbidity index (r:-0.174 p:0.013) (Table 3). There is a statistically significant positive correlation between mNutric Score and Apache-II (r:0.761 p:<0.001). There is a statistically significant positive correlation between the mNutric Score and the

Charlson comorbidity index (r: 0.534 p: <0.001). There is a statistically significant positive correlation between mNutric Score and SOFA (r:0.701 p:<0.001) (Table 3).

**Table 3.** Correlation analysis between Apache-II, CCI, SOFA and nutritional scores.

		PNI	Albumin	NRS -2002	mNutric Score
APACHE-II	r	-0.109	-0.186	0.189	0.761
	p	0.120	0.008	0.007	<0.001
CCI	r	-0.332	-0.338	0.465	0.534
	p	<0.001	<0.001	<0.001	<0.001
SOFA	r	-0.174	-0.273	0.098	0.701
	p	0.013	<0.001	0.161	<0.001

r:correlation coefficient. Statistically significant p-values were in bold. APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson comorbidity index, SOFA: Sequential Organ Failure Assessment Score

The Charlson comorbidity index values of patients with high risk for PNI were found to be significantly higher than those with low risk for PNI (Table 4). The Charlson comorbidity index and SOFA values of patients with high risk for albumin were found to be significantly higher than those with low risk for albumin (Table 4). Apache-II and Charlson comorbidity index values of patients with high risk according to NRS-2002 level were found to be significantly higher than those with low risk (Table 4). Apache-II, Charlson comorbidity index, and SOFA values were found to be significantly higher in cases with high risk according to the mNutric score level compared to cases with low risk (Table 4).

**Table 4.** Apache-II, SOFA and CCI by nutritional risk grouping

	±SD	Med (IQR)	±SD	Med (IQR)	P
		<b>Low-risk</b>		<b>High-risk</b>	
<b>PNI</b>					
APACHE II	22.60±5.72	21 (6)	20.87±6.29	20 (8)	0.140
CCI	4.84±2.34	4 (1)	5.82±1.86	6 (3)	0.002
SOFA	6.20±1.71	6 (2)	6.16±1.87	6 (2)	0.763
		<b>ALBUMIN</b>		<b>High-risk</b>	
APACHE II	20.06±4.83	19 (5)	21.64±6.83	20 (8)	0.206
CCI	4.97±1.59	5 (2)	6.10±2.01	6 (2)	<0.001
SOFA	5.68±1.17	5 (1)	6.43±2.08	6 (2)	0.014
		<b>NRS -2002</b>		<b>High-risk</b>	
APACHE II	19.86±6.13	19 (7)	22.10±6.16	21 (7)	0.005
CCI	4.83±1.66	5 (1)	6.43±1.87	6 (2)	<0.001
SOFA	5.98±1.77	5 (1)	6.32±1.90	6 (2)	0.065
		<b>mNUTRIC Score</b>		<b>High-risk</b>	
APACHE II	16.18±3.30	16 (5)	23.68±5.86	22 (7)	<0.001
CCI	4.58±1.43	4 (1)	6.30±1.92	6 (2)	<0.001
SOFA	5.17±0.79	5 (0)	6.69±2.02	6 (2)	<0.001

Continuous variables were expressed as either the mean±standard deviation (SD) and median (interquartile range). Continuous variables were compared with mann whitney u test. Statistically significant p-values were in bold. APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson comorbidity index, SOFA: Sequential Organ Failure Assessment Score, PNI: prognostic nutritional index, NRS-2002: nutritional risk score-2002, mNUTRIC: modified nutritional risk in critically ill

In the ROC analysis performed to determine a cut-off value for CCI according to nutritional parameters, the area under the treatment characteristic curve (AUC) for PNI, albumin, NRS-2002, mNutric score was calculated

as 0.692, 0.668, 0.768, and 0.767, respectively. CCI cut-off value was determined as 4.5 according to PNI and albumin, and 5.5 according to NRS-2002 and mNutric score (Table 5).

**Table 5. Cut-off values for CCI determined by ROC analysis**

	SE	P	AUC (95% CI)	Cut Off	Sensitivity	Specificity
PNI	0.059	0.002	0.692 (0.575-0.809)	4.5	73.9%	60%
ALBUMIN	0.039	<0.001	0.668 (0.590-0.745)	4.5	58.6%	65.3%
NRS-2002	0.034	<0.001	0.768 (0.700-0.835)	5.5	73.2%	77.4%
mNUTRIC SCORE	0.035	<0.001	0.767 (0.699-0.835)	5.5	65.7%	78.9%

SE:Standard Error, AUC: Area under the ROC Curve, CI: Confidence interval, CCI: Charlson comorbidity index, PNI: prognostic nutritional index, NRS-2002: nutritional risk score-2002, mNUTRIC: modified nutritional risk in critically ill

Univariate and multivariate linear regression analysis was applied to determine the factors affecting the length of stay in the intensive care unit. According to the results of the 5th step, which is the last step, the need for MV support and the increase in the Charlson comorbidity index were determined as the factors affecting the length of stay in the intensive care unit (Table 6).

**Table 6. Factors affecting the length of stay in intensive care unit according to univariate and multivariate linear regression analysis**

	Univariate Linear Regression			
	t	p	β	95,0% for β
Age	0.333	0.740	0.023	(-0.065-0.091)
Gender (reference: male)	-0.965	0.336	-0.068	(-2.735-0.938)
BMI	1.069	0.286	0.075	(-0.061-0.206)
MV Support	6.770	<0.001	0.429	(4.148-7.558)
PNI	-0.563	0.574	-0.039	(-0.141-0.078)
ALBUMIN	-2.066	0.040	-0.144	(-0.329--0.008)
NRS-2002	-1.135	0.258	-0.079	(-1.867-0.503)
mNUTRIC SCORE	3.33	0.001	0.226	(0.370-1.457)
APACHE-II	2.704	0.007	0.186	(0.053-0.336)
CCI	2.524	0.012	0.174	(0.127-1.038)
SOFA	3.202	0.002	0.219	(0.297-1.249)
Multivariate Linear Regression (Backward Step 5)				
MV Support	6.553	<0.001	0.415	(3.956-7.361)
CCI	2.024	0.044	0.128	(0.011-0.845)

t: test statistics, β:coefficient, CI: Confidence interval. Statistically significant p-values are in bold. BMI: body mass index, MV: mechanical ventilation, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson comorbidity index, SOFA: Sequential Organ Failure Assessment Score, PNI: prognostic nutritional index, NRS-2002: nutritional risk score-2002, mNUTRIC: modified nutritional risk in critically ill

**DISCUSSION**

In our study, a negative correlation was found between CCI and PNI and albumin, and a positive correlation between mNutric score and NRS-2002. There is no correlation between Apache-II and PNI, SOFA, and NRS-2002. Among the scorings, only the CCI value

was significantly higher in those found to be at high risk compared to all nutritional scoring systems. In ROC analysis, the cut-off value determined according to nutritional scoring for CCI was determined as 4.5 according to PNI and albumin, and 5.5 according to mNutric score and NRS-2002. According to the regression analysis, it was determined that CCI affects the length of stay in the intensive care unit.

Critical diseases seen in patients hospitalized in intensive care are seen as an important public health problem due to high mortality and high health expenditures (19). For this reason, it is aimed to reduce the length of stay in the intensive care unit by increasing the quality of medical care.

It is stated that scoring systems used in intensive care are effective in clinical decisions, evaluation of treatment effectiveness, and optimizing the use of resources (20). However, very few of the scoring systems developed for this purpose are used effectively in clinical practice (20). The reason for this may be the use of many different scoring systems and the fact that each of these scoring systems gives the risk status of patients with different numerical values. In our study, in the nutritional risk classification made according to PNI, NRS-2002, mNutric Score, and albumin, it was seen that each of these scoring systems determined patients in high and low-risk groups at different rates. In our study, 54.6% of the patients were at high risk according to NRS-2002, while 65.4% of the patients were at high risk according to the mNutric score. In PNI and albumin, these rates are 87.8% and 64.9%, respectively.

It is known that the nutritional status of the patients hospitalized in the intensive care unit is very important in the prognosis, nutritional support changes the course and outcome of the critical illness, yet malnutrition is a neglected condition in hospitalized patients (19,21). Scorings that evaluate organ failure, chronic disease, and morbidity conditions such as Apache-II, SOFA, and CCI, which are used to predict prognosis in intensive care units, are scoring systems that do not evaluate the nutritional status of patients. However, detecting a relationship or correlation between these scoring systems and nutritional scoring will contribute significantly to clinical practice. When we looked at the correlation between disease severity scores and nutritional scores in this study, we saw that only CCI had a significant correlation with all nutritional scores in our study. In addition, only the CCI value was found to be significantly higher in those with high risk compared to all nutritional scoring systems in our study. Therefore, we can say that CCI is in good agreement with nutritional scoring. The cut-off value determined according to nutritional scoring was determined as 4.5 according to PNI and albumin,

and 5.5 according to mNutric score and NRS-2002. We think that the cut-off value of 5.5 can be used in clinical practice since it also includes the cut-off value determined for PNI and albumin. CCI, which is the gold standard in comorbidity risk assessment, is a scoring system where a score ranging from 1 to 6 is given to each of the 19 comorbid disease categories and calculated by the sum of these scores (8,22,23). Therefore, the CCI value cannot be a decimal value. For this reason, we can say that if  $CCI \geq 6$  in COPD patients hospitalized in the intensive care unit, the patients are also at high risk in terms of malnutrition. In studies in the literature, values of 2 and above for CCI have been reported as high CCI (8,24,25). However, these studies are not studies that determine a cut-off value for CCI. Again, these studies do not evaluate the relationship of CCI with nutritional scoring. In addition, these studies do not address COPD patients in intensive care. The fact that it is the first study that deals with the relationship of CCI with nutritional scores and determines a cut-off value for CCI from a nutritional point of view distinguishes our article from other studies in the literature.

Many studies evaluate the effectiveness of scoring systems in predicting the mortality of patients (26-28). Although it is important to prevent mortality, shortening the length of stay in the intensive care unit is important in terms of demonstrating the quality of medical care and reducing costs.

Many studies have shown that CCI is useful in predicting the prognosis of patients and that high CCI is associated with mortality and disease severity (8,29,30). However, we could not find any study evaluating the relationship between CCI and length of stay in the intensive care unit. In one study, it was stated that higher CCI was associated with a longer hospital stay in older adults hospitalized for acute stroke (24). However, this study does not evaluate COPD patients hospitalized in intensive care. According to the univariate and multivariate regression analysis we performed to determine the factors affecting the length of stay in the intensive care unit in COPD patients, it was determined that CCI affects the length of stay in the intensive care unit.

The fact that our research is single-centered and retrospective is a limitation of this article.

## CONCLUSION

CCI is a scoring system that is compatible with nutritional parameters and affects the length of stay in the intensive care unit. Therefore, we think that CCI can be used to predict prognosis and nutritional risk in patients with COPD in the intensive care unit and to predict the length of stay in the intensive care unit. In terms of malnutrition risk, a cut-off value of  $\geq 6$  can be used for CCI.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was initiated with the approval of the Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (Date: 11.01.2022, number: 2012-KAEK-15/2451).

**Informed Consent:** All patients were informed about the application and their informed consent was obtained.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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