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What Is "Best Achievable" Practice in Implementing the Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol in Intensive Care Units in the United States? Results of a Multicenter, Quality Improvement Collaborative

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Abstract

Background: The purpose of this study was to determine what was "best achievable practice" with the implementation of a novel enteral feeding protocol (Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol [PEP uP protocol]). *Methods:* This study was a multicenter quality improvement collaborative wherein we describe nutrition practices and outcomes within PEP uP sites. We report the minimum, average, and maximal site-level performance on aspects related to nutrition practices and outcomes. *Results:* In 2014, 7 intensive care units (ICUs) in the United States implemented the PEP uP protocol. On average, over the first 5 ICU days, patients received 35% (site range, 26%–53%) of their prescribed energy requirements and 42% (site range, 29%–66%) of their prescribed protein requirements from enteral nutrition. In PEP uP sites, 71% (site range, 58%–95%) of patients received a semidigested formula within 72 hours of admission to the ICU, 72% had a volume-based goal as the initial feeding strategy (site range, 47%–100%), 56% had prophylactic protein supplements (site range, 0%–100%), and 19% received prophylactic motility agents (site range, 0%–85%). *Conclusions:* There was variable success with the implementation of the different components of the PEP uP protocol. Improving the implementation of the various components may further increase nutrition delivery. *(JPEN J Parenter Enteral Nutr. XXXX;xx:xx-xx)*

Keywords

critical care; nutrition therapy; nutrition status; caloric intake; energy balance; quality improvement; feeding protocols; underfeeding

Clinical Relevancy Statement

Iatrogenic underfeeding in the intensive care unit is associated with worse clinical outcomes in nutritionally high-risk patients. In 2010, the Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP protocol), a novel enteral feeding protocol, was introduced and has been shown subsequently to improve nutrition delivery. This multicenter quality improvement collaborative demonstrates that success with implementing the protocol in the United States has been variable. Improving the implementation of the various components may further increase nutrition delivery.

Introduction

Over the past several years, Heyland and colleagues[1] have introduced a novel enteral feeding protocol designed to safely initiate enteral nutrition (EN) in the broadest group of critically ill patients, the Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP protocol). The main features of this new protocol are using a 24-hour volume goal rather than an hourly goal rate for EN, enabling an option to initiate "trophic feeds" or a low volume of a concentrated feeding solution, use of a semidigested feeding solution instead of a standard polymeric solution, prophylactic use of protein supplements and motility agents, and setting a higher value for tolerated gastric residual volume (≥300 mL). The rationale and justification for these nutrition strategies were provided in previous publications.[1] In our prior work implementing this

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protocol, we have consistently demonstrated that patients fed via the PEP uP protocol received more EN than those fed via standard protocols.[1–3]

At the same time we have documented improved nutrition outcomes in patients fed via the PEP uP protocol, we have noted significant variability across sites in how successful they have been with overall nutrition outcomes and with changing the key practices related to the PEP uP protocol. As we continue to implement this protocol in other settings, a natural next step for quality improvement efforts is to audit clinical practice to determine "best achievable" practice.[4] We define "best achievable" practice as what is achievable by the top-performing sites on implementing the key components of the PEP uP protocol (use of volume-based feeds, prophylactic protein supplements, etc). Ideally, sites will achieve 100% adherence with these practice-changing behaviors, but often such performance may not be realistic and may be beyond the reach of some sites. By documenting best achievable performance, we can set more realistic targets for future performance improvement initiatives.

The purpose of this multicenter, observational study was to continue to evaluate the success of the PEP uP protocol by comparing nutrition process measures and outcomes in patients fed via the PEP uP protocol compared with patients in sites using a standard protocol. In addition, we describe the level and range of success in implementing key components of the PEP uP protocol (and overall nutrition performance) in those sites implementing the PEP uP protocol as part of a quality improvement collaborative. By defining best achievable performance targets, we aim to aid in future quality improvement initiatives related to implementing the PEP uP protocol.

Methods

This study is a prospective, multicenter quality improvement collaborative with an evaluation component. We recruited sites in the United States from our contact list and through our website (www.criticalcarenutrition.com). To be eligible to join the collaborative, intensive care units (ICUs) had to be able to identify a multidisciplinary team consisting of, at a minimum, the ICU dietitian and a physician and a nurse who were recognized by their peers as champions of best nutrition practices. In addition, they had to be willing to implement all aspects of the PEP uP protocol. Of 8 applications, because of limitations in funding, we were only able to select 5 hospitals for participation in this collaborative. One hospital implemented the protocol in 3 of its ICUs for a total of 7 distinct ICUs.

Each site was provided with implementation tools and an educational DVD presentation to train their multidisciplinary team (described more fully by McCall and colleagues[5]), a site visit and presentation from a member of the critical care nutrition team, a supply of EN product, access to a member of the critical care nutrition team for support in implementing the protocol, and access to a bedside monitoring tool to assist with nutrition monitoring. A semidigested solution with a very high protein content (37% of calories from protein; 92 g per 1000 mL) was used in study sites. Beginning in the spring of 2014, sites engaged their local clinical teams to implement the PEP uP protocol and received a site visit from Dr Heyland and coaching from his colleagues on aspects of implementation and system change.

Data Collection

To evaluate the success of our collaborative and describe the variation in practices, we used data collected from a large international multicenter observational study of nutrition practices in the ICU conducted starting in fall of 2014, the International Nutrition Survey (INS) 2014. The methods of this recurring survey are similar to previously published studies.[4,6] Critically ill adult patients mechanically ventilated prior to ICU admission or within the first 48 hours and who stayed in the ICU for at least 72 hours were eligible to be included in this evaluation. On the first day of the study (September 17, 2014), sites screened all patients located in their ICU on that day and began collecting data on all eligible patients. Sites continued to screen each new patient admitted to the ICU, with the goal of identifying 15–20 consecutive eligible patients. As per usual clinical practice, the decision to implement a feeding protocol and initiate feeds occurred when clinically indicated at the site level. For the purposes of this evaluation, we included only patients who met the described eligibility criteria above.

For each patient included in the INS, sites collected data describing patient characteristics, ICU admission information, baseline nutrition assessment, daily nutrition data, and 60-day patient outcomes. As per our usual INS practices, baseline nutrition assessment was not standardized across sites, but we did capture the total calories and protein prescribed and received. Prescribed calories and protein referred to the total calories and protein provided by the goal feeding regimen determined at the initial assessment, using EN or parenteral nutrition (PN), according to the physician or dietitian's recommendation. Daily nutrition data, which included the initial feeding strategy and type and amount of nutrition received, were collected from ICU admission until ICU discharge or death, or for a maximum of 12 days. Patient outcomes at day 60 were collected in hospital and included date mechanical ventilation was discontinued, date of ICU and hospital discharge, and date of death (if relevant). Data were abstracted from patient records and entered online using a secure web-based electronic data capture system.

After the end of the nutrition data collection, reports that demonstrated the nutrition adequacy of patients from participating sites benchmarked to other sites in the database were generated and sent back to all participating sites. We followed up with a questionnaire to dietitians at the PEP uP sites to evaluate the ease of implementation, as well as acceptability of and perceived barriers to implementation of the various

components of the PEP uP protocol. Answers to open-ended questions were analyzed for themes by 2 of the authors independently (D.K.H. and M.L.).

To compare the nutrition performance of PEP uP sites, we developed a concurrent control group. Since practice patterns vary across countries and are a significant determinant to nutrition performance,[7] we selected only the sites participating in the INS from the United States to form the control group. These ICUs elected to participate in the nutrition survey of their own accord and received no support or intervention from the study team beyond that which was available to all participants of the international survey. In these non-PEP uP sites, patient care, including the use of semidigested diets, protein supplements, gastric residual volume threshold, and so on, was not standardized or influenced at any point during this observational study. To be eligible for this control group, U.S. sites could not be using volume-based feedings or the PEP uP protocol.

Statistical Approach

We first describe and compare nutrition practices and nutrition adequacy between the PEP uP sites vs the concurrent control group. Adequacy of EN refers to percentage of prescribed calories and protein received from EN, while adequacy of total nutrition is expressed as the percentage of caloric and protein prescriptions received from a combination of EN, PN, and propofol. Given the focus of the PEP uP protocol is an EN initiation strategy, adequacy was calculated over the first 5 ICU days only. Days without EN or PN were included and counted as 0% adequacy, but only days prior to the date of death, ICU discharge, or permanent progression to exclusive oral intake were counted in the 5-day averages. Permanent progression to exclusive oral feeding occurred when a patient had begun oral feeding and subsequently did not receive any EN or PN during the remaining days of his or her data collection. Patients prescribed PN only were excluded from this analysis in both groups as they would not have received the PEP uP protocol. To further investigate nutrition adequacy in the 2 groups, we looked at the nutrition adequacy of high Nutrition Risk in the Critically Ill Score (NUTRIC) patients. A high NUTRIC score of ≥5 is associated with worse clinical outcomes, and these patients are more likely to benefit from aggressive nutrition therapy in comparison to low NUTRIC score patients.[8]

All categorical variables are described as counts and percentages. Continuous variables are described as means and standard deviations except for site characteristics, which are described as means and site ranges, and length of stay variables, which are summarized by medians and quartiles due to their positive skew. *P* values for all comparisons accounted for between-site clustering. Continuous variables were compared by the linear mixed-effects model with site as a random effect, except duration of stay variables, which were compared by the log-rank test with robust standard errors to account for site clustering. Categorical patient characteristics were compared by the Rao-Scott χ^2 clustered by site,[9,10] but categorical nutrition outcomes were compared by generalized estimating equations clustered by site (the logistic model was used for binary outcomes and the generalized logit for nominal outcomes). Since nutrition intake increases over the first few days in the ICU and admission type (medical vs surgical) is strongly predictive of nutrition outcomes, all adjusted differences and *P* values comparing nutrition outcomes controlled the number of evaluable days, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and the admission type (medical/surgical).[11,12] For nutrition outcomes, we also present an unadjusted analysis that used the site average of the first 5 ICU days of all patients and compared groups by an independent *t* test of the site averages. The range of site averages was also presented. All analysis used SAS version 9.4 (SAS Institute, Cary, NC). All *P* values were 2-sided. Given the hypothesis-generating and descriptive nature of these observations, we did not adjust for multiplicity of tests.

The Queen's University Research Ethics Board approved the INS. Individual sites also obtained local research ethics board approval as required by their local institutions. Informed consent from patients was not required given the quality improvement nature of this work.

Results

In 2014, a total of 244 ICUs from 29 countries participated in the INS. Of the 50 ICUs from the United States, 7 were part of the PEP uP Collaborative, and the remaining 43 served as concurrent control sites. Characteristics of participating sites are shown in Supplemental Table S1. Most participating hospitals were academic facilities with a "closed" administrative model of care. All sites had a dietitian dedicated to working in the ICU, but only 67% of the control sites acknowledged having a specific nurse-directed feeding protocol.

In total, 1108 patients were included in this analysis: 126 from PEP uP sites and 982 from control sites. Table 1 describes the baseline characteristics and clinical outcomes of patients included in this evaluation. Patients in PEP uP sites were more likely to have a medical admission diagnosis and a higher ICU mortality rate (22% vs 13%, $P = .01$; Table 1). In both groups, approximately one-fourth of patients had a high NUTRIC score.

Overall Nutrition Performance

Overall, most patients in both groups were fed via the enteral route (see Table 3). EN tended to be started faster in PEP uP sites compared with controls (mean, 34 hours from admission to ICU vs 51, $P = .08$). On average, patients were prescribed 23 kcal/kg/d and 1.4 g/protein/d across all sites. The amount of calories and protein actually received over the first 5 days from EN and total nutrition by patients in sites

Table 1. Characteristics and Outcomes of Participating Patients.[a]

Variable	Patients From PEP uP Sites (n = 126)	Patients From Other U.S. Sites (n = 982)	*P* Value
Age, y	62.9 ± 16.0	59.6 ± 16.8	.24
Sex, male	83 (65.9)	610 (62.1)	.59
Body mass index, kg/m^2	27.9 ± 7.9	28.5 ± 8.3	.34
Admission diagnosis			.009
Neurologic	19 (15.1)	201 (20.5)	
Respiratory	41 (32.5)	191 (19.5)	
(Cardio)vascular	16 (12.7)	214 (21.8)	
Gastrointestinal	6 (4.8)	88 (9.0)	
Sepsis	33 (26.2)	104 (10.6)	
Trauma	6 (4.8)	130 (13.2)	
Metabolic	3 (2.4)	22 (2.2)	
Other	2 (1.6)	32 (3.3)	
Admission type			.0004
Medical	112 (88.9)	598 (60.9)	
Surgical elective	3 (2.4)	152 (15.5)	
Surgical emergency	11 (8.7)	232 (23.6)	
APACHE II score	21.3 ± 6.9	22.1 ± 7.8	.70
Baseline SOFA score	5.7 ± 3.1	5.8 ± 3.4	.89
NUTRIC score	4.4 ± 1.9	4.1 ± 2.0	.57
% NUTRIC ≥5	35 (27.8)	258 (26.3)	.72
Charlson Comorbidity Index	2.1 ± 2.0	1.9 ± 2.1	.73
ICU mortality	28 (22.2)	131 (13.3)	.01
Died in hospital within 60 days of ICU admission	32 (25.4)	181 (18.4)	.08
Length of stay among 60-day survivors	n = 94	n = 801	
Days on mechanical ventilation	4.9 [2.8–10.2]	4.4 [2.0–9.9]	.74
Days in ICU	8.8 [5.6–15.1]	8.8 [5.4–15.9]	.95
Days in hospital	15.2 [10.3–29.8]	16.4 [10.0–29.4]	.48

APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; NUTRIC, Nutrition Risk in the Critically Ill Score; PEP uP, Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol; SOFA, Sequential Organ Failure Assessment.
[a]Values are number (%), mean ± standard deviation, or median [interquartile range]. To account for potential clustering by site, *P* values were calculated from a linear mixed-effects model with site as a random effect for continuous variables and the Rao-Scott χ^2 test clustering by site for categorical variables.

using the PEP uP protocol was greater than control sites (Table 2 and Figure 1). From enteral sources, patients at PEP uP sites received an average of 35% of their prescribed energy requirements (site range, 26%–53%) compared with 24% in patients from control hospitals (site range, 1%–48%; $P = .02$). Patients from PEP uP sites received significantly more protein over the first 5 ICU days (mean, 42% of prescribed requirements [site range, 29%–66%] compared with 25% in control sites [site range, 1%–48%]; $P = .001$). All patients, particularly high NUTRIC score patients, were more likely to achieve at least 80% of goal protein by after day 3 at PEP uP sites compared with control sites (Table 3). However, the proportion of high NUTRIC score patients who achieved this quality benchmark was only 12%. The increased protein delivery observed with the use of the PEP uP protocol was mainly the result of using the very high-protein formula as the EN source. The contribution of supplemental protein was minimal in both groups (Table 2).

Differences in PEP uP Sites in Key Nutrition Practices Related to PEP uP Protocol

A greater proportion of patients in PEP uP sites were initially started on volume-based feeds with a semidigested solution and received prophylactic use of motility agents and protein supplements compared with patients in control sites (Table 3). In PEP uP sites, 71% of patients received a semidigested formula within 72 hours of admission to the ICU (site range, 58%–95%), and the use of a volume-based goal as the initial feeding strategy ranged from 47%–100% (mean, 72%). Use of prophylactic protein supplements and motility agents ranged from 0%–100% (mean, 56%) and 0%–85% (mean, 19%) respectively. The variability in EN nutrition adequacy in PEP uP sites only is shown in Figure 2. Patients from the best-performing site received 53% of calories prescribed and 66% of protein prescribed over the first 5 days.

Table 2. Nutrition Outcomes Over First 5 ICU Days.

Variable	PEP uP ICUs (n = 7)[a]	Other U.S. ICUs (n = 43)[a]	Unadjusted		Adjusted	
			Difference	*P* Value[b]	Difference	*P* Value[c]
Proportion of prescribed calories from EN nutrition solution excluding supplements, %	33.0 ± 7.5	23.2 ± 10.6	9.8 (1.4–18.2)	.02	7.8 (1.0–14.7)	.03
Proportion of prescribed protein from EN nutrition solution excluding supplements, %	37.8 ± 8.0	22.1 ± 10.2	15.7 (7.6–23.8)	.0003	13.8 (6.9–20.6)	<.0001
Proportion of prescribed calories from EN nutrition including supplements, %	34.7 ± 9.5	24.2 ± 11.1	10.5 (1.5–19.4)	.02	8.5 (1.0–16.0)	.03
Proportion of prescribed protein from EN nutrition including supplements, %	41.7 ± 11.6	25.3 ± 11.8	16.4 (6.7–26.1)	.001	14.5 (6.1–22.8)	.0007
Proportion of prescribed calories from total nutrition, %	43.0 ± 10.5	31.8 ± 10.7	11.2 (2.4–19.9)	.01	8.7 (1.1–16.3)	.03
Proportion of prescribed protein from total nutrition, %	42.4 ± 10.9	27.1 ± 11.0	15.3 (6.3–24.3)	.001	13.9 (6.0–21.9)	.0006
Calories intake from EN by weight, kcal/kg	7.5 ± 2.7	5.7 ± 2.6	1.8 (−0.4 to 3.9)	.10	1.3 (−0.5 to 3.2)	.16
Protein intake from EN by weight, g/Kg	0.6 ± 0.3	0.3 ± 0.2	0.3 (0.2–0.4)	.0001	0.3 (0.1–0.4)	.0001
Total calorie intake by weight, kcal/kg	9.3 ± 3.3	7.5 ± 2.6	1.9 (−0.3 to 4.1)	.09	1.3 (−0.6 to 3.3)	.18
Total protein intake by weight, g/kg	0.6 ± 0.3	0.4 ± 0.2	0.3 (0.1–0.4)	.0002	0.3 (0.1–0.4)	<.0001

EN, enteral nutrition; ICU, intensive care unit; PEP uP, Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol.
[a]Values are mean ± standard deviation or median (interquartile range).
[b]Calculated by 2-sample *t* test comparing site averages between groups.
[c]Estimated by the linear mixed-effects model with patient average as the dependent variable, site as a random effect, and group, evaluable days, admission type (medical vs surgical) and Acute Physiology and Chronic Health Evaluation II score as fixed effects.

Postimplementation Questionnaire to Dietitians at the PEP uP Sites

Table 4 shows the ratings of acceptability of the various components of the PEP uP protocol, with the overall acceptability of the protocol rated as 9 (range, 8–10). Overall, most elements were considered acceptable with the exception of the prophylactic use of motility agents, which had a rating of 5 (range, 3–9). Perceived barriers to implementing the PEP uP protocol and its various components are listed in Table 5. Common barriers specific to implementing the protocol include the need for ongoing education of practitioners, receiving buy-in from practitioners, and concern with feeding certain patient populations (eg. surgical patients). Dietitians experienced variable levels of difficulty in implementing the components of the protocol (see Supplemental Figure S1). Of the 8 dietitians surveyed from the 7 ICUs, 3 found that implementing the protocol in their ICU increased their workload "a bit," and 1 found it increased their workload "a lot." The remaining felt it had a neutral effect (3/8 dietitians), and 1 felt it "decreased their workload a bit."

Discussion

The PEP uP protocol was designed as an initial starting strategy for EN that would optimize EN delivery compared with historic approaches to feeding via the enteral route. In the context of a national quality improvement collaborative, we implemented the PEP uP protocol in several ICUs in the United States and demonstrated significant increases in nutrition adequacy over the first 5 days compared with other ICUs in the United States participating in the 2014 INS. Greater protocolization of EN delivery, earlier introduction of EN, use of volume-based feeding, and the use of a high-protein formula in the PEP uP sites may explain this study's findings.

We also demonstrated that the PEP uP protocol and its various components are, for the most part, acceptable to dietitians working in the ICU. This is consistent with our prior publication documenting high levels of acceptability from bedside nurses.[2] Despite demonstrating improved protein and calorie delivery, the overall nutrition adequacy of patients in the PEP uP sites was still low and results were variable across sites. Some sites successfully implemented all aspects of the protocol

Table 3. Nutrition Process Variables.[a]

Variable	Patients From PEP uP Sites (n = 126)	Patients From Other U.S. Sites (n = 982)	*P* Value	
			Unadjusted	Adjusted
Patients achieving 80% of goal calories after day 3[b]	44 (39.3)	239 (28.6)	.08	.25
Patients achieving 80% of goal protein after day 3[b]	44 (39.3)	207 (24.8)	.02	.05
% of high NUTRIC patients achieving 80% of goal calories after day 3	11 (9.8)	44 (5.3)	.08	.15
% of high NUTRIC patients achieving 80% of goal protein after day 3	13 (11.6)	39 (4.7)	.0006	.004
Type of nutrition			.008	.03
EN only	118 (93.7)	715 (72.8)		
EN + PN	2 (1.6)	61 (6.2)		
None	6 (4.8)	206 (21.0)		
Time of initiation of EN, h	34.2 ± 34.6	51.1 ± 43.0	.05	.08
EN delivery strategy initially ordered			<.0001	<.0001
Keep nil per os	5 (4.0)	89 (9.1)		
Initiate EN: keep a low rate (trophic feeds: no progression)	18 (14.3)	84 (8.6)		
Initiate EN: start at low rate and progress to hourly goal rate	4 (3.2)	520 (53.0)		
Initiate EN: start at hourly goal rate	3 (2.4)	67 (6.8)		
Initiate EN: start at hourly rate determined by 24-hour volume goal	87 (69.0)	82 (8.4)		
Initiate EN: oral nutrition	4 (3.2)	116 (11.8)		
Initiate EN: bolus feeds	3 (2.4)	5 (0.5)		
Other	0 (0.0)	17 (1.7)		
Proportion of patients receiving semidigested solution within first 3 days of admission	92 (73.0)	138 (14.1)	<.0001	<.0001
Proportion of patients receiving Peptamen Bariatric[c] solution within first 3 days of admission	87 (69.0)	18 (1.8)	<.0001	<.0001
Proportion of patients receiving motility agents within the first 2 days of admission	25 (19.8)	39 (4.0)	.02	.04
Average duration of treatment with motility agents, d	0.9 ± 1.5	0.2 ± 0.7	.001	.002
Average morning glucose, mg/dL	8.3 ± 2.2	8.0 ± 2.3	.22	.79
Proportion of glucose values ≥10 mmol/L (180 mg/dL)	19.6 ± 26.1	16.4 ± 24.3	.49	.74

EN, enteral nutrition; ICU, intensive care unit; NUTRIC, Nutrition Risk in the Critically Ill Score; PEP uP, Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol; PN, parenteral nutrition.

[a]Values are number (%) or mean ± standard deviation. To account for clustering by site, we calculated *P* values from linear mixed-effect models with random site effect for continuous outcomes and generalized estimating equations clustering by site for categorical outcomes. In addition, adjusted *P* values control for admission type (medical vs surgical) and Acute Physiology and Chronic Health Evaluation II score.

[b]A total of 160 patients were not evaluable on day 4 (14 in PEP uP group) and thus were excluded from this comparison because they either left the ICU or transitioned to permanent oral feeding by the end of day 3.

[c]Nestlé HealthCare Nutrition (Florham Park, NJ).

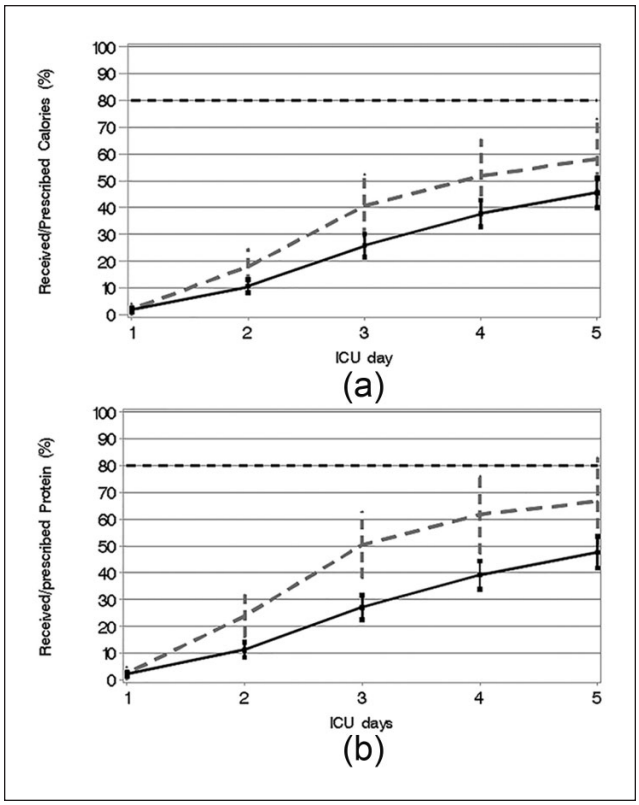

Figure 1. Proportion of prescription received from enteral nutrition. Figure depicts the overall daily mean with 95% confidence intervals of calories (a) and protein (b) provided via the enteral route. Dashed and solid lines depict Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol sites and U.S. control sites, respectively. ICU, intensive care unit.

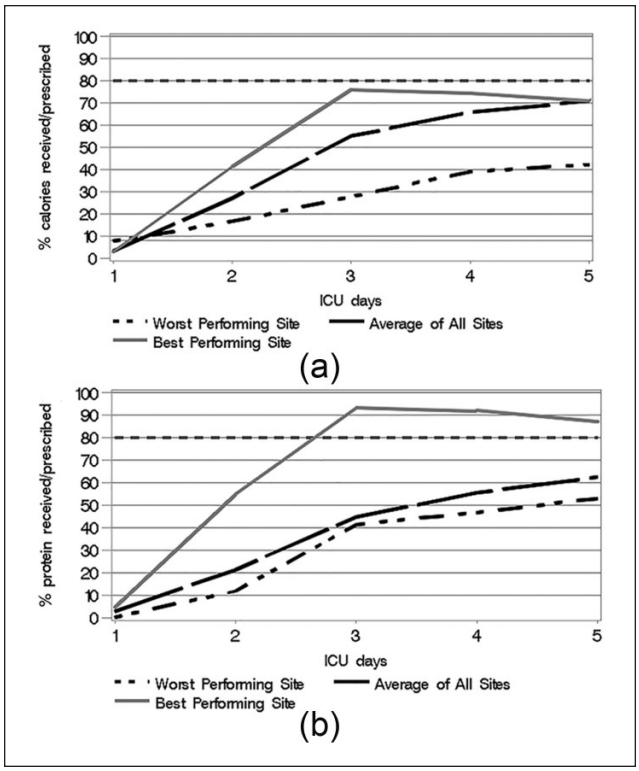

Figure 2. Enteral nutrition adequacy over the first 5 days in best, worst, and average Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP) sites. (a) The total amount of calories received via the enteral route as a percentage of the calories prescribed at baseline assessment in 7 PEP uP sites. The 5-day average for the worst site is 26%; the average is 35% and the best is 53%. (b) The amount of protein from all sources received via the enteral route as a percentage of the protein prescribed at baseline assessment in 7 PEP uP sites. The 5-day average for the worst site is 29%; the average is 42% and the best is 66%. ICU, intensive care unit.

while others struggled to fully implement the protocol and thus failed to improve nutrition delivery. Practice or culture change remains the main barrier for PEP-uP implementation.

Overall, the results of this study are consistent with the previous PEP uP studies that demonstrated improved nutrition delivery with the PEP uP protocol compared with usual feeding protocols that start at a low volume and advance to goal hourly rate based on tolerance.[1–3] We posit that not all ICU patients require such a cautious or conservative approach; some tolerate going right to goal rate from the beginning.[13] Thus, with the PEP uP protocol, we enable practitioners to decide which patients will go right to goal rate compared with others who may require a lower rate of infusion. More important, we shift the language from "hourly rate" to a 24-hour volume-based goal.[14] This enables the bedside nurse to adjust the hourly rate to make up for interruptions that frequently occur during the day when EN is temporarily suspended. We believe the earlier initiation of volume-based feeding to be integral to the success of the PEP uP protocol. As we observed in this collaborative, we saw variable success with the use of volume-based feeds as the initial order for EN (range, 47%–100%). Admittedly, in some patients, such as those taking vasopressors, a lower rate of infusion (trophic feeds) may be safer, but we leave this to bedside clinicians to decide.

Although our work with the PEP uP protocol continues to show improvements in protein and calorie delivery, the absolute increases in amounts of protein and calories are underwhelming and likely insufficient to affect clinical outcomes. Prior studies have shown that for an increase of 1000 calories or 30 g protein/d or 25% increase in protein/caloric adequacy, this translates into a meaningful and large reduction in mortality and infectious complications, as well as improved long-term health-related quality of life.[6,15–17] In this trial, we achieved only approximately an 8% increase in caloric adequacy and a 15% increase in protein adequacy. Moreover, if the goal of our artificial nutrition delivery is to provide >80% of estimated requirements overall, only 40% of all patients and 12% of high NUTRIC score patients in the PEP uP group achieved this quality metric.[11] Clearly, more work needs to be

Table 4. Ratings of Acceptability of the Various Components of the PEP uP Protocol.[a]

Question	Median (Range)
Do you find it acceptable to start enteral nutrition early (within 24–48 hours of ICU admission)?	10 (8–10)
Do you find it acceptable to start trophic feeds early (within 24–48 hours of ICU admission)?	10 (2–10)
Do you find it acceptable to provide 24-hour volume-based goals?	9 (6–10)
Do you find it acceptable to start enteral nutrition right away with a semidigested formula (eg, Peptamen Bariatric[b])?	10 (7–10)
Do you find it acceptable to start a motility agent (eg, metoclopramide) right away, as soon as feeds are initiated?	5 (3–9)
Do you find it acceptable to start protein supplements right away, as soon as feeds are initiated?	10 (5–10)
Overall, how acceptable is the PEP uP Feeding Protocol to you?	9 (8–10)

ICU, intensive care unit; PEP uP, Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol.
[a]Ratings of acceptability of the various components of the PEP uP protocol. Respondents were asked to rate acceptability on a 10-point scale where 1 = totally unacceptable and 10 = totally acceptable.
[b]Nestlé HealthCare Nutrition (Florham Park, NJ).

Table 5. Barriers to Implementation of the PEP uP Protocol.

Question	Responses
What do you see as the main barriers to starting EN early (within 24–48 hours of ICU admission)?	RN/MD belief that EN is contraindicated in hemodynamically unstable patients, GI bleeds, and surgical patients who have not shown clear evidence of bowel function
	EN order set issues (eg, merging it into the electronic medical record)
	Unable to get enteral access
What do you see as the main barriers to implementing trophic feeds early?	MDs/RNs hesitant to initiate EN early before evidence of bowel function in surgical patients, especially GI surgeries
	MDs/RNs hesitant to start feeds for patients with intra-abdominal hypertension
	Lack of understanding of the rationale for trophic feeds among healthcare professionals
What do you see as the main barriers to implementing the 24-hour volume-based goals?	RNs hesitant to use this method if patient has shown signs of intolerance (eg, high gastric residual volumes or vomiting) or is at risk of intolerance based on diagnosis/complications
	The calculation required if feeds are held
	Staff turnover and need for education on protocol and importance of early EN
What do you see as the main barriers to using a semidigested EN formula?	MD may request other product in certain populations
	Staff confused by the name of the product
	Concern over high-protein content in renal patients
What do you see as the main barriers to starting a motility agent (eg, metoclopramide) right away?	MD/PharmD concerns with using them prophylactically given potential side effects
	RD does not have order writing privileges for medications and therefore is unable to complete the PEP uP protocol
	Some medical conditions contraindicate the use of motility agents
What do you see as the main barriers to starting protein supplements right away?	Concern with renal function
	Difficulties documenting their use in the chart if not on the medication administration record
	RNs administering protein supplements
Any suggestions on how to improve the protocol?	Fourth option for surgical patients to start at a rate-based regimen and, once the goal rate is achieved, then switch to a volume-based regimen
	Electronic volume/rate calculator for RN to refer to based on volume goal entered by RD/MD
	Changing volume based feeds to every 12 hours rather than 24 hours so it is based on a single nurse's shift
	Education/tools for maintaining optimal blood sugar control when EN rates are being frequently adjusted
	Adding an option for bolus feeds
	Omitting routine use of motility agents
	Incorporating all aspects of the protocol onto the orders (eg, diarrhea guidelines, OR guidelines, gastric residual volumes)
	Further education/resources supporting the early use of motility agents

EN, enteral nutrition; GI, gastrointestinal; ICU, intensive care unit; MD, medical doctor; OR, operating room; PEP uP, Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol; RD, registered dietitian; RN, registered nurse.

done to consistently optimize the implementation of the PEP uP protocol to achieve a meaningful impact on nutrition delivery and thus on patient outcomes, but the focus should be on high NUTRIC score patients.

In this collaborative, we used a very high-protein-containing formula (37% of calories from protein) to optimize protein delivery, and this strategy alone (independent of protein supplements) may explain the increased protein delivery with the PEP uP protocol. We note that some ICU dietitians felt that protein supplements were not needed because of this fact, and this may explain why we observed such variable use of prophylactic protein supplements. However, we also note that protein adequacy was still suboptimal, despite the use of this high-protein-containing solution. Moving forward, we suggest practitioners continue to use high-protein-containing solutions as well as protein supplements to optimize protein delivery and to achieve a minimum of 80% of that which is prescribed. Although the PEP uP protocol recommends 14 g of protein supplements twice a day, this was meant to be a "starting dose," and certainly higher doses can be used (up to 28 g bid), and efforts should be made to compensate for missed doses. Achieving this threshold of 80% of prescribed amounts of protein has been shown to be associated with reduced mortality in nutritionally "at-risk" ICU patients and more important than achieving energy goals.[18]

By describing the upper range of site averages with nutrition adequacy and the success of implementing the various components of PEP uP protocol, we define what is "best achievable" in real practice. If one site can achieve this kind of success, why can we not expect that of others? By addressing the barriers to implementing the PEP uP protocol, we believe local sites can achieve greater success with the PEP uP protocol. In this quality improvement collaborative, we surveyed the dietitians participating in the PEP uP sites to get their anecdotal sense of main barriers to implementation. The barriers are shown in Table 5. Overall, we postulate that main barriers may be cultural (devaluation of nutrition in the ICU in general) and systematic (lack of nutrition education for ICU clinicians and inability to embed aspects of the PEP uP feeding protocol into electronic ordering). With the exception of the prophylactic use of motility agents, the PEP uP protocol and its components can be considered acceptable to clinicians. No safety issues were raised. Most dietitians did not report that the protocol increased their workload significantly. However, it has to be acknowledged that introducing practice changes into an ICU requires considerable resources to educate staff. Perhaps more dietitian and nurse educator time to more systematically educate all ICU clinicians would improve compliance with the PEP uP protocol and hence achieve greater improvements in nutrition delivery.[5] Moreover, the use of a more formal, quantitative barriers questionnaire in sites trying to implement the PEP uP protocol may further illuminate obstacles that need to be overcome to ensure successful implementation.[19]

The strengths of this work include that it occurred in a "real-life" setting where practice change work was facilitated by practicing clinicians and implemented in a heterogeneous, nonselective patient population in a variety of settings. One of the limitations of this study was that few surgical patients were enrolled at PEP uP sites. This may have been a selection bias due to the perception that surgical patients will not tolerate volume-based feeds or other aspects of the PEP uP protocol. Unfortunately, with all the studies done on the implementation and evaluation of the PEP uP protocol in the past 5 years, very few surgical patients have been enrolled, and so far the PEP uP protocol does not seem to improve their nutrition delivery.[20] Yet, these patients are some of the worst-fed ICU patients.[10] More work is required to reduce barriers to EN in this population and improve the success of the PEP uP protocol in surgical patients. There is an ongoing multicenter randomized controlled trial of the PEP uP protocol, and we await the results of this trial to inform future practice in these "difficult-to-feed" patients.[21] Another limitation of this quality improvement collaborative is the lack of process information detailing exactly what implementation efforts were made at each site. Future implementation efforts need to better document what exactly was done with what effect. Finally, the formal hypothesis testing should be interpreted as ancillary to the descriptive results since there may be some type I and type II errors due to the large number of comparisons and small number of PEP uP ICUs, respectively.

Conclusions

The PEP uP protocol can be effectively and safely implemented by critical care practitioners in the United States. As a consequence, participating sites observed a decrease in the time to initiate EN in ICUs and a marginal increase in nutrition adequacy. Implementation of the protocol and overall improvement in nutrition adequacy were variable across sites. Further work is required to improve the means by which the PEP uP protocol is implemented in an ICU to achieve greater success with improving nutrition delivery.

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Statement of Authorship

D. K. Heyland and M. Lemieux contributed to the conception/design of the research; D. K. Heyland, M. Lemieux, L. Shu, K. Quisenberry, and A. G. Day contributed to the acquisition, analysis, or interpretation of the data; and D. K. Heyland drafted the manuscript. All authors 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.

Supplementary Material

Table S1 and Figure S1 are available online at http://jpen.sagepub.com/supplemental.

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