Comparisons between short-peptide formula and intact-protein formula for early enteral nutrition initiation in patients with acute gastrointestinal injury: a single-center retrospective cohort study

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Background: Early enteral nutrition (EN) in critically ill patients is important and most of them have suffered acute gastrointestinal injury (AGI). In this study, we investigated the influence of short-peptide EN formula and intact-protein EN formula on the prognosis of patients with AGI grades I–II to provide some guidance.

Methods: A retrospective cohort study was performed. The primary outcomes were the percentage of EN calories (25 kcal/kg/d) and protein (1.2 g/kg/d) on the 3rd and 7th days of intensive care unit (ICU) admission, EN percent elevation in calories and protein on days 3–7, and the incidence of gastric retention and diarrhea after EN administration. Secondary outcomes included ICU and 28-day mortality, length of ICU stay, total hospitalization cost, and ventilator-free days. Univariate and multivariate Cox regression analysis was used to identify factors associated with gastric retention and diarrhea. And we used Kaplan-Meier survival curves to compare 28-day mortality rates between the two groups.

Results: There were no statistically significant differences in ICU and 28-day mortality, ICU length of stay, total hospitalization cost, or ventilator-free days in the short-peptide formula group compared with the intact-protein formula group. Kaplan-Meier survival curves of 28-day mortality also showed no statistically significant difference. The EN percent elevation in calories and protein on days 3–7 in the short-peptide formula group was significantly higher than the intact-protein formula group (48% *vs.* 38%, P=0.03 and 37% *vs.* 38%, P=0.04, respectively). For gastrointestinal (GI) adverse events, the incidence of gastric retention (15.5% *vs.* 29.8%, P=0.03) and diarrhea (8.5% *vs.* 19.8%, P=0.04) were lower in the short-peptide group. In the multivariate-adjusted model, the use of short-peptide formula was the only independent variable of reduction in gastric retention and diarrhea [HR =0.469 (95% CI: 0.239–0.922), P=0.028; and HR =0.394 (95% CI: 0.161–0.965), P=0.041, respectively].

Conclusions: Short-peptide formula is more easily tolerated by patients in the acute phase of AGI and can quickly achieve nutritional goals by EN provision, making it the preferred formula for the initiation of EN in the acute phase of AGI.

Keywords: Enteral nutrition (EN); acute gastrointestinal injury (AGI); prognosis; short-peptide formula; intensive care unit (ICU)

Submitted Mar 09, 2022. Accepted for publication May 10, 2022.

doi: 10.21037/atm-22-1837

View this article at: https://dx.doi.org/10.21037/atm-22-1837

Introduction

Enteral nutrition (EN) for critically ill patients can exert beneficial physiological effects, including downregulating systemic immune responses, reducing oxidative stress, maintaining gut microecology, promoting the recovery of intestinal function, and improving patient outcomes (1-5). Many guidelines (1,4,6,7) have referred to the importance of early EN in critically ill patients. Most patients in a critical condition have suffered acute gastrointestinal injury (AGI). Unfortunately, the mortality of critically ill patients with AGI is high. Furthermore, the severity or grade of AGI is correlated with mortality (4,8-13), and the advantage of early EN is often not exploited for AGI patients. Because of gastrointestinal (GI) digestion and absorption dysfunction, the provision of EN is more crucial in critically ill patients with AGI than those without AGI. Therefore, improving EN tolerance and maximizing its advantages may significantly improve the prognosis and clinical outcome for critically ill patients with AGI. There are numerous clinical nutritional guidelines for critically ill patients, but only the 2016 Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines have recorded specific recommendations for EN formulas. The SCCM and ASPEN guidelines suggest using a standard polymeric formula for initiating EN in the intensive care unit (ICU) setting and a short-peptide formula for persistent diarrhea (4). However, the above recommendations have low-quality evidence, are not combined with AGI grade, and have no clear selection of EN formulas for ICU patients with AGI. Specifically, incorrect selection of the EN initiation formula may cause feeding intolerance, which may reduce or even interrupt feeding. In turn, this may cause a delay in reaching the calorie and protein targets, affecting the prognosis and clinical outcomes of patients with AGI grade I–II. Currently, there are no evidence-based studies on the selection of EN initiation formulas for AGI patients. It is not clear whether selection of the EN initiation formula can decrease GI adverse events and benefit prognosis in critically ill patients with AGI grades I–II.

In this study, we aimed to investigate the influence of EN formulas (short-peptide formula and intact-protein formula) on the prognosis of critically ill patients with AGI grades I–II to provide some guidance for formulating EN strategies. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1837/rc).

Methods

Study design and samples

We performed a retrospective cohort study of critically ill patients admitted to the ICU of The First Hospital of Jilin University between March 2018 and September 2020 (*Figure 1*). The inclusion criteria were as follows: age ≥18 years, admitted to ICU for at least 7 days, AGI grade I (increased risk for the development of GI dysfunction or failure) or II (GI dysfunction) proposed by the 2012 Society of Critical Care Medicine (ESICM) guidelines (9), and short-peptide formula or intact-protein formula was used within 7 days of admission to ICU. Patients were excluded if they received nutrients via oral feeding, received EN prior to admission to ICU, had participated in other similar clinical studies, did not follow nutritional protocols, or were pregnant. Patients with missing clinical data or nutritional protocols were also excluded.

Patients were divided into a short-peptide formula group [EN suspension (SP): 500 mL, 1 kcal/mL, 20 g/500 mL of protein (Nutricia, Wuxi, China)] and an intact-protein formula group [EN suspension (TPF): 500 mL, 1.5 kcal/mL, 30 g/500 mL of protein (Nutricia, Wuxi, China)] according to the type of EN formula used. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The protocol was approved by The First Hospital of Jilin University Ethics Committee for Clinical Research (No. 19K032-001) and individual consent for this retrospective analysis was waived.

Nutrition protocols

Since publication of the ESICM guidelines in 2012 (9), clinicians in our center have gradually normalized and systematized enteral feeding (EF) for patients with AGI. Our center developed personalized nutrition protocols for each patient with AGI, including an EF starting dose of 20 mL/h (9) and nutritional target setting (the calorie target was set at 25 kcal/kg/d (14); the current recommendation for protein dosage in critically ill patients is 1.2–2.0 g/kg/d (4), so the patients' protein supplement target was set as 1.2 g/kg/d in this study). Adequate supplemental parenteral nutrition was conducted if the nutritional target was not achieved in the short term, and GI symptoms were re-evaluated daily to determine whether to increase EF or not. Additionally, clinicians provided nutrition for AGI patients in strict accordance with the 2016 nutritional protocols. Patients who did not follow the nutritional protocols were

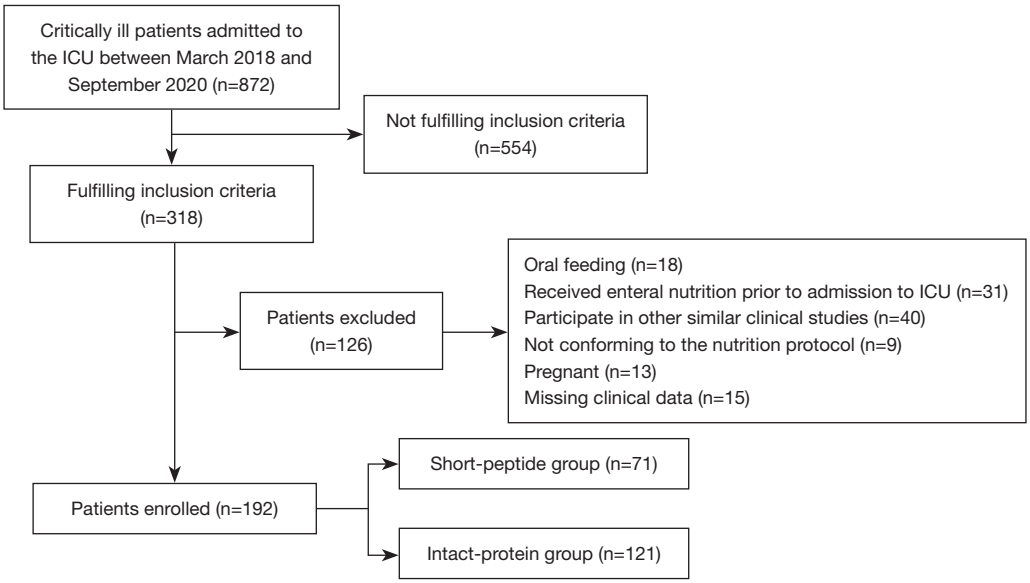

Figure 1 Patient inclusion flowchart. ICU, intensive care unit.

excluded from this study.

Clinical data collection

After carefully reviewing electronic medical records, the patients' information was collected, including demographics, diagnoses, medical history, time of EN initiation, feeding route, the occurrence of gastric retention and diarrhea and the time of first occurrence, Acute Physiology, Age and Chronic Health Evaluation II (APACHE II) scores, Sequential Organ Failure Assessment (SOFA) scores, Numeric Rating Scale (NRS) scores, Modified Nutrition Risk in the Critically III (mNUTRIC) scores, AGI grades, serum albumin, and daily intake of protein and calories from EN. The total APACHE II, SOFA, NRS, and mNUTRIC scores, AGI grades, and serum albumin levels were acquired based on the related parameters within the first 24 h of ICU admission.

Computational formulas

(I) Percentage of EN calories = calories from EN/target calories (target calories =25 kcal/kg/d);
(II) EN percent elevation in calories on days 3–7 = percentage of EN calories on the 7th day-percentage of EN calories on the 3rd day;
(III) Percentage of EN protein = protein from EN/target protein (target protein =1.2 g/kg/d);
(IV) EN percent elevation in protein on days 3–7 = percentage of EN protein on the 7th day-percentage of EN protein on the 3rd day.

Primary and secondary outcomes

The primary outcomes were percentage of EN calories (25 kcal/kg/d) and protein (1.2 g/kg/d) (4) on the 3rd and 7th days of ICU admission, EN percent elevation in calories and protein on days 3–7, the incidence of gastric retention (a single volume over 200 mL) and diarrhea (with three or more loose or liquid stools per day, and a stool weight higher than 200–250 g/d or 250 mL/d) (9) after EN administration. Secondary outcomes were ICU and 28-day mortality, ventilator-free days, length of ICU stay, total hospitalization cost, and serum albumin levels on the 7th day of ICU admission.

Statistical analysis

SPSS 26.0 (IBM, United States) and Graphpad Prism 8.0 (GraphPad Software, California) software were used for all statistical analyses. Continuous variables with normal distribution were expressed as means ± standard deviation; the variables distributed abnormally were represented by median values and interquartile ranges M (P25, P75). The Mann-Whitney U test for nonparametric data and *t*-tests for normally distributed continuous variables were used to

Table 1 Clinical characteristics and demographic data of patients at baseline

Characteristics	All (n=192)	Short-peptide (n=71)	Intact-protein (n=121)	P value
Sex (male), n [%]	121 [63]	45 [63]	76 [63]	1.0
Age, mean ± SD, years	60±17	61±18	59±16	0.41
Actual body weight (kg), median [IQR]	65 [60–70]	65 [60–70]	65 [60–70]	0.28
Feeding route, n [%]				
Feeding via nasogastric tube	185 [96]	68 [96]	117 [97]	0.71
Feeding via nasojejunal tube	7 [4]	3 [4]	4 [3]	0.71
Underlying conditions, n [%]				
Diabetes mellitus	51 [27]	15 [21]	36 [30]	0.24
Disease severity at defined time[a]				
APACHE II score, median [IQR]	15 [11–19]	16 [12–20]	15 [10–19]	0.39
SOFA score, median [IQR]	7 [5–10]	6 [4–10]	7 [5–10]	0.14
NRS score, median [IQR]	4 [3–4]	4 [3–5]	3 [3–4]	0.08
mNUTRIC score, median [IQR]	4 [3–5]	4 [3–5]	4 [3–5]	0.83
Mechanical ventilation, n [%]	163 [85]	59 [83]	104 [86]	0.68
ICU course prior to defined time[a]				
Serum albumin, mean ± SD, g/dL	28.3±7.2	28.4±7.6	28.3±7.0	0.91
AGI grade I, n [%]	141 [73]	51 [72]	90 [74]	0.70

[a], the defined time was the first 24 h of ICU admission. SD, standard deviation; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; NRS, nutrition risk screening 2002 score; mNUTRIC, modified Nutrition Risk in the Critically Ill score; AGI, acute gastrointestinal injury; IQR, interquartile range.

compare differences between the two groups. Categorical data comparisons between the two groups were performed with the Chi-square test. The 28-day mortality comparisons between the groups were conducted using Kaplan-Meier survival curves and log-rank tests. Univariate and multivariate Cox regression analysis was used to identify factors associated with gastric retention and diarrhea, the Forward method was used for selection of variables. A significance level of 5% (P<0.05) and confidence interval (CI) of 95% was adopted in all statistical tests.

Results

Among 872 patients, 192 patients who met the inclusion criteria were enrolled in this study. Reasons for patient exclusion were as follows: 554 patients did not fulfill the inclusion criteria, 18 patients had received nutrients via oral feeding, 31 patients received EN prior to admission to ICU, 40 patients had participated in other similar clinical studies, 9 patients did not meet the nutritional protocols, 13 patients were pregnant, and 15 patients had missing clinical data. Therefore, we assessed the effect of short-peptide and intact-protein formulas on the prognosis and clinical outcomes of 192 critically ill patients with AGI grades I–II (*Figure 1*).

The patients' baseline features are displayed in *Table 1*. The mean age and body weight were 60 years and 65 kg, respectively. In the first 24 h of ICU admission, the mean serum albumin level was 28.3 g/dL. There were no significant differences in disease severity, APACHE II scores, SOFA scores, NRS scores, mNUTRIC scores, AGI grades, mechanical ventilation ratio, feeding route, or other baseline characteristics between the short-peptide formula group and the intact-protein formula group (P>0.05).

In regard to the patients' clinical results (*Table 2*), there were no statistically significant differences in ICU and 28-day mortality, ICU length of stay, total hospitalization cost, or ventilator-free days between the short-peptide formula group and the intact-protein formula group (P>0.05).

Table 2 Comparison of clinical outcomes between the two patient groups

Clinical outcomes	Short-peptide (n=71)	Intact-protein (n=121)	χ^2/Z	P value
Length of ICU stay (day), median [IQR]	14 [9–21]	13 [9–22]	–0.36	0.72
Total hospitalization cost (×10^4 ¥), median [IQR]	12.5 [6.9–22.7]	10.6 [6.1–19.3]	–1.18	0.24
ICU mortality, n (%)	12 (16.9)	16 (13.2)	0.49	0.49
28-day mortality, n (%)	15 (21.1)	25 (20.7)	0.01	0.94
Ventilator-free time (day), median [IQR]	7 [2–13]	8 [3–14]	–1.06	0.29

ICU, intensive care unit; IQR, interquartile range.

Table 3 Comparison of nutritional and feeding tolerance outcomes between the two patient groups

Nutrition summary	Short-peptide (n=71)	Intact-protein (n=121)	χ^2/Z	P value
Timing of EN (h), median [IQR]	81 [24–109]	50 [12–96]	–2.13	0.03
Percentage of EN calories on the 3rd day (%), median [IQR]	0 [0–27]	0 [0–56]	–2.25	0.01
Percentage of EN calories on the 7th day (%), median [IQR]	64 [36–96]	68 [40–89]	–0.44	0.66
EN percent elevation in calories on 3–7 d (%), median [IQR]	48 [27–71]	38 [0–79]	–2.14	0.03
Percentage of EN protein on the 3rd day (%), median [IQR]	0 [0–21]	0 [0–46]	–2.61	0.01
Percentage of EN protein on the 7th day (%), median [IQR]	51 [27–74]	52 [30–68]	–0.37	0.72
EN percent elevation in protein on 3–7 d (%), median [IQR]	37 [21–59]	30 [0–59]	–1.99	0.047
Serum albumin on the 7th day (g/dL), median [IQR]	30.4 [29.0–31.8]	30.0 [27.5–32.4]	–0.71	0.48
Gastric retention, n (%)	11 (15.5)	36 (29.8)	4.40	0.03
Diarrhea, n (%)	6 (8.5)	24 (19.8)	4.92	0.04

EN, enteral nutrition; IQR, interquartile range.

For the nutritional and feeding tolerance outcomes of patients (*Table 3*), the median timing of EN provision in the short-peptide formula group was shorter than that of the intact-protein group (81 *vs.* 50 h; P=0.03) and the EN calorie percentage on the 3rd day was lower in the short-peptide formula group (P=0.01). Nonetheless, there were no statistically significant differences in the percentage of EN calories on the 7th day between the short-peptide and intact-protein formula groups (64% *vs.* 68%, P=0.66), but the EN percent elevation in calories on days 3–7 in the short-peptide formula group was significantly higher compared with the intact-protein formula group (48% *vs.* 38%, P=0.03). Similar to calories, the EN protein percentage on the 3rd day was lower in the short-peptide formula group (P=0.01). However, no statistically significant differences were observed in the percentage of EN protein on the 7th day between the short-peptide and intact-protein formula groups (51% *vs.* 52%, P=0.72), but the EN percent elevation in protein on days 3–7 in the short-peptide formula group was significantly higher compared with the intact-protein formula group (37% *vs.* 30%, P=0.047) (*Figure 2*). For GI adverse events, the incidence of gastric retention (15.5% *vs.* 29.8%, P=0.03) and diarrhea (8.5% *vs.* 19.8%, P=0.04) was lower in the short-peptide group (*Figure 3*). In the multivariate-adjusted model, the use of short-peptide formula was the only independent variable of reduction in gastric retention and diarrhea [HR =0.469 (95% CI: 0.239–0.922), P=0.028; and HR =0.394 (95% CI: 0.161–0.965), P=0.041 respectively] (*Figure 4*). There was no statistically significant difference in serum albumin levels on the 7th day of ICU admission between the two groups (30.4 *vs.* 30 g/dL, P=0.48). There was also no statistically significant difference in 28-day mortality according to the Kaplan-Meier survival curves (P=0.84) (*Figure 5*).

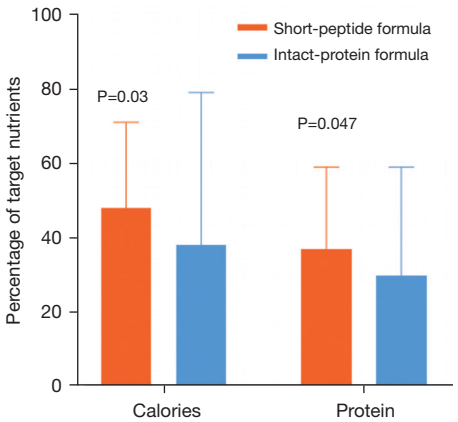

Figure 2 The EN percent elevation in calories and protein on days 3–7 are significantly higher in the short-peptide formula group compared with the intact-protein formula group (48% *vs.* 38%, P=0.03 and 37% *vs.* 30%, P=0.047, respectively). EN, enteral nutrition.

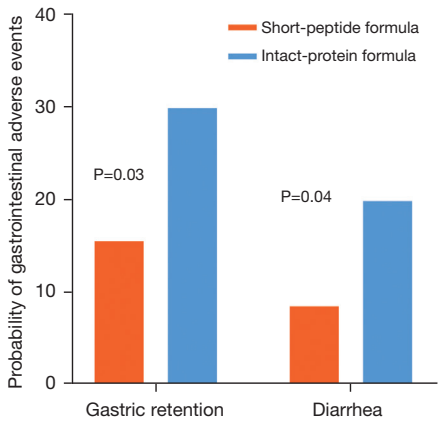

Figure 3 Gastrointestinal adverse events show that the incidence of gastric retention (15.5% *vs.* 29.8%, P=0.03) and diarrhea (8.5% *vs.* 19.8%, P=0.04) are lower in the short peptide group.

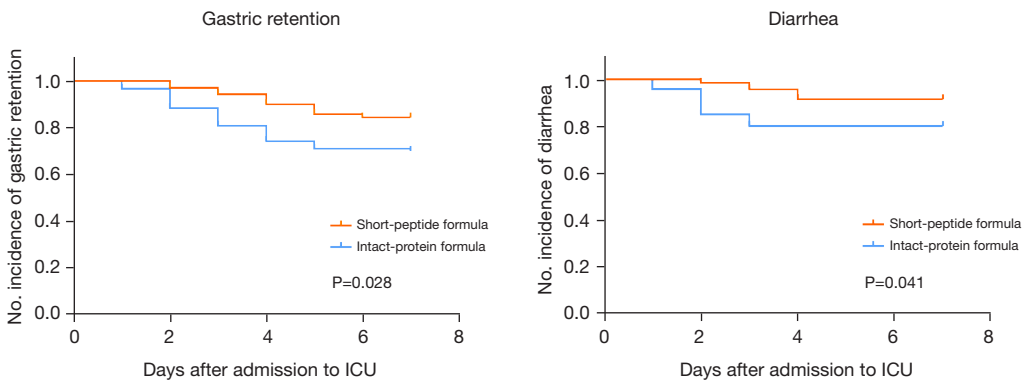

Figure 4 The use of short-peptide formula was the only independent variable of reduction in gastric retention and diarrhea [HR =0.469 (95% CI: 0.239–0.922), P=0.028; and HR =0.394 (95% CI: 0.161–0.965), P=0.041 respectively]. ICU, intensive care unit.

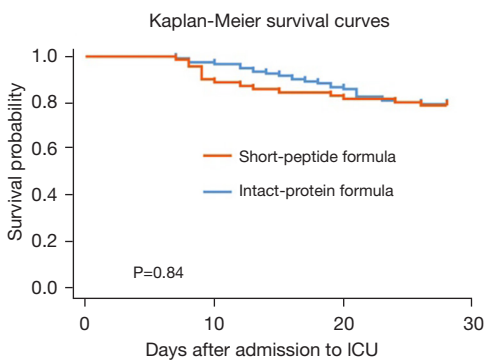

Figure 5 Kaplan-Meier survival curves of patients with AGI grade I–II. ICU, intensive care unit; AGI, acute gastrointestinal injury.

Discussion

Patients with AGI may have various degrees of feeding intolerance and GI symptoms (e.g., diarrhea, weakness, emesis, and high gastric residue) (9). AGI symptoms can lead to interruption or failure of feeding and low protein and calorie intake (15), resulting in delayed provision of EN and failure of early nutritional therapy. The 2016 SCCM and ASPEN guidelines suggest a standard-polymeric formula for EN initiation in the ICU setting, and a short-peptide formula recommendation for ischemia, suspected malabsorption, persistent diarrhea, or lack of response to fiber. However, the evaluation of most of the

above symptoms lacks objective monitoring and evidence and is highly subjective, so there is still confusion and uncertainty in the clinical implementation of the above recommendations. AGI grade is a relatively objective indicator for GI status assessment. Therefore, this study aimed to use AGI grade to guide the selection of EN initial formulas. Short-peptide formula is predigested and is widely used in clinical practice. However, should short-peptide formulation be used as an initial formula in AGI grade I–II patients to reduce the incidence of feeding intolerance and interruption due to incorrect initial formulation selection? Does this feeding strategy improve outcomes and tolerability in AGI grade I–II patients? There are no high-quality studies that can reliably answer these questions. This study revealed no statistically significant differences in ICU and 28-day mortality, ventilator-free days, total hospitalization cost, length of ICU stay, or serum albumin on the 7th day between the short-peptide and the intact-protein formula groups. The above results are similar to previous studies (16-21). However, this study showed that the provision of short-peptide EN formula could notably improve symptoms of GI adverse events (nausea and emesis, abdominal pain, diarrhea, and distention) (22-24). Experimental studies have shown that short-peptide formula plays a protective role in bacterial translocation (25), is absorbed without digestive enzymes (16), accelerates gut digestion and absorption of protein, and augments the postprandial availability of amino acids (26). Some studies have reported that when rats are diseased, the transport of the bacterial product N-formyl-methionyl-leucyl-phenylalanine (fMLP) in the rat colon increases the expression of oligopeptide transporter (PepT1), which may lead to colonic mucosa damage (27,28). Short peptides can reduce GI damage and play a protective role in the gut due to their greater transportability and the competitive suppressive effect on fMLP transport (29). In this study, the incidence of gastric retention and diarrhea was reduced in the short-peptide group (11% *vs.* 36%, P=0.03 and 6% *vs.* 24%, P=0.04, respectively), and the use of short-peptide formula was the only independent variable of reduction in gastric retention and diarrhea [HR =0.469 (95% CI: 0.239–0.922), P=0.028; and HR =0.394 (95% CI: 0.161–0.965), P=0.041 respectively]. Therefore, short-peptide formula is well tolerated and is more suitable for patients with intestinal injury or risk of GI injury (AGI grades I–II).

It is important to fully utilize the advantages of EN in maintaining gut barrier functions and gut microecology, shortening hospitalization time, and reducing postoperative complications (30,31) to achieve nutritional targets as early as possible by selecting the appropriate EN initiation time and formulations for critically ill patients with AGI. It has been reported (32) that an energy achievement rate ≤65% 3 days after provision of EN was significantly correlated with increased mortality, and patients who delayed reaching the target EN calories had higher mortality (33,34). Similarly, patients receiving adequate protein intake (achievement of >90% of target protein intake) were more likely not to require a ventilator, had lower in-ICU and in-hospital mortality, and had a higher 60-day survival rate than patients who did not receive an adequate protein intake (35). According to a new study (36), a higher average EN/EN + PN ratio within the first 7 days was correlated with lower hospital mortality. In this research, the percentage of EN calories and protein on the 3rd day in the short-peptide formula group was lower than that in the intact-protein formula group (P=0.01), which may be related to the later initiation of EN in the short-peptide formula group and its lower energy density compared to that of the intact-protein formula group (1.0 *vs.* 1.5 kcal/mL) with the same initial feeding speed. However, there was no statistical difference in the percentage of EN calories and protein on the 7th day between the two groups (P>0.05). In addition, the EN percent elevation in calories and protein on days 3–7 was notably higher in the short-peptide versus the intact-protein formula group (48% *vs.* 38%, P=0.03 and 37% *vs.* 30%, P=0.047, respectively). The reason for this result is that feeding intolerance in the two groups was rare, so increased EF was more likely in the short-peptide group. However, diarrhea and gastric retention were more common in the intact-protein group. Furthermore, the short-peptide formula has the advantages of improving the absorption of nutrients, reducing mucosal inflammation, promoting protein synthesis, and maintaining the integrity of intestinal mucosal microcirculation (25). Therefore, the short-peptide formula was selected as the initial EN formula because of its ability to reach the nutritional target early, making it more suitable for EN provision in the early stage of critically ill patients with AGI grades I–II (≤7 d).

An interesting problem was found in this study: The timing of EN was not consistent between the two groups (81 *vs.* 50 h; P=0.03), despite consistent baseline characteristics. The possible reasons were as follows: clinicians were more inclined to choose the short-peptide EN formula and later timing of EN for patients with a high risk of feeding intolerance, despite there being no statistical difference in AGI grades (AGI grade I, 72% *vs.*

74%) between the two groups. Provision of EN in the early phase of AGI (defined by unstable metabolism and severely increasing catabolism; ≤48 h) (1) may increase the burden and damage to the gut, so we employed the gut rest strategy. This strategy proposes that trophic feeding after 72 h might be the best choice for critically ill patients with AGI and is also an organ-protective strategy (37). In this study, the late initiation of EN coincided with the gut rest strategy. In addition, clinicians performed AGI grade assessments and formulated individualized nutritional strategies for patients in the early phase of the acute stage (≤48 h). Most patients with AGI did not start EN in this early phase, so we define this period as the time window of strategy formulation for patients with AGI grades I–II. When the patient was in the late phase of the acute stage (defined as obvious muscle wasting and stable metabolic disturbance; 3–7 d) (1), clinicians had already determined the AGI grade and understood the GI tract of the patient with AGI. Individual feeding strategies were adopted, and most patients were provided with EN during this period. Therefore, we define this phase (3–7 d) as the time window for EF of patients with AGI grades I–II.

Some shortcomings existed in this study. Firstly, data selection and information bias may have existed due to the retrospective nature of this study. Additionally, as most of the enrolled patients did not have dynamic changes of prealbumin recorded, we chose to use serum albumin as the nutritional assessment index, which may not accurately reflect the real differences between nutritional formulations. Lastly, the sample size of this study was small. Nevertheless, this study is the first to explore the influence of short-peptide EN formula provision on clinical outcomes and feeding tolerance in critically ill patients with AGI. The results of this study will require verification with further randomized controlled trials.

Conclusions

Although selection bias may appear in this study due to its retrospective nature, patients in the acute phase of AGI who received the short-peptide formula had a lower incidence of diarrhea and gastric retention and a greater EN percent elevation in calories and protein during days 3–7 of ICU admission. Therefore, the short-peptide formula is more easily tolerated by patients in the acute phase of AGI grades I–II. The short-peptide formula can also achieve nutritional goals quickly with EN provision, making it the preferred formula for the initiation of EN in the acute phase of AGI.

Acknowledgments

Funding: This work was supported by the Project of Jilin Provincial Department of Finance (The Standardized Implementation, Promotion, and Application of Enteral Nutritional Feeding Process for Severe Patients).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1837/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-1837/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-1837/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The protocol was approved by The First Hospital of Jilin University Ethics Committee for Clinical Research (No. 19K032-001) and individual consent for this retrospective analysis was waived.

References

1. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38:48-79.
2. McClave SA, Heyland DK. The physiologic response and associated clinical benefits from provision of early enteral nutrition. Nutr Clin Pract 2009;24:305-15.

3. Lankelma JM, van Vught LA, Belzer C, et al. Critically ill patients demonstrate large interpersonal variation in intestinal microbiota dysregulation: a pilot study. Intensive Care Med 2017;43:59-68.
4. Taylor BE, McClave SA, Martindale RG, et al. 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.). Crit Care Med 2016;44:390-438.
5. Slack E, Balmer ML, Macpherson AJ. B cells as a critical node in the microbiota-host immune system network. Immunol Rev 2014;260:50-66.
6. Reintam Blaser A, Starkopf J, Alhazzani W, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. Intensive Care Med 2017;43:380-98.
7. Al-Dorzi HM, Arabi YM. Nutrition support for critically ill patients. JPEN J Parenter Enteral Nutr 2021;45:47-59.
8. Zhang D, Li Y, Ding L, et al. Prevalence and outcome of acute gastrointestinal injury in critically ill patients: A systematic review and meta-analysis. Medicine (Baltimore) 2018;97:e12970.
9. Reintam Blaser A, Malbrain ML, Starkopf J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. Intensive Care Med 2012;38:384-94.
10. Li H, Zhang D, Wang Y, et al. Association between acute gastrointestinal injury grading system and disease severity and prognosis in critically ill patients: A multicenter, prospective, observational study in China. J Crit Care 2016;36:24-8.
11. Reintam A, Parm P, Redlich U, et al. Gastrointestinal failure in intensive care: a retrospective clinical study in three different intensive care units in Germany and Estonia. BMC Gastroenterol 2006;6:19.
12. Padar M, Starkopf J, Uusvel G, et al. Gastrointestinal failure affects outcome of intensive care. J Crit Care 2019;52:103-8.
13. Reintam A, Parm P, Kitus R, et al. Gastrointestinal failure score in critically ill patients: a prospective observational study. Crit Care 2008;12:R90. Erratum in: Crit Care 2008;12:435.
14. Warren M, McCarthy MS, Roberts PR. Practical Application of the Revised Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: A Case Study Approach. Nutr Clin Pract 2016;31:334-41.
15. Li H, Lu J, Li H, et al. Association between nutrition support and acute gastrointestinal injury in critically ill patients during the first 72 hours. Clin Nutr 2021;40:217-21.
16. Seres DS, Ippolito PR. Pilot study evaluating the efficacy, tolerance and safety of a peptide-based enteral formula versus a high protein enteral formula in multiple ICU settings (medical, surgical, cardiothoracic). Clin Nutr 2017;36:706-9.
17. TARGET Investigators, for the ANZICS Clinical Trials Group; Chapman M, Peake SL, et al. Energy-Dense versus Routine Enteral Nutrition in the Critically Ill. N Engl J Med 2018;379:1823-34.
18. Endo A, Shiraishi A, Fushimi K, et al. Comparative effectiveness of elemental formula in the early enteral nutrition management of acute pancreatitis: a retrospective cohort study. Ann Intensive Care 2018;8:69.
19. Antigua AD, Tran J, Lemon SJ, et al. Challenges of Administering Pancrelipase in Pancreatitis Patients. J Am Coll Nutr 2016;35:334-8.
20. Poropat G, Giljaca V, Hauser G, et al. Enteral nutrition formulations for acute pancreatitis. Cochrane Database Syst Rev 2015;(3):CD010605.
21. Ibrahim H, Mansour M, El Gendy YG. Peptide-based formula versus standard-based polymeric formula for critically ill children: is it superior for patients' tolerance? Arch Med Sci 2020;16:592-6.
22. Mundi MS, Velapati S, Kuchkuntla AR, et al. Reduction in Healthcare Utilization With Transition to Peptide-Based Diets in Intolerant Home Enteral Nutrition Patients. Nutr Clin Pract 2020;35:487-94.
23. Sanz-Paris A, Martinez-García M, Martinez-Trufero J, et al. Oligomeric Enteral Nutrition in Undernutrition, due to Oncology Treatment-Related Diarrhea. Systematic Review and Proposal of An Algorithm of Action. Nutrients 2019;11:1888.
24. Mohamed Elfadil O, Steien DB, Narasimhan R, et al. Transition to peptide-based diet improved enteral nutrition tolerance and decreased healthcare utilization in pediatric home enteral nutrition. JPEN J Parenter Enteral Nutr 2022;46:626-34.
25. Zhang J, Yu WQ, Wei T, et al. Effects of Short-Peptide-Based Enteral Nutrition on the Intestinal Microcirculation and Mucosal Barrier in Mice with Severe Acute Pancreatitis. Mol Nutr Food Res 2020;64:e1901191.
26. Koopman R, Crombach N, Gijsen AP, et al. Ingestion of a protein hydrolysate is accompanied by an accelerated in vivo digestion and absorption rate when compared with its intact protein. Am J Clin Nutr 2009;90:106-15.

27. Shi B, Song D, Xue H, et al. Abnormal expression of the peptide transporter PepT1 in the colon of massive bowel resection rat: a potential route for colonic mucosa damage by transport of fMLP. Dig Dis Sci 2006;51:2087-93.
28. Ziegler TR, Fernández-Estívariz C, Gu LH, et al. Distribution of the H+/peptide transporter PepT1 in human intestine: up-regulated expression in the colonic mucosa of patients with short-bowel syndrome. Am J Clin Nutr 2002;75:922-30.
29. Nosworthy MG, Brunton JA. Cysteinyl-glycine reduces mucosal proinflammatory cytokine response to fMLP in a parenterally-fed piglet model. Pediatr Res 2016;80:293-8.
30. Herbert G, Perry R, Andersen HK, et al. Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications. Cochrane Database Syst Rev 2018;10:CD004080.
31. Shen TY, Qin HL, Gao ZG, et al. Influences of enteral nutrition combined with probiotics on gut microflora and barrier function of rats with abdominal infection. World J Gastroenterol 2006;12:4352-8.
32. Wang WN, Yang MF, Wang CY, et al. Optimal Time and Target for Evaluating Energy Delivery after Adjuvant Feeding with Small Bowel Enteral Nutrition in Critically Ill Patients at High Nutrition Risk. Nutrients 2019;11:645.
33. 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;41:706-42.
34. 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;54:480-6.
35. Song JH, Lee HS, Kim SY, et al. The influence of protein provision in the early phase of intensive care on clinical outcomes for critically ill patients on mechanical ventilation. Asia Pac J Clin Nutr 2017;26:234-40.
36. Fu PK, Chao WC, Hsu CY, et al. Caloric Intake with High Ratio of Enteral Nutrition Associated with Lower Hospital Mortality for Patients with Acute Respiratory Distress Syndrome Using Prone Position Therapy. Nutrients 2021;13:3259.
37. Zhang D, Li H, Li Y, et al. Gut rest strategy and trophic feeding in the acute phase of critical illness with acute gastrointestinal injury. Nutr Res Rev 2019;32:176-82.

(English Language Editor: D. Fitzgerald)

Cite this article as: Wang YQ, Li YH, Li YT, Li HX, Zhang D. Comparisons between short-peptide formula and intact-protein formula for early enteral nutrition initiation in patients with acute gastrointestinal injury: a single-center retrospective cohort study. Ann Transl Med 2022;10(10):573. doi: 10.21037/atm-22-1837

