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ORIGINAL ARTICLE

Randomized Clinical Trial

Effect of high-protein peptide-based formula compared with isocaloric isonitrogenous polymeric formula in critically ill surgical patient

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Abstract

BACKGROUND

Malnutrition is common in critically ill patients, and it is associated with an increased risk of complications. Early enteral nutrition with adequate caloric and protein intake is critical nevertheless it is difficult to achieve. Peptide-based formulas have been shown to be beneficial in patients with feeding intolerance. However, there are limited studies showing the efficacy and safety of high-protein peptide-based formula in critically ill surgical patients.

AIM

To determine the effects of a high-protein peptide formulation on gastrointestinal tolerance, nutritional status, biochemical changes, and adverse events in patients

in the surgery intensive care unit (SICU) compared to an isocaloric isonitrogenous standard polymeric formulation.

METHODS
This study was a multi-center double-blind, randomized controlled trial. We enrolled adult patients in the surgical intensive care unit, age ≥ 15 years and expected to receive enteral feeding for at least 5-14 d post-operation. They were randomly assigned to receive either the high-protein peptide-based formula or the isocaloric isonitrogenous standard formula for 14 d. Gastric residual volume (GRV), nutritional status, body composition and biochemical parameters were assessed at baseline and on days 3, 5, 7, 9, 11, and 14.

RESULTS
A total of 19 patients were enrolled, 9 patients in the peptide-based formula group and 10 patients in the standard formula group. During the study period, there were no differences of the average GRV, body weight, body composition, nutritional status and biochemical parameters in the patients receiving peptide-based formula, compared to the standard regimen. However, participants in the standard formula lost their body weight, body mass index (BMI) and skeletal muscle mass significantly. While body weight, BMI and muscle mass were maintained in the peptide-based formula, from baseline to day 14. Moreover, the participants in the peptide-based formula tended to reach their caloric target faster than the standard formula.

CONCLUSION
The study emphasizes the importance of early nutritional support in the SICU and showed the efficacy and safety of a high-protein, peptide-based formula in meeting caloric and protein intake targets while maintaining body weight and muscle mass.

Key Words: Peptide-based formula; Surgical intensive care; Hydrolyzed protein; Surgery; Nutritional support

Core Tip: This study is to focus on early nutrition support by novel high protein, peptide-based formula in various surgical intensive care patients. The formula could help maintaining body weight and muscle mass of patients and help them to meet calories and protein requirement. In addition, this nutrition support improved serum albumin, prealbumin and retinol binding protein which lead to decrease risk of malnutrition. Besides nutritional status outcomes evaluation, we investigate wound healing improvement by plasma fibronectin which is protein for cell adhesion, wound healing and blood clotting in this study. This finding would be helpful for recovery surgical patients after operation.

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INTRODUCTION

Malnutrition is common in critically ill patients, and it is associated with an increased risk of complications, particularly in surgical intensive care (SICU) patients. Malnutrition increases infectious complications, delayed wound healing, prolonged hospital stays, and increased hospital cost and overall mortality[1,2]. Early enteral nutrition with adequate caloric and protein intake have been shown to successfully handle the metabolic demands that arise during the acute phase of critical illness, especially in surgical patients which increased metabolic needs for recovery and wound healing. Early enteral feeding could reduce length of hospital stay, ICU stay, ventilator days and mortality in critically ill patients [3]. Moreover, high protein intake during peri-operative period results in less negative nitrogen balance and decrease risk of muscle wasting. Nevertheless, high caloric and protein intake is difficult to achieve. Since the greater volumes and concentrations of enteral nutrition may be required, which may raise the risk of feeding intolerance. Using high volume enteral feeding may increase gastric residual volume (GRV) which leads to increased risk of aspiration pneumonia[4,5]. Fibronectin is a protein that is essential for cell adhesion, wound healing, and blood clotting. Plasma fibronectin is essential for host defense in critically ill patients, especially during sepsis. Low plasma fibronectin levels can promote phagocytic failure, reticuloendothelial system malfunction, and multiple organ failure[6,7].

Peptide-based formula is an enteral formula that incorporates partially or totally hydrolyzed protein in the form of dipeptides or tripeptides. Additionally, a peptide-based formula usually contains a significant amount of medium chain triglyceride (MCT) which is easier to absorb and utilize[8]. This form of enteral formula has several advantages over other forms of enteral nutrition. It contains smaller protein fragments that can be absorbed and utilize more efficiently[9]. It is also a beneficial nutrition support for patients with tube feeding-related diarrhea, feeding intolerance or malabsorption

[10]. However, there are limited studies showing the efficacy and safety of high-protein peptide-based formula in critically ill surgical patients. Thus, this study aimed to determine the effect of high-protein peptide-based formula, compared to the isocaloric isonitrogenous standard polymeric formula, on the gastrointestinal (GI) tolerability and changes of fibronectin levels in patients who were admitted to the SICU. The secondary objective was to investigate the nutritional status, biochemical changes (serum albumin, prealbumin, and retinol-binding protein) and adverse events of this peptide-based formula compared to the standard regimen. The study's findings will be beneficial and guide physicians in choosing the appropriate nutritional regimen for critically ill surgical patients.

MATERIALS AND METHODS

Participants

This study was a multi-center double-blind, randomized controlled trial. It was conducted at SICU of Ramathibodi Hospital (Mahidol University), Chonburi Hospital and Surin Hospital, Thailand. We enrolled adult patients, age 15 years or older, who were admitted to the SICU and expected to receive enteral feeding for at least 5-14 d post-operation. Any acute surgical conditions patients, not the high-risk postoperative observation, could be enrolled to cover clinical scenarios which have problem to achieve goal of calories by enteral feeding. They were randomly assigned to receive either the high-protein peptide-based formula or the isocaloric isonitrogenous standard formula. Block randomization was generated from computerized system by statistical center and transferred to study site location as opaque sealed envelopes at a ratio of 1:1. We excluded patients who required parenteral nutrition, high doses sedative agents (fentanyl > 2 mg/kg/h or morphine > 0.05 mg/kg/h), history of aspiration pneumonia, thyroid disease, severe hepatic or renal impairment, abdominal hypertension, fluid overload, allergy to any research food components, end stage cancer, and severe burn (grade 2 or grade 3 burn with a lesion greater than 50% of the body surface area).

The study was approved by the Institutional Review Board from all institutes and the study was registered at the Thai Clinical Trials Registry (TCTR20220507003) before the first patient's enrollment. All patients voluntarily signed and dated the written informed consent.

Research diets

The study formula is a high-protein peptide-based formula with a Protein: Carbohydrate: Fat ratio of 20:45:35. It contains whey protein hydrolysate and leucine as protein sources and MCT, fish oil and canola oil as fat sources. The formula is fiber-free and it has low osmotic properties. For the control group, casein is added to the standard polymeric formula to pro-duce isocaloric and isonitrogenous formula. The ingredients and nutritional content of both enteral diets are displayed in Table 1. Both diets were prepared at a concentration of 1 kcal/mL.

Feeding protocol

The feeding was started within 48 h after ICU admission and delivered continuously through NG tube. The daily calorie intake for the first 7 d was 20-25 kcal/kg body weight/d, then it was gradually increased to 25-30 kcal/kg of body weight/d over the following 8-14 d. The feeding started by providing at least 50% of the patient's total daily energy requirement, and then gradually increased the feeding rate until the protocol-set feeding rate is reached.

GRV assessment

GRV was measured before feeding, 6 times daily at 4-h intervals. If the GRVs was less than 250 mL, feeding was gradually increased until the target is reached. If the GRV was between 250-400 mL, the feeding was withholded for 1 h before reassessing GRV. If the amount is still over 250 mL, the feeding was stopped for another hour before reassessing the gastric content and the prokinetic agents was administered according to the physician judgement. If the GRV exceeded 400 mL, feeding was stopped, and medication was administered. Symptoms of GI intolerance including diarrhea (assessed using by the Hart and Dobb scale) nausea and vomiting during the study period were recorded daily.

Fibronectin and other biochemical outcomes

Serum fibronectin concentrations were analyzed using a Human Fibronectin Detection kit, PerkinElmer, Inc. The data was generated by white OptiplatedTM 384 microplate and the Envision® plate reader 2103, PerkinElmer, Inc. At baseline (day 1) and on days 3, 5, 11, and 14. The other blood samplings such as complete blood count, blood urea nitrogen, creatinine, glomerular filtration rate, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, albumin, prealbumin, retinol binding protein (RBP), total lymphocyte count (TLC), prothrombin time, total bilirubin, international normalized ratio, fasting blood glucose, free thyroxine, free triiodothyronine, thyroid stimulating hormone, serum electrolyte were also performed.

Other outcomes

The nutritional status was determined on days 1, 3, 5, 7, 9, 11, and 14 using Bhumibol Nutrition Triage (BNT) which was endorsed by Society of Parenteral and Enteral Nutrition of Thailand[10]. Body composition using Bioelectrical Impedance Analysis (Inbody®, Korea), and Sequential Organ Failure Assessment score on day 1 and 14 and Glasgow Coma Scale were also recorded on day 1, 3, 5, 7, 9, 11 and 14.

Table 1 The study formula (once peptide) at concentration of 1 kcal:1 mL

	Peptide-based formula	Standard formula
Caloric distribution (Protein: Carbohydrate: Fat)	20:45:35	20:52:28
Source of protein	Whey protein hydrolysate (96%); Leucine (4%)	Sodium caseinate (8%); Soy protein isolate (92%)
Source of carbohydrate	Maltodextrin (79%); Potato starch (21%)	Maltodextrin (64%); Sucrose (32%); Fructo-oligosaccharide (4%)
Source of fat	Fish oil (5%); Canola oil (43%); MCT oil (52%)	Rice bran oil (92%); MCT oil (8%)
Osmolality (mOsm/kg H_2O)	290	364
Osmolarity (mOsm/L)	242	307

MCT: Medium chain triglyceride.

Statistical analysis

The sample size calculation was based on estimated serum fibronectin amount of ICU patients who received small-peptide and whole protein enteral feeding[11]. Considering standard deviation of serum fibronectin in post-operative patients as 20[12], a 95% confidence level, 80% power of study, and a 10% drop-out rate, 10 subjects were required in each group.

Statistical analysis was carried out using the SPSS version 18.0 (SPSS Inc, Chicago, IL, United States). Continuous data are presented as mean ± SD or median (interquartile range) while categorical data are shown as number (percentage). Independence sample *t*-test or Mann-Whitney *U* test were used to determine the differences of continuous variables between groups. While dependence sample *t*-test or Wilcoxon signed-rank test were used to compare within-subject parameters. Test results of categorical variables were evaluated by Chi-square and Fisher exact tests as appropriate. Results were deemed statistically significant at *P*-value < 0.05.

RESULTS

Baseline characteristics

A total of 19 patients were enrolled, 9 patients were randomized to the peptide-based formula and 10 patients were randomized to the standard formula. Most of the subjects (77.8%) were men. Mean (SD) age of the participants in the peptide-based formula was slightly higher than the standard formula (60.1 ± 21.6 *vs* 49.1 ± 26.0 years, $P = 0.333$). Eighty percent of participants were classified as having a risk of malnutrition or mild malnutrition according to the BNT. Baseline characteristics were similar between groups (Table 2). Causes of ICU admission and type of surgery are shown in Table 3.

Primary outcome

GRV was measured before feeding, 6 times a day then it was calculated as a daily average GRV. There were no significant differences between groups in average GRV measurement over the first three, five, or seven days of ICU admission (Figure 1). There was no difference between the two groups' percentage changes in serum fibronectin levels between days 1 and 3, 5, 11, and 14 (Table 4).

Secondary outcomes and subgroup analysis

During the SICU admission, body weight, body mass index (BMI), skeletal muscle index were not significantly different between groups at day 14 after ICU admission. Mean calorie intake were slightly higher in the control group (peptide-based formula 25.6 ± 4.1 *vs* standard formula 27.3 ± 3.7 kcal/kg/d, $P = 0.402$). However, on day 14, participants in the standard formula lost their body weight, BMI and skeletal muscle mass significantly. While body weight, BMI and muscle mass were maintained in the peptide-based formula, from baseline to day 14 (Table 5).

Serum albumin, prealbumin, RBP and TLC increased from baseline in all participants from both groups. However, only serum prealbumin and RBP significantly increased at day 14 ($P \leq 0.05$) (Figure 2). The actual caloric and protein intake were similar between groups. Duration to achieved target calories, at 25 kcal/kg BW/d and 30 kcal/kg BW/d, in peptide-based formula was shorter than standard formula both as shown in Table 6. There was no observed readmission in either group within 90 d following hospital discharge, and the survival rate was 100% in both group at day 180.

Side effects

There were no severe adverse event, and the frequency of GI complications was similar between groups.

Table 2 Baseline characteristics of study participants, *n* (%)/mean ± SD

	Peptide-based formula (*n* = 9)	Standard formula (*n* = 10)	*P* value
Demographic			
Age (yr)	60.1 ± 21.6	49.1 ± 26.0	0.333
Gender (Male)	7 (77.8)	9 (90.0)	0.466
Weight (kg)	66.2 ± 14.3	62.6 ± 10.4	0.533
BMI (kg/m^2)	24.2 ± 3.1	22.4 ± 3.8	0.275
GCS score	10.7 ± 3.0	10.0 ± 3.1	0.864
SOFA score	4.0 ± 2.0	4.2 ± 2.0	0.769
[1]Nutrition status assessment			
Risk of malnutrition	4 (44.4)	3 (30.0)	0.752
Mild malnutrition	4 (44.4)	5 (50.0)	
Moderate malnutrition	0 (0.0)	1 (10.0)	
Severe malnutrition	1 (11.1)	1 (10.0)	
Biochemistry			
Hemoglobin (g/dL)	9.8 ± 2.4	10.1 ± 1.8	0.793
White blood cells count (× 10^3/μL)	14.8 ± 4.2	15.0 ± 7.5	0.955
Platelets count (× 10^3/μL)	218.8 ± 112.7	175.5 ± 85.5	0.253
Neutrophils	84.3 ± 8.5	83.5 ± 5.8	0.826
Monocytes	6.3 ± 3.5	7.2 ± 3.8	0.513
Total lymphocytes count (cell/μL)	1267.1± 1164.8	1006.0 ± 1005.6	0.288
Blood urea nitrogen (mg/dL)	22.3 ± 8.7	21.3 ± 20.6	0.327
Creatinine (mg/dL)	1.1 ± 0.4	1.0 ± 0.9	0.102
Urine urea nitrogen	12.0 ± 6.4	15.4 ± 22.2	0.441
GFR (mL/min/1.73 m²)	74.7± 31.6	103.5 ± 35.8	0.082
Fasting plasma glucose (mg/dL)	128.0 ± 26.7	128.1 ± 49.1	0.374
Alkaline phosphatase (U/L)	92.1 ± 41.2	96.3 ± 64.6	0.859
Aspartate transaminase (U/L)	84.5 ± 52.0	104.3 ± 66.5	0.501
Alanine transaminase (U/L)	32.5 ± 26.0	86.8 ± 99.8	0.154
Nutritional status			
Albumin (g/dL)	2.6 ± 0.6	2.5 ± 0.5	0.821
Prealbumin (mg/dL)	10.2 ± 5.3	14.1 ± 8.2	0.236
Retinol binding protein (mg/dL)	2.1 ± 1.7	2.0 ± 1.3	1.000

[1]Nutrition status were assessed with Bhumibol Nutrition Triage which is endorsed by Society of Parenteral and Enteral Nutrition of Thailand. NT-1 (score 0-4): Normal or risk of malnutrition; NT-2 (score 5-7): Mild malnutrition; NT-3 (score 8-10): Moderate malnutrition; NT-4 (score >10): Severe malnutrition. BMI: Body mass index; GCS: Glasgow coma scale; SOFA: Sequential organ failure assessment; GFR: Glomerular filtration rate.

DISCUSSION

Our study demonstrated that early nutrition support can lead to improvement of nutritional status for patients in SICU. Within the first week of ICU admission, all patients in this study reached their energy and protein targets according to the European Society for Parenteral and Enteral Nutrition guideline[3]. Even though, there were no differences of GRV and changes of body weight, body composition, nutritional status and biochemical parameters, including fibronectin levels, in patients receiving high-protein peptide-based formula, compared to the standard regimen. The participants in the standard formula lost their body weight, BMI and muscle mass significantly, while the participants receiving peptide-based formula could maintain their weight, BMI and muscle mass on day 14. Moreover, the participants in the peptide-

Table 3 Subject characteristics

Subject number	Cause of ICU admission	Type of surgery
1	Traumatic subdural hematoma	Non operative management, close neurological observation
2	Acute calculus cholecystitis, adult respiratory distress syndrome	Open cholecystectomy
3	Closed fracture of shaft of right of humerus, closed fracture of right tibia and fibula severe head injury, maxillofacial injury, traumatic subdural hematoma	Open reduction of fracture with internal fixation humerus. Closed reduction of fracture without internal fixation tibia and fibula. Non operative management, close neurological observation
4	AAST grade II liver injury severe head injury, traumatic subdural hematoma thoracic blunt aortic injury	Craniotomy, tracheostomy, thoracic endovascular repair of the aorta
5	Splenic injury grade 5 left hemothorax	Exploratory laparotomy with splenectomy
6	Large gastric ulcer perforation	Exploratory laparotomy, simple suture with omental patch
7	Omental twist causing omental infarction	Exploratory laparotomy, omentectomy with drainage
8	Sigmoid colon diverticulitis with perforation	Exploratory laparotomy c sigmoidectomy with Hartmann operation
9	Gastric ulcer perforation	Exploratory laparotomy, simple suture with omental patch
10	Traumatic subdural hematoma	Craniotomy
11	AAST grade 4 pancreatic injury	Exploratory laparotomy, distal pancreatectomy, total splenectomy
12	Malignant neoplasm of adrenal gland, gallstone	Unilateral adrenalectomy, total cholecystectomy
13	Acute calculus cholecystitis	Laparoscopic cholecystectomy
14	Closed fracture of acetabulum, fracture of right radius and ulnar bones	Open reduction of fracture with internal fixation of radius and ulnar bones
15	Severe head injury, traumatic subdural hematoma	Craniectomy for clot removal
16	Epidural hematoma, fracture zygoma, fracture orbit, fracture rib with hemothorax right	Craniotomy with clot removal, open reduction with internal fixation facial fractures
17	Distal rectal cancer	Abdominoperineal resection
18	Necrotizing fasciitis with septic shock	Debridement right leg
19	Necrotizing fasciitis right leg	Debridement right leg

AAST: The American Association for the Surgery of Trauma; ICU: Intensive care unit.

Table 4 Percentage change of serum fibronectin level, median (25th-75th percentiles)

	Peptide-based formula	Standard formula	*P* value
Day 3 *vs* Day 1	17.8 (39.5)	17.5 (100.4)	0.790
Day 5 *vs* Day 1	21.4 (41.9)	63.4 (150.4)	0.290
Day 11 *vs* Day 1	65.1 (106.8)	59.1 (211.8)	0.641
Day 14 *vs* Day 1	11.0 (115.6)	80.5 (357.0)	0.157

based formula tended to reach their caloric target faster than the standard formula.

Peptide-based formula is the enteral formula which contains proteins that are partially hydrolyzed to dipeptides or tripeptides. Moreover, it usually includes higher MCT content compared to the standard polymeric formula which can be absorbed in GI tract and used as source of energy immediately[13]. Previous studies indicated that peptide-based formula could ameliorate feeding intolerance in critically ill patients[14] particularly in malnourished patients who underwent abdominal surgery[15]. In our study, the average GRV were similar between patients receiving either the peptide-based formula or the standard regimen. The discrepancy of the result might be explained by the fact that there were only few patients who had moderate to severe malnutrition in our study. Moreover, clinical characteristics of our study participants were various and not all patients had undergone abdominal surgery. Moreover, the participants in both groups did not have any GI intolerance at baseline and the average GRV were in the normal range throughout the study period [16].

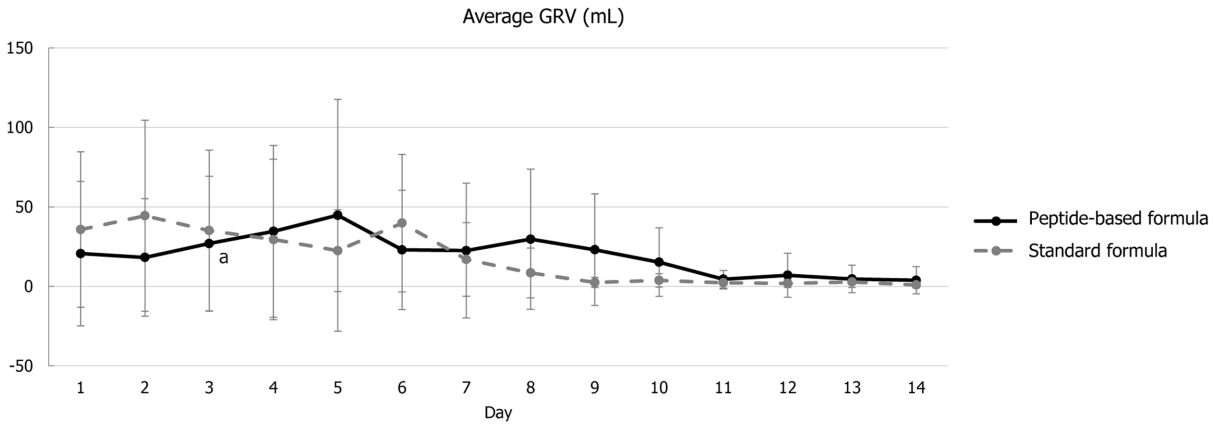
Table 5 Comparison of anthropometry between peptide-based formula and standard formula, mean ± SD

	Peptide-based formula			Standard formula			*P* value (compare between group for day 14)
	Day 1	Day 14	*P* value	Day 1	Day 14	*P* value	
Body weight (kg)	66.2 ± 14.3	65.2 ± 13.1	0.389	62.6 ± 10.4	58.4 ± 10.5	0.037	0.288
BMI (kg/m^2)	24.2 ± 3.1	23.0 ± 2.4	0.471	22.4 ± 3.8	20.9 ± 4.1	0.032	0.273
SMI (kg/m^2)	18.4 ± 5.0	15.7 ± 3.7	0.139	16.1 ± 3.2	13.6 ± 3.2	0.003	0.419

BMI: Body mass index; SMI: Skeletal muscle mass index.

Table 6 Comparison of duration to achieve goal of calories between peptide-based formula and standard formula, mean ± SD

Day to reach goal	Peptide-based formula	Standard formula	*P* value
Step 1 (25 kcal/kg/d up)	2.7 ± 0.6	3.8 ± 2.5	0.462
Step 2 (30 kcal/kg/d up)	7.5 ± 3.5	8.5 ± 0.7	0.733



Average GRV	Peptide-based formula (mean ± SD)	Standard formula (mean ± SD)	*P* value (compare between group)
First 3 d of study	22.03 ± 40.42	38.53 ± 51.79	0.380
First 5 d of study	29.09 ± 50.28	33.72 ± 47.26	0.955
First 7 d of study	27.27 ± 47.00	32.24 ± 44.15	0.885

Figure 1 Comparison of average daily gastric residual volume during study between peptide-based formula and standard formula. [a]*P* value ≤ 0.05. GRV: Gastric residual volume.

Even though, there were no differences of body weight, body composition, nutritional status and biochemical parameters between groups of patients on day 14. Interestingly, the participants in the standard formula lost their weight, BMI and muscle mass significantly, while the participants receiving peptide-based formula could maintain their weight, BMI and muscle mass during baseline through day 14. Muscle wasting is a crucial factor on the recovery of critically ill patients. Sarcopenia can lead to functional disability which can persists for years after discharge from the intensive care unit[17,18]. In a recent clinical study, it was found that patients who receiving peptide-based formula lost less weight and lean mass, compared to the isocaloric and isonitrogenous enteral nutrition[19]. The study suggests that a peptide-based formula is more effective in term of maintaining body weight and muscle mass in patients undergoing surgery. Notably, both groups included the same amount of protein, but the peptide-based formula, composed of whey protein and leucine which could accelerate muscle protein synthesis[20]. Recent study demonstrated that peptide-based formula could prevent significant muscle loss, in comparison with standard formula or β-hydroxymethy β-butyrate-rich product, in obese patients who underwent Roux-en-Y gastric bypass[21]. Moreover, the peptide-based formula contains leucine, a branch-chain amino acid that the World Health Organization recommends people get 39 micrograms/kg of body weight/d[22]. This may be helpful for ICU patients, as shown by the previous research, which presented leucine concentrations that lower normal range lead to decreased cumulative survival rate[23].

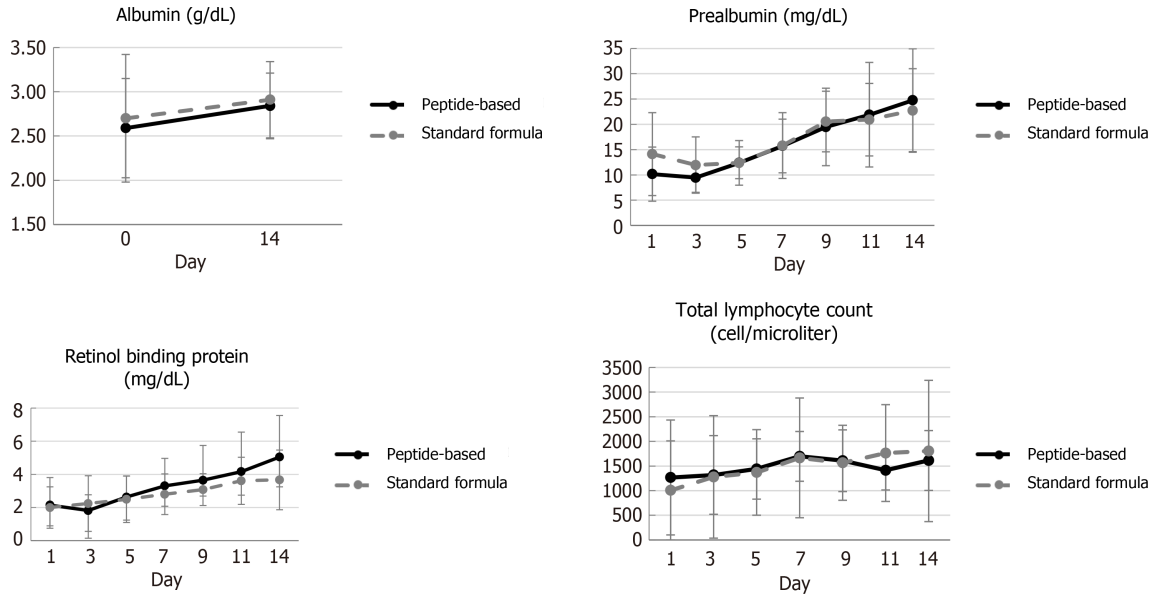


Figure 2 Comparison of nutritional status parameters during study between peptide-based formula and standard formula.

The average calorie and protein intake were similar between groups however participants in the peptide-based formula had a tendency to reach their energy goals earlier, compared to the control group. the study's finding were similar to the previous study which indicated that peptide-based formulas are more effective in achieving nutritional targets within a 7-d period compared to the intact-protein enteral nutrition formulas[24].

There was no significant difference in the change in plasma fibronectin levels between groups. This could be attributed to the fact that the level of plasma fibronectin varied greatly and was unpredictable. Previous research has shown that this value can be affected by several factors, such as the type of disease, severity of the infection, type of cancer, and blood transfusion[25-27]. Unlike previous studies[28,29], we only evaluated fibronectin levels after surgery, as we could not assess fibronectin levels before ICU admission[28,29]. Considering the factors mentioned above, the researcher concluded that the serum fibronectin value used in this study has a large variation, making it difficult to compare the degree of improvement among patients. Furthermore, it may not be specific enough to accurately measure the effect of the interventions.

This study has several strengths. Firstly, it was a multicenter, double-blind randomized controlled trial. Secondly, we used the isocaloric, isonitrogenous polymeric standard formula as a control. Thirdly, the feeding protocol was progressive and adjusted individually according to physician's judgement. Lastly, the study measured various outcomes including body composition, biochemistry, and gastrointestinal complications. Our important limitation of this study was the small sample size since we conducted the study during the coronavirus disease pandemic. The small sample size limits the ability to draw a definitive conclusion. Therefore, further study should be conducted to determine the long-term effect of peptide-based formula in larger patient populations, including various patient groups.

CONCLUSION

This study's results suggest that early nutritional support is a crucial aspect of health care for patients in the SICU. The high-protein, peptide-based enteral formula was not only well-received but also effective in helping critically ill patients meet their caloric and protein intake targets. This peptide-based enteral formula plays a significant role in preserving body weight and muscle mass. These findings have substantial implications for muscle strength, physical performance, and an individual's ability to participate in physical medicine and rehabilitation.

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FOOTNOTES

Author contributions: Sumritpradit P conceived the original idea, designed the study, enrolled subjects, patient care, performed the interpretation of data, wrote manuscript, and revised the manuscript and corresponding to submit for publication; Shantavasinkul PC

performed biochemistry analysis, took responsibility for integrity of data, wrote manuscript and revised the manuscript; Ungpinitpong W enrolled subjects, patient care, performed the statistical analysis data, took responsibility for accuracy of data, reviewed the manuscript and provided critical comments; Noorit P enrolled subjects, patient care, performed the interpretation of data, took responsibility for integrity of data, reviewed the manuscript and provided critical comments; Gajaseni C collected the data, coordinate with participants and site staff team for intervention. All authors read and approved the final manuscript.

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