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Impact of High-Protein Enteral Feeding on Skeletal Muscle Mass Changes in Critically Ill Patients: A Randomized Controlled Trial

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Abstract

Background: Increased protein intake is recommended for critically ill patients to prevent muscle breakdown and weakness. In this study, researchers compared protein delivery and muscle loss in mechanically ventilated intensive care unit (ICU) patients receiving high-protein enteral nutrition with those receiving standard care.

Methods: This was a randomized, open-label, controlled clinical trial conducted at a mixed medical-surgical ICU. Mechanically ventilated adult patients (age ≥18 years) who required enteral nutrition (EN) for at least 72 hours were randomized to receive either the intervention (target protein delivery of 1.5 g/kg per day) or standard care (provide 1.0 g/kg/day protein). Ultrasonography measured the muscle thickness of the biceps brachii for assessment at baseline and days 3, 6, 9, 12, 15, 18, and 21 after randomization. Adequacy of nutritional support was determined by measuring nitrogen balance (NB) at days 3 and 5 after the intervention. Descriptive statistics were used to summarize patient characteristics, and baseline demographic and clinical data were compared between groups using chi-square tests and independent samples t tests. Generalized estimating equations (GEE) were employed to analyze longitudinal data, assessing the effects of time, treatment group, and diabetes mellitus on muscle outcomes, while addressing missing data with the Last Observation Carried Forward method. The primary outcomes, changes in muscle mass and mid-upper arm circumference, were compared between treatment groups using independent samples t tests and further evaluated with analysis of covariance models adjusted for covariates.

Results: A total of 100 patients were studied in high protein (n = 50) and low protein (n = 50) groups. The mean muscle loss in the high-protein group [mean, -0.06 [95% CI, -0.09 to -0.02)] was significantly lower than the low-protein group [mean, -0.27 [95% CI, -0.34 to -0.22)] ($P < 0.001$). Patients in the high-protein group exhibited significantly higher nitrogen balance values compared to those in the low-protein group on day 3 ($P < 0.001$) and day 5 ($P < 0.001$).

Conclusion: This study showed that high-protein EN might have positive effects to attenuate the muscle loss and improve the nutritional status of mechanically ventilated ICU admitted patients.

Keywords: Intensive Care Unit, Muscle Loss, Protein, Ventilation

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Introduction

Muscle weakness and atrophy are common problems in critically ill patients and are associated with longer hospital length of stay (LoS) and a higher rate of morbidity, mortality, and rehospitalization (1, 2).

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↑What is "already known" in this topic:
Generally, patients hospitalized in the intensive care unit experience muscle loss. According to previous research, increasing the protein intake in patients' diets leads to an increase in muscle mass.

→What this article adds:
In this study, they used ultrasound to conduct this examination. They examined the biceps muscle of the patients participating in the test and ultimately confirmed the findings of previous studies.

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Prolonged bed rest, increased protein catabolism, and malnourishment are among the possible causes of skeletal muscle atrophy in critically ill patients (3). High protein demand during critical illness leads to enhanced skeletal muscle degradation for providing amino acids necessary for the synthesis of other proteins, such as acute phase reactants and other inflammatory factors (3). Distinct muscle wasting occurs early and rapidly during the first week of intensive care unit (ICU) stay and progressively worsens afterward (4). Remarkably reduced muscle mass was observed up to a year after ICU discharge (5). Preexisting malnutrition might be a risk factor for adverse events in patients who survive a critical illness (1).

Diagnosis and monitoring of muscle weakness and wasting are challenging in unconscious and mechanically ventilated patients because careful clinical examination requires cooperative patients. Ultrasonography is among the most valuable methods for screening for muscle atrophy in ICU-admitted patients (6). It is noninvasive and readily available at the bedside and applies to all patients regardless of their consciousness level (7).

To alleviate a negative protein catabolic state, recently published guidelines on clinical nutrition have recommended higher protein intake (1.2-2 g/kg per day) in critically ill patients as compared with healthy adults (0.8 g/kg per day) (8-10). Several observational studies demonstrated that higher protein intake is associated with improved outcomes in ICU patients (11-14). In 1 observational study, 17% lower risk of 90-day post-ICU discharge mortality was found for each 1g/kg increase in daily protein delivery (15). Optimal protein provision might also improve muscle function and hamper muscle loss (16, 17). Due to the small sample size and heterogeneity of previous observational studies, the correct interpretation of current data is difficult. Therefore, there is a substantial need for well-designed randomized clinical trials to assess the impact of high protein intake on clinical outcomes of ICU patients. The primary aim of the present study was to compare protein delivery and muscle loss among mechanically ventilated ICU patients who received a high-protein EN and standard care.

Methods

Study Design

This study was a randomized, open-label, controlled clinical trial conducted at the mixed medical-surgical intensive care unit of Imam Hossein Hospital, a referral teaching hospital associated with Shahid Beheshti University of Medical Sciences. The trial was carried out following the guidelines set forth by the International Conference on Harmonization for Good Clinical Practice and the Declaration of Helsinki.

Patients

Mechanically ventilated adult patients (age ≥18 years) who were admitted to the ICU and required EN through nasoenteric tube for at least 72 hours were eligible. We excluded patients with a Glasgow Coma Scale (GCS) of <5, fewer than 2 sonographic evaluations, unstable arm fractures, lacerations and infections of the arm, upper extremity paresthesias, thromboembolism of the upper extremities, musculoskeletal conditions, end-stage renal disease (ESRD), liver disease, and pregnant women. We also excluded patients whose stay in the ICU lasted <72 hours.

Intervention

The intervention group was administered enteral nutrition (EN) utilizing a high-protein formula aimed at achieving a target protein intake of 1.5 g/kg per day. The control group received standard nutrition care protocol, which aims to provide 1.0 g/kg/day protein. The assigned EN protocol was continued after intervention until 1 of the following events occurred: ICU discharge, death, extubation, change in route of nutrition delivery, or day 21. The need for changing the route of nutrition delivery or parenteral nutrition (PN) was determined by treating physicians who were not among the study investigators.

Sample Size

By reviewing similar studies, we assumed that the pooled standard deviation (SD) and effect size for the primary outcome (muscle mass) were 0.42 and 0.25, respectively (16, 17). Taking into account a 2-sided α of 0.05 and β of 0.20, it was determined that a total of 45 patients in each treatment group was required to achieve a minimum statistical power of 80%. By accounting for an anticipated 10% missing data rate, the final sample size needed per group was calculated to be 50. The following formula was used for sample size calculation:

$$n = 2 \times \left(\frac{(Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \times SD^2}{d^2}\right)$$

Randomization

Eligible patients were randomly assigned in a 1 to 1 ratio to either receive the intervention or standard care. Group allocation was performed using permuted block randomization with a block size of 4. Initially, we estimated a sample size of 100 participants to ensure statistical power, accounting for potential dropouts. To accommodate potential early dropouts and maintain the integrity of group allocations, we prepared a randomization list for 120 participants. This approach was intended to preemptively address any unforeseen reductions in participant numbers due to early exclusion from the study, which are not uncommon in clinical studies of this nature. During recruitment, depicted in Figure 1, six patients were excluded due to early death or extubation, finalizing recruitment with 100 participants. A randomization list was created using software that generates random numbers. Although the study was open-label due to the nature of the intervention, outcome assessment and statistical analyses were blinded. A blinded investigator undertook all outcome measurements to minimize detection bias. In addition, the individual responsible for conducting the statistical analyses was also blinded to the group allocation, further reducing the risk of bias in data interpretation. The pharmacist securely held the randomization list for the duration of the study.

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Clinical Measurements

Patient Characteristics

Patients' characteristics, comorbidities, admission diagnosis, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and admission Sequential Organ Failure Assessment (SOFA) score were recorded at baseline.

Muscle Outcomes

Diagnostic 2-dimensional ultrasonography was used to measure muscle thickness of the biceps brachii, according to the protocol determined by Reid et al (18), at baseline and days 3, 6, 9, 12, 15, 18, and 21 after randomization. Patients were asked to lie supine with the elbow passively extended and the forearm supinated. The probe was located midway between the tip of the acromion and the tip of the olecranon. A single experienced radiologist performed all ultrasound measurements. Mid-upper arm circumference (MAUC) at the mid-point between the tip of the acromion and olecranon was measured at baseline and day 3, 6, 9, 12, 15, 18, and 21 after randomization via a flexible measuring tape.

Nitrogen Balance

Adequacy of nutritional support was determined by measuring nutrition balance (NB) at days 3 and 5 after the intervention. Urinary urea nitrogen (UUN) excretion was evaluated by 24-hour urinary collection. The NB was calculated by subtracting nitrogen losses from nitrogen intake according to the standard formula: total protein intake (g)/6.25 –(UUN + 4 g).

Statistical Analysis

Descriptive statistics, including mean and standard deviation (SD), median and interquartile range (IQR), or counts and percentages, were utilized to represent the characteristics of the patients. Baseline demographic and clinical data were compared across groups using chi-square tests for categorical variables and independent samples *t* tests for continuous variables. For repeated measurements for the same patient over time, generalized estimating equations (GEE) were used. This approach provided a robust framework for analyzing longitudinal data, allowing us to assess the impact of time, group allocation (high protein vs standard care), and the presence of diabetes mellitus (DM) as a covariate on muscle outcomes. The GEE models were specified with an exchangeable working correlation structure and a Gaussian family distribution. Missing data were addressed using the Last Observation Carried Forward method. The primary outcome measures, which were the average changes in muscle mass and MUAC calculated as the difference between the initial and final measurements, were compared across treatment groups using independent samples *t* tests. To thoroughly assess the reliability of the treatment effect, analysis of covariance (ANCOVA) models were employed, adjusting for covariates such as baseline values and the number of days spent in the ICU (on the last measurement day) for the muscle outcomes. The data were analyzed using the IBM SPSS Software, Version 25.0. GraphPad Prism Version 10.0 was used to generate plots. Two-tailed testing was conducted, and $P < 0.05$ was considered statistically significant.

Results

During the study period, a total of 106 patients who were admitted to the ICU and mechanically ventilated were randomly assigned to either high protein (n = 53) or low protein (n = 53) groups. Three patients in each group were excluded due to death or extubation before 72 hours (Figure 1). In the remaining patients (50 patients in each group), measurements of MUAC and Biceps brachii muscle thickness were performed at least twice during the study, at baseline and on day 3 (Figure 1). These patients were included for outcome analysis. Baseline demographic data were similar across the study arms (Table 1).

Muscle Outcomes

Changes in muscle mass during the study period are shown in Figure 2. Using GEE, we examined the effects of high protein enteral nutrition versus standard care on muscle thickness in mechanically ventilated ICU patients. The results revealed a significant decrease in muscle thickness over time ($P < 0.001$). However, no significant difference was observed between the high protein and standard care groups in terms of muscle thickness change (B: -0.173; $P = 0.068$). Additionally, DM status did not significantly influence these changes (B: 0.035; $P = 0.750$). However, the mean muscle loss in the high-protein group (mean, -0.06 [95% CI, -0.09 to -0.02]) was significantly lower than the low-protein group (mean, -0.27 [95% CI, -0.34 to -0.22]) (Table 2). The last measured biceps muscle thickness in patients who received high-protein formula (1.5 ± 0.5 cm) was significantly higher than that of patients who received standard care (1.2 ± 0.3 cm) ($P = 0.008$). The difference between the groups continued to be significant even after accounting for baseline thickness and the day of the final measurement ($F = 46.1$; $P < 0.001$).

Changes in MUAC over the study period are shown in Figure 3. The results of GEE demonstrated a significant decrease in MUAC over time ($P < 0.001$). However, no significant difference was observed between the high-protein and low-protein groups regarding the MUAC change (B: -0.294; p = 0.724). These changes were not significantly influenced by DM status (B: 0.960; $P = 0.409$). The difference between groups regarding the last MUAC measured did not reach the level of significance (mean, 0.87 [95% CI, -0.64 to 2.38]; $P = 0.257$). However, the difference was significant after adjustment for baseline MUAC and last measurement day ($F = 77.1$; $P < 0.001$). The mean decrease in MUAC was also significantly higher in the low-protein group (mean, -1.58 [95% CI, -1.86 to -1.30]) compared to the high-protein group (mean, -0.41 [95% CI, -0.55 to -0.27]) (Table 2).

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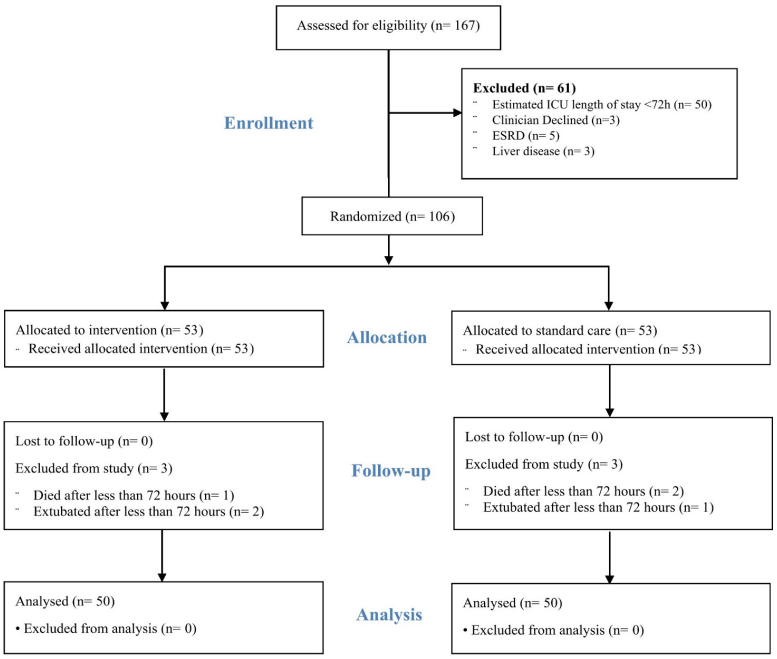

Figure 1. Presents the progression of participants through the phases of the study, including enrollment, allocation, follow-up, and analysis

Table 1. Baseline characteristics of study participants

Demographics	High-protein (n=50)	Standard care (n=50)	*P*-value
Age,y [Mean±SD]	51.5±14.2	52.2±10.8	0.794
Male gender [n (%)]	25 (50.0)	29 (58.0)	0.547
BMI [Mean±SD]	21.6 (2.8)	20.9 (2.7)	0.227
APACHE II score [Mean±SD]	17.7±6.0	17.4±6.0	0.828
SOFA score [Mean±SD]	8.4±2.9	8.1±3.2	0.672
Comorbidities [n (%)]			
Diabetes	14 (28.0)	5 (10.0)	0.040
Hypertension	7 (14.0)	9 (18.0)	0.786
Ischemic heart disease	9 (18.0)	8 (16.0)	1.000
Cerebrovascular disease	12 (24.0)	15 (30.0)	0.487
Malignancy	6 (12.0)	6 (12.0)	1.000
Asthma	2 (4.0)	1 (2.0)	1.000
COPD	1 (2.0)	2 (4.0)	1.000
Epilepsy	0 (0.0)	2 (4.0)	0.495
Thyroid disease	0 (0.0)	1 (2.0)	1.000
Any	39 (78.0)	35 (70.0)	0.495
Admission diagnosis [n (%)]			
Trauma	6 (12.0)	9 (18.0)	0.051
Infection/sepsis	2 (4.0)	2 (4.0)	0.051
Neurologic	24 (48.0)	16 (32.0)	0.051
Cardiovascular	4 (8.0)	0 (0.0)	0.051
Surgical	1 (2.0)	4 (8.0)	0.051
Medical	6 (2.0)	3 (6.0)	0.051
Unspecified	7 (14.0)	16 (32.0)	0.051

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; SOFA, Sequential Organ Failure Assessment; SD, standard deviation
Independent samples t-test was used for comparing age, BMI, APACHE II score, and SOFA score between groups.
Chi-square tests were used for comparing categorical variables (gender, each comorbidity, and admission diagnosis).

The primary outcome, changes in MUAC, was first analyzed using an unadjusted *t* test, which provided an initial *P* value of 0.257, indicating no significant difference between groups. However, given the possibility of baseline imbalances and the need to control for key covariates such as baseline MUAC and the number of days in the ICU, an ANCOVA was subsequently conducted. This model adjusted for these potential confounders, yielding an adjusted *P* value of < 0.001.

The role of the covariates in the ANCOVA model explains the substantial difference between the unadjusted and adjusted P-values. By accounting for baseline MUAC and ICU stay duration, the model isolated the effect of the intervention more effectively. This adjustment highlighted a statistically significant difference between groups that was not apparent in the unadjusted analysis. This adjusted analysis is standard practice to improve the robustness and validity of results, particularly when baseline

[DOI: 10.47176/mjiri.39.114]

Table 2. Study outcomes

Outcome	High-protein (n=50)	Standard care (n=50)	Between-group difference		
			Mean (95% CI)	*P*-value	Adjusted *P*-value[c]
Biceps muscle thickness (cm)					
Baseline[a]	1.5 (0.5)	1.5 (0.4)	0.02 (-0.17 to 0.21)	0.826	-
Last measurement	1.5 (0.5)	1.2 (0.3)	0.24 (-0.42 to -0.07)	0.008	<0.001
Change from[b] baseline	-0.06 (-0.09 to -0.02)	-0.27 (-0.34 to -0.22)	0.22 (0.15 to 0.29)	<0.001	<0.001
MUAC (cm)					
Baseline[a]	29.4 (3.7)	29.8 (4.0)	-0.30 (-1.84 to 1.24)	0.698	-
Last measurement[a]	29.0 (3.7)	28.2 (3.9)	0.87 (-0.64 to 2.38)	0.257	<0.001
Change from[b] baseline	-0.41 (-0.55 to -0.27)	-1.58 (-1.86 to -1.30)	1.17 (0.87 to 1.48)	<0.001	<0.001
Nitrogen balance[a] (g/day)					
Day 3	0.9 (12.6)	-8.4 (14.8)	9.32 (2.46 to 16.17)	0.009	-
Day 5	3.1 (8.4)	-7.3 (20.3)	10.32 (-19.25 to -1.39)	0.024	-
Mortality, n (%)	17 (35.4)	11 (23.9)	-	0.264	-

[a]. Data are shown as Mean (SD)
[b]. Mean (95% CI) is presented.
[c]. Adjusted for baseline values and number of days in the ICU.
Change from baseline values were calculated using paired samples t-tests.
Between-group differences were calculated using independent samples t-tests.
Analysis of covariance (ANCOVA) models with adjustment for baseline values and number of days in the ICU was used to calculate adjusted between-group difference *P*-values.

characteristics could confound the primary outcome.

Nitrogen Balance

As is demonstrated in Table 2, patients within the high-protein group had significantly higher nitrogen balance values compared to the low-protein group at day 3 ($P < 0.001$) and day 5 ($P < 0.001$).

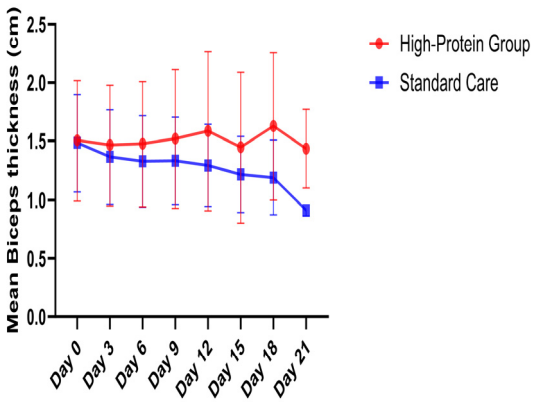

Figure 2. Depicts the changes in biceps muscle thickness over the course of the study, with error bars representing the standard deviation (SD).

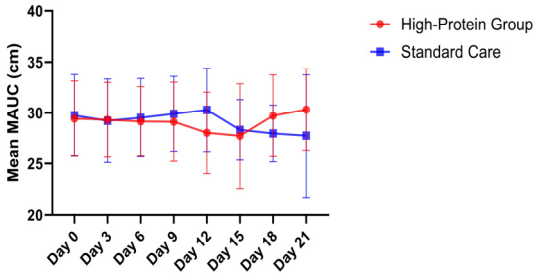

Figure 3. Shows the changes in Mid-Upper Arm Circumference (MUAC) observed during the study period, where error bars indicate the standard deviation (SD).

Mortality Rate

Seventeen patients (34%) in the high-protein group and 11 patients (22%) in the low-protein group died during the study period. There was no significant difference between the study groups regarding the mortality rate ($P = 0.181$) (Figure 4).

Discussion

Appropriate delivery of protein is essential for preventing muscle loss. In this trial, we compared the high-protein enteral feeding protocol and standard care about muscle mass changes in critically ill patients. We demonstrated that high-protein enteral feeding was superior to standard care in attenuation of biceps muscle mass loss. Moreover, in contrast to the standard care group, a positive nitrogen balance was found in the high-protein group, which may indicate that protein delivery was adequate in this group.

Previous observational studies have reported conflicting results regarding the efficacy of high-protein intake in the ICU population (11, 12, 14, 19). Although the majority of these studies reported improved outcomes with higher protein intake (11, 13, 14), harmful associations were also

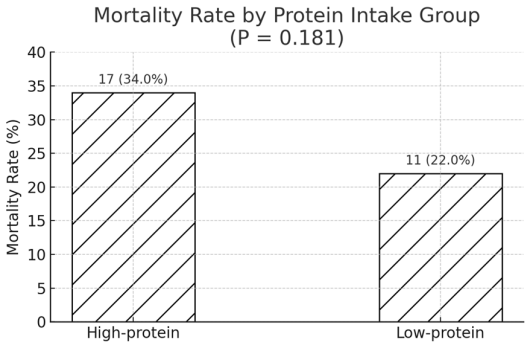

Figure 4. Mortality rates in high- and low-protein groups. No significant difference was observed ($P = 0.181$)

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found with early high-protein delivery (4, 19). Only a few randomized clinical trial studies have evaluated the efficacy of high-protein feeding protocols in these patients (16, 17).

In a study conducted by Ferrie et al (16), standard amino acid delivery (0.8 g/kg) was compared with higher recommended levels (1.2 g/kg) in critically ill patients receiving PN. The authors assessed efficacy via measuring muscle outcomes (handgrip strength, arm, and leg anthropometric and ultrasound measures) as well as fatigue score, nitrogen balance, length of stay, ICU and hospital mortality, and the 6-month mortality rate (16). Although handgrip strength at study day 7 was significantly better in the group receiving the higher level of amino acids, there was no significant difference between groups in handgrip strength at ICU discharge (16). The high amino acid group had significantly smaller fatigue scores (16). Greater forearm muscle thickness (on ultrasonography) and better NB were found in patients receiving a higher level of amino acids, and the mortality rate was similar between the groups (16). Our study has several methodological and nutritional differences from this study (16). First, all our patients received EN, and we excluded patients who shifted to PN. Second, we focused on mechanically ventilated patients. Third, daily protein intake in our patients in both standard care and high-protein groups was higher.

Although accepted clinical guidelines have recommended high-protein intake (1.5-2 g/kg per day) in ICU patients (8, 9), evidence regarding the efficacy of high protein delivery via enteral feeding is limited. In another clinical trial similar to our study, high-protein enteral feeding (1.5 g/kg) was compared with standard care (target protein delivery: 1g/kg) in 60 mechanically ventilated critically ill patients (17). The mean daily protein and energy delivery, change in quadriceps muscle layer thickness (QMLT, ultrasound), malnutrition, mortality, and LoS were the primary outcome measures in this study (17). The authors found that a high-protein feeding protocol provided higher amounts of protein and energy and was associated with significant attenuation of QMLT loss and lower prevalence of malnutrition at discharge (17). Likewise, they did not observe any significant difference between groups regarding the mortality rate and duration of ICU hospitalization (17).

Combined results of the trials mentioned above and the current study may indicate that high-protein delivery in critically ill patients may hamper muscle loss, but has no significant impact on patients' survival.

Study Limitations

The present study has some limitations, such as an open-label design without blinding. Regarding our primary objective, which was the measurement of MUAC, this could not be a source of bias. Also, we did not assess functional muscle outcomes, such as handgrip strength. We recommend conducting multicenter studies with larger sample sizes.

Conclusion

This single-center randomized clinical trial showed that high-protein EN might be effective in attenuating muscle loss and improving the nutritional status of mechanically ventilated ICU-admitted patients. Further randomized clinical trials with primary objective of ICU mortality and morbidity and longer duration of follow-up are needed to address the clinical relevance of high-protein EN in critically ill patients.

Authors' Contributions

M.K. and M.S.: study design. S.S., M.S., and T.S.: literature review, drafting of the proposal, and searching. S.S. and T.S.: data collection. M.S. and R.T.: data analysis and interpretation. All authors contributed to improving the manuscript and finalizing the article for publication.

Ethical Considerations

The protocol of this study was approved by the ethics committee of the Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1398.600). Written informed consent was obtained from the patients or the surrogate decision-maker. This study was registered at the Iranian Registry of Clinical Trials (www.irct.ir), number: IRCT (http://en.irct.ir/trial/ 45326).

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Conflict of Interests

The authors declare that they have no competing interests.

References

1. Weijs PJ, Looijaard WG, Dekker IM, Stapel SN, Girbes AR, Oudemans-van Straaten HM, Beishuizen A. Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients. Crit Care. 2014 Jan 13;18(2):R12.

2. Ju S, Choi SM, Park YS, Lee CH, Lee SM, Yoo CG, Kim YW, Han SK, Lee J. Rapid Muscle Loss Negatively Impacts Survival in Critically Ill Patients With Cirrhosis. J Intensive Care Med. 2020 Jul;35(7):663-671.

3. Arabi YM, Al-Dorzi HM, Sadat M. Protein intake and outcome in critically ill patients. Curr Opin Clin Nutr Metab Care. 2020 Jan;23(1):51-58.

4. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, Hopkinson NS, Phadke R, Dew T, Sidhu PS, Velloso C, Seymour J, Agley CC, Selby A, Limb M, Edwards LM, Smith K, Rowlerson A, Rennie MJ, Moxham J, Harridge SD, Hart N, Montgomery HE. Acute skeletal muscle wasting in critical illness. JAMA. 2013 Oct 16;310(15):1591-600.

5. Chan KS, Mourtzakis M, Aronson Friedman L, Dinglas VD, Hough CL, Ely EW, Morris PE, Hopkins RO, Needham DM; National Institutes of Health National Heart, Lung, and Blood Institute (NHLBI) Acute Respiratory Distress Syndrome (ARDS) Network. Evaluating Muscle Mass in Survivors of Acute Respiratory Distress Syndrome: A 1-Year Multicenter Longitudinal Study. Crit Care Med. 2018 Aug;46(8):1238-1246.

6. Bunnell A, Ney J, Gellhorn A, Hough CL. Quantitative neuromuscular ultrasound in intensive care unit-acquired weakness: A systematic review. Muscle Nerve. 2015 Nov;52(5):701-8.

7. Palakshappa JA, Bakhru RN. Bedside Ultrasonography Can and Should Be Used in the Intensive Care Unit to Evaluate

[DOI: 10.47176/mjiri.39.114]

Muscle Atrophy. Ann Am Thorac Soc. 2019 Sep;16(9):1107-1111.

8. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, Hiesmayr M, Mayer K, Montejo JC, Pichard C, Preiser JC, van Zanten ARH, Oczkowski S, Szczeklik W, Bischoff SC. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019 Feb;38(1):48-79.

9. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, McCarthy MS, Davanos E, Rice TW, Cresci GA, Gervasio JM, Sacks GS, Roberts PR, Compher C; Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016 Feb;40(2):159-211. doi: 10.1177/0148607115621863. Erratum in: JPEN J Parenter Enteral Nutr. 2016 Nov;40(8):1200.

10. Lee ZY, Yap CSL, Hasan MS, Engkasan JP, Barakatun-Nisak MY, Day AG, Patel JJ, Heyland DK. The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. Crit Care. 2021 Jul 23;25(1):260.

11. Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical Outcomes Related to Protein Delivery in a Critically Ill Population: A Multicenter, Multinational Observation Study. JPEN J Parenter Enteral Nutr. 2016 Jan;40(1):45-51.

12. 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 Feb 10;18(1):R29.

13. Weijs PJ, Looijaard WG, Beishuizen A, Girbes AR, Oudemans-van Straaten HM. Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients. Crit Care. 2014 Dec 14;18(6):701.

14. Compher C, Chittams J, Sammarco T, Nicolo M, Heyland DK. Greater Protein and Energy Intake May Be Associated With Improved Mortality in Higher Risk Critically Ill Patients: A Multicenter, Multinational Observational Study. Crit Care Med. 2017 Feb;45(2):156-163.

15. Weijs PJM, Mogensen KM, Rawn JD, Christopher KB. Protein Intake, Nutritional Status and Outcomes in ICU Survivors: A Single Center Cohort Study. J Clin Med. 2019 Jan 4;8(1):43.

16. Ferrie S, Allman-Farinelli M, Daley M, Smith K. Protein Requirements in the Critically Ill: A Randomized Controlled Trial Using Parenteral Nutrition. JPEN J Parenter Enteral Nutr. 2016 Aug;40(6):795-805.

17. Fetterplace K, Deane AM, Tierney A, Beach LJ, Knight LD, Presneill J, Rechnitzer T, Forsyth A, Gill BMT, Mourtzakis M, MacIsaac C. Targeted Full Energy and Protein Delivery in Critically Ill Patients: A Pilot Randomized Controlled Trial (FEED Trial). JPEN J Parenter Enteral Nutr. 2018 Nov;42(8):1252-1262.

18. Reid CL, Campbell IT, Little RA. Muscle wasting and energy balance in critical illness. Clin Nutr. 2004 Apr;23(2):273-80.

19. Koekkoek WACK, van Setten CHC, Olthof LE, Kars JCNH, van Zanten ARH. Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study. Clin Nutr. 2019 Apr;38(2):883-890.

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