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A Volume-Based Enteral Nutrition Support Regimen Improves Caloric Delivery but May Not Affect Clinical Outcomes in Critically Ill Patients

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Abstract

Introduction: Meeting enteral nutrition goals is an ongoing challenge in the intensive care unit (ICU). Most hospitals use rate-based (RB) protocols for nutrient delivery. Previous studies have found that volume-based (VB) protocols improve delivery of prescribed calories. However, these studies did not assess clinical outcomes. We hypothesize that a VB method will improve the delivery of prescribed calories and lead to improved clinical outcomes. *Methods:* A before-and-after study was performed following implementation of a VB feeding protocol in an adult mixed medical-surgical ICU. Formal institutional review board approval was obtained. The effect of RB and VB protocols on percentage of goal calories received, ICU length of stay (LOS), hospital LOS, mortality, days on the ventilator, and rates of infection were investigated using the Kruskal-Wallis test of differences. Multivariate regression was used to identify independent predictors of outcome. Significance was defined as $P < .05$. *Results:* A total of 77 patients were included (RB = 39, VB = 38). There were no differences in demographics between the 2 groups with the exception of the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, which was significantly higher in the VB group. VB patients received significantly more prescribed calories (74% vs 57%, $P < .001$). VB patients had significantly longer ICU LOS and duration of mechanical ventilation on univariate analysis. These differences did not persist after controlling for APACHE II score. *Conclusion:* VB enteral feeding allows for a significantly greater provision of prescribed calories but may not affect clinical outcomes. A larger sample size is needed for adequate power to corroborate these findings. (*JPEN J Parenter Enteral Nutr*. XXXX;xx:xx-xx)

Keywords

critically ill; enteral nutrition; parenteral nutrition; underfeeding

Clinical Relevancy Statement

Underfeeding in the critically ill patient is associated with increased morbidity and mortality. A volume-based protocol is a superior method to a rate-based protocol for the delivery of prescribed calories in the intensive care unit (ICU). This finding is clinically relevant for guiding intensivists and dietitians who implement enteral nutrition in the ICU.

Introduction

Although the importance of enteral nutrition (EN) support in critically ill patients is well established, how to optimize adequate delivery of prescribed calories remains controversial.[1,2] Appropriate nutrition support of critically ill patients has both direct and indirect benefits. Indirect benefits of EN include the maintenance of structural and functional gut integrity, a decrease in intestinal permeability, and the attenuation of the inflammatory response and oxidative stress.[1,2] Direct benefits include mitigating the development of a protein-calorie deficit that can rapidly occur in conjunction with critical illness.[1,2]

Discrepancies between prescribed EN goals and actual delivery of EN in the critically ill patient are common.[3] In fact, multiple studies show that patients in North America routinely receive between 51.3% and 59% of goal calories.[4–6] Exacerbating this dilemma is the fact that baseline malnutrition in hospitalized patients has been reported to be as high as 50%.[7–9] This high percentage of malnutrition, coupled with underfeeding in the setting of an acute stress response, increases the propensity for adverse patient outcomes, including impaired

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immune response, poor wound healing, increased mortality, longer lengths of hospital stay, and, in turn, increased cost of healthcare.[7] Because of these reasons, meeting EN goals is an important part of patient care in the intensive care unit (ICU).

Historically, patients in the ICU receive EN through a rate-based (RB) protocol. This strategy provides a fixed, hourly rate of EN regardless of feeding interruptions. Despite data demonstrating inefficacy in delivering prescribed calories, this approach continues to be widely used in the ICU.[10] An alternative form of enteral feeding is through a volume-based (VB) protocol. In this strategy, a 24-hour calorie goal is established for each patient, allowing for adjustment in the hourly rate to compensate for feeding interruptions. Previous studies have found that a VB protocol improves the delivery of prescribed calories, but no study has evaluated the effect of an RB or a VB feeding protocol on clinical outcomes.[11,12] The purpose of our study is to investigate the effect of an RB and a VB protocol on delivery of prescribed calories and clinical outcomes using data from a single institute. We hypothesize that a VB method will improve the delivery of prescribed calories and lead to improved clinical outcomes.

Methods

Study Design and Participants

All patients admitted to the ICU who were 18 years of age or older and who received continuous EN for at least 24 hours at any point during their stay in the ICU were included in our study. All routes of enteral feeding, including gastric and postpyloric feeding, were included. Patients younger than 18 years, patients not admitted to the ICU, and patients who received any parenteral nutrition (PN) support were excluded from the study. A registered dietitian assessed all patients included in the study within 48 hours of admission to the ICU and calculated the nutrition prescription for both the RB and the VB cohorts using EN dosing guidelines from the 2009 Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral (A.S.P.E.N.) guidelines for the adult critically ill patient.[13] Data were collected on all patients until they were transferred out of the ICU or died. This study was approved by the George Washington University Institutional Review Board (study number 071412).

RB Delivery Subgroup

Consecutive medical and surgical patients admitted to the ICU from April 2013 through July 2013 comprised the RB protocol group. Patients in this cohort received EN without alteration in the traditional RB protocol. Enteral formula selection was determined by the dietitian. The use of promotility agents and the decision to begin enteral support at the goal hourly rate or to initiate at a trophic level (10–20 mL/h) and advance to goal were intensivist specific. Admission Acute Physiology and Chronic Health Evaluation II (APACHE II) score, calories ordered and received, ICU length of stay (LOS), hospital LOS, mortality, days on the ventilator, and rates of infection were collected for all patients.

VB Delivery Subgroup

Consecutive medical and surgical patients admitted to the ICU from December 2013 through February 2014 comprised the VB protocol group. Education regarding the VB protocol was carried out by the Department of Clinical Nutrition using in-services, problem-based cases, and one-on-one bedside teaching with the ICU physician and nursing staff from August through November 2013. Algorithms for adjustment in the hourly rate of EN to compensate for feeding interruptions were standardized and placed on each bedside nursing computer station to optimize adherence to the new protocol. As with the RB protocol, enteral formula selection was left to the discretion of the dietitian. No other concomitant strategies, such as trophic initiation or motility agents, were routinely employed. EN was started at the target rate using the VB protocol algorithm with a maximum hourly infusion rate of 150 mL/h per the previously established maximum rate at our institute only when required to make up for missed EN volume. Similar to the RB arm, admission APACHE II score, calories ordered and received, ICU LOS, hospital LOS, mortality, days on the ventilator, and rates of infection were collected for all patients.

Statistical Analysis

Primary outcomes investigated included percent goal calories delivered, total number of days on the ventilator, length of ICU stay, total length of hospital stay, and mortality. Secondary outcomes investigated included rates of nosocomial infections, including ventilator-associated pneumonia (VAP) and urinary tract infection (UTI). All primary and secondary outcomes were investigated using the Kruskal-Wallis test of differences. Stepwise, multivariate regression was used to identify independent predictors of clinical outcomes while controlling for relevant covariates. Significance was defined as $P < .05$.

Results

Patient Demographics

A total of 77 patients were enrolled in the study, 38 patients in the RB protocol arm and 39 patients in the VB protocol arm. Fifty-eight percent of patients in the RB group were female, while 59% of patients in the VB group were female. The median age of patients in the RB protocol arm was 58 years, while the median age of patients in the VB protocol arm was 61 years (Table 1). The median body mass index (BMI) for both groups was 27 kg/m^2. The VB group was sicker than the RB group based on median admission APACHE II score (17 vs 10, $P < .01$). An equal number of patients within each protocol arm were

Table 1. Patient Demographics.

Variable	Rate-Based Protocol (n = 38)	Volume-Based Protocol (n = 39)	*P* Value
Female sex, %	58	59	.92
Age, median (IQR), y	58 (48, 68)	61 (49, 71)	.66
BMI, median (IQR), kg/m^2	27 (25, 30)	27 (22, 34)	.99
APACHE II, median (IQR)	10 (8, 16)	17 (12, 19)	.01
Mechanically ventilated patients, No. (%)	34 (90)	35 (90)	.94
Days of EN received, median (IQR)	11.4 (4, 15)	11.8 (5, 17)	.97
No. of patients requiring promotility agents, No. (%)	0	1 (3)	.32

APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; EN, enteral nutrition; IQR, interquartile range.

Table 2. Effect of Enteral Feeding Protocol on Underfeeding and Length of Stay.

Variable	Rate-Based Protocol (n = 38)	Volume-Based Protocol (n = 39)	*P* Value (Univariate)	*P* Value (Multivariate)
Percentage of goal calories received	57.02	74.01	<.001	NA
Average ICU LOS, median (IQR), d	9 (5, 19)	14 (10, 21)	.05	.12
Average hospital LOS, median (IQR), d	19 (9, 29)	25 (16, 29)	.19	.38
Duration of mechanical ventilation, median (IQR), d	5 (3, 12)	9 (7, 16)	.04	.12
Mortality, No. of people	5	4	.90	.88

ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; NA, not applicable.

Table 3. Effect of Enteral Feeding Protocol on Rates of Infection.

Type of Infection	Rate-Based Protocol (n = 38), No. (%)	Volume-Based Protocol (n = 39), No. (%)	*P* Value
Ventilator-associated pneumonia	0	2 (5)	.16
Urinary tract infection	8 (21)	8 (21)	.78

mechanically ventilated. Similarly, patients in each arm required an equal number of days of EN support. The incidence of gastric vs postpyloric feeding was not recorded for either group.

Effect of RB vs VB on Underfeeding and Quality Outcome Measures

Patients in the VB protocol group received a significantly greater percentage of prescribed calories than those in the RB protocol arm (74% vs 57%, $P < .001$). In addition, patients in the VB protocol arm had a significantly longer length of ICU stay (14 vs 9, $P = .05$) as well as days on the ventilator (9 vs 7, $P = .04$). When controlling for the admission APACHE II score, however, these differences in clinical outcomes between the RB and VB protocol arms did not persist (Table 2). There was no difference in the overall hospital LOS or mortality between the 2 groups.

Effect of RB vs VB on Rates of Infection

The differences in the rates of infection for each group were not statistically significant (Table 3). No patient in the RB protocol was diagnosed with a VAP, while 2 patients in the VB protocol were diagnosed with a VAP. Eight patients from each cohort were diagnosed with a UTI.

Discussion

There is a rapidly growing body of literature surrounding nutrition in the critically ill patient. These studies show that early EN (initiation within 24–48 hours of ICU admission) is associated with decreased morbidity and mortality.[14] Despite these findings, however, there remains an ongoing debate regarding the optimal dose of EN in the ICU setting. Our study sought to determine the ideal method of EN that allows for a greater provision of prescribed calories and the clinical outcomes associated with such an approach. We found that compared with an RB protocol, a VB protocol is a superior method in optimizing nutrition delivery but may not affect clinical outcomes.

Meeting EN goals is an inherent challenge in the ICU due to both avoidable and unavoidable interruptions in feeding.[15] Underfeeding can both exacerbate preexisting malnutrition and contribute to iatrogenic malnutrition, which is often seen in the critically ill patient.[16] A recent study found that underfeeding was associated with significantly higher mortality and

worse functional outcomes, even after correcting for possible covariates.[17] In a study authored by Alberda et al[18] in 2009, increased caloric delivery led to reduced 60-day mortality and increased ventilator-free days. The findings were most pronounced in patients who were at highest nutrition risk (defined as BMI <25 or BMI ≥35). Another randomized, controlled trial comparing rate of initiation of EN in patients with severe head injury found that patients who started receiving EN at the goal rate received 20% more calories than those whose EN was started at a trophic rate. This study found a trend toward improved neurologic outcome and fewer infections in the intervention group.[19]

Conversely, the Early versus Delayed Enteral Feeding to Treat People With Acute Lung Injury or Acute Respiratory Distress Syndrome (EDEN Study) investigated the effect of trophic vs full-dose enteral feeding on clinical outcomes in patients with acute lung injury (ALI). This study concluded that full-dose enteral feeding did not improve the number of ventilator-free days, reduce 60-day mortality, or reduce infectious complications.[20] However, this study has several limitations. First and foremost, the patients included in this study were mostly young, healthy individuals. In fact, patients who were underweight (often categorized as malnourished) were excluded.[18] Furthermore, there existed a significant confounding variable, with nearly 27% of the study's population receiving concomitant ω-3 fatty acids, which has been shown to improve clinical outcomes in patients with ALI.[18,20,21] Also, patients may have been overfed in the intervention arm because prescribed caloric need was based on nonprotein calories. Finally, this study investigated the effect of EN dosing during early ICU admission and in mechanically ventilated patients only.[20]

More recently, a randomized controlled trial by Arabi et al[22] investigated the effect of permissive underfeeding on clinical outcomes in critically ill patients. This study revealed no difference in clinical outcomes between permissively underfed patients (defined as receiving 40%–60% of caloric requirements) vs patients who received standard enteral feeding (defined as receiving 70%–100% of caloric requirements). This study, too, has several limitations. Similar to the EDEN trial, this study investigated the effect of EN dosing during early ICU admission only. Furthermore, patients in the permissively underfed group received a statistically significant and greater amount of supplemental enteral protein (27 g/d vs 6 g/d) to compensate for the restriction in the amount of nonprotein calories received.[22]

In congruence with other studies supporting early goal EN, our study shows that selective and proactive strategies can enhance EN caloric provision to the critically ill patient. Contrary to our clinical hypothesis, our study did not find any difference in clinical outcomes between the RB and VB protocol arms, which may be explained by a variety of factors. Despite extensive education for physician and nursing staff on the VB protocol prior to implementation, patients in the VB protocol received only 74% of their goal calories (Table 1). This discrepancy between goal calories and actual calories received may be related to inaccurate or lack of recalculation of the hourly rate after feeding interruptions. In addition, if EN was held for a significant amount of time within a 24-hour period, there may have been insufficient time to make up for the lost volume due to restrictions on the maximum hourly infusion rate (150 mL/h). The lack of difference in clinical outcomes may also be related to measurement of inappropriate end points. For instance, assessment of baseline nutrition status was not directly measured for patients in this study. Instead, we measured duration of mechanical ventilation as an index of respiratory muscle performance and strength and presence of infection as an index of immunocompetence, both of which are related to nutrition.[1,2] However, each of these end points can be affected by a myriad of other factors and therefore may not change significantly based on alteration of the method of EN delivery alone.

This is the first prospective study to evaluate the efficacy of a VB protocol for the delivery of goal calories as well as clinical outcomes. However, we acknowledge several limitations. First, the study groups were not randomized as this was a before-and-after study, although they do appear to be well matched and equally represent both medical and surgical patients. Second, this study is a single-center study and may not be generalizable to all hospitals or patient populations. Third, the number of patients included in our study is small, which may make our results underpowered to detect a statistical difference. Fourth, the enteral formula chosen was not standardized, and therefore fatty acid and protein intake differed among the patients. Fifth, increased awareness of EN goals following education on the VB protocol may have contributed to the increased percentage of goal calories received in this cohort. However, the VB cohort still received only 75% of their goal calories, which may have masked any clinical benefit to improved calories received.

Conclusions

In conclusion, we found that a VB protocol is one method to improve the delivery of prescribed calories. Considering the consequences of underfeeding in the ICU, we recommend the employment of a VB strategy. Future studies with a larger sample size are needed to further investigate the effect of such a protocol on clinical outcomes.

Statement of Authorship

I. N. Haskins, M. Baginsky, M. Gergely, and B. Sarani contributed equally to the conception and the design of the research; N. Gamsky, K. Sedghi, and S. Yi contributed equally to the acquisition of data; and I. N. Haskins, M. Baginsky, R. L. Amdur, M. Gergely, and B. Sarani contributed equally to the analysis and interpretation of the data. All authors drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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