An Early Enteral Nutrition (EEN) Protocol for Adult Critically Ill Patients

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ABSTRACT

Background: Enteral nutrition (EN) is the preferred feeding route for critically ill patients who are unable to maintain volitional intake due to intubation with mechanical ventilation, as it attenuates the metabolic response to critical illness. Established guidelines support early EN (EEN) initiation within the first 24-48 hours of intubation to improve various clinical outcomes.
Objectives: To determine if implementation of an EEN protocol increases the number of patients that receive EEN within 48 hours of intubation, as well as to assess the effect of EN timing on certain nutritional and clinical patient outcomes.
Methods: A quasi-experimental, single-center, retrospective study involving analysis of electronic medical record (EMR) data of critically ill, intubated and mechanically ventilated, adult patients admitted to two ICUs of a community hospital was performed before (control group) and following implementation of the protocol (intervention group). The EEN protocol involved a flowchart and education sessions for staff. Demographic, clinical, and nutrition data were collected and analyzed.
Results: The EEN protocol resulted in a statistically significant increase the number of patients that received early EN (p = <0.001), from 33.3% to 74.1% of patients, but this did not translate into a reduction in the primary nutrition endpoints of constipation and pressure injury progression or development, nor other clinical patient outcomes of reduced mechanical ventilation duration, mortality, or ICU and hospital length of stay (LOS).
Conclusions: Implementation of an EEN protocol successfully increased the number of patients that received EEN within the recommended 48 hours of intubation, however, patient outcomes did not improve as intended. A larger study of longer duration may have been more efficacious.

INTRODUCTION

Nutrition is known to play an essential role in the clinical outcomes of critically ill patients.[1] Early initiation of enteral nutrition (EN) support within 48 hours of intubation is a best practice guideline recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) due to its association with reduced morbidity and mortality.[1] Despite this recommendation, delayed EN remains a prevalent occurrence in intensive care units (ICU)s due to various barriers that impede timely initiation.[2,3]

The catabolic state and severe inflammatory response to critical illness can quickly lead to metabolic complications such as negative nitrogen balance, multi-organ failure, and impaired glucose metabolism among others.[1] These complications increase the risk for detrimental patient outcomes, like prolonged hospitalization and ICU length of stay (LOS), delayed wound healing, difficulty weaning from mechanical ventilation, and increased infections and mortality.[1] However, research shows that provision of EN support maintains the functional integrity of the intestines, prevents oxidative cellular injury, modulates

stress and the systemic immune response, and can attenuate disease severity.[1] Thus, early enteral nutrition (EEN) during critical illness can reduce disease severity and infectious complications, decrease ICU and hospital LOS, and improve patient outcomes overall.[1]

EN may be delayed beyond 48 hours of intubation for several reasons, including delays in feeding tube placement, patient intolerance to EN (e.g., high gastric residual volume, vomiting), withholding EN for tests and surgical procedures, hemodynamic instability, provider-level factors, and lack of clear policies and procedures regarding EEN.[2,4]

To address this problem, researchers have implemented enteral nutrition protocols and studied the effects on different patient outcomes.[3,5,6,7,8,9,10,11] A recent retrospective study of 694 patients found that 17.7% of patients were not started on EN during the first 48 hours of intubation, 53% of which did not have appropriate reasons for delayed initiation.[5] The study's data assisted in educating providers about the importance of EEN and modifying hospital protocols to prevent delayed EN initiation.[5] A similar retrospective quality improvement study identified initiation and advancement of EN as the most common reason for insufficient EN volume delivery, and concluded that avoiding delayed EN results in greater overall EN delivery.[6]

Until now, the literature has failed to show the effects of an EEN protocol on pressure injury development and progression or bowel regularity specifically—two nutritional endpoints of particular interest in the critically ill population.[12] Critical illness carries the highest prevalence of pressure injuries compared to all other healthcare settings, at about 12–33% of patients.[13] Critically ill patients are four times more likely to develop a more severe pressure injury (stage III, IV, deep tissue injury, or unstageable) than a stage I or stage II.[13] Critical illness increases constipation prevalence as well, ranging from 5 to 83% of patients.[14] This is due to several potential factors, such as shock, use of sedatives and opioids, electrolyte disturbances, dietary changes, and gastrointestinal dysmotility.[14]

The purpose of this study was to determine the prevalence of delayed EN in an ICU, as well as identify barriers to early EN initiation, and implement an EEN protocol aimed at addressing those barriers and increasing the number of patients who receive EEN within 48 hours of intubation. It was hypothesized that increasing the number of patients who receive EEN would result in improved skin integrity and bowel regularity.

METHODS

Study Design

This was a single-center retrospective study of critically ill patients at Ellis Hospital in Schenectady, NY. To increase the number of patients who receive EEN within 48 hours of intubation and to determine if EEN reduces constipation and pressure injury development and/or progression, an EEN protocol was implemented consisting of a written flowchart and staff education sessions. Data from patient's electronic medical records (EMR)s were retroactively collected and analyzed. This included demographic data such as sex, age, and BMI; patient characteristics such as ICU admission reason and use of vasopressor support; and outcomes such as time to EN initiation, mechanical ventilation duration, ICU length of stay (LOS), hospital LOS, in-hospital mortality, constipation, and pressure injury development or progression. Outcome changes were assessed by comparing data

from a pre-intervention group to a post-intervention group. Institutional Review Board approval was obtained from SUNY Oneonta and Ellis Medicine.

Intervention

The EEN protocol was designed to address the barriers to EEN initiation and provide clear guidance to staff (nurses, physicians, and physicians assistants) regarding how to safely initiate EN in a timely manner in the absence of registered dietitian (RD) recommendations or availability (e.g., once volume resuscitated and hemodynamically stable, no concern for gastrointestinal bleeding, etc.), along with EN formula selection and rate initiation (see **Appendix**). This intervention was based on the Social Ecological Model as it targeted individuals (staff members) as well as the larger system of the ICU/hospital to positively influence the health outcomes of patients.[15] It involved a written flowchart that the author created and posted throughout the two ICUs at Ellis Hospital. A combination of ten minute group and individual education sessions were provided to staff on site to increase knowledge of ASPEN's recommendation to initiate EN within 48 hours of intubation (known as EEN) including the purpose and benefits, explain the EEN protocol (flowchart), review the pre-intervention data highlighting the need for this intervention, and clarify each discipline's role in the protocol. The education sessions occurred over one week, with implementation of the protocol beginning once all staff received education. The data of patients who met inclusion criteria were obtained from their EMRs for approximately four weeks until a sufficient sample size was collected.

Participants

Patients were selected to participate if they remained intubated for greater than 48 hours. There were 45 patients in the pre-intervention group and 27 patients in the post-intervention group. All participants were adults. The mean age of the pre-intervention group was 62.6 years, ranging from 20 to 93 years, compared to the post-intervention group with a mean age of 70.3 years, ranging from 53 to 89 years. Approximately 56 percent (n = 25) of the pre-intervention group were females and 44 percent (n = 20) were males, and 53 percent (n = 16) of the post-intervention group were females and 47 percent (n = 14) were males. The average BMI of the pre-intervention group was 30.0, ranging from 16.9 to 52.3. The post-intervention group's average BMI was 27.3, ranging from 18.3 to 47.5. Patients were admitted to the ICU predominantly for medical reasons (86.7% in the pre-intervention group, 77.8% in the post-intervention group), but surgical patients were included as well (13.3% in the pre-intervention group and 22.2% in the post-intervention group).

Tools

The evidence-based flowchart included in the EEN protocol was developed by the study author, but drew influence from a similar study.[16] It was a guideline created by reviewing up-to-date practice guidelines and literature searches, and was agreed upon by the critical care dietitians and physicians. It includes when to start EN based upon different patient parameters, what EN formula to order and at what rate.

Data Analysis

The pre-intervention and post-intervention groups were further split into EEN and delayed enteral nutrition (DEN) groups based upon timing of EN initiation. Using SPSS software, two-way ANOVA tests were run for the continuous variables (age, BMI, time to EN initiation, mechanical ventilation duration, ICU LOS, and hospital LOS) and

Pearson's Chi-Squared tests were used for the categorical variables (ICU admission reason, sex, vasopressor support, in-hospital mortality, constipation, and pressure injury development or progression). A p-value of 0.05 was considered statistically significant.

RESULTS

Implementation of the protocol resulted in a statistically significant increase in the number of patients who received EEN within the recommended 48 hours of intubation—33.3% of patients (n = 15) received EEN in the pre-intervention group compared to 74.1% of patients (n = 20) in the post-intervention group (see **Figure 1**).

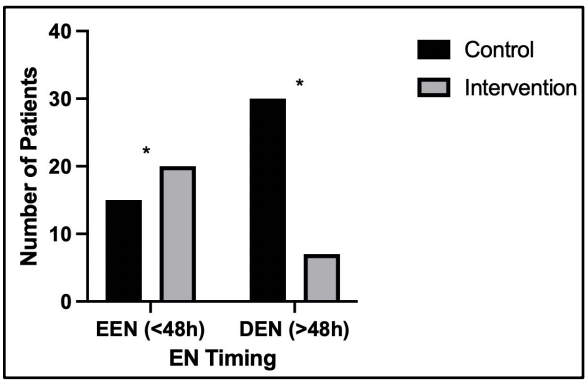

Figure 1: Comparing EN timing of pre-intervention to post-intervention. * = $p < 0.05$

As shown in **Table 1**, there were no significant differences found for patient characteristics like sex, age, and BMI. However, a significant difference in ICU admission reason (medical or surgical) was discovered (p = 0.007), as the majority of patients were admitted for various medical reasons as opposed to surgery.

Table 1: Baseline Patient Characteristics

	Pre-Intervention			Post-Intervention			
	All Patients (n=45)	**EEN (< 48 hr) (n=15)**	**DEN (> 48 hr) (n=30)**	**All Patients (n=27)**	**EEN (< 48 hr) (n=20)**	**DEN (> 48 hr) (n=7)**	***P*-value**
Admission Reason							
Medical	39 (86.7%)	15 (100%)	24 (80%)	21 (77.8%)	18 (90%)	3 (42.9%)	0.007[b]
Surgical	6 (13.3%)	0 (0%)	6 (20%)	6 (22.2%)	2 (10%)	4 (57.1%)	
Sex							
Male	20 (44.4%)	6 (40%)	14 (46.7%)	10 (37%)	7 (35%)	3 (57.1%)	0.874[b]
Female	25 (55.6%)	9 (60%)	16 (53.3%)	17 (63%)	13 (66%)	4 (42.9%)	
Age (y)	62.6 (20-93)	59.5 (20-82)	64.2 (20-93)	70.3 (53-89)	71.7 (55-89)	68.6 (53-87)	0.612[a]
BMI (kg/m^2)	30.0 (16.9-52.3)	29.5 (16.9-52.3)	30.3 (21.7-51.1)	27.3 (18.3-47.5)	27.5 (18.6-47.5)	27.7 (18.3-35.0)	0.94[a]
Vasopressors at 48 hrs	19 (42.2%)	4 (26.7%)	15 (50%)	7 (25.9%)	5 (25%)	2 (28.6%)	0.228[b]
High dose	8	0	8	1	0	1	
Low dose	11	4	7	6	5	1	0.063[b]

Abbreviations: EEN, early enteral nutrition; DEN, delayed or no enteral nutrition

[a] Two-way ANOVA test

[b] Pearson's Chi-Square test

Two-way ANOVA tests were used to evaluate for variance between patients receiving EEN and DEN in the pre- and post-intervention groups for various patient outcomes outlined in **Table 2**. As previously mentioned, a significant difference was found in the time to EN initiation between these groups, which was the primary endpoint of this study. However, no differences were found for the remaining patient outcomes, including mechanical ventilation duration, ICU and hospital length of stay (LOS), in-hospital mortality, constipation, and pressure injury development or progression.

Table 2: Patient Outcomes

	Pre-Intervention			Post-Intervention			
	All Patients (n=45)	**EEN (< 48 hr) (n=15)**	**DEN (> 48 hr) (n=30)**	**All Patients (n=27)**	**EEN (< 48 hr) (n=20)**	**DEN (> 48 hr) (n=7)**	***P*-value**
Time to EN initiation (hours)	68 (0-168)	22.6 (0-43.8)	93.2 (48.8-168)	55.5 (3.9-282.1)	24.6 (3.9-43.3)	143.9 (64.4-282.1)	<0.001[a]
Mechanical ventilation (days)	13.3 (2-47)	14.7 (2-47)	12.6 (3-45)	8.8 (2-36)	9.2 (2-36)	7.7 (3-19)	0.837[a]
ICU LOS (days)	16.7 (4-48)	17.9 (4-48)	16.1 (5-44)	11.4 (4-42)	12.3 (4-42)	8.9 (4-19)	0.671[a]
Hospital LOS (days)	23.7 (6-61)	27.1 (8-61)	22.0 (6-57)	15.1 (5-42)	14.9 (5-42)	15.7 (5-37)	0.487[a]
In-hospital mortality	17 (37.8%)	7 (46.7%)	10 (33.3%)	4 (14.8%)	3 (15%)	1 (14.3%)	0.138[b]
Constipation (≥ 4 days)	19 (42.2%)	5 (33.3%)	14 (46.7%)	9 (33.3%)	5 (25%)	4 (57.1%)	0.313[b]
Pressure injury development or progression	19 (42.2%)	6 (40%)	13 (43.3%)	8 (29.6%)	5 (25%)	3 (42.9%)	0.595[b]

Abbreviations: EEN, early enteral nutrition; DEN, delayed or no enteral nutrition; EN, enteral nutrition; ICU, intensive care unit; LOS, length of stay
[a] Two-way ANOVA test
[b] Pearson's Chi-Square test

The reasons for delayed initiation of EN were identified for both the pre- and post-intervention groups and are displayed in **Table 3**. They included hemodynamic instability, abdominal surgery, presence of gastric tube output, 48 hours after intubation falling on a weekend day, gastrointestinal bleeding, presence of an intra-aortic balloon bump (IABP) without a post-pyloric feeding tube (thus inhibiting the ability to raise the patient's head of bed greater than 30 degrees which is a prerequisite for safe feeding), and no identifiable reason for delayed EN initiation for the pre-intervention group. However, in the post-intervention group, only hemodynamic instability, abdominal surgery, and gastrointestinal bleeding resulted in DEN.

DISCUSSION

Implementation of an EEN protocol in critically ill, intubated patients was shown to positively increase the number of patients who receive EN within 48 hours of intubation, but did not translate into a

Table 3: Reason for delayed EN (> 48 hr)

Reason for delayed EN (DEN)	Pre-Intervention (n=30)	Post-Intervention (n=7)
Hemodynamic instability	7	1
Abdominal surgery	6	3
Unknown reason	5	1
Gastric tube output	4	0
Weekend	4	0
GI bleeding	3	2
IABP	3	0

Abbreviations: IABP, intra-aortic balloon pump

reduction in the primary nutrition endpoints of constipation and pressure injury progression or development, nor other clinical patient outcomes like reduced mechanical ventilation duration, mortality, or length of stay (LOS).

Nutrition Outcomes

An interesting finding of this study was that pressure injuries in the post-intervention group were primary caused by medical devices (7 out of 8 or 87.5% of pressure injuries) whereas roughly half (9 out of 19 or 47.4%) of pressure injuries in the pre-intervention group were attributable to medical devices. Further testing should be done to determine whether the reduction in non-medical device pressure injuries was due to the increase in receipt of EEN or if these findings are attributable to other causes, such as the implementation of the new LEAF patient monitoring system for pressure injury prevention that was initiated in these ICUs after the pre-intervention and during the intervention phase of this study. Since this was the first study of its kind to evaluate the effects of EEN on constipation and pressure injuries, more research in this area should be conducted.

Clinical Outcomes

Contrary to prior research, this study failed to find any correlation between EN timing and the clinical outcomes of mechanical ventilation duration, ICU and hospital LOS, and in-hospital mortality.[1] The duration of data collection and subsequent small and unmatched sample sizes of this study were major limitations that may have affected our ability to achieve results similar to that in the literature. Although buy-in from hospital staff regarding the relevance and benefits of this intervention was resounding (a major strength of the intervention), the ability to demonstrate positive effects on end points of particular interest to hospital administration such as cost reduction would have further highlighted the benefits of continued implementation of this protocol.

Barriers to Early EN

Identifying the reasons EN was delayed for the pre-intervention group was imperative in designing an intervention to best target these barriers. The findings in **Table 3** showcase that the intervention was successful in doing so, given post-intervention patients received delayed EN for only three reasons: abdominal surgery, hemodynamic instability, and gastrointestinal bleeding—of

which the latter two are true contraindications to early EN for which EN should be delayed. Thus, abdominal surgery remained the number one inappropriate reason for delayed EN initiation. Although the protocol's written flowchart does list "recent gastrointestinal surgery" as *not* a contraindication to trickle feeds, awaiting return of bowel function before feeding is a common practice by the General Surgery team at this facility. Increasing critical care physician awareness of the large body of evidence in support of early EN in post-surgical patients resulted in their support and willingness initiate EEN in these patients, however, a major challenge of this study was the inability to coordinate educational sessions with the General Surgery group to address this prior to the data collection period.

CONCLUSION

Implementation of the early EN protocol successfully increased the number of intubated patients to receive EEN. Although this did not translate into improved patient outcomes, a larger study of longer duration may have. Adoption of the protocol by all involved departments is imperative for optimal compliance.

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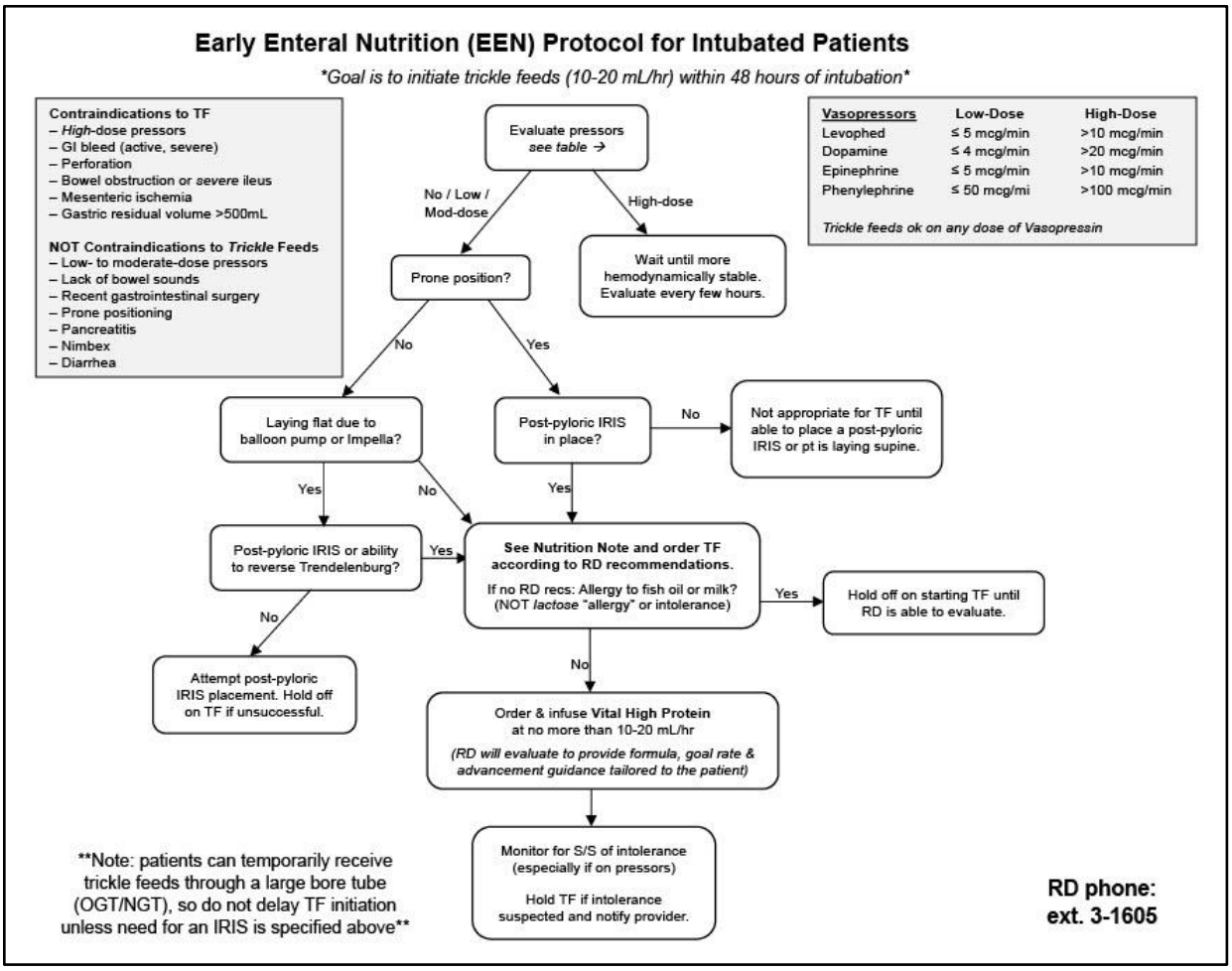
APPENDIX


Early Enteral Nutrition (EEN) Protocol for Intubated Patients
Goal is to initiate trickle feeds (10-20 mL/hr) within 48 hours of intubation
Contraindications to TF
– High-dose pressors
– GI bleed (active, severe)
– Perforation
– Bowel obstruction or severe ileus
– Mesenteric ischemia
– Gastric residual volume >500mL
NOT Contraindications to Trickle Feeds
– Low- to moderate-dose pressors
– Lack of bowel sounds
– Recent gastrointestinal surgery
– Prone positioning
– Pancreatitis
– Nimbex
– Diarrhea
Evaluate pressors see table →
No / Low / Mod-dose
High-dose
Wait until more hemodynamically stable. Evaluate every few hours.
Vasopressors | Low-Dose | High-Dose
Levophed | ≤ 5 mcg/min | >10 mcg/min
Dopamine | ≤ 4 mcg/min | >20 mcg/min
Epinephrine | ≤ 5 mcg/min | >10 mcg/min
Phenylephrine | ≤ 50 mcg/mi | >100 mcg/min
Trickle feeds ok on any dose of Vasopressin
Prone position?
No
Yes
Laying flat due to balloon pump or Impella?
Post-pyloric IRIS in place?
No
Not appropriate for TF until able to place a post-pyloric IRIS or pt is laying supine.
Yes
No
Yes
Post-pyloric IRIS or ability to reverse Trendelenburg?
Yes
See Nutrition Note and order TF according to RD recommendations.
If no RD recs: Allergy to fish oil or milk? (NOT lactose "allergy" or intolerance)
Yes
Hold off on starting TF until RD is able to evaluate.
No
Attempt post-pyloric IRIS placement. Hold off on TF if unsuccessful.
No
Order & infuse Vital High Protein at no more than 10-20 mL/hr
(RD will evaluate to provide formula, goal rate & advancement guidance tailored to the patient)
Monitor for S/S of intolerance (especially if on pressors)
Hold TF if intolerance suspected and notify provider.
Note: patients can temporarily receive trickle feeds through a large bore tube (OGT/NGT), so do not delay TF initiation unless need for an IRIS is specified above
RD phone: ext. 3-1605