CLINICAL SCIENCE OF NUTRITION

Original Article

DOI: 10.5152/ClinSciNutr.2023.221341

Enteral Nutrition Challenge in Patients Requiring Vasoactive Agents: A National Survey

Özlem Özkan Kuşcu[1], Nursel Sürmelioğlu[2], Kutay Demirkan[3], Hasan Murat Gündüz[4]

[1]Department of Intensive Care, Başkent University, Faculty of Medicine, Ankara, Turkey
[2]Department of Clinical Pharmacy, Çukurova University, Faculty of Pharmacy, Adana, Turkey
[3]Department of Clinical Pharmacy, Hacettepe University, Faculty of Pharmacy, Ankara, Turkey
[4]Department of Anesthesiology and Reanimation, Çukurova University, Faculty of Medicine, Adana, Turkey

Cite this article as: Özkan Kuşcu Ö, Sürmelioğlu N, Demirkan K, Gündüz HM. Enteral nutrition challenge in patients requiring vasoactive agents: A national survey. *Clin Sci Nutr.* 2023;5(1):1-7.

ABSTRACT

Objective: In this study, it was aimed to determine the approaches of physicians with intensive care unit experience to enteral nutrition therapy in patients requiring vasoactive drugs.
Methods: A 14-question electronic questionnaire was applied to physicians practicing in intensive care units.
Results: A total of 244 physicians (54.5% women) with a mean (SD) age of 39.76 (8.45) years participated in the study. The specialties of the participants were intensive care (35.2%), anesthesiology and reanimation (30.7%), and general surgery (16.4%). Interestingly, 39.3% of the study participants were not using any screening tool for the nutrition of critical patients. Although most of the physicians encountered enteral nutrition intolerance and gastrointestinal system complications as the most common reasons for enteral feeding interruption in patients receiving vasoactive drugs, it is demonstrated that the rate of vasoactive drug dose threshold use, routine assessment of organ failure, and follow-up organ perfusion was low.
Conclusion: Based on the results of this study, it is seen that there are differences among physicians in terms of nutritional approach to critically ill patients. It is obvious that these differences are more pronounced in doctors of different titles and institutions. In order to provide a standard treatment, especially in this critically ill patient population, it will be beneficial to increase the importance given to "nutrition therapy" in both specialist training and in-service training. In addition, it is thought that standardization will be achieved in patient care by including "nutrition therapy" in treatment protocols, considering the recommendations made by current guidelines.

Keywords: Enteral nutrition, critical illness, shock, vasoactive drugs, enteral nutrition intolerance

INTRODUCTION

Critical illness progresses with catabolic pathophysiological changes. Mucosal integrity is impaired and enterocytes become hyperpermeable. Enteral nutrition (EN) has been shown to alleviate the catabolic state by increasing the blood flow to the gastrointestinal system (GIS). Enteral nutrition preserves the structural integrity and barrier function of the gut, promotes symbiosis, maintains normal immune function, and prevents GIS complications.[1-7] Some of the critically ill patients with hemodynamic instability need to receive intensive treatments such as vasoactive drugs. Vasoconstriction at the splanchnic circulation and peripheral tissues maintains vital organ perfusion with redistribution of blood flow in the case of vasoactive treatment. Vasoconstriction and redistribution may lead to impaired oxygen supply/demand ratio and intestinal ischemia.[8] Thus, potential benefits of early EN should be balanced with the risks.

In the first 24 to 48 hours of intensive care unit (ICU) admission, EN is recommended.[9-11] For patients with shock, firstly providing the hemodynamic and tissue perfusion goals with fluid resuscitation/vasopressor/inotrope after low-dose EN is recommended. The American Society for Parenteral and Enteral Nutrition (ASPEN) recommends initiation/continuation of EN to patients who receive a stable vasoactive drug dose and who progress with a decrease in lactate level with sufficient perfusion pressure; European Society of Intensive Care Med suggests initiating low-dose EN if the patient has fluid response shock or hemodynamic stability is achieved with vasopressor

The study was presented as an oral presentation in KEPAN 2021, Antalya, Turkey.

Corresponding author: Özlem Özkan Kuşcu, e-mail: ozlemozkankuscu@gmail.com

Received: September 23, 2022 Accepted: January 16, 2023
Publication Date: February 16, 2023

support at a fixed or decreasing dose and if there is no increase in the level of lactate during the follow-up.[12,13]

In the NUTRIREA trial and some of the observational studies, it is suggested that the frequency of intestinal ischemia was higher in patients who are receiving vasopressors if early EN is started.[14-16] During this period, remaining vigilant for the signs of bowel ischemia is also recommended.

In this study, we aimed to examine the approaches of physicians with ICU experience to nutritional therapy of critically ill patients receiving vasoactive drugs.

METHODS

Cukurova University Faculty of Medicine Non-interventional Clinical Research Institutional Ethics Committee approved the study protocol (date: 2021, decision no. 2021/109-51).

Study Participants

This crosssectional survey study was performed between February 2 and 9, 2021, via an electronic questionnaire among physicians currently practicing in Turkey with ICU experience. Pediatricians were not included in the study.

Survey Development and Distribution

A questionnaire consisting of 19 questions was prepared to evaluate physicians' approach to nutritional therapy in patients requiring vasoactive drugs. After a comprehensive literature review, survey questions were developed by the researchers specifically for this study. The survey was created on Google® Forms online survey platform. The questionnaire was piloted with the researchers' colleagues (medical residents) before the initialization. The total time to completely answer these 19 questions was approximately 10 minutes. The questionnaire consisted of 2 parts; the first part includes 6 questions regarding the participants' demographic information (age, gender, medical specialty, employing healthcare facility, duration of professional experience, and title) and the second part includes 13 multiple-choice questions regarding the participants' approaches and experiences on EN of patients who require a vasoactive agent. While 11 of those questions have only 1 answer option, 2 of them (3rd and 11th questions) have more than 1 answer option. Answers were evaluated groups that are composed according to demographic information.

The participants of the survey were physicians with ICU experience who were individually invited to participate in the survey via professional email groups. Participation in the survey was on a voluntary basis, and reminder emails were sent only once. Participants who voluntarily participated in the study first approved the informed consent form via the survey link and then answered the questions online. Only entirely completed surveys were included in the study analysis.

Statistical Analysis

IBM Statistical Package for Social Sciences 20.0 (IBM SPSS Corp., Armonk, NY, USA) software program was used for statistical analysis. Mean (±SD) or median (minimum-maximum) values were given for numerical variables as descriptive statistics, and number (percentage) values were given for categorical variables. The *t*-test, Mann–Whitney *U*-test, and post-hoc analysis were used to compare quantitative data. In terms of normal distribution, the Kolmogorov–Smirnov test was used. The chi-square and Fischer's exact tests were used to compare categorical variables. For all the tests, $P < .05$ was considered statistically significant.

According to power analysis, a total of 240 participants were required for a 0.20 effect size with 95% power and 5% error margin (G* Power 3.0.10 software).

RESULTS

The number of participants was 244 (55% female). The mean ± SD age was 39.76 ± 8.45 years. Participants' demographic data (medical specialty, title, employing healthcare facility, and duration of professional experience) are given in Table 1.

Thirteen multiple-choice questions in order to evaluate the physicians' approaches and answers to these questions are summarized in Tables 2 and 3.

Participants were grouped according to their age, gender, medical specialty, employing healthcare facility, duration of professional experience, and title. The answers of the 13 multiple-choice questions evaluated according to these groups. The results are stated below.

Nutritional Screening

With regard to the specialty, pulmonologists were not using screening tools ($P < .001$); intensive care specialists were using the Nutric score and nutritional risk screening (NRS) 2002 scales ($P < .001$); associate professors, professors, and intensivists were using NRS 2002 ($P < .001$), while the others were not using a screening scale ($P < .001$). With regard to the experience, those with more than 20 years of professional experience were using the NRS 2002 scale ($P < .05$). According to the institution, physicians practicing in secondary-level public and private hospitals were not tending to use a screening scale ($P < .05$).

Table 1. Demographic Information of the Participants	
	n (%)
Specialties	
Intensive care	86 (35.2)
Anesthesiology and reanimation	75 (30.7)
General surgery	40 (16.5)
Internal medicine	26 (10.6)
Pulmonology	12 (4.9)
Neurology	5 (2.1)
Title	
Specialist doctor	95 (38.9)
Intensivist	60 (24.6)
Research assistant	55 (22.6)
Professor	19 (7.8)
Associate professor	15 (6.1)
Duration of professional experience	
<5 years	45 (18.4)
5-10 years	76 (31.1)
10-15 years	52 (21.3)
15-20 years	27 (11.1)
>20years	44 (18.1)
Employing healthcare facility	
University and Training and Research Hospitals	135 (55.4)
State Hospital	64 (26.2)
Private and Foundation Hospitals	45 18.4)

Table 2. Approaches of Physicians to EN Therapy in Patients Requiring Vasoactive Drugs—Questions
1. What is your preferred nutritional screening score?
2. When do you start EN in hemodynamically stable shock patient?
3. When do you interrupt/stop EN?
4. What is the lactate level to interrupt EN?
5. Which is true for shock patients?
6. While planning to start EN therapy in shock patients, would you also consider organ failure?
7. What would be your preference of nutrition treatment for patients requiring vasoactive drugs until hemodynamic stability is achieved?
8. What is the maximum dose range of norepinephrine in patients receiving EN treatment?
9. What is the maximum dose range of dopamine in patients receiving EN treatment?
10. Have you experienced any EN intolerance during vasoactive drug therapy?
11. If the answer is yes, which complications did you notice during EN intolerance due to vasoactive drug therapy?
12. Would you do GRV control in hemodynamically stable patients receiving vasopressor and EN?
13. Would you consider starting PN in patients whose EN could not reach the target?
EN, enteral nutrition; GRV, gastric residual volume; PN, parenteral nutrition.

Time to Initiate Enteral Nutrition

Time to initiate EN to hemodynamically stable shock patients was questioned, and most of the participants (55.7%, n = 136) declared that they initiate immediately. There was no difference detected between the groups ($P > .05$).

Reasons of Enteral Nutrition Interruption

More than 1 answer option is provided to the question of "In which cases do you interrupt/stop your patient's EN therapy while in the presence of vasoactive agents." The top 3 answers given by the physicians to this question were abdominal distension (n = 208, 85.2%), vomiting (n = 196, 80.3%), and excess gastric residual volume (GRV) (n = 187, 76.6%).

Organ Failure Assessment

Lactate threshold to interrupt EN questioned 54.9% of the participants answered as above 4 mmol/L while 35.2% of them were not considering the lactate level. There was no significant difference detected between the groups ($P > .05$).

Routine assessment of organ failure was evaluated with the question "While planning to start EN therapy in shock patients, would you also consider organ failure?" About 9.8% of the participants were not considering organ failure, 31.6% were evaluating with "sequential organ failure assessment" score, and 57.8% declared that they were evaluating on a patient basis. There was no significant difference detected between the groups ($P > .05$).

Nutrition of Vasoactive Agent Requiring Patient

There were significant differences with regard to the specialty of the physicians to the question "What would

Table 3. Approaches of Physicians to EN Therapy in Patients Requiring Vasoactive Drugs—Top 3 Answers (%)		
1. I don't use any screening tool (39.3)	NRS 2002 (34.4)	Nutric score (21.7)
2. Immediately (55.7)	Within the first 72 hours (37.3)	Within 3-7 days (4.9)
3. Abdominal distention (85.2)	Vomiting (80.3)	GRV excess (76.6)
4. >4 mmol/L (54.9)	I do not consider lactate level (35.2)	>2 mmol/L (9.8)
5. Nutrition is not a priority (79.5)	Nutrition is priority (20.5)	—
6. I evaluate on a patient basis (57.8)	I consider SOFA's ≥2-point increase (23.4)	I do not consider the presence of organ failure (9.8)
7. Trophic EN (36.9)	Intravenous dextrose (30.7)	PN (13.5)
8. I do not use a dose threshold (41.4)	0.3-0.5 μg/kg/min (18.0)	0.05-0.1 μg/kg/min (14.8)
9. I do not use a dose threshold (44.7)	5-10 μg/kg/min (24.6)	10-20 μg/kg/min (15.6)
10. Yes (74.2)	No (25.8)	—
11. GRV excess (79.9)	Abdominal distention (72.4)	Vomiting (69.8)
12. I do it on selected patients (34.4)	I do it every day in all patients (32.0)	I don't (12.3)
13. Yes (70.9)	No (29.1)	—

EN, enteral nutrition; GRV, gastric residual volume; NRS, nutritional risk screening; PN, parenteral nutrition; SOFA, sequential organ failure assessment.

be your preference of nutrition treatment for patients requiring vasoactive agent until hemodynamic stability is achieved?" While 53.8% of internists and 47.4% of general surgeons stated that they preferred intravenous dextrose, 53.5% of intensive care specialists and 40% of anesthesiology and reanimation specialists stated that they prefer trophic nutrition ($P < .05$). The rate of trophic nutrition was higher in female physicians than male ($P < .05$).

It was determined that 41.4% (n = 101) and 44.7% (n = 109) of the physicians did not use a threshold dose value for norepinephrine and dopamine while managing EN treatment, and there were no significant differences detected between the groups. In addition, 74.2% of the physicians stated that they had previously experienced EN intolerance in patients receiving vasoactive drugs and mostly noticed this with abdominal distention, excess GRV, and vomiting.

Measurement of Gastric Residual Volume

Gastric residual volume practices of participants were evaluated with the question "Would you do GRV control in hemodynamically stable patients receiving vasopressor and EN?" There was no significant difference detected between the groups ($P > .05$).

Supplemental Parenteral Nutrition

Supplemental parenteral nutrition (PN) support was questioned for vasoactive agent receiving patients whose energy target could not be reached with EN, nearly one-third of the participants declared that they were not considering supplemental PN.

DISCUSSION

To our knowledge, this is the first study evaluating the approach of physicians to the nutrition therapy of patients requiring vasoactive drugs, and we determined that physicians with ICU experience had varied approaches to EN in patients requiring vasoactive agents. The main results of our study could be specified as follows.

Nutritional Screening

Screening of nutrition with a scale is questioned. It has been detected that 39.3% of the participants declared that they did not tend to use a nutrition scale, although screening of all critical patients' nutritional status is recommended by the guidelines.[17,18] The rate of nutrition screening with a scale was found to be statistically significantly low in pulmonology and neurology specialists and secondary level hospital employees ($P < .05$). Use of the nutrition screening scale was evaluated according to the title, associate professors, professors, and intensivists were using nutrition screening tools more than the others ($P < .05$).

Time to Initiate Enteral Nutrition

Most of the participants stated that they initiate EN in the first 72 hours of ICU admission. This finding was

found to be in line with the recommendation of nutrition guidelines;[9,10,15] however, there are contrary studies demonstrating EN latency in the literature.[19-21]

Organ Dysfunction Assessment

Critically ill patients with hemodynamic instability need to receive intensive treatments such as fluid replacement and vasoactive drugs. Approach to EN may be a determinant factor for outcome of patients with hemodynamic instability and should be individualized. Organ failure scoring systems are used to predict the degree of organ dysfunction, course of the disease serially over time, and decrease in complications.[22,23,29-31] However, a significant number of the study participants declared that they do not tend to use determinants of tissue perfusion such as organ failure scoring systems, threshold value for vasopressor therapy, or a threshold value for the lactate level.

Reasons for Enteral Nutrition Interruption

Reasons for EN interruption were questioned, and GIS symptoms such as excess GRV, abdominal distention, and vomiting were stated as the common causes. We demonstrated that the declared frequency of GIS symptoms was higher than the literature.[12,19,24] We think that the lack of attention to tissue perfusion and organ failure may have resulted with increased GIS complications.

Measurement of Gastric Residual Volume

Routine measurement of GRV as evidence of digestive system dysfunction is not recommended in the recent guidelines because of the difficulties and infectious risks such as SARS-CoV-2.[17,18,25] Nearly a third of the participants declared that they routinely measure GRV. Gastrointestinal system symptoms are reported as the most common cause of EN latency,[17,21,26,27] and similarly EN complications are suggested as the most common cause of failure to achieve nutritional targets;[27] in this situation, supplemental PN is suggested.[28,29]

Supplemental Parenteral Nutrition

Nearly one-third of the participants declared that they were not considering supplemental PN, although it is recommended in the randomized controlled trials and guidelines.[13,30] A higher ratio of supplemental PN could be expected because of the high ratio of EN complications.

Considering all the answers, the nutritional status screening is not sufficient at ICU admission, the timing of EN initiation is compatible with the guidelines, and tissue perfusion and organ failure follow-up is not enough as expected in patients receiving vasoactive agents. Despite the high rate of GIS complications declared by the participants, the rate of supplemental PN considering participants was low.

Study Limitations

The survey was designed online. Only completed forms could be included in the study. The number of dropout/nonresponsive surveys could not be calculated.

In conclusion, based on the results of this study, it is seen that there are differences among physicians in terms of nutritional approach to critically ill patients. It is obvious that these differences are more pronounced in doctors of different titles and institutions. In order to provide a standard treatment, especially in this critically ill patient population, it will be beneficial to increase the importance given to "nutrition therapy" in both specialist training and in-service training. In addition, it is thought that standardization will be achieved in patient care by including "nutrition therapy" in treatment protocols, considering the recommendations made by current guidelines. The main points that are emphasizing the results of the study are listed below:

- The rate of participants' nutrition screening during the ICU admission was low.
- Time to EN initiation was compatible with the guidelines, but there were issues that need attention during the follow-up period.
- The ratio of using threshold dose for vasoactive agents, also follow up for tissue perfusion with lactate level organ failure assessment scales and the ratio of supplemental PN was found to be low. The rate of GIS complications declared by the participants was high.
- Qualification of the hospital (secondary/tertiary-level hospitals), specialty of the physician, professional experience period, and titles of physicians were the main determinants for approach to EN therapy in patients requiring vasoactive drugs.

Ethics Committee Approval: The study protocol was approved by the Cukurova University Ethics Committee (Date: February 2, 2021, decision no. 2021/109-51).

Informed Consent: Participants who voluntarily participated in the study first approved the informed consent form via the survey link and then answered the questions online.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Ö.Ö.K., N.S., K.D., H.M.G.; Design – Ö.Ö.K., N.S., K.D.; Supervision – K.D., H.M.G.; Resources – Ö.Ö.K., N.S., K.D.; Data Collection and/or Processing – Ö.Ö.K., N.S.; Analysis and/or Interpretation – Ö.Ö.K., N.S., K.D.; Literature Search – Ö.Ö.K., N.S., K.D.; Writing Manuscript – Ö.Ö.K., N.S., K.D.; Critical Review – K.D., H.M.G.

Declaration of Interests: The authors declare that they have no competing interest.

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

REFERENCES

1. Patel JJ, Rice T, Heyland DK. Safety and outcomes of early enteral nutrition in circulatory shock. *JPEN J Parenter Enteral Nutr*. 2020;44(5):779-784. [CrossRef]
2. McClave SA, Chang WK. Feeding the hypotensive patient: does enteral feeding precipitate or protect against ischemic bowel? *Nutr Clin Pract*. 2003;18(4):279-284. [CrossRef]
3. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. *Crit Care Med*. 2001;29(12): 2264-2270. [CrossRef]
4. Kusdk K, Croce M, Fabian T. Enteral vs. parenteral feeding: effects on septic morbidity following blunt and penetrating abdominal trauma. *Ann Surg*. 1992;215:503-511. [CrossRef]
5. Jabbar A, Chang WK, Dryden GW, McClave SA. Gut immunology and the differential response to feeding and starvation. *Nutr Clin Pract*. 2003;18(6):461-482. [CrossRef]
6. Nguyen NQ, Besanko LK, Burgstad C, et al. Delayed enteral feeding impairs intestinal carbohydrate absorption in critically ill patients. *Crit Care Med*. 2012;40(1):50-54. [CrossRef]
7. Hu Q, Ren H, Hong Z, et al. Early enteral nutrition preserves intestinal barrier function through reducing the formation of neutrophil extracellular traps (NETs) in critically Ill surgical patients. *Oxid Med Cell Longev*. 2020;2020:8815655. [CrossRef]
8. Lasierra JF, Pérez-Vela J, González JM. Enteral nutrition in the hemodynamically unstable critically ill patient. *Med Intensiva*. 2015;39(1):408. [CrossRef]
9. Merchan C, Altshuler D, Aberle C, Papadopoulos J, Schwartz D. Tolerability of enteral nutrition in mechanically ventilated patients with septic shock who require vasopressors. *J Intensive Care Med*. 2017;32(9):540-546. [CrossRef]
10. Moore FA, Feliciano DV, Andrassy RJ, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Ann Surg*. 1992;216(2):172-183. [CrossRef]
11. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. *Am J Crit Care*. 2010;19(3):261-268. [CrossRef]
12. 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(3):380-398. [CrossRef]
13. McClave SA, Taylor BE, 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 (ASPEN). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211. [CrossRef]
14. Melis M, Fichera A, Ferguson MK. Bowel necrosis associated with early jejunal tube feeding: a complication of postoperative enteral nutrition. *Arch Surg*. 2006;141(7):701-704. [CrossRef]
15. Mancl EE, Muzevich KM. Tolerability and safety of enteral nutrition in critically ill patients receiving intravenous vasopressor therapy. *JPEN J Parenter Enteral Nutr*. 2013;37(5):641-651. [CrossRef]
16. Reignier J, Boisramé-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet*. 2018;391(10116):133-143. [CrossRef]
17. 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 (ASPEN). *Crit Care Med*. 2016;44(2):390-438. [CrossRef]
18. Heyland DK, Ortiz A, Stoppe C, et al. Incidence, risk factors, and clinical consequence of enteral feeding intolerance in the mechanically ventilated critically ill: an analysis of a multicenter, multiyear database. *Crit Care Med*. 2021;49(1):49-59. [CrossRef]
19. De Jonghe B, Appere-De-Vechi C, Fournier M, et al. A prospective survey of nutritional support practices in intensive care unit patients: what is prescribed? What is delivered? *Crit Care Med*. 2001;29(1):8-12. [CrossRef]
20. Binnekade JM, Tepaske R, Bruynzeel P, Mathus Vliegen EMH, Haan RJ. Daily enteral feeding practice on the ICU: attainment of goals and interfering factors. *Crit Care Med*. 2005;9(3):1-8. [CrossRef]
21. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Crit Care Med*. 1999;27(7):1252-1256. [CrossRef]
22. Arts DG, de Keizer NF, Vroom MB, De Jonge E. Reliability and accuracy of sequential organ failure assessment (SOFA) scoring. *Crit Care Med*. 2005;33(9):1988-1993. [CrossRef]
23. Hejazi N, Mazloom Z, Zand F, Rezaianzadeh A, Amini A. Nutritional assessment in critically ill patients. *Iran J Med Sci*. 2016;41(3):171-179.
24. Fernández-Ortega JF, Herrero Meseguer JI, Martínez García P, Metabolism and Nutrition Working Group of the Spanish Society of Intensive Care Medicine and Coronary units. Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus SEMICYUC-SENPE: indications, timing and routes of nutrient delivery. *Nutr Hosp*. 2011;26(2):7-11. [CrossRef]
25. Gungabissoon U, Hacquoil K, Bains C, et al. Prevalence, risk factors, clinical consequences, and treatment of enteral feed intolerance during critical illness. *JPEN J Parenter Enteral Nutr*. 2015;39(4):441-448. [CrossRef]
26. Adam S, Batson S. A study of problems associated with the delivery of enteral feed in critically ill patients in five ICUs in the UK. *Intensive Care Med*. 1997;23(3):261-266. [CrossRef]

27. Mentec H, Dupont H, Bocchetti M, Cani P, Ponche F,Bleichner G. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med*. 2001;29(10):1955-1961. [CrossRef]
28. Uozumi M, Sanui M, Komuro T, et al. Interruption of enteral nutrition in the intensive care unit: a single-center survey. *J Intensive Care*. 2017;5(1):52. [CrossRef]
29. Salciute-Simene E, Stasiunaitis R, Ambrasas E, et al. Impact of enteral nutrition interruptions on underfeeding in intensive care unit. *Clin Nutr*. 2021;40(3):1310-1317. [CrossRef]
30. Heidegger CP, Berger MM, Graf S, et al. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. *Lancet*. 2013;381(9864):385-393. [CrossRef]