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Association of the enteral nutrition support with mortality, biochemical parameters, and health markers in geriatric patients with COVID-19: A retrospective cohort study

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Abstract

This study aims to evaluate the association of the enteral nutrition support on mortality, biochemical parameters, and health markers in geriatric patients with COVID-19 treated in intensive care units (ICUs). A retrospective cohort analysis was conducted on 226 patients aged 60 years and older admitted to the COVID-19 adult ICU of Yıldırım Beyazıt University Training and Research Hospital in 2021. Demographics, ICU stay characteristics, biochemical parameters, and nutrition therapy details were collected from hospital records. Patients receiving enteral nutrition were categorized by product type (e.g., diabetic, immunonutrition, glutamine-containing, etc.), and their association on mortality, biochemical markers, and ICU outcomes were evaluated. The mortality rate was 50.4%, with an mean ICU stay of 9.63±6.50 days. Most patients (90.3%) had chronic conditions. Nutrition therapy was administered to 138 patients using various products. Immunonutrition products were associated with improved albumin levels and reduced mortality ($p<0.05$). Chronic conditions significantly increased mortality risk and ICU stay duration ($p<0.05$). Multivariate analysis revealed that longer ICU stays and the presence of chronic diseases independently reduced survival probability. Enteral nutrition support, particularly immunonutrition, may benefit geriatric ICU patients with COVID-19 by improving biochemical parameters and reducing mortality risk. Although patients receiving diabetic and glutamine-enriched products have a higher incidence of pressure ulcers, it should be considered that such products are likely to have been used in higher-risk patients.

Keywords: Aged, COVID-19, enteral nutrition, intensive care unit

Introduction

The novel coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus, is a multisystemic disease that may more severely affect geriatric individuals and patients with chronic conditions and that may be more severe and lethal compared to other viral types of pneumonia [1,2]. Yet, improving patients' nutritional status may alleviate the disease severity [3]. It is often reported that geriatric patients, particularly those with a chronic disease, are at high risk for micronutrient deficiency in COVID-19. Furthermore the presence of a nutritional deficiency before and during the disease aggravates the course of the disease [4,5]. Moreover, it is argued that preventing or eliminating protein and energy deficiencies is a protective factor for mortality in COVID-19 that is highly linked with disease-related malnutrition [6,7].

The global need for beds due to the COVID-19 disease was reported to be 13.7 in inpatient services and 2.1 in intensive care units (ICU) per 100,000 people [8]. A previous study comparing

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the international COVID-19 data indicated that mortality among COVID-19 patients hospitalized in an ICU was highly variable between cohorts [9]. Besides, ICU admission, age, and length of hospital stay are thought to have a significant association on patients' nutritional status [10]; therefore, monitoring and correcting patients' nutritional patterns seems critical to mitigating the severity and course of COVID-19. Monitoring micronutrient intake is feasible in enteral nutrition for patients with COVID-19; thus, nutritional intervention should be integrated into the patient care policies of hospitals [11]. Enteral nutrition can be administered to and well tolerated in COVID-19 patients with extracorporeal membrane oxygenation or mechanical ventilation [12,13]. It was previously revealed that adopting a simplified nutrition protocol in COVID-19 ICU patients significantly increased the percentage of days when the energy intake target was accomplished (80-100%), but it was not the case for the percentage of days when the protein intake target was accomplished [14]. In another study exploring the nutritional status of patients with SARS-CoV-2, the authors reported that 36% of patients and 100% of ICU patients were at risk of severe malnutrition. They also found that those at risk were older and had a higher mortality rate [15].

It is thought that enteral nutrition may affect mortality and biochemical markers in elderly COVID-19 patients in intensive care through different pathways. Recent studies conducted in intensive care units, have associated the initiation of rapid enteral feeding with a reduction in the length of stay in intensive care and a decrease in mortality [16]. The literature has demonstrated that immunonutritional formulas modulate immune cell function, reduce proinflammatory cytokine production, and support intestinal barrier integrity [17]. Glutamine supports intestinal integrity as an energy source for enterocytes [18], while omega-3 fatty acids suppress inflammation in tissues by modulating eicosanoid synthesis and neutrophil activation [19]. These mechanisms are particularly important in COVID-19, where intestinal barrier dysfunction and the immune system are thought to play a significant role.

While nutrition supplements in COVID-19 were consistently investigated in the literature, there is a rarity of research on enteral nutrition of COVID-19 ICU patients. Hence, the present study aimed to examine the association of the nutrition support on mortality, biochemical parameters, and health markers in geriatric COVID-19 patients receiving enteral nutrition.

Material and Methods

In this retrospective cohort study, we considered the data of patients aged 60 and older who were discharged or died after being admitted to the COVID-19 adult ICU in the Yenimahalle Training and Research Hospital of Yıldırım Beyazıt University between January 1 and December 31, 2021.

Data Collection and Statistical Analysis

Considering the relevant statements in Law on the Protection of Personal Data, we properly utilized the hospital information management system and patient archive files to extract patients' demographic characteristics and hospital stay information (e.g., sex, age, length of hospital stay, survival status, state of consciousness during the hospital stay, medications, and presence of a chronic disease before ICU admission, bedsores, and nosocomial infections), their blood parameters on the day of ICU admission and the day of discharge or death (e.g., the levels of glucose, urea, creatinine, albumin, total bilirubin, direct bilirubin, gamma-glutamyl transferase (GGT), alanine transaminase (ALT), aspartate aminotransferase (AST), ferritin, magnesium, phosphorus, sodium, potassium, chlorine, calcium, and C-reactive protein (CRP)), and their nutrition therapy status (e.g., the type and duration of nutrition products received if the patient received nutrition therapy). Adequate energy and protein targets were calculated and applied according to ESPEN recommendations [20]. Nutritional support was not provided to patients without haemodynamic stability.

In the statistical analysis, descriptive statistics were first used to summarize the data. The normality of continuous variables was assessed using the Shapiro-Wilk test. For variables that showed normal distribution, independent samples t-test was used to compare two independent groups. For variables that did not follow a normal distribution, non-parametric tests were preferred: Mann-Whitney U test was applied for comparisons between two groups, and the Kruskal-Wallis test was used for comparisons among more than two groups. The Chi-square test was employed to examine associations between categorical variables. Furthermore, Binary Logistic Regression analysis was conducted to identify factors independently associated with the binary outcome variable. All statistical analyses were performed on SPSS 26.0, and a p-value of<0.05 was considered statistically significant.

Exclusion criteria

Below are the exclusion criteria of the study.

a. Being younger than 60 years,

b. Not being admitted to the COVID-19 adult ICU,

c. Inability to ensure hemodynamic stability following ICU admission,

d. Missing data in patient files (i.e., the data sought for in this study),

e. Being referred to other medical centers for various reasons or receiving no intervention.

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Ethical considerations

Prior to the study, we obtained relevant permission from the Ministry of Health and ethical approval from the Clinical Research Ethics Committee Yenimahalle Training and Research Hospital (No: E-2022-06 dated 02.02.2022).

Result

We considered the data of 226 patients, 95 females (42%) and 131 males (58%), with a mean age of 75.99±9.19 years. The mortality rate of the patients was found to be 50.4%, and the mean length of ICU stay was 9.63±6.50 days. While the majority of patients had a chronic condition (90.3%), slightly more than half of them were conscious during their ICU stay (52.7%). The mean body mass index (BMI) of the patients was noted to be 29.92±4.16 kg/m2. Our findings demonstrated that the majority of the patients (75.7%) had ICU-acquired nosocomial infections. While 47 patients suffered catheter infection, 34 had urinary tract infection. Moreover, 71.7% of the geriatric patients had pneumonia, 34.1% had septic shock, and 30.9% had acute renal failure. Yet, most patients (72.6%) did not develop bedsores (Table 1).

As a routine treatment modality for COVID-19, all patients were administered favipiravir at a loading dose of 2x1600 mg followed by 2x600 mg for five days from the moment they were admitted to the ICU. Besides, while 91.6% of the patients received Clexane 2x0.4IU, vitamin C was administered to 96.5%, vitamin D to 88.1%, vitamin B to 89.4%, and Prednol to 73.0%. Finally, 11.1% of the patients received albumin supplementation. Since 138 patients received nutrition therapy, we categorized the applied nutrition products into seven groups: diabetic products, immunonutrition products (arginine, zinc, omega-3 fatty acids), disease-specific products, fibrous products, glutamine-containing products, standard products, and hypercaloric products. Of these patients, diabetic products were administered to 51.4%, immunonutrition products to 11.6%, glutamine-containing products to 42.0%, disease-specific products to 0.7%, fibrous products to 4.3%, standard products to 2.9%, and hypercaloric products to 7.2% (Table 2).

In this study, we investigated the association of the above-mentioned enteral nutrition products (i.e., nutrition support) on the biochemical parameters - intensive care markers - of the patients. Since only one patient was administered disease-specific products, we excluded their data from our analyses. The findings showed that those using diabetic products had increased levels of urea, creatinine, total bilirubin, direct bilirubin, ALT, ferritin, magnesium, phosphorus, and potassium but decreased albumin levels. Those receiving immunonutrition products had increased levels of albumin and glucose but reduced levels of urea, ferritin, and phosphorus. It was also revealed that while the levels of rea, total bilirubin, ferritin, phosphorus, and potassium increased in the patients using fibrous products, it was vice versa for their chlorine levels. Those using glutamine-containing products had decreased levels of albumin, glucose, and calcium but increased levels of urea, creatinine, total bilirubin, direct bilirubin, ALT, AST, ferritin, magnesium, phosphorus, and potassium. Increased phosphorus and potassium levels were revealed in those using standard products. In those using hypercaloric products, the measurements yielded increased levels of urea, ALT, AST, ferritin, and phosphorus but decreased albumin levels. We could not conclude significant relationships between the use of any enteral nutrition products and the patients' CRP, GGT, and sodium levels Tables 3).

Our non-parametric analysis yielded that the geriatric patients receiving diabetic, immunonutrition, glutamine-containing, and standard products had a significantly more prolonged length of ICU stay than those not using them ($p<0.05$; Table 4). The chi-square test showed that those not receiving immunonutrition products had a significantly higher mortality rate. However, we could not conclude any association of using other nutrition products on the patients' survival ($p<0.05$; Table 5).

In addition, we found that the patients receiving diabetic and glutamine-containing products had significantly more bedsores ($p<0.05$). However, we did not discover significant relationships between the use of immunonutrition, fibrous, standard, and hypercaloric products, and bedsores ($p>0.05$). The results showed no association between receiving nutrition therapy (i.e., receiving any type of nutrition products) and ICU-acquired nosocomial infection ($p>0.05$; Table 6).

When it comes to the patients' demographics, our analyses yielded that although sex, BMI, and age were not related to their length of ICU stay, the presence of a chronic disease significantly reduced it ($p<0.05$). Accordingly, the length of ICU stay was found to be 9.82±6.3 days in the patients with a chronic disease and 7.81±7.92 days in those without (Supplementary Table 1). While the mortality rate was found to be 53.9% in those with a chronic disease, it was 18.2% in those without; the difference was statistically significant ($p<0.05$). Moreover, the mean BMI was found to be lower in survivors than in those passing away ($p<0.05$; Supplementary Table 2). On the other hand, we concluded that the survivors had a shorter length of ICU stay than the patients who died ($p<0.05$; Table 7).

Finally, we analyzed the variables that were discovered to be associated with survival with a logistic regression model and determined that the presence of a chronic disease and length of ICU stay reduced the likelihood of the patients' survival ($p<0.01$; Table 8).

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Table 1. Patients general information

General information		n (%)
Sex		
Female		95 (42.0)
Male		131 (58.0)
Survival		
Mortality		114 (50.4)
Recovery		112 (49.6)
State of consciousness		
Conscious		119 (52.7)
Unconscious		107 (47.3)
Chronic disease		
Yes		204 (90.3)
No		22 (9.7)
		M±SD
Age (years)		75.99±9.19
BMI (kg/m2)		29.92±4.16
Length of hospital stay (days)		9.63±6.50
Infection	**n (%)**	**Duration**
ICU-acquired nosocomial infection		
Yes	171 (75.7)	5.7±2.6
No	55 (24.3)	
Catheter infection		
Yes	47 (20.8)	4.7±1.1
No	179 (79.2)	
Urinary tract infection		
Yes	34 (15.0)	4.4±1.4
No	192(85.0)	
Pneumonia		
Yes	162 (71.7)	5.9±2.6
No	64 (28.3)	
Septic shock		
Yes	77 (34.1)	2.2±1.4
No	149 (65.9)	
Acute renal failure		
Yes	70 (30.9)	4.0±2.3
No	156 (69.1)	
Bedsore		
Yes	62 (27.4)	Unknown
No	164 (72.6)	

Table 2. Treatment regimens and enteral nutrition therapy for patients

Regimen	n(%)
Clexane (enoxaparin sodium)	
Yes	207 (91.6)
No	107 (8.4)
Vitamin C	
Yes	218 (96.5)
No	8 (3.5)
Vitamin D	
Yes	199 (88.1)
No	27 (11.9)
Vitamin B	
Yes	202 (89.4)
No	24 (10.6)
Albumin supplementation	
Yes	25 (11.1)
No	201 (88.9)
Prednol (methylprednisolone)	
Yes	165 (73.0)
No	61 (27.0)
Enteral nutrition therapy	
Yes	138 (61.1)
No	88 (38.9)
Diabetic products	
Yes	71 (51.4)
No	67 (48.6)
Immunonutrition products	
Yes	16 (11.6)
No	122 (88.4)
Disease-specific products	
Yes	1 (0.7)
No	137 (99.3)
Fibrous products	
Yes	6 (4.3)
No	132 (95.7)
Glutamine-containing products	
Yes	58 (42.0)
No	80 (58.0)
Standard products	
Yes	4 (2.9)
No	134 (97.1)
Hypercaloric products	
Yes	10 (7.2)
No	128 (92.8)

Table 3. Types of enteral nutrition products and the patients' biochemical parameters

Biochemical parameter	Diabetic product			Immunonutrition products			Fibrous products			Glutamine-containing products			Standard products			Hypercaloric products		
	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*
Albumin level at ICU admission	71	29.05±3.75	**p<0.001**	16	30.93±5.87	**p<0.001**	6	27.56±4.56	0.13	58	29.70±3.91	**p<0.001**	4	30.82±3.13	0.39	10	28.45±4.65	**0.01**
Albumin level at final measurement		24.75±3.89			26.71±3.42			23.66±3.60		58	24.57±4.34		4	28.02±6.07		10	23.97±3.50	
CRP level at ICU admission	71	140.87±76.96	0.23	16	91.56±66.76	0.68	6	164.50±85.39	0.24	58	127.66±78.61	0.80	4	153.55±81.33	0.63	10	114.79±44.71	0.80
CRP level at final measurement		122.65±104.8			82.05±72.11			272.81±191.25		58	131.73±102.40		4	171.61±132.04		10	107.32±75.44	
Glucose level at ICU admission	71	193.99±96.55	0.19	16	203.65±87.32	**0.03**	6	292.98±153.24	0.65	58	197.30±96.27	**p<0.001**	4	127.05±11.53	0.52	10	197.33±115.45	0.21
Glucose level at final measurement		173.37±147.46			153.09±64.68			355.0±410.35		58	157.46±78.15		4	180.08±143.10		10	137.61±62.98	
Urea level at ICU admission	71	78.45±47.85	**p<0.001**	16	62.65±49.57	**0.01**	6	78.93±12.96	0.02	58	64.45±34.19	**p<0.001**	4	145.25±15.31	0.13	10	88.39±61.65	**p<0.001**
Urea level at final measurement		150.85±99.92			101.31±65.70			159.85±65.31		58	150.53±92.96		4	89.89±48.30		10	171.79±81.33	
Creatinine level at ICU admission	71	1.13±0.60	**p<0.001**	16	1.10±0.92	0.69	6	1.43±0.57	0.25	58	1.02±0.45	**p<0.001**	4	0.92±0.13	0.99	10	1.30±0.75	0.45
Creatinine level at final measurement		1.74±1.34			1.18±0.69			2.35±1.56		58	1.66±1.08		4	0.92±0.41		10	1.52±0.75	
Total bilirubin level at ICU admission	71	0.73±0.99	**p<0.001**	16	0.84±0.89	0.34	6	0.45±0.30	0.03	58	0.66±0.54	**p<0.001**	4	0.84±0.56	0.51	10	0.63±0.26	0.16
Total bilirubin level at final measurement		1.40±1.75			1.37±2.16			1.24±0.82		58	1.33±1.35		4	1.27±0.97		10	1.84±2.60	
Direct bilirubin level at ICU admission	71	0.25±0.56	**p<0.001**	16	2.66±9.69	0.42	6	0.16±0.07	0.05	58	0.20±0.22	**p<0.001**	4	0.21±0.13	0.43	10	0.17±0.09	0.17
Direct bilirubin level at final measurement		0.70±1.14			0.62±1.35			0.58±0.45		58	0.62±0.90		4	0.24±0.17		10	0.92±1.66	

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Table 3. Types of enteral nutrition products and the patients' biochemical parameters

Biochemical parameter	Diabetic product			Immunonutrition products			Fibrous products			Glutamine-containing products			Standard products			Hypercaloric products		
	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*
GGT level at ICU admission	71	58.69±62.48	0.28	16	57.10±45.81	0.98	6	38.78±20.57	0.35	58	57.58±50.09	0.28	4	63.92±40.95	0.47	10	47.47±77.84	0.08
GGT level at final measurement		65.46±54.79			57.36±46.41			70.55±71.97		58	65.42±43.23		4	112.70±151.84		10	73.52±75.35	
ALT level at ICU admission	71	42.05±85.10	**0.04**	16	32.15±20.87	0.07	6	23.38±10.86	0.35	58	29.89±20.39	**0.01**	4	51.50±25.67	0.31	10	27.30±22.13	**0.03**
ALT level at final measurement		118.85±303.19			60.39±51.51			33.55±27.87		58	144.90±341.84		4	91.67±79.24		10	65.42±43.66	
AST level at ICU admission	71	68.92±159.43	0.10	16	38.38±29.18	0.18	6	59.63±20.10	0.73	58	41.76±23.22	**p<0.001**	4	73.27±22.20	0.42	10	33.02±20.39	**0.02**
AST level at final measurement		148.39±359.17			75.03±95.48			68.16±53.0		58	220.92±492.95		4	86.05±42.88		10	82.51±52.76	
Ferritin level at ICU admission	71	696.80±524.02	**p<0.001**	16	466.48±454.97	**0.04**	6	612.64±446.54	**p<0.001**	58	659.69±568.74	**p<0.001**	4	1085.89±409.62	0.93	10	512.70±467.62	**p<0.001**
Ferritin level at final measurement		972.94±629.40			872.60±656.39			1293.06±446.54		58	976.19±594.43		4	1075.00±425.55		10	1201.30±610.49	
Magnesium level at ICU admission	71	2.01±0.28	**0.03**	16	1.90±0.37	0.85	6	2.02±0.27	0.44	58	2.01±0.31	**0.01**	4	2.24±0.40	0.74	10	2.04±0.24	0.21
Magnesium level at final measurement		2.13±0.41			1.92±0.50			2.17±0.50		58	2.17±0.48		4	2.16±0.30		10	2.13±0.26	
Phosphorus level at ICU admission	71	3.39±1.11	**p<0.001**	16	3.25±0.73	**0.01**	6	3.59±1.45	**0.04**	58	3.28±1.04	**p<0.001**	4	2.42±0.29	0.04	10	3.27±0.82	p<0.001
Phosphorus level at final measurement		5.32±2.99			4.29±1.70			6.24±2.77		58	5.29±2.87		4	4.14±1.10		10	5.36±2.60	

Table 3. Types of enteral nutrition products and the patients' biochemical parameters

Biochemical parameter	Diabetic product			Immunonutrition products			Fibrous products			Glutamine-containing products			Standard products			Hypercaloric products		
	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*	n	M±SD	p*
Sodium level at ICU admission	71	138.14±6.25	0.55	16	131.75±13.40	0.13	6	140.66±8.98	0.27	58	138.03±5.79	0.32	4	133.00±5.09	1.00	10	137.20±3.91	0.11
Sodium level at final measurement		138.74±6.33			137.87±4.96			136.66±4.41		58	139.03±6.28		4	133.00±5.09		10	141.60±8.79	
Potassium level at ICU admission	71	4.28±0.61	**p<0.001**	16	4.34±0.66	0.16	6	4.01±0.49	**0.03**	58	4.17±0.60	**p<0.001**	4	4.10±0.24	**0.02**	10	4.54±0.49	0.81
Potassium level at final measurement		4.87±1.11			4.63±0.59			5.80±0.87		58	4.98±1.21		4	5.57±0.78		10	4.48±0.90	
Chlorine level at ICU admission	71	102.01±13.60	0.86	16	97.62±11.18	0.36	6	107.0±8.64	**0.04**	58	103.18±5.89	0.07	4	99.00±2.94	0.67	10	106.40±4.97	0.51
Chlorine level at final measurement		101.73±5.97			100.68±5.13			99.50±4.59		58	101.46±6.18		4	97.25±5.73		10	104.40±9.29	
Calcium level at ICU admission	71	9.50±11.39	0.20	16	9.17±1.22	0.79	6	7.71±0.71	0.45	58	8.26±0.56	**p<0.001**	4	8.09±0.36	0.57	10	8.16±0.54	0.16
Calcium level at final measurement		7.78±0.82			8.24±0.71			7.48±0.57		58	7.70±0.69		4	8.27±0.61		10	7.75±0.79	

*Paired Samples T-Test

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Table 4. Types of enteral nutrition products and the patients' length of ICU stay

Type of nutrition products	n	Length of ICU Stay			p*
		M±SD	Median	Min-Max	
Diabetic products					
Yes	71	14.63±7.27	12.0	3.0-35.0	**p<0.001**
No	67	9.22±5.08	9.0	1.0-24.0	
Immunonutrition products					
Yes	16	17.31±8.93	18.0	5.0-34.0	**0.01**
No	122	11.31±6.23	10.0	1.0-35.0	
Fibrous products					
Yes	6	11.50±3.01	11.0	8.0-15.0	0.77
No	132	12.03±6.97	11.0	1.0-35.0	
Glutamine-containing products					
Yes	58	14.17±7.21	12.0	2.0-35.0	**p<0.001**
No	80	10.43±6.14	9.0	1.0-26.0	
Standard products					
Yes	4	19.50±5.44	21.0	12.0-24.0	**0.02**
No	134	11.78±6.77	10.0	1.0-35.0	
Hypercaloric products					
Yes	10	16.10±8.39	13.0	9.0-34.0	0.08
No	128	11.68±6.64	10.0	1.0-35.0	

*Mann-Whitney U Test

Table 5. Types of enteral nutrition products and the patients' survival

Type of nutrition products	Survival			p*
	Mortality n (%)	Recovery n (%)	Total n (%)	
Diabetic products				
Yes	49 (69.0)	22 (31.0)	71 (100.0)	0.11
No	54 (80.6)	13 (19.4)	67 (100.0)	
Immunonutrition products				
Yes	8 (50.0)	8 (50.0)	16 (100.0)	**0.02**
No	95 (77.9)	27 (22.1)	122 (100.0)	
Fibrous products				
Yes	6 (100.0)	0 (0.0)	6 (100.0)	0.33
No	97 (73.5)	35 (26.5)	132 (100.0)	
Glutamine-containing products				
Yes	45 (77.6)	13 (22.4)	58 (100.0)	0.49
No	58 (72.5)	22 (27.5)	80 (100.0)	
Standard products				
Yes	3 (75.0)	1 (25.0)	4 (100.0)	1.00
No	100 (74.6)	34 (25.4)	134 (100.0)	
Hypercaloric products				
Yes	8 (80.0)	2 (20.0)	10 (100.0)	1.00
No	95 (74.2)	33 (25.8)	128 (100.0)	

*Chi-square Test

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Table 6. Types of enteral nutrition products and the patients' bedsores and nosocomial infection

Types of nutrition products	Bedsore			p*
	Yes n (%)	No n (%)	Total n (%)	
Diabetic products				
Yes	40 (56.3)	31 (43.7)	71 (100.0)	**p<0.001**
No	22 (32.8)	45 (67.2)	67 (100.0)	
Immunonutrition products				
Yes	5 (31.3)	11 (68.8)	16 (100.0)	0.24
No	57 (46.7)	65 (53.3)	122 (100.0)	
Fibrous products				
Yes	2 (33.3)	4 (66.7)	6 (100.0)	0.69
No	60 (45.5)	72 (54.5)	132 (100.0)	
Glutamine-containing products				
Yes	51 (87.9)	7 (12.1)	58 (100.0)	**p<0.001**
No	11 (13.8)	69 (86.3)	80 (100.0)	
Standard products				
Yes	2 (50.0)	2 (50.0)	4 (100.0)	1.00
No	60 (44.8)	74 (55.2)	134 (100.0)	
Hypercaloric products				
Yes	6 (60.0)	4 (40.0)	10 (100.0)	0.32
No	56 (43.8)	72 (56.3)	128 (100.0)	
	ICU-acquired Nosocomial Infection			
Types of nutrition products	**Yes n (%)**	**No n (%)**	**Total n (%)**	**p***
Diabetic products				
Yes	66 (93.0)	5 (7.0)	71 (100.0)	1.00
No	63 (94.0)	4 (6.0)	67 (100.0)	
Immunonutrition products				
Yes	15 (93.8)	1 (6.2)	16 (100.0)	0.96
No	114 (93.4)	8 (6.6)	122 (100.0)	
Fibrous products				
Yes	6 (100.0)	0 (0.0)	6 (100.0)	0.50
No	123 (93.2)	9 (6.8)	132 (100.0)	
Glutamine-containing products				
Yes	55 (94.8)	3 (5.2)	58 (100.0)	0.58
No	74 (92.5)	6 (7.5)	80 (100.0)	
Standard products				
Yes	4 (100.0)	0 (0.0)	4 (100.0)	1.00
No	125 (93.3)	9 (6.7)	134 (100.0)	
Hypercaloric products				
Yes	10.0 (100.0)	0 (0.0)	10 (100.0)	0.38
No	119 (93.0)	9 (7.0)	128 (100.0)	

*Chi-square Test

Table 7. The patients' length of ICU stay and survival

ICU stay	Survival			p*
	Mortality M±SD	Recovery M±SD	Total M±SD	
Length of ICU stay	11.31±6.82	7.91±5.69	9.63±6.50	**p<0.001**

* Independent Samples T-Test

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Table 8. The binary logistic regression model for the patients' survival

Variables	B	Standard Error (SE)	p*	Odds Ratio (OR)	Confidence Interval (CI)	
					Lower	Upper
Constant	4.60	1.26	0.000	99.92		
BMI	-0.06	0.03	0.088	0.94	0.879	1.009
Immunonutrition products	0.89	0.61	0.144	2.451	0.735	8.167
Chronic disease	-1.65	0.61	0.007	0.192	0.058	0.640
Length of ICU stay	-0.09	0.02	0.000	0.907	0.863	0.953

*Binary logistic regression

Supplementary Table 1. The patients' demographics and length of ICU stay

Demographics	Length of ICU stay			p
	M±SD	Median	Min-Max	
Sex				
Female	9.90±6.67	9.0	1.0-34.0	0.56*
Male	9.43±6.39	8.0	1.0-35.0	
Chronic disease				
Yes	9.82±6.3	9.0	1.0-34.0	**0.02***
No	7.81±7.92	5.9	1.0-35.0	
BMI				
<23 kg/m² (risky)	11.44±8.81	9.0	2.0-25.0	0.67**
23-33 kg/m² (normal)	9.43±6.38	8.0	1.0-35.0	
>33 kg/m² (risky)	10.02±6.53	9.5	1.0-35.0	
	r		p	
BMI	0.062		0.35***	
Age	-0.069		0.30***	

* Mann-Whitney U Test; **Kruskal-Wallis H Test; ***Spearman's Correlation Analysis

Supplementary Table 2. The patients' demographics and survival

Demographics	Survival			p
	Mortality n (%)	Recovery n (%)	Total n (%)	
Sex				
Female	51 (53.7)	44 (46.3)	95 (100)	0.407*
Male	63 (48.1)	68 (51.9)	131 (100)	
Chronic disease				
Yes	110 (53.9)	94 (46.1)	204 (100)	**0.001***
No	4 (18.2)	18 (81.8)	22 (100)	
BMI				
<23 kg/m² (risky)	6 (66.7)	3 (33.3)	9 (100)	0.078*
23-33 kg/m² (normal)	79 (46.2)	92(53.8)	171 (100)	
>33 kg/m² (risky)	29 (63.0)	17 (37.0)	46 (100)	
	Mortality M±SD	**Recovery M±SD**	**Total M±SD**	**p**
BMI	66.44±9.35	75.53±9.05	75.99±9.19	0.458**
Age	30.48±4.71	29.35±3.44	29.92±4.16	**0.042****

*Chi-square Test; **Independent Samples T-Test

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Discussion

In this retrospective cohort study, we considered the data of 226 patients (42% females, 58% males) aged 60 and older who were discharged or died after being admitted to the COVID-19 adult ICU in the Yenimahalle Training and Research Hospital of Yıldırım Beyazıt University University - Ankara between January 1 and December 31, 2021. 226 patients. Immunonutrition products were associated with improved albumin levels and reduced mortality ($p<0.05$). Chronic conditions significantly increased mortality risk and ICU stay duration ($p<0.05$). Multivariate analysis revealed that longer ICU stays and the presence of chronic diseases independently reduced survival probability.

The patients had a mean age of 75.99±9.19 years, a mean mortality rate of 50.4%, and a mean length of ICU stay of 9.63±6.50 days. While the majority of patients had a chronic condition (90.3%), their mean BMI was noted to be 29.92±4.16 kg/m^2. Consistent with prior studies, the most prevalent risk factors for ICU admission at our hospital are male gender, advanced age, chronic diseases (e.g., diabetes mellitus (DM), cardiac conditions, and hypertension (HT)), obesity, low peripheral oxygen saturation, and high leukocyte count [21-24]. Besides, a previous study reported that the in-hospital mortality rate was 31% among COVID-19 patients [25]. Older age, male gender, presence of comorbidities, and high BMI are often associated with mortality in COVID-19 ICU patients [26-29]. In this study, we found that mortality was significantly higher in those with a chronic condition and that the mean BMI was significantly higher in the patients who died ($p<0.05$). Unlike the literature, we concluded no relationship between age and mortality ($p>0.05$). This may be attributable to our sample, which exclusively comprised geriatric patients, narrowing the age variability. Further research comparing younger and older populations could help elucidate these findings. At the time of this study, favipiravir treatment was administered to all patients as a routine treatment regime in Türkiye, as well as other countries. In addition, some patients received enoxaparin, corticosteroid, and vitamin B, C, and D supplements when necessary. Similar procedures were also adopted in previous Türkiye-based studies [30-33].

Our study underscores the critical role of nutritional support in managing geriatric COVID-19 patients. Among the various nutritional products analysed, immunonutritional products were associated with reduced mortality, consistent with existing evidence suggesting their potential benefits in modulating the immune response and improving recovery in critically ill patients [14,31-33]. However, logistic regression analysis showed that the significance of immunonutrition products decreased after adjustment for confounders such as chronic disease and length of ICU stay. This indicates that while nutrition plays a role, other factors, particularly comorbidities, and longer ICU stays, may have a greater impact on patient outcomes.

The results of the biochemical analysis were mixed with regard to the effect of the different nutritional products. In a previous retrospective study, the authors investigated intensive care indicators in COVID-19 patients for ICU admission and concluded that neutrophil counts and the levels of AST, lactate dehydrogenase (LDH), and CRP may be relevant predictors for ICU support in these patients [34]. Moreover, it was stated that invasive mechanical ventilation, bacterial superinfections, being older than 75 years, and the levels of serum ferritin, CRP, and interleukin 6 (IL-6) may affect survival in COVID-19 patients at intensive care hospitalization [35]. Our findings showed that no enteral nutrition products had a significant effect on the patients' CRP levels. Looking at ferritin and AST, which are thought to be predictive of intensive care support and may affect survival, while diabetic, immunonutrition, fibrous, glutamine-containing, and hypercaloric products contributed to the patients' ferritin levels, glutamine-containing and hypercaloric products increased their AST levels. These findings highlight the complexity of nutritional management in critically ill patients and emphasise the need for individualised approaches to optimise outcomes. This suggests that it may be the advanced stage of disease in elderly patient cohort where inflammation may be driven by factors beyond dietary modulation.

Length of ICU stay was another critical factor influencing patient outcomes. The literature predicates that the length of ICU stay and mortality may be affected by body weight, chronic diseases, age, sex, and type of medications [24-30]. In this study, we discovered that deceased patients had a more prolonged ICU stay than their surviving counterparts. In addition, we found that while the length of ICU stay was significantly longer in those using immunonutrition products, those who did not receive immunonutrition products had a significantly higher mortality rate. In our logistic regression model with the use of immunonutrition products, BMI, presence of a chronic disease, length of ICU stay, and mortality, while the use of immunonutrition products lost its significance on mortality, we discovered that the presence of a chronic disease and length of ICU stay reduced the probability of the patients' survival ($p<0.01$). Patients receiving immunonutrition and glutamine-containing products had significantly longer ICU stays, possibly due to their more severe initial conditions requiring intensive nutritional interventions. In addition, longer ICU stays were independently associated with higher mortality rates, highlighting the importance of early and effective interventions to reduce ICU dependency and associated complications such as infections and pressure ulcers.

Our findings revealed that chronic disease prevalence, BMI, and length of ICU stay were significantly associated with patient outcomes, including survival and mortality rates. Additionally, the type of enteral nutrition product appeared to influence specific biochemical markers, yet their direct impact on survival and overall health markers was limited.

This study has several important strengths. First, the study's focus on a vulnerable and under-researched population, such as elderly COVID-19 patients admitted to the ICU, provides important

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information to the literature on clinical nutrition management during critical illness. Secondly, the study comprehensively assessed numerous outcome measures, including mortality, biochemical parameters, and ICU-related health indicators. These results enable a multidimensional assessment of relationships. Thirdly, the comparative evaluation of different types of enteral nutrition products investigated in the study is limited in the literature. Finally, the study presents clinically important results that could guide nutritional support strategies in elderly COVID-19 intensive care patients.

Limitations

There are limitations to our study, although it provides valuable information. First, as a retrospective study, it cannot establish causality between nutritional support and patient outcomes. Secondly, the lack of standardised nutritional protocols between patients may have led to variability in the results. Third, the study was conducted in a single hospital during a specific timeframe, potentially limiting the generalizability of findings to other settings or patient populations. One of the limitations of the study is that both deceased and discharged patients were included in the same analyses, which made it difficult to determine group-specific differences and limited the interpretability of the results.

Another limitation of the study is that the patients included in the study used more than one nutrition product and the products may have more than one content. This situation makes it difficult to interpret the analyses. Although the nutritional formulas used in the study were standardised, it should be taken into consideration that the contents and compositions that may develop depending on other brands may affect the results. The study only compared the mean values of laboratory markers at the time of hospitalisation and at the end of hospitalisation without adjusting for the clinical status of the patients, which limits the conclusions that can be drawn from these comparisons.

Sufficient energy and protein targets were calculated and implemented for patients as a hospital procedure in accordance with ESPEN recommendations. However, as there was no data on the extent to which individuals achieved their energy and protein targets, this could not be collected. Calculating the extent to which energy and protein targets were achieved is also important for evaluating the results in future studies.

Conclusion

Our findings highlight the importance of addressing nutritional status in geriatric COVID-19 patients, particularly in those with chronic diseases and prolonged ICU stays. While specific enteral nutrition products, such as immunonutrition, may offer benefits, their impact on survival appears to be mediated by other critical factors. Future prospective studies with standardised dietary protocols and larger, more diverse populations are needed to confirm these findings and guide clinical practice. In addition, exploring the integration of nutritional interventions with other treatment modalities may provide a holistic approach to improving outcomes in this vulnerable.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
This study was approved by the Clinical Research Ethics Committee Yenimahalle Training and Research Hospital (No: E-2022-06 dated 02.02.2022).

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