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Effect of high or low protein nutrition on diaphragm thickness using ultrasonography in mechanically ventilated intensive care patients

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ABSTRACT

Background: Diaphragmatic dysfunction is associated with difficulties from weaning and have worse patient outcomes in intensive care unit (ICU). It is still not clear how to prevent diaphragmatic dysfunction. Protein may be one of the modifiable factors that can prevent diaphragmatic dysfunction. We aimed to compare the effects of low protein and high protein support on diaphragm thickness using ultrasonography in mechanically ventilated patients in the ICU.

Methods: This study was performed in intensive care patients over the age of 18 who were mechanically ventilated and administered enteral nutrition. Patients were randomly (using a computer-generated list: 1/1 block randomization) allocated to low protein group (1.1 g/kg/day) or a high protein group (1.5 g/kg/day). The patients' demographics, diagnosis and comorbidities, length of stay (APACHE II), NRS 2002 scores were recorded on the first day of intubation. Diaphragm thickness and mid arm muscle circumference measurements were taken on the 1st, 7th, and 14th days on mechanically ventilation and day of weaning.

Results: 42 Intubated critically ill patients (age 69 ± 15 years, 12 women/30 men) enrolled in this study. Demographics BMI, Apache II score, duration of mechanical ventilation, length of intensive care stay and hospital stay were not different between groups. The diaphragm thickness measured on the 7th day was 1.81 ± 0.29 mm (n=21) in low protein group and 2.00 ± 0.23 mm (n=21) in the high protein group (p= 0.028). The diaphragm thickness measured on the weaning day were 1.73 ± 0.14 mm (n=9) and 2.01 ± 0.21 mm (n=10) in the low protein group and in the high protein group respectively (p= 0.004).

Conclusions: Large-scale and long-term studies on this subject may help reveal the differences between the high protein and low protein support for ICU patients.

Keywords: diaphragm, malnutrition, mechanical ventilation, nutrition, nutritional assessment, proteins

Introduction

Critical illness is associated with a protein catabolic state, causing in muscle wasting ICU patients. Loss of muscle mass and function during ICU has a negative impact on long-term quality of life as well as short- and long-term outcomes. Mechanical ventilation is one of the most important treatments in ICU. Mechanically ventilated patients have difficulties being weaned from mechanical ventilation when respiratory support is no longer needed.[1] Mechanical ventilation has also negative effects on respiratory muscles that causes atrophy and

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dysfunction in the diaphragm muscle.[2] The diaphragm is the main muscle involved in ventilation, and its dysfunction causes various respiratory complications.[3] Diaphragmatic ultrasonography has recently become a valuable tool in intensive care for the evaluation of diaphragmatic dysfunction.[4]

Insufficient protein intake and increased protein loss cause weakening of the respiratory muscles, especially the diaphragm, and deterioration of their structure and function. Current American and European nutrition guidelines recommend 1.2–2.0 g/kg/day and 1.3 g/kg/day, respectively, for protein support in the absence of high-quality studies.[5,6] In the systematic review and meta-analysis of nineteen randomized controlled trials (n=1731 patients), Lee at al.[7] compared higher vs lower protein delivery (with similar energy delivery between groups) in critically ill patients. The pooled mean protein delivery for the higher versus lower protein group were 1.31±0.48 vs 0.90±0.30 g/kg/day respectively. They reported that a 0.48 g/kg/day higher protein support didn't show any significant effect on mortality and other outcomes. On the other hand, higher protein, was linked to a tendency toward shorter mechanical ventilation and ICU length of stay. Higher protein was related with a shorter duration of mechanical ventilation (0.73 days) and a one-day reduction in the length of stay in the ICU ($p = 0.07$), in the subset group of trials. Higher protein delivery is associated with a muscle loss attenuation (−3.44% per week, 95% CI −4.99 to −1.90, $p<0.0001$) in five studies.

In this study, it was aimed to compare low protein and high protein support on diaphragm thickness using ultrasonography in patients undergoing invasive mechanical ventilation in the ICU.

Main Points

- Mechanical ventilation causes atrophy and dysfunction in the diaphragm muscle.
- Diaphragma ultrasonography is a valuable tool in intensive care for the evaluation of diaphragmatic dysfunction.
- Insufficient protein intake and increased protein loss cause weakening of the respiratory muscles, especially in the diaphragm.
- So, nutrition must include adequate provision of protein. This is particularly important for icu patients.

Materials and Methods

After the Local Ethics Committee of the Pamukkale University, Medical School, this study was performed in 42 intensive care patients over the age of 18 who were mechanically ventilated and administered enteral nutrition. Patients with known primary or secondary muscle disease (systemic disorders secondary affect the skeletal muscle manifesting as myositis or rhabdomyolysis) , anatomical diaphragm malformation, chronic obstructive pulmonary disease, severe malnutrition (BMI<18,5 kg/m2 if <70 years old or BMI <20 kg/m2 if >70 years old) advanced organ failure, mechanical ventilation support for more than 24 hours in the ICU in the 6 months prior to inclusion, those who required positive end expiratory pressure ≥ 20 cm H_2O and FiO_2 > 60% during indirect calorimetry measurement, and those whose enteral feeding was discontinued were excluded from the study.

Patients who received enteral nutrition under mechanical ventilation support in the ICU were divided into two groups by randomization using a computer-generated list (1: 1 block randomization), with 21 patients in each group such as low protein group (1.1 g/kg/day) or a high protein group (1.5 g/kg/day).

After the patients admitted the ICU with stable hemodynamics and enteral nutrition was indicated, enteral nutrition was started within 24–48 hours. In the ICU, the intensive care team inserted a 12F feeding tube into the patients.The position of the tube was confirmed by taking a chest radiograph, followed by enteral nutrition with a standard or protein-rich polymeric formula. For the low protein group, Nutrison (Nutricia, Zoetermeer, the Netherlands; 1 mL/kcal; this product provided 20 g protein, 19.5 gr fat, 61.5 gr carbohydrate /500 mL) was used. For the high protein group, Nutrison Protein Plus (Nutricia, Zoetermeer, the Netherlands; 1.25 kcal/1 mL; this product provided 31.5 g protein, 24.5 gr fat, 71 gr carbohydrate /500 mL) was used. Enteral feeding was started at the flow rate of 20 mL/h in the ICU and was increased by 20 mL/h every 6 h, depending on clinical signs of intolerance, until the target calorie rate was reached. Residual gastric volumes was routinely monitored as a measure of digestive intolerance four times daily. Patients who developed high gastric residue (greater than 300ml in 12h) within the first 24h of the enteral nutritional therapy, intravenous metoclopramide were given. In both groups, the resting energy expenditure of the patients was measured daily by indirect calorimetry using the Datex Ohmeda M-CAiOVX module (Datex- Ohmeda, Finland). Actual nutrition delivery was monitored daily based on the volumes delivered relative to the predefined daily caloric targets. If there was a feeding interruption due to gastric intolerance the delivery rate was not increased after resumption to compensate for the interruption and feeding was resumed at the initial rate after 6 hours without a new episode of intolerance. The rate of administration was not increased to compensate for nutrition not received. For all patients who underwent enteral nutrition, the head of the bed was kept in an upward position of 30–45 degrees.

Diaphragm thickness and mid arm muscle circumference measurements were taken on the 1st, 7th, and 14th days on mechanically ventilation and day of weaning from the ventilator. Mid arm muscle circumference measurements were obtained from the same location using a skin marker. Patient age, gender, body mass index, hospitalisation diagnosis and comorbidities, acute physiology and chronic health evaluation (APACHE II), NRS 2002 scores and daily hemogram, albumin, and total protein values were also recorded. Total protein and albumin values were measured on the 1^{st} day, 7^{th} day, 14^{th} day, and day of weaning from mechanical ventilation. Patients were fed the same enteral nutrition product during mechanical ventilation. Thirteen patients in the low protein group and sixteen patients in the high protein group have 14^{th} day measurements for diaphragm thickness and mid arm muscle circumference. Nine patients in the low protein group and 10 in the high protein group were successfully weaned from mechanical ventilation within 21 days. Measurements were performed in these patients.

Measurements

The diaphragm was visualised by placing the ultrasonography probe vertically between the 9^{th} and 10^{th} ribs between the anterior-mid-axillary lines while the patient was in the supine position. Diaphragm thickness was measured at the end of expiration with ultrasound using a 6–13 MHz linear probe in B mode. Measurement with ultrasound was performed only by the responsible authors.

Indirect calorimetry measurements were started after haemodynamic stability was achieved in the intubated patients who were admitted to our ICU. Indirect calorimetry measurements were performed in the first 24–48 hours after admission to the ICU, with the Datex-Ohmeda M-CAiOVX module (Datex-Ohmeda, Helsinki, Finland) for 24 h without interruption. Average of the measurements was recorded by pressing the "trend" button and enrolled. Measurements were repeated daily by trained staff during mechanical ventilation and enteral nutrition therapy.

Statistical analysis

As a result of the power analysis made hypothetically in the direction of expectations, assuming that a strong degree effect size (d=0.8) will be obtained for the difference to be obtained between the two groups It has been calculated that at least 42 people (21 people for each group) should be included in the study in order to achieve 80% power with 95% confidence. The data were analysed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY). Continuous variables were presented using the mean ± standard deviation, median, and minimum–maximum value. The number and percentage calculations were performed for categorical variables. When the parametric test assumptions were met, the independent-samples T test and one-way analysis of variance were used for the enteral nutrition groups to compare the differences between the groups. In cases where the parametric test assumptions were not met, the Mann–Whitney U test and Friedman repeated-measures analysis of variance were used to compare the differences between the enteral nutrition groups. Pearson's chi-square test was applied to compare categorical variables and examine the relationship between the variables of the two groups. Median values were compared to determine statistical significance.

Results

The mean age of 42 patients included in the study was 69.00 ± 15.69 years. The mean height, weight, and body mass index were 164.52 ± 6.61 cm, 67.48 ± 10.35 kg, and 25.54 ± 3.93, respectively. There were 12 women (28.6%) and 30 men (71.4%). Higher NRS 2002 scores were obtained in the high protein group (Table 1). Pneumonia was the most admission diagnosis (31/42 patients). Other reasons for icu admission were pulmonary edema (3/42 patients), massive pulmonary embolism (2/42 patients), diabetic foot ulcer (2/42 patients), acute heart failure (2/42 patients), pneumococcal meningitis (1/42 patients) and acute intraalveolar hemorrhage (1/42 patients).

During the study, the number of patients decreased because there were patients who were extubated, died or transferred to another hospital before the 14^{th} day and the weaning day. There were totally 29 patients on 14^{th} day and 19 patients on the weaning day.

Table 1. Demographic data of the patients and analysis results of some variables according to enteral nutrition status

Parameters	Low Protein (n=21)	High Protein (n=21)	p
Age (Year)	64.38 ± 18.16	73.62±11.41	0.055
Sex (F/M)	8 (%38.1)	4 (%19)	0.153
Height (cm)	163.33 ± 7.80	165.71±5.07	0.248
Weight (kg)	65.10 ± 9.47	69.86±10.87	0.138
BMI	24.33 ± 2.75	25.38±4.20	0.347
NRS 2002	3.81 ± 0.60	4.29 ± 0.46	0.006
APACHE 2	13.62 ± 3.81	15.05 ± 2.50	0.158
Energy requirement (kcal)	1877.71 ± 154.19	1900±64.67	0.541
MV time (day)	24 ± 25.48	21.48±12.69	0.687
Length of ICU stay (day)	27.33 ± 24.06	25.43±11.34	0.744
Length of hospital stay (day)	32.33 ± 26.58	30.71±11.98	0.801

*p<0.05, statistically significant difference; mean; SD: standard deviation

Table 2. Diaphragm thickness measurements on day 1, day 7, day 14, and on the day of weaning from mechanic ventilation

	Low Protein n=21		High Protein n=21		p value
	Mean ± SD (mm)	Median (Min–max)	Mean ± SD (mm)	Median (Min–max)	
Day 1	1.94 ± 0.27	1.80 (1.70–2.90)	2.10 ± 0.23	2.20 (1.7–2.50)	0.054
Day 7	1.81 ± 0.29	1.70 (1.50–2.90)	2.00 ± 0.23	2.00 (1.70–2.40)	0.028
Day 14	1.80 ± 0.33 (n=13)	1.70 (1.50–2.80)	1.86 ± 0.25 (n=16)	1.95 (1.50–2.30)	0.628
Day of weaning	1.73 ± 0.14 (n=9)	1.70 (1.60–2.00)	2.01 ± 0.21 (n=10)	2.00 (1.70–2.40)	0.004

*p<0.05 statistically significant difference; SD, standard deviation; Min–max, minimum and maximum values

Diaphragm thickness measurements on the first day and 14th day did not show a statistically significant difference between groups. There was a statistically significant difference in diaphragm thickness measurements on the 7th day and on the day of weaning from mechanical ventilation between the groups (Table 2). Diaphragm thicknesses of the patients showed a significant difference within groups on 7th day, 14th day, and day weaning from mechanical ventilation for both groups. Diaphragm thickness levels tended to decrease with time in both groups (Table 3). We found that the decrease in diaphragm thickness in the first 7 days was 0.10 mm in the high protein group and 0.13 mm in the standard protein group.

Mid arm muscle circumferences data did not show statistically significant difference between groups (Table 4). Measured energy expenditure data did not different between groups (Table 1). There was not any difference between groups according to the total protein and albumin levels (Table 5, Table 6). No statistically significant differences in protein and albumin levels were found within the groups. (Table 5, Table 6). Duration of ICU stay; mechanical ventilation time and hospital stay of the groups were similar

Discussion

In this study, it was compared high protein (1.5 g/kg per day) enteral nutrition with low protein enteral nutrition (1.1 g/kg per day) on diaphragm thickness using ultrasonography and outcomes in patients undergoing invasive mechanical ventilation in ICU. There was no statistically significant difference between groups in the first and 14th day control measurements of diaphragm thickness. This may be related to the low number of intubated patients on the 14th day. On the 14th day, the

Table 3. Changes in diaphragm thicknesses measurements within group					
Group	**Measurement**	**Mean ± SD**	**Median (Min–max)**	**P**	**Difference**
Low Protein	Day 1	1.94 ± 0.27	1.80 (1.70–2.90)	0.000* §	1 – 2* ‡ 1 – 3* ‡ 1 – 4* ‡ 2 – 3* ‡ 2 – 4* ‡
	Day 7	1.81 ± 0.29	1.70 (1.50–2.90)		
	Day 14	1.80 ± 0.33 (n=13)	1,70 (1,50 – 2,80)		
	Day of weaning	1.73 ± 0.14 (n=9)	1.70 (1.60–2.00) (n=10)		
High Protein	Day 1	2.10 ± 0.23	2.20 (1.7–2.50)	0.000* §	1 – 2* ‡ 1 – 3* ‡ 1 – 4* ‡ 2 – 3* ‡ 2 – 4* ‡
	Day 7	2.00 ± 0.23	2.00 (1.70–2.40)		
	Day 14	1.86 ± 0.25 (n=16)	1.95 (1.50–2.30)		
	Day of weaning	2.01 ± 0.21 (n=10)	2.00 (1.70–2.40)		

*p<0.05 statistically significant difference; SD: standard deviation; Min–max: minimum and maximum values; 1: day 1; 2: day 7; 3: day 14; 4: day of weaving from mechanical ventilation; §: Wilcoxon repeated two-measure difference test; ‡: Friedman repetitive ANOVA.

Table 4. Mid arm muscle circumference measurements on day 1, day 7, day 14, and on the day of weaning from mechanic ventilation					
	Mid arm muscle circumference Low Protein n=21		**High Protein n=21**		**P value**
	Mean ± SD (cm)	**Median (Min–max)**	**Mean ± SD (cm)**	**Median (Min–max)**	
Day 1	25,31±3,60	26 (18 – 30)	23,66±3,89	27 (19,5-31,5)	0.470
Day 7	24,38±3,55	25 (17 – 28)	23,70±6,68	26 (18,5-30)	0.583
Day 14	24,46±3,38(n=13)	24 (16 – 28)	23,66±3,89 (n=16)	23,75 (17-29	0.562
Day of weaning	23,67±3,95(n=9)	23,5 (18 – 28)	23,70±3,68 (n=10)	23,25 (19-29)	0.985

*p<0.05 statistically significant difference; SD, standard deviation; Min–max, minimum and maximum values.

Table 5. Blood total protein levels of the groups					
	Low Protein (n=21)		**High Protein (n=21)**		**P**
	Mean ± SD	**Median (Min–max)**	**Mean ± SD**	**Median (Min–max)**	
Day 1	5.46 ± 0.71	5.60 (4.10–6.50)	5.66 ± 0.91	5.70 (3.59–7.30)	0.430
Day 7	5.35 ± 0.81	5.30 (3.60–6.70)	5.40 ± 0.70	5.50 (4.01–6.75)	0.834
Day 14	5.07 ± 0.68 (n=13)	5.01 (3.59–6.10)	5.32 ± 0.64 (n=16)	5.25 (4.40–6.60)	0.322
Day of weaning	5.97 ± 0.53 (n=9)	6.07 (4.90–6.70)	5.54 ± 0.74 (n=10)	5.90 (3.90–6.10)	0.181

*P<0.05 statistically significant difference; SD: standard deviation; Min–max: minimum and maximum values.

number of intubated patients was 29. However, there was a statistically significant difference between the two groups in the measurements on the 7th day and the day of weaning from the mechanical ventilator. Diaphragm thickness decreased as the measurement period progressed in both the groups. In addition, in our study, we found that the decrease in diaphragm thickness in the first 7 days was 0.10 mm in the high protein group and 0.13 mm in the low protein group. It caught our attention that the difference of 0.03 mm was in favour of the high protein group, but we could not find any statistical significance.

A protein catabolic condition associated with critical illness causes significant muscle atrophy when a patient is in the ICU. It has been observed that ICU patients lose

Table 6. Blood albumin levels of the groups					
	Low Protein (n=21)		**High Protein (n=21)**		**P**
	Mean ± SD	**Median (Min–max)**	**Mean ± SD**	**Median (Min–max)**	
Day 1	3.05 ± 0.5	3.03 (2.06–3.80)	3.01 ± 0.57	3.17 (1.56–3.87)	0.810
Day 7	2.80 ± 0.52	2.87 (1.89–3.83)	2.62 ± 0.38	2.53 (2.06–3.38)	0.217
Day 14	2.73 ± 0.53	2.92 (1.76–3.83)	2.56 ± 0.57	2.61 (1.68–3.53)	0.311
Day of weaning	2.81 ± 0.57	2.94 (1.94–3.70)	2.54 ± 0.67	2.62 (1.61–3.57)	0.209

*p<0.05, statistically significant difference; mean mean; SD: standard deviation; Med: median; min–max: minimum and maximum values.

about 10% of muscle mass during the first 10 days of ICU admission.[8] Attenuating the catabolic state during critical illness could be one way to improve quality of life and post-ICU functional recovery while also slowing down the amount of muscle loss. For healthy individuals, maintaining muscle mass is crucial and requires dietary protein, which is a significant anabolic stimulation. Multinational, registry-based, randomised, single-blind, research was conducted in 85 ICU in sixteen countries. In order to compare the prescription of high-dose protein (≥2.2 g/kg per day) with usual dose protein (≤1.2 g/kg per day), they enrolled nutritionally high-risk adults (≥18 years) undergoing mechanical ventilation. The nutrition was started within 96 hours of ICU admission and continued for up to 28 days, or until death or the start to oral feeding. There were no differences in 60-day mortality or time-to-discharge-alive between the groups in their study. They suggested that excessive protein may be detrimental to patients who are admitted to the ICU and who have acute renal injury.[9]

Recent meta-analysis was published by van Ruijven et al.[10] was included 29 studies written between 2012 and 2022 were included. They included that studies including patients ≥18 years with an ICU stay of ≥2 days and a administered mean amount of protein ≥1.2 g/kg as compared to <1.2 g/kg. They reported outcomes such as ICU and hospital length of stay, ICU, hospital, 28-day, 30-day, 42-day, 60-day, 90-day and 6-month mortality, length of mechanical ventilation, gastric residual volume, vomiting, diarrhoea, infections, nitrogen balance, destination at hospital discharge, changes in muscle mass, physical performance and psychological status. Muscle mass changes were measured between baseline and five weeks after admission. They showed differences between groups in favour of high protein support for sixty-day mortality, nitrogen balance and changes in muscle mass. Muscle mass changes was reported in six studies which included total of 187 patients. They reported a significant difference between groups in favour of high protein. We could not find a difference for diaphragm thickness in our study. This may be since our study was a shorter study than their study or may be the different muscle mass.

In critical illness, diaphragmatic dysfunction and muscle wasting are recognised to be associated with each other and bigger catabolic activity may be seen in the diaphragm after only fifteen h of mechanical ventilation.[11] Animal and human studies in recent years have shown that also mechanical ventilation causes diaphragm dysfunction and atrophy of the respiratory muscles. Levine et al.[12] conducted a similar study in humans and showed that there was significant atrophy of myofibrils in the patient group that underwent 18–69 hours of mechanical ventilation and related diaphragm inactivity. The course of diaphragmatic atrophy in mechanically ventilated patients was evaluated using the ultrasound, and it was shown that mechanical ventilation causes atrophy in the diaphragm, decreases in diaphragm muscle thickness, and the greatest decrease in diaphragm thickness occurs during the first 72 h of mechanical ventilation.[13] In addition, the degree of atrophy was associated with the duration of mechanical ventilation. Similarly, the decrease in diaphragm thickness was directly proportional to time, and the mean diaphragm thickness decreased as the measurement days progressed in our study.

In the multicentre observational study, it was aimed search modifiable risk factors for loss of diaphragmatic function during mechanical ventilation. They studied one hundred and twenty-six critically ill patients who were ventilated for at least forty eight h and used ultrasound imaging to prospectively identify patients who experienced diaphragmatic dysfunction. They reported that patients who experienced diaphragmatic dysfunction were two times more likely to die, eight times more likely to develop extubation failure and required longer ICU stays. Amino acid intake during the first 24 h of ICU admission found the only significant independent predictors of diaphragmatic dysfunction. Amino acid intake during the first 24 h of ICU stay might reduce the relative risk of developing diaphragmatic dysfunction (10 to 48%) and might reduce the relative risk of mortality (25 to 73%).[14] In our study, diaphragm thickness decreased as the measurement period progressed in both the groups. Although the 0.03 mm difference for diaphragm thickness in favour of the high protein group, we were unable to determine any statistical significance.

In a randomised controlled study by Nakamura et al.[15], patients in ICU were divided into two groups, and the same calorie target was achieved with high-protein nutrition in one group and standard protein nutrition in the other. Patients in both groups underwent rehabilitation with electrical muscle stimulation throughout the treatment, and femoral muscle volume was evaluated using computed tomography on the 1st and 10th days. The decrease in the femoral muscle volume was lower in the high-protein group. Albumin levels were compared on the 10th day, and no significant differences were observed. Albumin levels of the patients did not show a statistically significant difference between the groups in our study.

In a meta-analysis published in 2017, the amount of protein administered to intensive care patients and its effects on mortality, hospital stay, mechanical ventilation, and infection incidence were investigated. It showed that administration of different amounts of protein to patients had no effect on mortality. In addition, there was no significant difference between the patient groups receiving high protein and low protein in terms of length of hospital stay, duration of mechanical ventilation, and incidence of new pneumonia and bacteraemia.[16] We also found no statistically significant difference between the groups in terms of APACHE II score, mechanical ventilation time, length of ICU stay, and length of hospital stay.

Mid arm circumference measurement is considered as a useful indicator of muscle mass and nutritional status.[17] In our study, mid arm muscle circumference measurements did not show statistically significant difference between groups. This may be related to preexisting protein-energy malnutrition, sarcopenia, immobility, and disuse-related muscle atrophy in all patients.[18]

The NRS 2002 screening test is related to the degree of malnutrition. Although our patients in the protein rich group were at risk of severe malnutrition, we observed less thinning in the diaphragm thickness in this group in our study. High protein nutritional support may have affected this result.

Our study has some limitations. First, this study involved a small number of participants. Furthermore, a follow-up period of more than 14 days and a larger number of patients may be needed to show the effect of high protein nutrition on diaphragmatic thickness. We also did not record the presence of sepsis, steroid use, vasopressor use, or their effects on the diaphragm, which may have caused diaphragmatic dysfunction. Protein dosing may not be achieved reasonable between-group separation of actual protein dose delivered. We did not calculate the actually delivered protein doses. We provided the nutrition required to reach the target calories by using enteral products with high or standard protein content. The NRS 2002 scores were not the same between the groups, which may have affected the study results.

Conclusion

In this study, we found statistically significant difference between the two groups in the measurements on the 7th day and the day of weaning from the mechanical ventilator. But there was no statistically significant difference between groups in the first and 14th day control measurements of diaphragm thickness. Also, there was no significant difference between the two enteral nutrition groups in terms of diaphragm mid arm muscle circumference measurements, duration of mechanical ventilation, length of hospital stays and length of stay in the ICU. Large-scale and long-term studies on this subject may help reveal the differences between the high protein and low protein support for ICU patients.

Ethical approval

This study has been approved by the Pamukkale University Faculty of Medicine (approval date 30.08.2018, number 03). Informed consent was obtained from patients' relatives.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: DH, HS; data collection:

DH, HS; analysis and interpretation of results: DH, HS; draft manuscript preparation: DH, HS. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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