Clinical Nutrition (2006) **25**, 51–59

Clinical
Nutrition

http://intl.elsevierhealth.com/journals/clnu

ORIGINAL ARTICLE

Enteral nutrition delivery and energy expenditure in medical intensive care patients

Sirak Petros*, **Lothar Engelmann**

Medical ICU, Center of Internal Medicine, University of Leipzig, Liebigstr. 20, D-04103 Leipzig, Germany

Received 25 January 2005; accepted 24 August 2005

KEYWORDS
Enteral nutrition;
Nutrition delivery;
Post-pyloric feeding;
Energy expenditure;
Critical illness

Summary
Background and aims: Delivery of enteral nutrition (EN) in critical illness is often inadequate. This prospective observational study addresses the implementation of enteral feeding in critically ill medical patients and its relation to energy expenditure.
Methods: All admissions to a university medical ICU over a period of one year were screened. Patients receiving EN for at least 7 days were followed up. The caloric target was a minimum of 20 kcal/kg/day. The feeding volume was increased daily by 500 ml and a maximum of 2000 ml/day was targeted to be achieved by day 4 of admission. Energy expenditure was measured with indirect calorimetry on day 3 or 5.
Results: Two hundred and thirtyone patients required artificial nutrition, of which 61 patients were enterally fed for $\geqslant$7 days. This group was followed for a total of 750 feeding days. The gastric route was used at the start, with a post-pyloric feeding required during follow-up in 36.1% of patients due to high gastric residual. EN was interrupted in 32.1% of the feeding days. The daily administered volume was 86.2±30.4% of the prescribed. The mean enteral caloric supply in relation to energy expenditure was between 39.2±34.6% on day 1 and 83.1±31.1% on day 6. The targeted maximum feed volume was achieved on day 4 in 75.4% of the patients. Patients with a delayed target time had a higher mortality rate than those with a target time of $<$4 days (73.3% vs. 26.1%),
Conclusions: A high delivery-to-prescription rate could be achieved with a standardized enteral feeding protocol in critically ill medical patients. However, caloric delivery is much less than measured energy expenditure. Enteral feeding intolerance is associated with a high mortality rate.

Introduction

Nutritional support is important in the management of the critically ill patient when oral food intake is

---

*Corresponding author. Tel.: +49 341 97 12706;
fax: +49 341 97 12719.
E-mail address: pets@medizin.uni-leipzig.de (S. Petros).

0261-5614/$ - see front matter © 2005 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.
doi:10.1016/j.clnu.2005.08.013

inadequate or not possible. Enteral nutrition (EN) has to a great extent replaced parenteral nutrition (PN) in intensive care medicine.[1,2] EN reverses the loss of gastrointestinal mucosal integrity,[3,4] maintains intestinal blood flow,[5] preserves the IgA-dependent immunity[6,7] and contributes to the maintenance of host immune response.[8] However, the clinical implication of these findings is not yet clear.[9] Meta-analyses of clinical studies have reported that EN is associated with a lower risk of infection.[10–12] There are also cost savings with EN as opposed to PN.[13] Early EN is associated with a lower incidence of infections and a reduced length of hospital stay.[14] Clear conclusions have been difficult to make due to the heterogeneity of nutritional studies.[15] Despite existing controversies, nutrition should be administered by the enteral route whenever possible.[9]

A major concern with EN is the discrepancy between prescribed and delivered amount of nutrient, the major causes of which are diarrhea, vomiting or gastric stasis. Furthermore, enteral nutrient delivery is gradually increased in critically ill patients in order to avoid the possibility of gastrointestinal intolerance, so that a few days are required to achieve the caloric target. Administering the total nutritional requirement of mechanically ventilated medical patients starting on day 1 was associated with greater infectious complications and prolonged length of hospital stay compared to patients in whom a gradual approach was implemented.[16] Despite the caloric deficiency, EN is still superior than PN so that non-energetic effects of EN, such as immune modulation or protection of the intestinal mucosal barrier, seem to be of greater value in the critically ill than the mere energetic supply.[9]

The issue of the better enteral access (gastric vs. post-pyloric route) is not yet settled. However, available evidence does not support the routine insertion of post-pyloric tubes as long as the gastric route is effective.[17–19]

EN is the standard feeding route in critically ill patients at the medical ICU of the University of Leipzig as long as there are no contraindications to this strategy. In this prospective observational study on critically ill medical patients, it was aimed to achieve the maximum enteral feed volume on day 4 of admission. We further report our experience with the implementation of EN in this patient population, compare data on delivery with energy expenditure measurements and discuss common problems associated with this strategy.

Patients and methods

All medical patients admitted to the medical ICU of the University of Leipzig between August 2001 and July 2002 were screened for an indication for artificial nutrition. Patients were considered in need of artificial nutrition if oral food intake was not possible. Contraindications to EN were continuous diarrhea (defined as more than 3 stools per day or the need for an incontinence bag), massive gastric stasis, paralytic ileus and acute upper gastrointestinal bleeding. A nasogastric tube was inserted immediately after considering a patient eligible for EN. In those patients with a gastric residual of >300 ml in the first 6 h, a post-pyloric feeding tube was inserted under an endoscopic guidance. A commercially available high molecular diet with a caloric concentration of 1 kcal/ml was started (Fresubin® original fibre, Fresenius Kabi, Bad Homburg, Germany). The nutrient composition of the solution was: carbohydrate 138 g/l, fat 34 g/l, protein 38 g/l, fiber 20 g/l, osmolality 300 mosmol/kg. EN was administered as a bolus every 2 h over a period of 14 h daily (from 08:00 a.m. to 10:00 p.m.). The nutrition regimen was outlined by the first author, and trained staff nurses documented the volume administered as well as problems during feeding. The amount of feeding solution was increased daily by 500 ml with the aim to provide the maximum feed volume by day 4 with a caloric goal of at least 20 kcal/kg/day. This caloric target was based on the assumption that using the mean adjusted body weight of our ICU population (about 75 kg) and the planned rate of feeding increment, a maximum feed volume of 2000 ml/day or 25 ml/kg/day would be achieved by day 4 using the solution mentioned earlier. Providing for possible difficulties in implementation, a caloric target of at least 20 kcal/kg/day was considered feasible. For calculations of energy supply, the actual body weight of the patient was used if this was $<125\%$ of the ideal weight calculated with the Hamwi equation[20]: for men: 48 kg for first 152 cm+1.1 kg for every cm above 152 cm; for women: 45.5 kg for first 152 cm+0.9 kg for every cm above 152 cm. In patients with an actual body weight of $>125\%$ of the ideal, the adjusted body weight was used. Since fat tissue is metabolically active to a certain degree, 25% of the difference between the actual and the ideal body weight was added to the ideal weight in order to compute the adjusted body weight.[21]

Since short periods of feeding would not precisely demonstrate the problems associated with EN, only those patients with a minimum feeding period of 7 days were included in this analysis.

Patients were followed up until leaving the ICU or for a maximum of 14 days. In the initial screening, patients were classified into those who did not need artificial nutrition (group 1), those who required EN for less than 7 days (group 2) and those fed enterally for at least 7 days (group 3). Furthermore, patients in group 3 were classified into those who achieved the targeted feed volume in time (3A) and those who did not (3B). Because EN is the standard feeding route in our ICU, informed consent or a vote from the ethics commission was not required.

Energy expenditure was measured with indirect calorimetry either on day 3 or 5 (Deltatrac II MBM-200 Metabolic Monitor, Datex-Ohmeda, Finland). Measurements were performed in supine position in the morning between 7:00 and 08:00 for at least 30 min with patients in unfed state. According to a predefined algorithm, the first 5 min of measurement were omitted during data processing. In mechanically ventilated patients, ventilatory parameters were left unchanged for at least 60 min before and during the calorimetry.[22,23] Gas exchange measurements were carried out in spontaneously breathing patients with a canopy. Patients were left undisturbed during indirect calorimetry, so that the data were considered to represent resting energy expenditure (REE).

Based on our own data from continuous 24 h indirect calorimetry measurements on ten patients on controlled ventilation and another ten patients on assisted ventilation (unpublished data), a multiplication factor of 1.0635 for controlled mode and 1.098 for assisted mode was used to compute total daily energy expenditure (TEE) from measured REE of mechanically ventilated patients. Computing TEE for spontaneously breathing patients is complicated, and a uniform correction factor is difficult to calculate.[24,25] In our spontaneously breathing patients, only 10% was added to the measured REE to compute TEE because these patients remained in bed throughout the day without any significant physical activity.

To demonstrate the relationship between energy provision and energy expenditure, the following classification was adapted[26]:

> Energy supply $<90\%$ of expenditure: hypoenergetic.
> Energy supply 91–110% of expenditure: normoenergetic.
> Energy supply $>110\%$ of expenditure: hyperenergetic.

Data on the use of vasopressors and sedatives, the ventilatory status, stool frequency and consistency, and the amount of gastric residual were recorded for every study day. The APACHE-II score and the sequential organ function assessment (SOFA) score [27] were also calculated.

Data are given as mean$\pm$SD unless stated otherwise. The *t*-test and the χ^2 were applied for data comparison. A *P* value of <0.05 was considered statistically significant.

Results

Seven hundred and thirty patients of Caucasian origin were admitted to the medical ICU during the study period. Forty eight patients (6.6%) were excluded because they were referred after a major surgical procedure within the last 2 weeks, thus considered surgical. Therefore, the analysis included 682 medical patients aged 63.0 ± 16.9 years, of which 397 (58.2%) were men and 285 (41.8%) women. Their mean body weight was 76.5 ± 17.2 kg with a body mass index (BMI) of 26.4 ± 5.8. 6.9% of the patients had a BMI of <18.5 and 21.7% a BMI of >30. Coronary heart disease and sepsis were the leading causes of admission (Table 1).

Artificial feeding was considered unnecessary in 66.1% of the patients (group 1). Two hundred and thirty one patients (33.9%) required artificial nutrition, of which 170 patients (group 2) were fed for less than 7 days and 61 patients (group 3) for at least 7 days. Severity of the clinical condition and organ dysfunction states were markedly higher in groups 2 and 3 compared to group 1 (Table 2). The reasons for the short EN period in group 2 are given in Table 3.

Further analysis was thus limited to the 61 patients in group 3 (35 men and 26 women; median age 62 years [range 18–84]). Major diagnoses in this group were sepsis (32) and congestive heart failure (12). The remaining were 9 patients admitted for respiratory insufficiency due to exacerbation of their chronic obstructive lung disease, 2 patients with acute pancreatitis, and one each with alcoholic polyneuropathy, cerebral insult, Child C liver cirrhosis, pulmonary embolism, hypoxic brain damage and systemic lupus erythematodes. The cause of sepsis was bacterial pneumonia in 31/32 patients. 11/61 patients were suffering from hematological malignancies. Diabetes mellitus was known in 23 patients before hospital admission. In 6/61 patients, cardiopulmonary resuscitation was performed immediately before admission. Mechanical ventilation was required in 54/61 patients (88.5%) and vasopressors were administered in 57.4% of the patients.

Table 1 Major diagnoses of the total study population on study admission.

Major diagnosis	N	Frequency (%)
Cardiovascular		
Coronary heart disease	163	23.9
Congestive heart failure	65	9.5
Cardiac arrhythmias	37	5.4
Arterial occlusive disease	47	6.9
Venous thromboembolism	20	3.0
Bacterial endocarditis	6	0.9
Hypovolemic shock	5	0.7
Infectious sepsis		
Due to pneumonia	85	12.4
Urinary tract infection	8	1.2
Other causes	10	1.5
Pneumonia	67	9.9
Gastrointestinal		
Acute upper gastrointestinal bleeding	48	7.0
Acute pancreatitis	10	1.5
Child C liver cirrhosis	13	1.9
Poisoning	29	4.3
Chronic obstructive lung disease	15	2.2
Acute and chronic renal failure	17	2.5
Diabetic coma	5	0.8
Others	64	9.4

Table 2 Severity of disease and organ dysfunction on admission in the study population (data are mean±SD).

Group	ICU stay (days)	APACHE-II score	SOFA score
1	2.8±2.7*	13.4±6.3*	2.7±3.3*
2	5.2±6.7†	27.7±8.6	10.4±4.7
3	23.0±13.8	25.9±8.0	10.4±4.0

*Significantly lower compared to groups 2 and 3 ($P = 0.0001$).

†ICU stay significantly shorter compared to group 3 ($P < 0.001$). Scores were not significantly different between group 2 and 3.

Patients were followed for a mean of 12.5±2.5 days. There were a total of 750 patient days available for analysis. EN was started 13.9±1.8 h after admission to the ICU. The gastric route was used at the start in 93.3% of the patients.

Table 3 Causes for the short period of enteral nutrition in patients with less than 7 days of feeding (group 2).

Causes	N	Frequency (%)
EN required for less than 7 days	75	44.1
Patient died within the first 24 h	42	24.7
Acute upper gastrointestinal bleeding	15	8.8
Diarrhea and/or frequent vomiting	14	8.2
ICU stay for not more than 1 day	8	4.7
Severe abdominal distension/paralytic ileus	11	6.5
Refusal of the patient	5	2.9

During the follow-up, a post-pyloric feeding tube was required in 22/61 (36.1%) patients due to a high gastric residual that impeded further gastric feeding. These patients had a significantly higher gastric residual than those tolerating gastric feeding (689.6±808.7 vs. 158.7±331.3 ml/day, $P = 0.0001$). Analgesia and sedation ($\chi^2 = 22.4$, $P = 0.001$) and the need for vasopressors ($\chi^2 = 15.5$, $P = 0.0001$) were associated with a high gastric residual. There was also a moderate correlation between the SOFA score and the amount of gastric residual ($r = 0.334$, $P = 0.001$). A post-pyloric tube with a gastric aspiration port was placed in every case under endoscopic guidance. The median time from decision to tube placement was 21 h (range 7–31).

Supplemental PN was administered in 18.7% of patient feeding days to compensate for temporary reduction in the amount of daily EN due to diarrhea and/or high gastric residual. PN was continued until diarrhea had subsided, or, in patients with a high gastric residual, until EN was resumed with a post-pyloric feeding tube. There were episodes of diarrhea on 40.9% of the patient feeding days, but these lead to a discontinuation of EN and switch to total PN in only 6.5% of the patient feeding days.

The daily administered amount of EN was 86.2±30.4% of the prescribed (between 70.3±41.8% on day 12 and 92.7±25.2% on day 5). The prescribed amount of EN was fully administered in 78.9% of patient feeding days. EN was interrupted in 241 patient feeding days (32.1%). The interruption could be compensated on the same day in 31.1% of the cases by extending the feeding period further into the night, while this was not possible in 68.9%. The most common reasons for interruption in the ''compensated'' group were diagnostic or therapeutic procedures (81.4%), while gastrointestinal disorders posed a major problem in the ''uncompensated'' group (Table 4).

The target amount of at least 20 kcal/kg/day was achieved in 47.5% patients on day 3, reaching the best mark of 68.9% on day 6 (Fig. 1).

The median energy expenditure was 25.2 kcal/kg/day (23.7–27.5). Assuming the same energy expenditure for each study day, the median daily caloric deficit was between 16.0 (9.8–23.7) kcal/kg on day 1 and 2.3 (−5.0–8.7) kcal/kg on day 6. The mean enteral caloric supply in relation to the energy expenditure was between 39.2 ± 34.6% on day 1 and 83.1 ± 31.1% on day 6. Fig. 2 depicts the relationship between the daily caloric supply and energy expenditure according the classification into hypo-, normo- and hyper-energetic states, with the proportion of hypo-energetic episodes quite high.

The aim to administer the targeted maximum feed volume of 2000 ml or 25 ml/kg by day 4 was achieved in 46 patients (75.4%) (group 3A). The mean target day in this group was 3.5 ± 1.0. In the remaining 15 patients (group 3B), the target volume was achieved after 10.4 ± 5.7 days, the difference between the two groups being statistically significant ($P < 0.0001$). The enteral caloric supply on day 4 was 23.2 ± 7.5 kcal/kg in group 3A, while this was only 10.4 ± 6.1 kcal/kg in group 3B ($P < 0.0001$). The major cause of inadequate enteral feeding in group 3B was gastrointestinal intolerance, i.e. high gastric residual, abdominal distension and diarrhea (58.0%) followed by diagnostic and therapeutic procedures (25.0%). Analyzing their admission state, there was no significant difference in APACHE-II score (26.2 ± 8.5 vs. 23.6 ± 4.6) and the need for mechanical ventilation (84.8 vs. 100.0%) between group 3A and 3B. However, the SOFA score was lower in group 3A than 3B, and this difference was significant on days 7, 9 and 11–13 (Fig. 3). The serum albumin concentration on admission to the ICU was also significantly higher in group 3A than 3B (28.9 ± 6.6 g/l vs. 21.3 ± 4.4, $P < 0.0001$). 6/46 (13.0%) patients in group 3A but 5/15 (33.3%) in group 3B were in septic shock on admission. The ICU mortality rate was

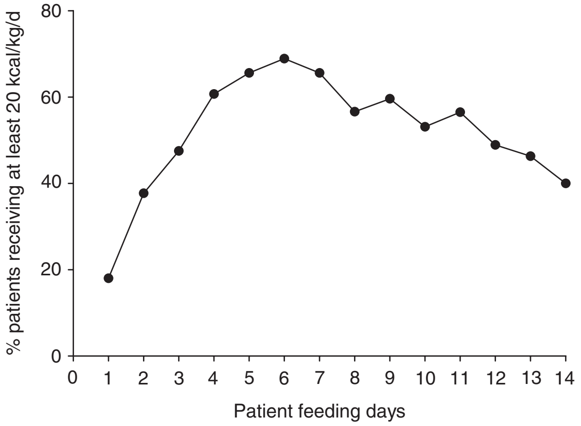

Figure 1 Proportion of patients who received a daily enteral supply of at least 20 kcal/kg.

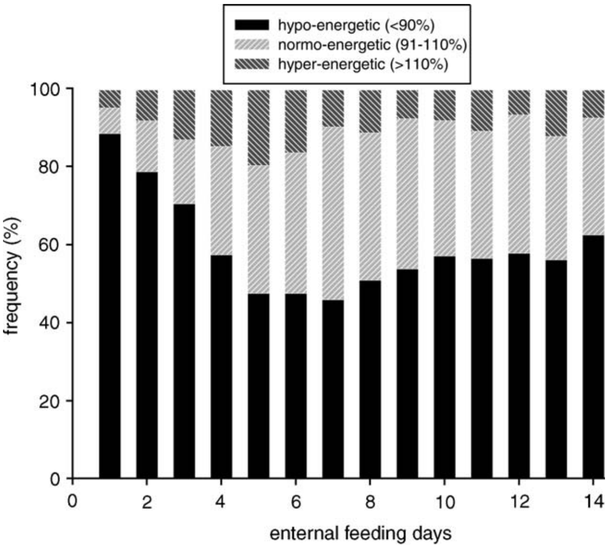

Figure 2 The day-to-day relationship between the amount of enteral caloric supply and energy expenditure classified into three categories based on the study by McClave et al.[26] (<90%: hypo-energetic; 91–110%: normo-energetic; >110%: hyper-energetic).

Table 4 Causes of interruption of enteral feeding.

Compensated interruption		Uncompensated interruption	
Diagnostic procedures	60.0%	Vomiting/high gastric residual	31.9%
Therapeutic procedures	21.4%	Therapeutic procedures	30.7%
Vomiting/high gastric residual	4.0%	Diagnostic procedures	10.8%
Patient removed feeding tube	2.7%	Diarrhea	9.6%
Others	11.9%	Patient removed feeding tube	6.0%
		Gastrointestinal bleeding	3.0%
		Others	7.8%

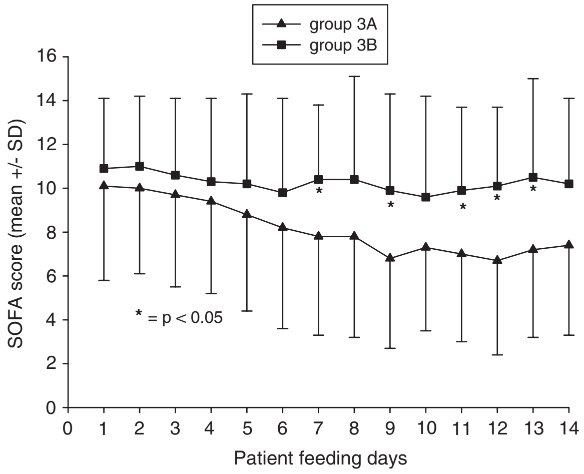

Figure 3 The course of the SOFA score in patients who reached the targeted feed volume on day 4 (group 3A) and those who did not (group 3B).

significantly lower in group 3A than in group 3B (26.1% vs. 73.3%, $P = 0.002$).

Discussion

EN is physiologic and prevents atrophic changes of the intestinal mucosa.[3,4] The healthy enterally fed bowel is metabolically active and builds an effective barrier through peristalsis, secretory IgA, intact intercellular junctions, mucus and diverse inhibitory factors. Malnutrition, infection, chemotherapy, radiation, shock and total PN result in damage to this barrier.[8,28–31] The injured bowel releases proinflammatory cytokines, which may trigger multiple organ dysfunction.[32,33]

Extrapolating data from animal studies into clinical practice is often difficult. Animal experiments are usually done using healthy animals, while the majority of patients in an ICU are old and frequently suffer from multiple underlying disease states. Nutritional interventions have been conducted in animal experiments before or immediately after the acute stress. In contrast, such interventions are started in patients in an ICU after they are already suffering from one or more organ dysfunction states.

A major drawback in enteral feeding strategies is the insufficient caloric intake. In the present study, the nutrition target was achieved on day 4 in about three-fourth of the patients, and this was about two-third of the measured energy expenditure. The proportion of hypo-energetic episodes, which was defined as the provision of $<90\%$ of the recommended caloric supply,[26] was high. A study by McClave et al.[34] showed the provision of even lesser amount of feeding volume. A major cause of insufficient supply is feeding interruption due to gastrointestinal intolerance or diagnostic or therapeutic procedures.[34–36] By applying a flexible strategy in the time stipulated for enteral feeding, the nutrition volume can be maintained in patients with interruptions for diagnostic or therapeutic reasons.[35] In contrast, volume reduction or even cessation of EN may not be avoided in patients with gastrointestinal intolerance. Genton et al.[37] reported that increasing the prescribed feeding volume by 5 kcal/kg resulted in improvement in the amount administered. However, it is not yet proven whether such a strategy is associated with a better clinical outcome.

In a study by Bauer et al.,[38] additional PN in the early phase of enteral feeding resulted in optimal caloric supply and improvement in such laboratory parameters as retinol binding protein and prealbumin, but this was not associated with a better clinical outcome.

It is still not clear how much caloric supply the critically ill patient needs in order to overcome the critical condition with an optimal metabolic state. There is no evidence that a normocaloric feeding strategy must be pursued in this patient group. Definitions of hypo-, normo- and hypermetabolic nutrition, although useful for research purposes, are too narrow for the clinical routine.[15] A crucial issue is not only the caloric supply but also the metabolic and non-energetic influence of EN. Neither hypercaloric nor normocaloric feeding was found to prevent protein catabolism in critically ill patients.[39–41] On the contrary, such a strategy may result in a metabolic burden, increased thermogenesis, azotemia and hyperglycemia.[40] In a study on survivors of burn injury,[42] a caloric supply of more than 120% of the REE led to an increase in fat mass, but the lean body mass remained unchanged.

In a prospective non-randomized study[43] in critically ill patients, those patients with a moderate caloric supply (33–65% of the target amount) have had a better prognosis than those with higher caloric supply. However, underfeeding has also to be avoided by any means. In a prospective cohort study, Rubinson et al.[44] showed that failing to provide the critically ill patient $\geqslant 25\%$ of the recommended calories was associated with a significantly higher risk of bloodstream infection. Further investigations are still required to define the optimal energy supply of a critically ill patient beyond the mere measurement of and adaptation to the energy expenditure. Pre-existent malnutrition has also to be considered in defining nutritional goals.

In the present study, the mortality rate among patients with increasing gastrointestinal intolerance was very high. In a study on children with severe burn injury,[45] intolerance to EN, defined as increased gastric regurgitation or severe diarrhea, was associated with the development of sepsis and a high mortality rate. Sedation and the need for vasopressors were also associated with a high intolerance rate in our study. Similar observations were also made by Mentec et al.[46]

PN could be avoided in patients with gastrointestinal intolerance by implementing post-pyloric feeding. Similar observations were also reported in a retrospective study by Boulton-Jones et al.[47] However, the correct insertion of the required tube was often delayed for logistic reasons, so that temporary PN could not be avoided in some of the patients. In the present study, post-pyloric feeding was implemented only in patients with a high gastric residual, so that comparison with the routine gastric feeding could not be made. In a prospective randomized study,[48] the rate of gastroesophageal regurgitation was significantly higher in patients on gastric than post-pyloric feeding (39.8% vs. 24.9%). Microaspirations were also more often seen under gastric than post-pyloric feeding (7.5% vs. 3.9%); however, this difference was not significant. In another study,[49] the rate of gastrointestinal complications was also lower with jejunal than gastric feeding. However, this advantage was not associated with a reduction in nosocomial pneumonia. In contrast, a prospective study by Esparza et al.[17] did not reveal any significant difference in the regurgitation rate between gastric and post-pyloric feeding. Neumann et al.[18] did also not observe any advantage of post-pyloric feeding compared to the gastric route. In their study, the target feeding volume was achieved faster with a gastric tube than with the post-pyloric route. A meta-analysis by Marik and Zaloga[19] did not show any advantage of a routine post-pyloric feeding over the gastric route regarding the rate of nosocomial pneumonia, length of ICU stay und mortality rate. However, the number of patients in most of the cited studies was too small and the patients were heterogeneous, so that the data must be interpreted cautiously.

There are certain limitations to our study that should be considered in interpreting the data. A single energy expenditure measurement was extrapolated for the total observation period. Day-to-day variations in the TEE may be considerable in the critically ill patient.[50] However, our approach still helps demonstrate the dilemma of EN delivery and energy expenditure. Data on the relationship between the use of vasopressors and EN intolerance should also be cautiously interpreted. Due to the small number of patients, the different combinations of vasopressors used, and the dose diversity, a causal relationship cannot be extrapolated from our data. The association we found should been seen mainly as a sign of the serious disease state the affected patients were into rather than a direct effect of vasopressors on gastrointestinal motility. Our decision to limit the feed volume by 2000 ml/day should by no means be taken as the optimum. Some patients surely tolerate larger volumes or higher caloric concentrations. However, in a population of seriously sick patients like ours, larger feed volumes would increase the likelihood of gastrointestinal intolerance.

In conclusion, there are significant discrepancies between measured energy expenditure and enteral feeding in critically ill medical patients. Implementation of EN is hampered by interruptions due to gastrointestinal intolerance and diagnostic or therapeutic procedures. The development of standard infusion protocols and continuous education of critical care physicians and nurses may improve the delivery of EN. The post-pyloric route is useful in patients with a high gastric residual that prevents gastric feeding. Intolerance to EN is associated with a poor outcome.

Acknowledgments

We would like to thank the staff of our medical ICU for the dedicated support in the implementation of the study and data collection.

References

1. Berger MM, Chiolero RL, Pannatier A, Cayeux MC, Tappy L. A 10-year survey of nutritional support in a surgical ICU: 1986–1995. *Nutrition* 1997;**13**:870–7.
2. Ochoa JB, Magnuson B, Swintowsky M, et al. Long-term reduction in the cost of nutritional intervention achieved by a nutrition support service. *Nutr Clin Pract* 2000;**15**:174–80.
3. Buchman AL, Moukarzel AA, Bhuta S, et al. Parenteral nutrition is associated with intestinal morphologic and functional changes in humans. *J Parenter Enteral Nutr* 1995;**19**:453–60.
4. Hadfield RJ, Sinclair DG, Houldsworth PE, Evans TW. Effects of enteral and parenteral nutrition on gut mucosal permeability in the critically ill. *Am J Resp Crit Care Med* 1995;**152**:1545–8.
5. Niinikoski H, Stoll B, Guan X, et al. Onset of small intestinal atrophy is associated with reduced intestinal blood flow in TPN-fed neonatal piglets. *J Nutr* 2004;**134**:1467–74.
6. Kudsk KA, Li J, Renegar KB. Loss of upper respiratory tract immunity with parenteral feeding. *Ann Surg* 1996;**223**:629–35.

7. Renegar KB, Johnson CD, Dewitt RC, et al. Impairment of mucosal immunity by total parenteral nutrition: requirement for IgA in murine nasotracheal anti-influenza immunity. *J Immunol* 2001;**166**:819–25.
8. Shou J, Lappin J, Daly JM. Impairment of pulmonary macrophage function with total parenteral nutrition. *Ann Surg* 1994;**219**:291–7.
9. Jolliet P, Pichard C, Biolo G, et al. Enteral nutrition in intensive care patients: a practical approach. Working Group on Nutrition and Metabolism, ESICM. European Society of Intensive Care Medicine. *Intensive Care Med* 1998;**24**:848–59.
10. Heyland DK. Nutritional support in the critically ill patients. A critical review of the evidence. *Crit Care Clin* 1998;**14**: 423–40.
11. Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: a meta-analysis. *Am J Clin Nutr* 2001;**74**:534–42.
12. Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. *Intensive Care Med* 2005;**31**: 12–23.
13. Kalfarentzos F, Kehagias J, Mead N, Kokkinis K, Gogos CA. Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. *Br J Surg* 1997;**84**:1665–9.
14. Marik PE, Zaloga GP. Early enteral nutrition in critically ill patients: a systematic review. *Crit Care Med* 2001;**29**: 2264–70.
15. Preiser JC, Chiolero R, Wernerman J. Nutritional papers in ICU patients: what lies between the lines? *Intensive Care Med* 2003;**29**:156–66.
16. Ibrahim EH, Mehringer L, Prentice D, et al. Early versus late enteral feeding of mechanically ventilated patients: results of a clinical trial. *J Parenter Enteral Nutr* 2002;**26**:174–81.
17. Esparza J, Boivin MA, Hartshorne MF, Levy H. Equal aspiration rates in gastrically and transpylorically fed critically ill patients. *Intensive Care Med* 2001;**27**:660–4.
18. Neumann DA, DeLegge MH. Gastric versus small-bowel tube feeding in the intensive care unit: A prospective comparison of efficacy. *Crit Care Med* 2002;**30**:1436–8.
19. Marik PE, Zaloga GP. Gastric versus post-pyloric feeding: a systematic review. *Crit Care* 2003;**7**:R46–51.
20. Hamwi GJ. Therapy: Changing dietary concepts. Danowski TS, editor. *Diabetes mellitus: diagnosis and treatment*, vol. 1. New York: American Diabetes Association; 1964. p. 73–8.
21. Kushner RF, Wall-Alonso E, Alverdy J. Obesity. In: Merritt RJ, Rombeau JL, editors. *A.S.P.E.N. Nutrition Support Practice Manual*. Silver Springs, MD: A.S.P.E.N; 1988. p. 21/1–21/11.
22. Henneberg S, Söderberg D, Groth T, Stjernström H, Wiklund L. Carbon dioxide production during mechanical ventilation. *Crit Care Med* 1987;**15**:8–13.
23. Brandi LS, Bertolini R, Santini L, Cavani S. Effects of ventilator resetting on indirect calorimetry measurement in the critically ill surgical patient. *Crit Care Med* 1999;**27**:531–9.
24. Madden AM, Morgan MY. Resting energy expenditure should be measured in patients with cirrhosis, not predicted. *Hepatology* 1999;**30**:655–64.
25. Barak N, Wall-Alonso E, Sitrin MD. Evaluation of stress factors and body weight adjustments currently used to estimate energy expenditure in hospitalized patients. *J Parenter Enteral Nutr* 2002;**26**:231–8.
26. McClave SA, Lowen CC, Kleber MJ, et al. Are patients fed appropriately according to their caloric requirements? *J Parenter Enteral Nutr* 1998;**22**:375–81.
27. Vincent JL, de Mendonca A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on sepsis-related problems of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;**26**:1793–800.
28. Alverdy JC, Aoys E, Moss GS. Total parenteral nutrition promotes bacterial translocation from the gut. *Surgery* 1988;**104**:185–90.
29. Deitch EA, Winterton J, Li M, Berg R. The gut as a portal of entry for bacteremia. Role of protein malnutrition. *Ann Surg* 1987;**205**:681–92.
30. Maxson RT, Dunlap JP, Tryka F, Jackson RJ, Smith SD. The role of the mucus gel layer in intestinal bacterial translocation. *J Surg Res* 1994;**57**:682–6.
31. Shou J, Lappin J, Minnard EA, Daly JM. Total parenteral nutrition, bacterial translocation, and host immune function. *Am J Surg* 1994;**167**:145–50.
32. Mester M, Tompkins RG, Gelfand JA, Dinarello CA, Burke JF, Clark BD. Intestinal production of interleukin-1 alpha during endotoxemia in the mouse. *J Surg Res* 1993;**54**:584–91.
33. Meyer TA, Noguchi Y, Ogle CK, et al. Endotoxin stimulates interleukin-6 production in intestinal epithelial cells. A synergistic effect with prostaglandin E2. *Arch Surg* 1994;**129**:1290–4.
34. 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**:1252–6.
35. 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**:261–6.
36. 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**:8–12.
37. Genton L, Dupertuis YM, Romand JA, et al. Higher calorie prescription improves nutrient delivery during the first 5 days of enteral nutrition. *Clin Nutr* 2004;**23**:307–15.
38. Bauer P, Charpentier C, Bouchet C, Nace L, Raffy F, Gaconnet N. Parenteral with enteral nutrition in the critically ill. *Intensive Care Med* 2000;**26**:893–900.
39. Streat SJ, Beddoe AH, Hill GL. Aggressive nutritional support does not prevent protein loss despite fat gain in septic intensive care patients. *J Trauma* 1987;**27**:262–6.
40. Muller TF, Muller A, Bachem MG, Lange H. Immediate metabolic effects of different nutritional regimens in critically ill medical patients. *Intensive Care Med* 1995; **21**:561–6.
41. Frankenfield DC, Smith JS, Cooney RN. Accelerated nitrogen loss after traumatic injury is not attenuated by achievement of energy balance. *J Parenter Enteral Nutr* 1997;**21**:324–9.
42. Hart DW, Wolf SE, Herndon DN, et al. Energy expenditure and caloric balance after burn. Increased feeding leads to fat rather than lean mass accretion. *Ann Surg* 2002;**235**: 152–61.
43. Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric intake in medical ICU patients. Consistency of care with guidelines and relationship to clinical outcomes. *Chest* 2003;**124**:297–305.
44. Rubinson L, Diette GB, Song X, Brower RG, Krishnan JA. Low caloric intake is associated with nosocomial bloodstream

infections in patients in the medical intensive care unit. *Crit Care Med* 2004;**32**:350–7.

45. Wolf SE, Jeschke MG, Rose JK, Desai MH, Herndon DN. Enteral feeding intolerance: an indicator of sepsis-associated mortality in burned children. *Arch Surg* 1997; **132**:1310–4.
46. 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**:1955–61.
47. Boulton-Jones JR, Lewis J, Jobling JC, Teahon K. Experience of post-pyloric feeding in seriously ill patients in clinical practice. *Clin Nutr* 2004;**23**:35–41.
48. Heyland DK, Drover JW, MacDonald S, Novak F, Lam M. Effect of postpyloric feeding on gastroesophageal regurgitation and pulmonary microaspiration: results of a randomized controlled trial. *Crit Care Med* 2001;**29**: 1495–501.
49. Montejo JC, Grau T, Acosta J, et al. Multicenter, prospective, randomized, single-blind study comparing the efficacy and gastrointestinal complications of early jejunal feeding with early gastric feeding in critically ill patients. *Crit Care Med* 2002;**30**:796–800.
50. Vermeij CG, Feenstra BW, van Lanschot JJ, Bruining HA. Day-to-day variability of energy expenditure in critically ill surgical patients. *Crit Care Med* 1989;**17**:623–6.