



Turkish Journal of Geriatrics  
DOI: 10.31086/tjgeri.2022.300  
2022; 25(3): 409-421

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Received : Mar 30, 2022  
Accepted : Jul 20, 2022

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## RESEARCH

# NUTRITIONAL SUPPORT IN GERIATRIC PATIENTS IN INTENSIVE CARE: THE RELATIONSHIPS BETWEEN PREALBUMIN, ALBUMIN AND TOTAL PROTEIN LEVELS AND THE ROUTE OF NUTRITION ADMINISTRATION

## ABSTRACT

**Background:** Adequate nutrition for geriatric elderly patients hospitalized in the intensive care unit (ICU) is of great importance.

**Objective:** This study included critically-ill patients hospitalized in the ICU and aimed to determine the relationships between nutritional status, patient severity and the time-bound changes in various parameters known to be associated with malnutrition.

**Methods:** The study was conducted by retrospectively examining the files of 112 patients (63 women and 49 men) who received inpatient treatment in the ICU of Bartın State Hospital for at least 21 days.

**Results:** Apache II score ( $p=0.001$ ), mortality risk score ( $p=0.003$ ), intermittent nutrition ( $p = 0.046$ ), low energy intake on day 7 ( $p=0.008$ ), total protein level on day 30 ( $p=0.016$ ), prealbumin level on day 21 ( $p=0.021$ ), the change in prealbumin level from the 1<sup>st</sup> to the 21<sup>st</sup> day ( $p<0.001$ ), and CRP level on day 30 ( $p=0.025$ ) were significantly different between the groups. Multivariate analysis performed with these variables revealed that the change in prealbumin level from the 1<sup>st</sup> to the 21<sup>st</sup> day was the only parameter to be independently associated with length of stay ( $p=0.003$ ).

**Conclusions:** In geriatric elderly patients admitted to the ICU, it was observed that albumin and total protein values did not change significantly during feeding, whereas prealbumin levels increased significantly on the 21<sup>st</sup> day compared to the 1<sup>st</sup> day.

**Keywords:** Nutritionists; Hospitals; Malnutrition; Albumins; Prealbumin.

## INTRODUCTION

Malnutrition is a broad term and covers not only protein-energy malnutrition but also deficiencies of other nutrients such as micronutrients (1). Malnutrition can occur when patients are admitted for intensive care as a result of the metabolic response caused by factors such as insufficient nutrition and the severity of the disease (2). Malnutrition is more common in people admitted for intensive care and those with a critical illness. Providing appropriate nutritional support in malnourished patients prevents the increase of complications and purveys clinical, functional, financial benefits, and can increase survival (3).

Old age is usually defined as 65 years of age or older. In geriatric patients with age-related degenerative changes, there is an increase in the frequency of disease as a result of acute and/or chronic disease, restriction, regression, and changes in physical, mental and/or social functions. As age progresses, impaired cognitive function, increased frequency of chronic disease, and postural balance or walking disorders occur, and the frequency of hospitalization increases (4,5).

Protein and energy malnutrition is a common finding in patients admitted to intensive care units (ICU) (40% of patients). In practice, anthropometric measurements, laboratory results, and indirect calorimetry tests help in evaluating nutritional status; however, these measurements are known to be insensitive to short- or mid-term changes in nutrition (4-6). Serum albumin and prealbumin levels are indicated as markers of nutritional status. Low serum albumin and prealbumin levels in ICU patients have been associated with a higher risk of infection and death (7). In addition, low serum albumin and prealbumin levels are also an indicator of inflammation. Care should be taken when assessing a patient's nutritional status based purely on visceral protein markers, as they are non-specific and are affected by changes in homeostasis such as inflammation. The entire clinical context of a patient should be

considered when using these values (8). However, levels of C-reactive protein (CRP), which is a non-specific acute phase reactant, is known to be negatively correlated with albumin and prealbumin levels (8,9,10). Assessment of prealbumin levels in combination with CRP levels is more clinical. The main assessment system for determining the risk of nutrition in critical ICU patients is nutritional risk screening-2002 (NRS). NRS is defined as the first step in identifying hospitalized patients who may benefit from the practice of nutrition (10,11). Early enteral and parenteral nutrition positively changes the duration of hospitalization and the clinical picture of patients in the ICU (12-14).

We believe that there is a correlation between the level of CRP values, low serum prealbumin levels, high NRS-2002 values and Apache II values used to determine nutritional status in hospitalized patients.

This study included critically-ill patients hospitalized in the ICU and aimed to determine the relationships between nutritional status (NRS-2002), patient severity (Apache II score) and the time-bound changes in various parameters known to be associated with malnutrition (CRP, serum albumin, prealbumin, total protein level). In addition, we aimed to determine the differences between patients receiving enteral or parenteral nutrition in terms of malnutrition-related parameters and the aforementioned relationships. Finally, we also aimed to identify nutritional parameters associated with the length of ICU stay.

## MATERIALS AND METHODS

In this retrospective cohort study, the files of 112 patients hospitalized in the ICU of our hospital between February 2018 and October 2018 were reviewed retrospectively. Patients over 65 years of age who were hospitalized for at least 21 days and were included in a nutrition protocol were included in the study. Data were collected and recorded from



the hospital information system, ICU database, patient files and physician order forms. Study approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Karabuk University (Date: January 3, 2018, Decision no: 1/13).

Total blood protein, albumin, prealbumin and CRP parameters of patients who started treatment in the ICU and received nutritional support were examined on the 1<sup>st</sup>, 3<sup>rd</sup>, 7<sup>th</sup>, 14<sup>th</sup>, and 21<sup>st</sup> days. Comparison of prealbumin, albumin, total protein values and CRP levels measured on the 1<sup>st</sup> and 21<sup>st</sup> days were performed among patients and longitudinal analyses of the changes were also performed. Values on the 30<sup>th</sup> and 60<sup>th</sup> days were also recorded in patients who had a relatively longer stay in the ICU.

Patients' demographic characteristics, admission diagnosis, underlying diseases, duration of hospitalization, Apache II score on admission, mortality, nutrition duration, the route of continuous feeding (enteral, parenteral), the method of feeding administration [nasogastric tube or percutaneous endoscopic gastrostomy (PEG)], and decubitus ulcers were recorded. Target energy and protein values were calculated for each patient (per kilogram weight). The number of calories to be given was determined between 25-30 kcal per kilogram, while obese patients received 18-20 kcal. Target protein was calculated to be 1.2-2 grams per kilogram. Energy and protein requirements were determined on the 1<sup>st</sup>, 3<sup>rd</sup>, 7<sup>th</sup>, and 21<sup>st</sup> days (and further when ICU stay was longer).

Patients were fed within the first 24-72 hours of their admission to the ICU. Enteral nutrition was used as the initial approach when applicable. Parenteral nutrition was initiated in patients whose gastrointestinal functions or disease course were not suitable for enteral nutrition. Patients receiving parenteral nutrition were switched to enteral nutrition at the earliest possible time when appropriate. Abdominal signs (pain, distension, diarrhea, vomiting, etc.) and residue was closely followed (every 4 hours). Enteral nutrition was discontinued for a

short period of time in patients who developed abdominal signs or residue. If necessary, the product was replaced or reductions in the rate of infusion were made. Peripheral parenteral nutrition (PPN) or central parenteral nutrition (CPN) were added to patients who could not attain target levels via enteral administration. Parenteral nutrition was gradually discontinued in patients showing clinically-relevant improvement (determined by the attending physicians).

NRS 2002 values were evaluated separately in each patient. NRS-2002 values, serum albumin, prealbumin, total protein and CRP levels, APACHE II and mortality scores were compared in all patients. Serum albumin, total protein and prealbumin levels were compared in patients who underwent either the enteral or parenteral nutrition program, only. When the patient switched from parenteral nutrition to enteral nutrition, the patient was included in the enteral nutrition group when parenteral nutrition administration was performed for less than 80% of the total calories. The levels of total calories and protein given were recorded at first hospitalization and before the discontinuation of feeding.

### **Statistical analysis**

All analyses were conducted with SPSS v21 (SPSS Inc. Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to check the normality of distribution in continuous variables. Data were given as mean  $\pm$  standard deviation or median (25%-75% interquartile values) for continuous variables according to the normality of the distribution, and as frequency (percentage) for categorical variables. Repeated measurements of continuous variables were analyzed by the repeated measures analysis of variance (ANOVA) test for normally distributed variables, and non-normally distributed variables were analyzed by Friedman's analysis of variance. Repeated measurements of categorical variables were made by the Cochran's Q test. Post-hoc pairwise comparisons were done with the Bonferroni correction. In 2-group analyses, comparisons were done with the independent samples t-test for variables

with normal distribution, while the Mann-Whitney U test was used for variables without normal distribution. Linear regression analysis was performed to determine factors associated with the duration of stay in the ICU.  $p < 0.05$  values were considered statistically significant results

## RESULTS

The study included 112 elderly patients (63 women and 49 men), with a median age of 78 (66.5–84) years. The most common causes of hospitalization were respiratory problems (36.61%), neurological problems (33.93%), and poor overall condition (13.39%). Seventy-six (67.86%) patients had a nasogastric tube and 36 (32.14%) patients had a PEG for enteral nutrition. Eighty-one (72.32%) patients underwent continuous nutrition and 31 (27.68%) patients underwent intermittent nutrition. Forty-four (39.29%) patients had a decubitus ulcer. The average duration of stay in the ICU was 38.5 days (Table 1).

The percentage of parenteral nutrition (only parenteral or with enteral support) on the 1st and 3rd days were significantly higher than that of the 30th day ( $p < 0.001$ ). Total energy intake on the 1st and 3rd days were significantly lower than that of the 30th day ( $p < 0.001$ ). Total protein intake on the 1st and 3rd days were significantly lower than that of the 21st and 30th days ( $p < 0.001$ ).

Energy intake for each kg on the 1st and 3rd days, were significantly lower than that of the 21st and 30th day ( $p < 0.001$ ). Protein intake for each kg on the 1st and 3rd days were significantly lower than that of the 21st and 30th day ( $p < 0.001$ ). Albumin levels on the 3rd days were significantly lower than that of the 30th day ( $p = 0.036$ ). Prealbumin levels on the 1st and 7th day were significantly lower than that of the 21st and 30th day ( $p < 0.001$ ). CRP levels on the 1st day was significantly higher than that of the other days ( $p = 0.001$ ). Blood sugar levels on the 1st day was significantly higher compared to the 21st and 30th day ( $p < 0.001$ ) (Table 2)

**Table 1.** Summary of patients' characteristics

Age	78 (66.5 - 84)
Gender	
Male	63 (56.25%)
Female	49 (43.75%)
Height	163 (158 - 170)
Weight	63.77 ± 14.49
Body mass index	23.86 ± 5.09
Ideal body weight	58.46 (54.92 - 63.58)
Arm circumference	24.5 (23 - 27)
Basal metabolic rate	1248.97 ± 195.70
ICU indication	
Neurological	38 (33.93%)
Respiratory	41 (36.61%)
Metabolic	1 (0.89%)
Renal	4 (3.57%)
Cardiovascular	7 (6.25%)
Poor general condition	15 (13.39%)
Gastrointestinal	6 (5.36%)
Hematological	0 (0.00%)
Type of ICU	
Level 3	32 (28.57%)
General	55 (49.11%)
Thoracic	24 (21.43%)
Emergency	1 (0.89%)
Energy requirement	
Minimum	1461.51 (1373.02 - 1589.50)
Maximum	1753.82 (1647.62 - 1907.40)
Protein requirement	
Minimum	76.52 ± 17.39
Maximum	127.53 ± 28.98
APACHE II score	18 (14 - 23)
Mortality risk score	29 (21 - 40)
Type of tube	
Nasogastric	76 (67.86%)
PEG	36 (32.14%)
Method of nutrition	
Continuous	81 (72.32%)
Intermittent	31 (27.68%)
Decubitus ulcer	44 (39.29%)
Length of stay in ICU, days	38.5 (28 - 57.5)

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables



**Table 2.** Summary of nutritional status and laboratory measurements with regard to time

	1st day (n=112)	3rd day (n=112)	7th day (n=112)	21st day (n=112)	30th day (n=94)	p
Parenteral nutrition	41 (36.61%) <sup>a</sup>	31 (27.68%) <sup>a</sup>	13 (11.61%) <sup>b</sup>	8 (7.14%) <sup>b</sup>	5 (5.26%) <sup>b</sup>	<0.001
Calorie intake, total	1000 (790-1400) <sup>a</sup>	1285.5 (1018-1627.6) <sup>b</sup>	1429 (1200-1782.8) <sup>c</sup>	1518.5 (1266.5-1773.6) <sup>c</sup>	1536 (1360-1773.6) <sup>c</sup>	<0.001
Lower than required	92 (82.14%) <sup>a</sup>	66 (58.93%) <sup>b</sup>	55 (49.11%) <sup>bc</sup>	49 (43.75%) <sup>bc</sup>	36 (38.71%) <sup>c</sup>	<0.001
Protein intake, total	40.25 (30-69.65) <sup>a</sup>	63 (46.75-88.2) <sup>b</sup>	75.6 (62.6-90.5) <sup>bc</sup>	77.2 (63.04-90.5) <sup>c</sup>	81.05 (63.54-100.5) <sup>c</sup>	<0.001
Lower than required	91 (81.25%) <sup>a</sup>	67 (59.82%) <sup>b</sup>	57 (50.89%) <sup>bc</sup>	55 (49.11%) <sup>bc</sup>	37 (39.78%) <sup>c</sup>	<0.001
Calorie intake, for each kg	16.37 (11.76-22.81) <sup>a</sup>	20.97 (16.76-26.62) <sup>b</sup>	23.42 (18.23-28.2) <sup>c</sup>	23.72 (19.32-29.94) <sup>c</sup>	24.72 (20-29.87) <sup>c</sup>	<0.001
Protein intake, for each kg	0.69 (0.48-1.1) <sup>a</sup>	1.01 (0.76-1.38) <sup>b</sup>	1.19 (0.88-1.52) <sup>bc</sup>	1.21 (0.96-1.62) <sup>c</sup>	1.26 (0.99-1.63) <sup>c</sup>	<0.001
Total protein	5.07 ± 0.98 <sup>a</sup>	5.28 ± 0.88 <sup>b</sup>	5.46 ± 0.81 <sup>c</sup>	5.68 ± 0.90 <sup>d</sup>	5.73 ± 0.87 <sup>d</sup>	<0.001
Albumin	2.5 (2.1-2.9) <sup>ab</sup>	2.3 (2.1-2.8) <sup>a</sup>	2.5 (2.1-2.8) <sup>ab</sup>	2.45 (2.2-2.8) <sup>ab</sup>	2.5 (2.2-2.9) <sup>b</sup>	0.036
Prealbumin	8 (5-11) <sup>a</sup>	9 (7-12.5) <sup>ab</sup>	10 (8-13.5) <sup>bc</sup>	12 (9-14) <sup>cd</sup>	13 (10-16) <sup>d</sup>	<0.001
CRP	105 (63-157.5) <sup>a</sup>	100 (47.1-128) <sup>b</sup>	82.5 (50.3-121) <sup>b</sup>	89.5 (53.3-121.5) <sup>b</sup>	90 (47-110) <sup>b</sup>	0.001
Glucose	135 (100-182) <sup>a</sup>	120 (98.5-164.5) <sup>ab</sup>	116 (95-160) <sup>ab</sup>	111 (95-155) <sup>b</sup>	111 (92-157) <sup>b</sup>	<0.001

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables. The same letters denote the lack of statistically significant difference between groups.

Laboratory measurements on days 1, 21 and 30, and the changes in these measurements were analyzed according to the type of nutrition received by the individuals (enteral or parenteral). It was found that the decrease in glucose levels was significantly higher in the parenteral nutrition group compared to the enteral nutrition group ( $p = 0.005$ ). No significant difference was found between the groups with respect to other laboratory measurements (Table 3).

We additionally analyzed laboratory measurements on the 7<sup>th</sup>, 21<sup>st</sup> and 30<sup>th</sup> days and the changes in these measurements with respect to protein intake. In the low protein intake group, the prealbumin levels were found to be significantly lower compared to the normal/high intake group ( $p = 0.043$ ) on the 30<sup>th</sup> day. No significant difference was found between the groups with respect to other laboratory measurements (Table 4).

Linear regression analysis was performed to determine factors that were independently associated with the length of stay in the ICU. Univariate analysis showed that the Apache II score ( $p = 0.001$ ), mortality risk score ( $p = 0.003$ ), intermittent nutrition ( $p = 0.046$ ), low energy intake on day 7 ( $p = 0.008$ ), total protein level on day 30 ( $p = 0.016$ ), prealbumin level on day 21 ( $p = 0.021$ ), the change in prealbumin level from the 1<sup>st</sup> to the 21<sup>st</sup> day ( $p < 0.001$ ), and CRP level on day 30 ( $p = 0.025$ ) were significantly different between groups. Multivariate analysis performed with these variables revealed that the change in prealbumin level from the 1<sup>st</sup> to the 21<sup>st</sup> day was the only parameter that was independently associated with length of stay ( $p = 0.003$ ) (Table 5).

According to these results, an increase in prealbumin levels in the first 21 days reduces the duration of stay in the ICU.

**Table 3.** Summary of laboratory measurements with regard to the type of nutrition on the 1<sup>st</sup> day

	Type of nutrition on 1 <sup>st</sup> day		p
	Only enteral (n=71)	Parenteral (n=41)	
Total protein			
21 <sup>st</sup> day	5.65 ± 0.88	5.72 ± 0.95	0.685
30 <sup>th</sup> day	5.73 ± 0.85	5.74 ± 0.92	0.979
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	0.53 ± 0.80	0.73 ± 1.02	0.253
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	0.57 ± 0.71	0.84 ± 1.17	0.223
Albumin			
21 <sup>st</sup> day	2.5 (2.2-2.9)	2.4 (2.0-2.8)	0.167
30 <sup>th</sup> day	2.6 (2.3-3.0)	2.3 (2.2-2.7)	0.104
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	0 (-0.2-0.2)	-0.1 (-0.5-0.4)	0.636
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	0 (-0.2-0.3)	0.1 (-0.5-0.4)	0.962
Prealbumin			
21 <sup>st</sup> day	11 (9-15)	12 (9-14)	0.872
30 <sup>th</sup> day	13 (10-17)	12 (8-16)	0.278
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	3 (0-6)	4 (1-7)	0.325
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	4 (1-8)	5 (1-9)	0.546
CRP			
21 <sup>st</sup> day	86 (52-123)	90.3 (54.6-120)	0.830
30 <sup>th</sup> day	88.2 (47-118)	90 (40-110)	0.863
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	-20 (-55-20)	-24.9 (-70-12)	0.461
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	-20 (-62-20)	-40 (-95-6)	0.177
Glucose			
21 <sup>st</sup> day	110 (92-151)	111 (100-174)	0.244
30 <sup>th</sup> day	103 (92-155)	116 (100-160)	0.159
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	0 (-22-0)	-28 (-54-0)	0.005
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	0 (-29-0)	-16 (-77-0)	0.119

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution. (1) Negative values represent a decrease in measurements and positive values represent increase in measurements.



**Table 4.** Summary of laboratory measurements with regard to protein intake on the 7<sup>th</sup> day

	Protein intake on 7 <sup>th</sup> day		p
	Low (n=57)	Normal & High (n=55)	
Total protein			
21 <sup>st</sup> day	5.78 ± 0.87	5.57 ± 0.93	0.224
30 <sup>th</sup> day	5.86 ± 0.88	5.61 ± 0.85	0.165
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	0.62 ± 0.94	0.59 ± 0.84	0.833
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	0.67 ± 1.04	0.67 ± 0.79	0.994
Albumin			
21 <sup>st</sup> day	2.6 (2.2-2.8)	2.4 (2.1-2.8)	0.334
30 <sup>th</sup> day	2.5 (2.3-2.8)	2.5 (2.1-2.9)	0.480
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	-0.1 (-0.3-0.2)	0 (-0.3-0.3)	0.427
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	0 (-0.2-0.2)	0.1 (-0.2-0.4)	0.466
Prealbumin			
21 <sup>st</sup> day	12 (9-14)	11 (9-15)	0.809
30 <sup>th</sup> day	12 (9-15)	15 (10-18)	0.043
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	4 (1-7)	4 (0-6)	0.304
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	4 (1-7)	5 (2-9)	0.377
CRP			
21 <sup>st</sup> day	86 (55.8-118)	90 (50-128)	0.802
30 <sup>th</sup> day	90.3 (40.5-104.7)	85.8 (49.3-117)	0.753
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	-30 (-58.5-19.4)	-11.8 (-60-20)	0.476
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	-40 (-81-5.9)	-20 (-54-12)	0.212
Glucose			
21 <sup>st</sup> day	116 (95-160)	106 (92-150)	0.278
30 <sup>th</sup> day	121 (95-159)	104 (92-151)	0.239
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day <sup>(1)</sup>	-13 (-48-0)	0 (-38-0)	0.071
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day <sup>(1)</sup>	-16 (-59-0)	0 (-34-0)	0.165

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution. (1) Negative values represent a decrease in measurements and positive values represent an increase in measurements.

**Table 5.** Significant factors of the length of stay in ICU, linear regression analysis

	Univariate		Multivariate	
	$\beta$	p	$\beta$	p
Age	-0.153	0.107		
Apache II score	0.302	0.001	0.149	0.437
Mortality risk score	0.274	0.003	0.011	0.957
Type of tube, PEG	0.174	0.066		
Intermittent nutrition	-0.189	0.046	-0.046	0.665
Parenteral nutrition, 1 <sup>st</sup> day	-0.177	0.062		
Low calorie intake, 7 <sup>th</sup> day	-0.250	0.008	0.144	0.170
Low protein intake, 7 <sup>th</sup> day	-0.088	0.354		
Total protein				
21 <sup>st</sup> day	-0.097	0.311		
30 <sup>th</sup> day	-0.248	0.016	-0.165	0.115
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day	0.030	0.754		
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day	-0.185	0.074		
Albumin				
21 <sup>st</sup> day	-0.077	0.421		
30 <sup>th</sup> day	-0.077	0.460		
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day	-0.054	0.574		
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day	-0.054	0.606		
Prealbumin				
21 <sup>st</sup> day	-0.218	0.021	0.216	0.059
30 <sup>th</sup> day	-0.022	0.830		
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day	-0.390	<0.001	-0.310	0.003
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day	-0.179	0.084		
CRP				
21 <sup>st</sup> day	0.062	0.518		



30 <sup>th</sup> day	0.232	0.025	0.135	0.195
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day	0.113	0.234		
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day	0.174	0.093		
Glucose				
21 <sup>st</sup> day	-0.084	0.379		
30 <sup>th</sup> day	-0.122	0.242		
Change, 1 <sup>st</sup> & 21 <sup>st</sup> day	-0.043	0.650		
Change, 1 <sup>st</sup> & 30 <sup>th</sup> day	0.002	0.984		

β: Standardized Beta coefficient. Adjusted R<sup>2</sup> of the multivariate model = 0.202

## DISCUSSION

Early nutritional intervention has beneficial effects in patients with high nutritional risk (11). Early initiation of patients into nutrition therapy within 24-48 hours is recommended by the guidelines for critically ill patients who are unable to provide adequate oral intake (12-15). Regarding the effect of early nutritional nutrition, Tian et al. 's study of 1895 patients showed that the rates of mortality and gastrointestinal intolerance were significantly reduced. Four recent meta-analyses involving up to 25 studies with 3816 patients comparing EN and PN indicated that early onset nutrition has a significant effect on mortality in high-risk groups. According to these studies it also significantly reduces the risk of infectious complications and positively improves the clinical picture of patients (9,16-18). In our ICU, nutritional support begins at an early stage, within the first 24 hours.

Although the negative effects of malnutrition on ICU inpatients have been known for a long time, the issue of screening tests or approaches that can be used to determine malnutrition is still controversial. The European Association for Enteral and Parenteral nutrition (ESPEN) recommends the NRS 2002 screening test to determine the risk of malnutrition in hospitalized adult patients (11). But the effective-

ness of this screening test in assessing malnutrition in intensive care patients is still unknown. There is currently no specific algorithm, screening test, or specific marker that enables the assessment of malnutrition in patients admitted to the ICU. Nutritional risk is only evaluated with the NRS-2002 and it has not been effective in reducing undesirable clinical results (16,19). In a study conducted on critical patients in an ICU in Thailand, the effects of nutrition on sepsis and mortality were evaluated and having an NRS-2002 risk score of  $\geq 3$  was found to be associated with death and septic shock (12,19). In this study, the NRS-2002 score was used as a screening test and an NRS-2002 risk score of  $>3$  was identified in 99.4% of the patients. NRS 2002  $>3$  means the presence of malnutrition in patients and the need for urgent nutritional support therapy. The reasons for such a high rate of malnutrition may be that patients were elderly and had at least one underlying chronic disease.

For the last 20-30 years, the importance and necessity of enteral nutrition have been advocated. It is recommended that early nutrition is started in intensive care patients if possible (within the first 24 hours), unless there is a contraindication. Many studies have found that early enteral nutrition reduces hospitalization time in intensive care patients, duration of stay on mechanical ventilators, infec-

tious or other complications (such as organ failure), or mortality. Early enteral nutrition has advantages over parenteral nutrition, and has been demonstrated to shorten patients' recovery times (20,21). In this study, the effects of enteral and parenteral nutrition on biochemical data and anthropometric measurements in intensive care patients were examined. In intensive care patients followed for 21 days who received enteral and parenteral nutrition, the daily calorie and protein intake in the enteral-fed patients reduced their energy requirements.

It remains unclear what the optimal protein energy goals should be and exactly when they should be achieved (22,23). In a recent meta-analysis discussing the importance of early nutrition therapy the authors state that excess protein and energy intake may be associated with increased mortality in patients at risk of malnutrition (24,25). The number of macronutrients for critically ill patients should be carefully tailored to each individual patient. The optimal amount of energy, what the goals should be and when they should be achieved should be determined, especially in the acute phase of the critical illness, and not just calorie sufficiency should be targeted (22). A multicenter study conducted in Europe found that nutritional support started at an average of 46.5 hours (8.2-149.1 hours) in ICUs participating in the study, and the target calorie and protein levels were fully delivered in only 2.5% of patients (24). In a study of 201 ICUs from 26 countries, Heylan et al., found that enteral nutrition was initiated at an average of  $38.8 \pm 39.6$  hours. Patients in this study were found to have received 61.2% of their calorie requirements and only 57.6% of their protein requirement. It was found that 80% of the calories needed to be reached within the first week were reached in only 26% of patients. The authors emphasized that European ICUs are better relative to other regions at achieving target calories and protein levels (19,20). In this study, only 50% of the targeted calories and only 36% of the targeted protein were given on the third day of nutritional sup-

port. The target calorie was reached only in 31.4% of patients, and the target protein was reached only in 33.3% of patients. Energy consumption per kilogram increased gradually from the first day to the second day. The decrease in daily glucose levels in the parenteral nutrition group was significantly higher than in the enteral nutrition group when analyzed according to dietary pattern.

Prealbumin acts as a protein transporter that binds thyroxine and retinol and its plasma half-life is 21 days. Changes in nutrient intake are observed within 1 week. In the presence of metabolic stress, a faster change is observed (24). Compared to albumin, prealbumin shows nutritional changes in a shorter time. Evaluating prealbumin levels together with CRP levels may result in better clinical guidance (25). A previous study showed a negative correlation between serum albumin levels and CRP, white blood cell count and neutrophil-to-lymphocyte ratio in critically-ill ICU patients (23). Serum albumin is a negative acute phase reactant; therefore, CRP, white blood count and neutrophil-to-lymphocyte ratio decrease while albumin increases if the critical ICU patient begins to recover (21). In this study, it was observed that albumin and total protein values did not change statistically during nutrition, while prealbumin levels were significantly higher on the 13th day compared to the first day. Daily prealbumin levels were significantly lower in the group receiving low protein. According to these results, an increase in prealbumin levels within the first 21 days may reduce the length of stay in the ICU. CRP levels were found to be relatively high at first hospitalization in patients undergoing both enteral and parenteral nutrition in this study. The CRP levels on the 21<sup>st</sup> day were found to be significantly lower compared to day one and day seven. The long-term "enteral or parenteral" issue is debated and emotionally debated as it happens. Two large multicenter randomized controlled trials (RCTs) showed no fatal differences in the treatment of early nutrition, while



they were found to benefit the clinical picture of patients (24,25).

In this study, early nutritional evaluation was performed, the degree of risk was determined via NRS-2002 values, and early nutritional support was started in all patients. No statistically significant difference was found between different feeding methods in terms of hospitalization or NRS-2002 values. But statistically significant differences in baseline and pre-discharge NRS-2002 values (the latter was higher) were found. This suggested that even if the calculated caloric and protein needs of patients were determined and nutrition was started promptly, nutritional support was still not fully achieved in critically-ill ICU patients. This finding may also put into question the utility of the NRS-2002 system as a reliable method of monitoring the nutritional status of ICU patients; however, this particular conclusion requires further studies on the subject.

#### **Limitations of the study**

Our study was retrospectively planned which carries all related limitations, and it is clear that patients are not diagnostically homogeneous. Because of the exclusion criteria, only patients over 65 and those who received clinical nutrition therapy were included in the study, resulting in a small number of patients. The fact that this was a single-center and retrospective study may have reduced the strength of the study and the availability of some data. Finally, this study was conducted under the supervision of a dietitian. It should not be overlooked that the nutritional support received by each patient was not decided directly by a dietitian, but by a group of individuals, including the attending physician. Therefore, nutrition calculations and administration of feeding were based on patient-, dietitian- and physician-related decisions; thus, applying the same criteria and approach to these decisions may not have been possible. In the future,

we recommend prospective, observational studies in which diagnostically homogeneous ICU patients are included.

#### **CONCLUSIONS**

The prealbumin, albumin and total protein levels of geriatric intensive care patients were evaluated and the effect of reducing the development of malnutrition in geriatric patients by assessing early nutritional therapy (enteral compared to parenteral nutrition) is highlighted. Albumin and total protein values did not change statistically during nutrition, while prealbumin levels were significantly higher on the 13<sup>th</sup> day when compared with the first day. Planning nutrition by evaluating values such as prealbumin, albumin, total protein at an early stage facilitates the nutritional treatment of patients. Independent of which nutrition method is used, prealbumin should be followed primarily, because changes in prealbumin levels can indicate ICU stay and prognosis of elderly patients. Further studies are needed to evaluate the effects of nutritional support therapy on malnutrition in the elderly. We recommend that new systems be developed to monitor the nutritional status of patients during their stay in the ICU.

#### **Acknowledgment**

This study was completed without any financial support.

#### **Authors' Contribution**

**PG:** Conceptualization, Methodology, Writing-review & editing, Visualization. All authors have read and approved the final version of the manuscript; **HDG:** Conceptualization, Data curation, Project administration, original draft, Writing-review & editing.

#### **Conflicts of Interest**

The authors declare no conflicts of interest in this study.

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