Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2022.22108

The Effects of Protein Intake on Clinical Outcome in Pediatric Intensive Care Units

Merve Mısırlıoğlu[1], Dinçer Yıldızdaş[1], Faruk Ekinci[1], Özden Özgür Horoz[1], Yasemin Özkale[2], Murat Özkale[2], Ahmet Yöntem[1], İlknur Arslan[3], Gökhan Tümgör[4]

[1]Department of Pediatric Intensive Care, Çukurova University Faculty of Medicine, Adana, Turkey
[2]Department of Pediatric Intensive Care, Başkent University, Faculty of Medicine, Adana Dr Turgut Noyan Teaching and Medical Research Center, Adana, Turkey
[3]Department of Pediatric Intensive Care, Adana City Training and Research Hospital, Adana, Turkey
[4]Department of Pediatric Gastroenterology, Çukurova University, Faculty of Medicine, Adana, Turkey

What is already known on this topic?

- *The development of malnutrition in the pediatric intensive care unit (PICU) is associated with increased adverse outcomes. To provide appropriate nutritional support, it is necessary to obtain the patient's nutritional history, calculate the appropriate energy requirement, and evaluate their anthropometric data.*

What does this study add on this topic?

- *Monitoring the anthropometric conditions of the patients admitted to the PICU is important in terms of providing early and adequate nutritional support. The development of malnutrition in the PICU is associated with increased adverse outcomes, such as susceptibility to infection, prolonged hospital stay, mechanical ventilation, and mortality.*

ABSTRACT

Objective: Factors such as increased metabolic needs and inadequate calorie and protein intake increase the risk of malnutrition in critically ill children admitted to the pediatric intensive care unit. This study aimed to determine the risk of malnutrition and associated clinical outcomes.

Materials and Methods: Data from all patients aged 1 month to 18 years in 4 pediatric intensive care units in Adana, Turkey, were prospectively collected. Patient anthropometric data, the duration of mechanical ventilation, the length of stay in pediatric intensive care unit, 60-day mortality, nutritional status, and calorie and protein intake were recorded.

Results: A total of 111 patients were included in the study. There was a significant difference between survivor and non-survivor patients in terms of calorie and protein intake 48 hours after admission and protein intake on the seventh day after admission ($P = .001$, $P = .000$, and $P = .003$, respectively). No significant correlation was found between the length of pediatric intensive care unit stay, sepsis, and calorie intake in the first week. It was found that 1 g/kg/day increase in protein intake on the seventh day of intensive care hospitalization decreased the risk of mechanical ventilation by 0.49 times ($P = .035$; sensitivity: 83.3%; specificity: 34.5%).

Conclusion: Nutritional status should be evaluated fully in patients admitted to the pediatric intensive care unit and early detected malnutrition should be monitored closely to determine the need for early intervention. The risk of developing malnutrition is high in critically ill children. Providing the necessary energy and protein intake with nutritional therapy affects the clinical course in children with critical illness. Protein intake causes prolongation of mechanical ventilation time, delaying clinical recovery.

Keywords: Calorie, malnutrition, nutritional assessment, pediatric intensive care, protein

INTRODUCTION

It has long been known that nutritional status affects disease prognosis. The relationship between nutrition and prognosis was first emphasized by Hippocrates in the fifth century BC; it was reported that good nutrition facilitated healing in patients.[1] There are not enough data on nutritional support in critically ill pediatric patients, and nutritional support is one of the controversial issues in pediatric intensive care practice. The development of malnutrition in children in the pediatric intensive care unit (PICU) is associated with increased adverse outcomes, such as susceptibility to infection, delay in wound healing, impaired gastrointestinal function, prolonged hospital stay, mechanical ventilation, and mortality.[2,3]

Corresponding author:
Merve Mısırlıoğlu
✉ mervemisirlioglu@gmail.com
Received: April 20, 2022
Accepted: October 17, 2022
Publication Date: December 29, 2022

Cite this article as: Mısırlıoğlu M, Yıldızdaş s D, Ekinci F, et al. The effects of protein intake on clinical outcome in pediatric intensive care units. *Turk Arch Pediatr.* 2023;58(1):68-74.

To provide appropriate nutritional support, it is necessary to obtain the patient's nutritional history, calculate the appropriate energy requirement, and evaluate their anthropometric data. The malnutrition rate determined in a study conducted on critically ill children in the Netherlands to evaluate their nutritional status at PICU admission and discharge was 24%.[4] The American Society for Parenteral and Enteral Nutrition (ASPEN) and European Society of Pediatric and Neonatal Intensive Care (ESPNIC) recommend screening all children admitted to the PICU to determine their nutritional status, especially those who are at high risk of malnutrition.[5,6] The purpose of evaluating nutritional status is to adopt an appropriate treatment approach and determine the type and degree of malnutrition.

Dietary protein sufficient is the most important nutrition intervention in critically ill children to facilitate wound healing and inflammatory response and preserve skeletal muscle protein mass. The quantities of protein recommended for critically ill neonates and children are based on limited data. Certain severely stressed states, such as significant burn injury, may require additional protein supplementation to meet metabolic demands.[7] A similar evaluation of the effects of high protein administration using new formulas is desirable. Estimated protein requirements for children of various age groups are as follows: 0-2 years, 2-3 g/kg/day; 2-13 years, 1.5-2 g/kg/day; and 13-18 years, 1.5 g/kg/day.[8] In this study, we aimed to evaluate the nutritional status of the patients being treated in the PICUs in our province and to investigate the effects of calorie and protein intake in the first week of their hospitalization on mortality, nosocomial sepsis, mechanical ventilation, and PICU stay.

MATERIALS AND METHODS

Data from all patients aged 1 month to 18 years were collected prospectively from October 2019 to November 2019 in 4 pediatric intensive care units in Adana, Turkey. We searched malnutrition in 111 patients in first days and weeks in 4 PICUs within 2 study days. Not all patients who were admitted to the intensive care unit for 2 months but the patients who met the criteria on the randomly determined study day were included in the study, and the data of these patients were collected. Ethical committee approval was received from the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Approval No: 94/5, Date: December 6, 2019). Families participating in the study were informed about the study and provided the necessary consent by signing an informed consent form.

Patient anthropometric data, degree of malnutrition, reason for hospitalization, calorie intake, dietitian evaluation status, duration of mechanical ventilation, length of PICU stay, 60-day mortality, nutritional status, required calories, and actual calorie intake were recorded. Patients who were hospitalized in the PICU for less than 24 hours or longer than 6 months were excluded from the study.

Body height and weight were measured by doctors at each hospital. Height was measured with patients in the supine position and recorded in centimeters. Body weight was measured in kilograms using weight-measuring beds after calibration. After measuring the body length and weight as anthropometric parameters, height for age, body weight for age, height for body weight, and body mass index (BMI) were calculated. Body mass index was calculated by dividing the weight by the square of the height (m). The standard deviation (SD) score (z score), which is the most commonly used method for standardizing data on height, body weight, and BMI, was calculated using the CHILD METRICS computer program.[9,10] According to the anthropometric data, nutritional status and degree of malnutrition were evaluated. Patients who fulfilled one of the following criteria were defined as under nutrition: BMI z-score <-2, weight-for-height (W/H) $< 90\%$, or height-for-age (H/A) $< 95\%$.[11,12]

The energy required by the patients was calculated in kilocalories by using calorimetry calculations according to the Schofield equation and the World Health Organization (WHO) basal metabolic rate equation.[5,6] Estimated protein requirements for children of various age groups are as follows: 0-2 years, 2-3 g/kg/day; 2-13 years, 1.5-2 g/kg/day; and 13-18 years, 1.5 g/kg/day.[8] In the first 24-48 hours of hospital feeding, early enteral nutrition containing 25% of the target calories should be provided. The recommended goal for feeding and increasing nutrition in patients is to reach 2/3 of the calculated calorie intake by the end of the first week.[5] Various screening methods have been used to evaluate the nutritional risk of hospitalized children; the Screening Tool for Risk of impaired Nutritional Status and Growth (STRONGkids) score is currently the most commonly used method. In the STRONGkids, a subjective general evaluation of the patient is performed, and the presence of high-risk disease, nutritional intake and loss, and weight loss or low weight gain are evaluated. Nutritional risk is classified according to a score ranging from 0 to 5 on the evaluation; a score of 1-3 indicates that patients have a moderate nutritional risk and a score of 4-5 indicates that they have a high nutritional risk.[13,14]

Statistical Analysis

All statistical analyses were carried out with the Statistical Package for Social Sciences (SPSS for Windows v20.0). Categorical variables are expressed as numbers and percentages. In numerical continuous data, it was stated that the mean ± SD was given for those with normality distribution, and the median (minimum–maximum) value was given for those without normality distribution. The Kolmogorov–Smirnov normality test (and also some additional tests for normality; like skewness, kurtosis, and Detrended plots) was used to determine whether the variables are normally distributed or not. The independent *t* test was used to compare 2 normally distributed variables among independent groups. The Fisher's exact test was used to compare categorical data. The related-samples Wilcoxon signed-rank test was used to compare 2 dependent variables with non-normal distribution. The Mann–Whitney *U* test was used to compare continuous variables between 2 independent groups with non-normal distribution. Explanatory variables (risk factors) with $P \leq .25$ in univariate analysis were used in the forward multiple logistic regression analysis to find predictive risk factors for sepsis and mechanical ventilation in the first week of hospitalization. The statistical significance level was $P < .05$.

RESULTS

A total of 111 patients in 4 PICUs in Adana in October 2019 and November 2019 were included in the study. Of these, 66.7% (n = 74) were male, and the mean age was 55.96 ± 63.25

(minimum: 2–maximum: 275) months. The mean duration of hospitalization was 12.74 ± 18.28 (minimum: 2–maximum: 130) days. Among our patients, 50.5% (n = 56) required mechanical ventilation, and 8.1% (n = 9) received inotropic support. The mortality rate of patients in PICUs was 11.7 % (n = 14), and the rate of nosocomial sepsis was 20% (n = 24). The rate of diagnosis of respiratory system diseases on admission was 28.8% (n = 32). When evaluated in terms of nutritional status, nasogastric feeding was the most common feeding method, accounting for 45% (n = 50). A total of 23 patients (20.7%) were not fed on the study days. Evaluation by a dietician revealed that 17.1% (n = 19) of the patients were to be fed regularly. The most commonly used calorimetry method was the WHO basal metabolic rate equation, which was used in 79.3% (n = 88) of patients, followed by the STRONGkids score, which was used in 36.0% (n = 40) of patients. When all the patients in the study were evaluated using the STRONGkids tool, 27.9% (n = 31) were at high risk of malnutrition. The distribution of all patients in the study according to their characteristics is shown in Table 1.

Our patients could not be fed enterally for an average of 2 days. The total number of parenteral nutrition use days ranged from a minimum of 3 to a maximum of 10. Out of 57 patients who were hospitalized in the intensive care unit for more than a week, 64.3% (n = 36) had achieved their target calorie intake. The average calorie (enteral and parenteral, both) intake at the end of the first week was 91.91 ± 43.86 kcal/kg/day. The mean STRONGkids score was 2.69 ±1.14 (Table 2).

Anthropometric data (body weight, height, BMI, and z scores) were compared in terms of hospitalization and nutritional status on the study days; no statistically significant difference was found ($P > .05$) (Table 3). Nutrition and malnutrition status assessments of the patients are shown in Table 1. Our patients received an average of 95.08 ± 46.04 kcal/kg/day according to the Schofield equation and 95.79 ± 47.48 kcal/kg/day according to the WHO equation.

There was not a statistically significant difference between the mortality rates of patients who achieved and did not reach target calories in the first 48 hours and at the end of the first week ($P = .052, .054$; respectively) (Table 4). We found differences in length of stay and calorie intake on the seventh day after admission between the survivor and non-survivor group ($P = .008, .016$; respectively) but did not find any differences in duration of mechanical ventilation ($P > .05$). There was a significant difference between survivor and non-survivor groups in terms of calories and protein intake at the end of the first 48 hours after admission and protein intake on the seventh day after admission ($P = .001$, $P = .000$, $P = .003$, respectively). The comparison of survivor and non-survivor patient characteristics in patients admitted to the PICUs is shown in Table 5. Chronic malnutrition frequency at PICUs admission in our study is 24.2% (n = 29). There was no difference between those with and without chronic malnutrition in terms of hospital stay, stay in the PICU, MV duration, and mortality. There is no significant difference in the amount of calories; even the amount of protein on the fifth day of chronic malnutrition is higher than others ($P = .048$) (Supplementary Table 1).

The number of patients staying in PICU for at least 7 days or more was 71. The effects of calorie and protein intake in the

Table 1. The Distribution of All Patients and Nutrition Evaluations

Reason for Hospitalization	**n (%)**
Respiratory system diseases	32 (28.8)
Neurological system diseases	27 (24.3)
Infectious diseases	12 (10.8)
Gastrointestinal tract disease	8 (7.2)
Metabolic disease	7 (6.3)
Others	25 (22.6)
Nutritional status	**n (%)**
Nasogastric tube	50 (45.1)
Peroral	26 (23.4)
Gastrostomy	11 (9.9)
Parenteral	1 (0.9)
Not fed	23 (20.7)
STRONGkids malnutrition risk	**n (%)**
Low risk	14 (12.6)
Medium risk	66 (59.5)
High risk	31 (27.9)
Evaluation by a dietitian	**n(%)**
Yes, regularly	19 (17.1)
Yes, if needed	32 (28.8)
No	60 (54.1)
Energy calculation	**n(%)**
Schofield equation	21 (18.9)
WHO equation	88 (79.3)
Indirect calorimetry	2 (1.8)
Body mass index z-score	**n (%)**
Morbidly obese	6 (5.4)
Obese	13 (11.7)
Overweight	11 (9.9)
Normal	40 (36.0)
Underweight	8 (7.3)
Severely underweight	33 (29.7)
Weight for height	**n (%)**
Obese	14 (12.6)
Overweight	12 (10.8)
Normal	31 (27.9)
Mildly malnourished	19 (17.1)
Moderately malnourished	19 (17.1)
Severely malnourished	16 (14.5)
Weight for age	**n (%)**
Normal	39 (35.1)
Mildly malnourished	26 (23.4)
Moderately malnourished	27 (24.3)
Severely malnourished	19 (17.2)
Height for age	**n (%)**
Normal	52 (46.9)
Mildly malnourished	21 (18.9)
Moderately malnourished	15 (13.5)
Severely malnourished	23 (20.7)
Duration of malnutrition	**n (%)**
Normal	31 (27.9)
Acute: weakly	22 (19.9)
Acute-chronic malnutrition	29 (26.1)
Chronic: Short	29 (26.1)

STRONGkids, screening tool for risk of impaired nutritional status and growth; WHO, World Health Organization.

Table 2. All Patients' Characteristics in PICUs

	Mean ± Standard Deviation Median (Minimum–Maximum)
Time to initiating enteral feeding after admission (n = 94) (day)	2.5 ± 1.7 2.0 (1-10)
Number of days without enteral feeding (n = 83) (day)	2.4 ± 1.9 2.0 (1-11)
Number of days with parenteral nutrition (day)	4.6 ± 3.1 3.0 (3-10)
STRONGkids score	2.7 ± 1.1 3.0 (0-5)
Calories received at the end of the first week after admission (kcal/kg/day)	91.9 ± 43.9 86.0 (13-243)
Length of stay (day)	23.34 ± 39.92 13.00 (2-279)
Duration of mechanical ventilation (day) (n = 62)	24.85 ± 48.78 12.00 (1-279)
Calories received at the end of the first 48 hours after admission (kcal/kg/day)	41.93 ± 29.41 35.60 (3.00-144.00)
Protein received at the end of the first 48 hours after admission (g/kg/day)	1.17 ± 0.88 1.03 (0.00-4.00)
Calories received on the seventh day after admission (kcal/kg/day)	50.18 ± 25.68 47.50 (5.00-100.00)
Protein received on the seventh day after admission (g/kg/day)	1.41 ± 0.77 1. 63 (0.00-4.00)
% of total target calories reached in the first 48 hours	89.21 ± 96.45 75.14 (2.96-909.09)

STRONGkids, screening tool for risk of impaired nutritional status and growth; SD, standard deviation.

first week of hospitalization in the intensive care unit of these 71 patients on the outcome were examined. No significant correlation was found between the length of stay in PICU, sepsis, and protein and calorie intake in the first week ($P > .05$). No significant difference was found between patients with and without ventilation support in terms of calories intake ($P > .05$) (Supplementary Table 2). Logistic regression analysis with protein and calorie intake could not be performed because mortality was observed in 9 of our patients, and explanatory variables (risk factors) with $P \leq .25$ in univariate analysis were used in the forward multiple logistic regression analysis to find predictive risk factors for sepsis and mechanical ventilation in the first week of hospitalization (Supplementary Table 3). It was found that 1 g/kg/day increase in protein intake on the seventh day of intensive care hospitalization decreased the risk of mechanical ventilation by 0.49 times (0.252-0.942) ($P = .035$) (sensitivity: 83.3%, specificity: 34.5%) (positive predictive index: 0.64, negative predictive index: 0.58).

Table 3. Body Weight, Height, Body Mass Index, and z Scores on Hospitalization and Study Day

	Hospitalization Date Mean ± Standard Deviation Median (Min–Max)	Study Day Mean ± Standard Deviation Median (Min–Max)	*P**
Body weight (kg)	16.8 ± 16.3 10.2 (3.6 to 85)	16.6 ± 15.7 11.8 (3.7 to 85.0)	.415
Body weight z scores	−2.3 ± 3.2 −1.6 (−14.3 to 2.5)	−2.2 ± 3.1 -0.81 (−14.3 to 3.6)	.331
Height (cm)	93.0 ± 32.6 78.0 (50 to 177)	93.1 ± 32.6 78.0 (50.0 to 177.0)	.059
Height z scores	−1.5 ± 2.4 −1.5 (−6.3 to 4.7)	−1.5 ± 2.4 −1.5 (−6.3 to 4.7)	.362
BMI (kg/m²)	16.3 ± 4.9 15.9 (8.4 to 40.9)	16.8 ± 5.3 16.6 (6.1 to 28.5)	.662
BMI z scores	−1.7 ± 3.9 −0.7 (−12.8 to 4.3)	−1.6 ± 4.0 0.7 (−16.4 to 4.7)	.683

BMI, body mass index.
*Related-samples Wilcoxon signed-rank test.

DISCUSSION

The deterioration in nutritional status in critically ill patients, the presence of malnutrition, and inadequate nutritional support cause infection, deterioration of protein balance in these patients, prolongation of mechanical ventilation time, and delaying clinical recovery. The quantities of protein recommended for critically ill neonates and children are based on limited data.[7,8] Our main findings in this study are: protein intake on the seventh day of PICU admission is associated with the risk of prolonged mechanical ventilation, in addition, the calorie and protein intake at the 48th hour and the calorie intake at the 72nd hour was different in the survivor and non-survivor groups. We found that 1 g/kg/day increase in protein intake on the seventh day of intensive care hospitalization decreased the risk of mechanical ventilation by 0.49 times. In our study, no significant correlation was found between the length of stay in PICU, sepsis, and protein and calorie intake in the first week. In the acute phase of critical illness, there is a negative protein balance. Giving the necessary protein in the diet increases protein synthesis and positively affects protein synthesis in this period. Hauschild et al[15] reported that in critically ill children, total daily protein intake > 1.1 g/kg was associated with positive effects on clinical outcomes and protein balance. A minimum of 1.5 g/kg/day of protein intake may be necessary to achieve a positive protein balance in critically ill children.[6,16] Mehta et al[17] reported that the protein goal was 1.9 ± 0.7 g/kg/day. The adequacy of enteral protein intake was significantly associated with 60-day mortality. Adequacy of enteral protein intake was significantly associated with mortality in this prospective cohort study in mechanically ventilated children. Similarly, there was a statistically significant difference between the survivor and non-survivor groups in terms of protein intake in our study. In critically ill septic adults, an increase of 30 g/day of actual protein intake was associated with reduced 60-day mortality and increased ventilator-free days.[18]

The recommended goal for feeding and increasing nutrition in patients is to reach 2/3 of the calculated calorie intake by the end of the first week.[5] In our study, 71 patients had been hospitalized in the PICU for more than a week, and 64.3% (n = 36) of them had achieved their target calorie intake. The average calorie intake of our patients at the end of the first week was 91.9 ± 43.9 kcal/kg/day. In a study involving 90 patients in the PICU, the calorie intake at the end of the first week was reported to be 82 ± 47 kcal/kg/day.[19] In another study, the calorie intake of critically ill children was 64 ± 29 kcal/kg/day.[20]

Table 4. Comparison of Mortality Rates in Patients Achieving Versus Not Achieving Target Calories at the End of the First 48 Hours and First Week in Pediatric Intensive Care Units

	Mortality (n; %)		Mortality (n; %)
Achieving target calories at the end of the first week (n = 37)	3 (8.1)	Achieving target calories at the end of the first 48 hours (n = 90)	10 (11)
Not achieving target calories at the end of the first week (n = 18)	5 (27.8)	Not achieving target calories at the end of the first 48 hours (n = 11)	3 (30.8)
*P**	.054	*P**	.052

*Fisher's exact test.

The risk of malnutrition is high in critically ill children with limited calorie intake due to fluid restriction during hospitalization, interruption of feeding during intervention, or gastrointestinal intolerance due to sedatives and analgesics. A patient may be malnourished prior to hospitalization in the PICU or malnutrition may develop during hospitalization.[21] The WHO defines malnutrition as the imbalance between nutrient and energy intake and the needs of the body to perform growth, maintenance, and specific functions.[22] Nutritional status can be evaluated using anthropometric methods such as height, body weight, or biochemical parameters; however, height and weight measurements are non-invasive, inexpensive, and easily applicable.[23] A study conducted on critically ill children reported that 24% of patients were malnourished on admission to the PICU.[4] Various studies have reported that there are different degrees of malnutrition, ranging from 40% to 70%.[2,19,24,25] In our study, we found that 41% of our patients were malnourished; in addition, there was no significant difference between the rates on the admission and study days. To evaluate a patient's nutritional status on admission to the PICU, their height, body weight, and BMI z score should be observed. In addition, it is recommended that head circumference should be measured in children under 36 months of age.[5] The malnutrition rate was 30% in a multinational study in mechanically ventilated children in 31 PICUs; 13.2% of patients had a BMI z score >2 SD, while 17.1% had a BMI z score<−2 SD.[16] A study involving 2432 children from 27 PICUs reported that 18.5% had a BMI z score <−2 SD and 7.4% had a BMI z score >2 SD.[26] In our patients, 17.1% had a BMI z score >2 SD, and 36.9% had a BMI z score <−2 SD. In the abovementioned studies, the morbid obesity rate was close to that in our patients; however, the rate of critically ill patients with malnutrition was higher in our study.

The guidelines recommend screening all children admitted to the PICU for nutritional status, especially those who are at high risk of malnutrition.[5,6] Various screening methods are used to evaluate the nutritional risk in hospitalized children; currently, the STRONGkids score is the most commonly used method. STRONGkids scores, which were calculated in 36.0% of our patients, were evaluated, and it was found that 59.5% of patients were in the medium-risk group, and 27.9% were in the high-risk group. In another study, 8% of children hospitalized in Iran were in high-risk group according to the STRONGkids score,[27] whereas 3.6% of children hospitalized in Turkey were in the high-risk group.[28] In a study evaluating 211 patients in the PICU, 32.2% of patients had malnutrition during the first

Table 5. Comparison of Survivor and Non-survivor Patients' Characteristics in 4 Pediatric Intensive Care Units

	Total Patients in 4 PICUs (n = 111)			Patients Stay in 4 Pediatric Intensive Care Units for Atleast 7 Days or More (n = 71)		
	Non-survivor Patients (n = 14) Mean ± SD Median (min–max)	Survivor Patients (n = 97) Mean ± SD Median (min–max)	*P**	Survivor Patients (n = 62) Mean ± SD Median (min–max)	Non-survivor Patients (n = 9) Mean ± SD Median (min–max)	*P**
Length of stay (day)	67.21 ± 94.95 27.00 (3-279)	16.59 ± 13.92 12.00 (2-60)	.008	18.60 ± 11.03 14.50 (7-52)	25.56 ± 9.77 26.00 (12-42)	.04
Duration of mechanical ventilation (day) (n = 62)	61.46 ± 97.44 23.00 (1-279)	15.14 ± 13.85 10.00 (1-52)	.117	8.97 ± 12.28 4.50 (0-52)	24.67 ±14.36 23.00 (0-46)	.01
Calories received at the end of the first 48 hours after admission (kcal/kg/day)	20.43 ± 19.23 10.60 (5.00-72.00)	45.28 ± 29.38 40.85 (3.00-144.00)	.001	43.74 ± 31.03 35.86 (3.00-144.00)	22.32 ± 23.38 10.00 (5.00-72.00)	.02
Protein received at the end of the first 48 hours after admission (g/kg/day)	0.42 ± 0.52 0.32 (0-1.73)	1.28 ± 0.88 1.08 (0-4.00)	.000	1.22 ± 0.95 1.03 (0.00-4.00)	0.39 ± 0.63 0.00 (0.00-1.73)	.07
Calories received on the seventh day after admission (kcal/kg/day)	34.16 ± 25.00 25.39 (5.00-72.00)	53.02 ± 24.93 49.00 (10.59-100.00)	.016	55.56 ± 25.99 53.80 (10.59-110.0)	38.15 ± 28.06 29.90 (5.00-72.00)	.08
Protein received on the seventh day after admission (g/kg/day)	0.78 ± 0.64 0.65 (0.00-1.73)	1.52 ± 0.74 1.51 (0.00-4.00)	.003	1.60 ± 0.76 1.60 (0.00-4.00)	0.81 ± 0.75 0.64 (0.00-1.73)	.01

SD, standard deviation. *Mann–Whitney *U* test.

hospitalization, and according to the STRONGkids score, 73.0% were found to be in the medium- and high-risk groups.[29] In our study, 87.4% of the patients were in the medium- and high-risk group.

It is more difficult for children with insufficient nutritional intake to manage serious disease attacks and disease complications than healthy children; therefore, their mortality risk is increased.[21] In a study conducted in Brazil, the presence of malnutrition was shown to increase mortality in patients admitted to the PICU.[30] Patients can be malnourished due to the postponement of nutrition for various reasons or an inability to consume the appropriate number of calories. In the first 24-48 hours of hospital feeding, early enteral nutrition containing 25% of the target calories should be provided. A study conducted on critically ill children in Turkey found that achieving intake of the target calories in the first 48 hours was a protective factor, as starting early enteral nutrition helped to reduce mortality in the PICU.[31] Although there is not enough evidence on the optimal time to start feeding in intensive care patients, it is recommended to start feeding within 24-48 hours of hospitalization in patients with a hemodynamically stable and functional gastrointestinal system since every day without food can be compensated with additional calories later.[32] In our study, we found that on average, feeding in our patients started within 2 days.

The ASPEN and ESPNIC guidelines on nutrition in critically ill children recommend the evaluation of nutrition in patients admitted to the PICU, a continuous review of energy delivered, the monitoring of anthropometric data during the hospitalization period, and the initiation of feeding as soon as possible, with the enteral route preferred over parenteral nutrition if there is no contraindication.[6,8] In a study conducted in Brazil, the enteral nutrition rate in the PICU was 80%, while the parenteral nutrition rate was 10%.[19] In our study, 78.4% of the patients received enteral nutritional support, while 20.7% of the patients were not fed on the study day. Among our patients, 0.9% (n = 1) received parenteral nutritional support, which was lower than that in the Brazilian study.[19]

The objectives of optimal nutritional support during critical illness include the careful evaluation of energy needs and the provision of the necessary nutrients in an appropriate way.[21] If indirect calorimetry cannot be performed, the guide published by Mehta et al[5] in 2017 recommends the use of the Schofield equation or the WHO equation for energy calculation. The use of the Harris-Benedict equation is not recommended in critically ill children. In our study, no center used the Harris-Benedict equation in accordance with the guidelines. In our study, indirect calorimetry was used in 1.8% of the patients. The most frequently used equation for energy calculation was the WHO basal metabolic rate equation. In previously conducted studies, many PICUs use only formulas for energy calculation.[33] We calculated the energy needs of the patients according to the Schofield equation. Healthcare professionals and intensivists sometimes overlook nutrition issues because they are concentrating on the primary problem of the patients. Accurate measurement of energy expenditure is not always possible, whereas energy requirements can be determined by using standard equations and indirect calorimetry recommended in the guidelines to calculate energy consumption.

In recent years, the important effects of nutritional support on mortality and morbidity of diseases have been described in several studies and are well-known issues.[5] The risk of developing malnutrition is high in critically ill children. Providing the necessary energy and protein intake with nutritional therapy affects the clinical course in children with critical illness. Protein intake is the most important nutrition intervention in critically ill children to facilitate wound healing and the inflammatory response and preserve skeletal muscle protein mass. According to the results of our study, protein intake causes prolongation of mechanical ventilation time, delaying clinical recovery. There is a need for studies in the pediatric age group to be conducted in this area.

Several major limitations need to be considered when interpreting our findings. The first is the small sample size. The study was conducted in only 4 hospitals, limiting the generalizability of the results. Another limitation of our study is that we do not have access to the anthropometric data of the patients discharged from the PICU. Third, the cross-sectional design of the study rendered it impossible to identify the relationship between nutrition practices and outcomes in the patients. It is also important to acknowledge the limitation inherent in a cross-sectional study; it is not possible to establish a cause–effect relationship without longitudinal data. Other measurements, such as triceps thickness and middle arm circumference, were missing from the anthropometric data. Disorders severity scores and comorbidity are our missing values. Finally, the centers were not asked whether there were nutrition protocols in place.

Ethics Committee Approval: Ethical committee approval was received from the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Approval No: 94/5, Date: December 6, 2019).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.M., D.Y., F.E., O.O.H., A.Y., I.A., Y.O., M.O., G.T.; Design – M.M., D.Y., F.E., O.O.H., A.Y., I.A., Y.O., M.O., G.T; Supervision – D.Y., F.E., O.O.H., I.A., Y.O., M.O., G.T.; Funding – M.M., D.Y., F.E., O.O.H., A.Y., I.A., Y.O., M.O., G.T.; Materials – M.M., D.Y., F.E., O.O.H., A.Y., I.A., Y.O., M.O., G.T.; Data Collection and/or Processing – M.M., F.E.; Analysis and/or Interpretation – M.M., D.Y., F.E., O.O.H., A.Y., I.A., Y.O., M.O., G.T.; Literature Review – M.M., D.Y., O.O.H., F.E.; Writing – M.M., D.Y., O.O.H., F.E.; Critical Review – M.M., D.Y., O.O.H., F.E.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Sahinoglu AH. *Intensive Care Problems and Their Treatments.* 2nd ed. Ankara, Turkey Clinics; 2003:251-280.
2. Skillman HE, Wischmeyer PE. Nutrition therapy in critically ill infants and children. *JPEN J Parenter Enteral Nutr.* 2008;32(5): 520-534. [CrossRef]

3. Joffe A, Anton N, Lequier L, et al. Nutritional support for critically ill children. *Cochrane Database Syst Rev. Art.No.* 2016;2018(12): CD005144. [CrossRef]
4. Hulst J, Joosten K, Zimmermann L, et al. Malnutrition in critically ill children: from admission to 6 months after discharge. *Clin Nutr.* 2004;23(2):223-232. [CrossRef]
5. Mehta NM, Skillman HE, Irving SY, et al. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient:Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr.* 2017;41(5):706-742. [CrossRef]
6. Tume LN, Valla FV, Joosten K, et al. Nutritional support for children during critical illness: European Society of Pediatric and Neonatal Intensive Care (ESPNIC) metabolism, endocrine and nutrition section position statement and clinical recommendations. *Intensive Care Med.* 2020;46(3):411-425. [CrossRef]
7. Premji SS, Fenton TR, Sauve RS. Higher versus lower protein intake in formula-fed low birth weight infants. *Cochrane Database Syst Rev.* 2006;(1):CD003959. [CrossRef]
8. Mehta NM, Compher C, A.S.P.E.N. Board of Directors. A.S.P.E.N. Clinical Guidelines: Nutrition support of the critically ill child. *JPEN J Parenter Enteral Nutr.* 2009;33(3):260-276. [CrossRef]
9. Demir K, Özen S, Konakçı E, Aydın M, Darendeliler F. A comprehensive online calculator for pediatric endocrinologists: ÇEDD Çözüm /TPEDS Metrics. *J Clin Res Pediatr Endocrinol.* 2017;9(2):182-184. [CrossRef]
10. Neyzi O, Bundak R, Gökçay G, et al. Reference values for weight, height, head circumference, and body mass index in Turkish children. *J Clin Res Pediatr Endocrinol.* 2015;7(4):280-293. [CrossRef]
11. Yalcin SS. Evaluation of nutritional status by anthropometric measurements. *Clin Pediatr.* 2011;33:441-464.
12. World Health Organization Multicentre Growth Reference Study Group. *WHO Child Growth Standards: Length/Height-Forage, Weight-for-Age, Weight-for-Length, Weight-For Height and Body Mass Index-for-Age: Methods and Development.* Geneva: World Health Organization; 2006.
13. Hulst JM, Zwart H, Hop WC, Joosten KF. Duch national survey to test the STRONG kids nutritional risk screening tool in hospitalized children. *Clin Nutr.* 2010;29(1):106-111. [CrossRef]
14. Erkan T. Methods to evaluate the nutrition risk in hospitalized patients. *Turk Pediatri Ars.* 2014;49(4):276-281. [CrossRef]
15. Hauschild DB, Ventura JC, Mehta NM, Moreno YMF. Impact of the structure and dose of protein intake on clinical and metabolic outcomes in critically ill children: a systematic review. *Nutrition.* 2017;41:97-106. [CrossRef]
16. Mehta NM, Bechard LJ, Cahill N, et al. Nutritional practices and their relationship to clinical outcomes in critically ill children- An international multicenter cohort study. *Crit Care Med.* 2012; 40(7):2204-2211. [CrossRef]
17. Mehta NM, Bechard LJ, Zurakowski D, Duggan CP, Heyland DK. Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study. *Am J Clin Nutr.* 2015;102(1):199-206. [CrossRef]
18. Elke G, Wang M, Weiler N, Day AG, Heyland DK. Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database. *Crit Care.* 2014;18(1):R29. [CrossRef]
19. Zamberlan P, Delgado AF, Leone C, Feferbaum R, Okay TS. Nutrition therapy in a pediatric intensive care unit: indications, monitoring, and complications. *JPEN J Parenter Enteral Nutr.* 2011;35(4): 523-529. [CrossRef]
20. Leite HP, Isatugo MK, Sawaki L, Fisberg M. Anthropometric nutritional assessment of critically ill hospitalized children. *Rev Paul Med.* 1993;111(1):309-313.
21. Mehta NM. Approach to enteral feeding in the PICU. *Nutr Clin Pract.* 2009;24(3):377-387. [CrossRef]
22. Grover Z, Ee LC. Protein energy malnutrition. *Pediatr Clin North Am.* 2009;56(5):1055-1068. [CrossRef]
23. Nangalu R, Pooni PA, Bhargav S, Bains HS. Impact of malnutrition on pediatric risk of mortality score and outcome in pediatric intensive care unit. *Indian J Crit Care Med.* 2016;20(7):385-390. [CrossRef]
24. Oosterveld MJ, Van Der Kuip M, De Meer K, De Greef HJ, Gemke RJ. Energy expenditure and balance following pediatric intensive care unit admission: a longitudinal study of critically ill children. *Pediatr Crit Care Med.* 2006;7(2):147-153. [CrossRef]
25. López-Herce Cid J. Nutrition in the critically ill child. *An Pediatr (Barc).* 2009;71(1):1-4. [CrossRef]
26. Jacquot A, Valla FV, Mura T, et al. NUTRI-REAPED study: nutritional assessment of French critically ill children and nutrition practice survey in French-speaking pediatric intensive care units. *Ann Intensive Care.* 2019;9(1):15. [CrossRef]
27. Imani B, Gholampour Z, Hosseininasab M, Khademi G, Sezavar M, Abdollahpour N. Assessment of nutritional status based on STRONGkids tool in Iranian hospitalized children. *Int J Child Health Nutr.* 2015;4(1):61-66. [CrossRef]
28. Beser OF, Cokugras FC, Erkan T, Kutlu T, Yagci RV, TUHAMAR Study Group. Evaluation of malnutrition development risk in hospitalized children. *Nutrition.* 2018;48:40-47. [CrossRef]
29. Qiao JY, Guo FF, Li F, Chen LX, Luan B. Nutritional assessment and clinical application of nutritional risk screening tools in critically ill children. *Zhongguo Dang Dai Er Ke Za Zhi.* 2019;21(6):528-533. [CrossRef]
30. El Halal MG, Barbieri E, Filho RM, Trotta Ede A, Carvalho PR. Admission source and mortality in a pediatric intensive care unit. *Indian J Crit Care Med.* 2012;16(2):81-86. [CrossRef]
31. Bağci S, Keleş E, Girgin F, et al. Early initiated feeding versus early reached target enteral nutrition in critically ill children: an observational study in paediatric intensive care units in Turkey. *J Paediatr Child Health.* 2018;54(5):480-486. [CrossRef]
32. Mehta NM, Skillman HE, Irving SY, et al. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *Pediatr Crit Care Med.* 2017;18(7):675-715. [CrossRef]
33. Campos Miño S, Sasbón JS. The Latin-American survey on nutrition in Pediatric Intensive Care (ELAN-CIP). *An Pediatr (Barc).* 2009;71(1):5-12. [CrossRef]

Supplementary Table 1. Comparison of patients with chronic malnutrition vs. no chronic malnutrition in terms of nutrition issues and outcomes.			
	Chronic malnutrition (n=21)	**No Chronic malnutrition (n=50)**	**p-value**
Age (month)	60.8 ± 51.3	55.8 ± 65.3	0.753
Length of hospital stay (day)	28.1 ± 14.4	27.4 ± 13.9	0.851
Length of PICU stay (day)	19.9 ± 11.4	19.3 ± 11.0	0.835
Duration of mechanical ventilation (day)	13.4 ± 14.6	9.9 ± 13.0	0.331
Calories received at the end of the first 48 hours after admission (kcal/kg/day)	40.3 ± 27.5	41.3 ± 32.4	0.90
Protein received at the end of the first 48 hours after admission (g/kg/day)	1.24 ± 1.0	1.06 ± 0.9	0.478
Calories received at the 5th day after admission (kcal/kg/day)	51 ± 24.6	45.9 ± 28.7	0.487
Protein received at the 5th day after admission (g/kg/day)	1.6 ± 0.8	1.2 ± 0.8	0.048
Calories received at the 7th day after admission (kcal/kg/day)	55.3 ± 24.6	52.5 ± 27.7	0.691
Protein received at the 7th day after admission (g/kg/day)	1.7 ± 0.9	1.4 ± 0.8	0.210
Mortality n (%)	2 (9.5%)	7 (14%)	0.605

Supplementary Table 2.			
	Mechanical Ventilation (n:56)	**No Mechanical Ventilation (n:55)**	**p-value***
Calories received at the end of the first 48 hours after admission (kcal/kg/day) (n=104)	39.4 ± 26.3	44.3 ± 32.2	0.605
Calories received at the 5th day after admission (kcal/kg/day)(n=88)	43.8 ± 26.5	47.1 ± 24.8	0.373
Calories received at the 7th day after admission (kcal/kg/day) (n=80)	46.4 ± 26.9	55.0 ± 23.5	0.095
*Mann-Whitney U Test			

Supplementary Table 3.								
Variables in the backward logistic regression Equation (Sepsis)								
							95% C.I.for EXP(B)	
	B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(B)**	**Lower**	**Upper**
Calories received at the end of the first 48 hours after admission	.075	.032	5.444	1	.020	1.078	1.012	1.149
Protein received at the end of the first 48 hours after admission	-1.621	.841	3.716	1	.054	.198	.038	1.027
Calories received at the 7th day after admission	-.038	.021	3.143	1	.076	.963	.923	1.004
Constant	-.603	.533	1.280	1	.258	.547		
Variables in the backward logistic regression Equation (Mechanical Ventilation)								
	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Protein received at the 7th day after admission	-.714	.339	4.437	1	.035	.490	.252	.952
Constant	1.466	.585	6.279	1	.012	4.333		