Curr Trauma Rep (2016) 2:73–78
DOI 10.1007/s40719-016-0045-z

Early Enteral Nutrition in Trauma: Is There Still Any Doubt?

Keith R. Miller[1] · **Jason W. Smith**[1] · **Brian G. Harbrecht**[1] · **Matthew V. Benns**[1]

Published online: 29 April 2016

Abstract Early enteral nutrition support has been standard in the care of the injured patient for nearly three decades. The Eastern Association for the Surgery of Trauma (EAST) provided the most recent management recommendations for nutritional support of trauma patients in 2004. Simply stated, the recommendation provided by the authors described the superiority of support via the enteral route within the first 72 h of injury when feasible. This statement implied that both the timing of initiation and route of support had potential to impact patient outcomes. The American Society of Parenteral and Enteral Nutrition (ASPEN) in conjunction with the Society of Critical Care Medicine (SCCM) published a broader set of guidelines in 2009 and 2016 that generally agreed with the EAST recommendations and were applicable to critically ill patients. The superiority of the enteral route for delivery of nutritional support has been theorized to be associated with the non-nutritional benefits of substrate provision at the level of the gastrointestinal tract within a 72-h therapeutic window. These concepts, at least in part, were the product of trials performed by surgeons in the setting of severe trauma and are now applied broadly to critically ill patients. However, as is clearly stated in the above guidelines, there are significant limitations inherent in the available literature. The breadth of literature in clinical nutrition has been plagued with issues including small trial size, the presence of multiple confounding variables, diverse control groups, and heterogeneous patient populations. Trials examining the role of early enteral nutrition support in injured patients have similar limitations. Over the last decade several significant trials have been conducted examining questions regarding nutrition support in the ICU, many of which conflict with historical findings. As a result of these trials, the practice of clinical nutrition is evolving rapidly. The objectives of this review include the following: discussion of the historical perspective on nutrition support in the setting of trauma, brief summary of existing data and more recent trials of importance, and how these trials may impact longstanding dogma.

Keywords Critical care · Intensive care · Nutrition · Enteral nutrition · Parenteral nutrition · Permissive underfeeding

Introduction

Early enteral nutrition support has been the mainstay of care in the critically injured trauma patient for decades. “Early” has generally implied the initiation of enteral support within 48 to 72 h of the initial insult, be that injury or admission to the ICU for a variety of illnesses. Guidelines specific to the trauma patient have not been revised since the Eastern Association for the Surgery of Trauma (EAST) published a review of the evidence in 2004 [1••]. Two broader sets of guidelines, in 2009 and recently in 2016, have since been published by the American Society of Parenteral and Enteral Nutrition in conjunction with the Society of Critical Care Medicine suggesting an evidence-based approach to the nutritional care of the critically ill patient [2••, 3]. Within these guidelines, trauma patients are included but are only rarely individually addressed. In the interval between the 2004 EAST guidelines and the 2016 revised ASPEN guidelines, very few studies have been published addressing specifically the benefit of early enteral

This article is part of the Topical Collection on *Nutrition After Severe Trauma*

✉ Keith R. Miller
krmill10@louisville.edu

[1] Department of Surgery, Trauma/ Critical Care, University of Louisville, Louisville, KY 40202, USA

support in trauma patients. The available literature for review is limited by patient heterogeneity, small numbers, alterations in ICU care over time, and variable control groups. Most recommendations are made based on extrapolation from mixed populations of critically ill patients that include sepsis, post-cardiac, and medical ICU patients. Despite these limitations, decisions in nutrition support in critically ill and injured patients continue to be necessary and the available data can assist clinicians in these decisions. In addition, surgeons and physicians caring for injured and critically ill patients should be aware of several recent large clinical trials published in the last decade (in journals not typically reviewed by the trauma surgeon).

Historical Perspective

Three options exist for nutrition support in the critically ill patient: no support, enteral nutrition (EN), and parenteral nutrition (PN). The teleological argument has traditionally suggested that during illness and injury, appetite is diminished as a protective mechanism due to the inability to utilize substrate and the risk of increased metabolic demand in the stress state. Therefore, early nutrition support of any kind could have adverse consequences. The alternative perspective would suggest that due to the hypermetabolic, catabolic state of severe illness and trauma, provision of substrate (either EN or PN) during times of increased demand could improve outcome. In fact, following critical illness, multiple observational trials have suggested that cumulative caloric debt is a powerful prognostic predictor [4, 5]. Thus patients that received fewer calories had poorer outcomes. Proponents of early nutrition support suggest that through early initiation of EN or PN, the caloric debt is decreased and outcomes improved. However, an alternative perspective would suggest that due to the observational nature of these trials, patients with higher morbidity and mortality are more likely to be intolerant of nutrition support and thereby quickly accumulate larger caloric deficits. These opposing perspectives would define the fundamental question regarding nutrition support in the critically ill patient for decades.

Interestingly, trauma surgeons were at the forefront as proponents of the early nutrition support movement that characterized the 1990s and permeates all disciplines today. Moore et al. in 1986 demonstrated that severely injured trauma patients (ATI > 15) undergoing laparotomy with concurrent jejunostomy placement and early initiation (at 18 h post laparotomy, goal in 72 h) of enteral support fared better with regard to septic complications (pneumonia, abscess) when compared to controls with no supplemental nutrition [6]. Proponents of early enteral nutrition have suggested that there is a therapeutic window (lasting anywhere from 24 to 72 h from the time of insult) whereby nutrition support can positively impact outcomes and improve future gastrointestinal tolerance. The initial study by Moore et al. was followed by a second study from the same group that suggested a physiologic advantage through anti-inflammatory mechanisms as the etiology of the differences observed. Acute phase reactants (alpha 1-antitrypsin and orosomucoid) were decreased in the enteral nutrition (EN) group when compared to parenteral nutrition (PN) in abdominal trauma patients [7]. Kudsk et al. demonstrated similar findings with regard to decreased acute phase reactants in a trial examining EN versus PN in 68 trauma patients [8]. These studies, as highlighted in the 2004 EAST recommendations, supported reduced risk of septic and infectious complications in patients receiving EN post injury when compared to either PN or no support control groups. These findings, in part, led to the concept of "non-nutritional" benefits of early EN.

The non-nutritional benefits of early EN have long been purported as the underlying mechanism contributing to the observed outcome differences when the enteral route is compared to the parenteral route or no support groups. There are several proposed advantages of enteral nutrition over parenteral nutrition. First, the maintenance of gastrointestinal structural integrity, and mucosal perfusion allow for the preservation of barrier function of the GI tract. Second, the maintenance of immune function as well as the preservation of gastrointestinal-associated lymphatic tissue (GALT) mass preserves both the systemic and locoregional immune response to infectious and inflammatory stimuli. The concept of the gastrointestinal tract serving as the "motor of sepsis" is an old concept [9]. This principal implies that the vulnerable ecosystem within the gut involves dynamic interplay between microbiome and human host. This homeostasis depends on multiple variables within a delicate system and is dependent upon intact barriers separating the visceral lumen from the lymphatic, portal and, ultimately, systemic circulation (host from outside world). These principles theoretically explained the advantages of EN over PN despite the reduction in caloric deficit achieved through both interventions. Finally, the notion that early initiation of enteral nutrition improves future gastrointestinal tolerance alludes to the therapeutic window following injury. Evidence for improved gastrointestinal motility with the initiation of early EN is lacking in trauma patients and has been demonstrated predominately in the setting of major burn injuries and acute care surgical patients [10, 11]. Following severe trauma, ischemia, hypoxia, and sepsis, the gastrointestinal barrier function is disrupted [12]. Derangements in visceral physiology can lead to alteration in GI cellular structure such as uncoupling of tight junctions, thinning of visceral mucous layers, and increased mucosal cell membrane permeability. Due to these changes in GI permeability, traditional studies have focused on assessing whether or not bacterial translocation occurs from the GI tract following critical illness, trauma, and shock. These studies to date

have been mixed and inconclusive. However, more current thinking identifies that increased permeability of the intestinal barrier to bacterial cell fragments, free bacterial DNA fragments, and necrotic intestinal cellular debris are enough to activate both the local and systemic inflammatory processes following critical illness and injury. This activation can lead to worsening of the inflammatory response or, if persistent, can lead to a reduction in the body's ability to fight off future inflammatory/infectious stimuli. Increased permeability does not tell the complete story, however, as variables such as electrolyte concentrations and pH within the gastrointestinal lumen can significantly affect the overall virulence and distribution of the host microbiome [13]. These alterations in host physiology can directly impact the interaction between the host and the microbiome which can subsequently lead to remote organ dysfunction and failure. A more thorough discussion of these findings are beyond the scope of this manuscript, but the end result is selection of more virulent strains of GI bacteria while at the same time compromising the organs' ability to contain that bacterium away from the host organism.

EN has been suggested to be more efficacious in the maintenance of the structural integrity of the gastrointestinal tract when compared to PN. Mucosal atrophy has been observed in the absence of intraluminal substrate on serial small bowel biopsy in acute pancreatitis and restored with the initiation of EN [14]. Animal studies have demonstrated restoration of GALT and intestinal IgA levels with administration of EN following PN-induced atrophy [15]. EN has also been shown to reduce mucosal atrophy in traumatic brain injury models comparing early EN to parenteral saline alone [16]. In a small study by Hadfield et al., mucosal integrity was restored following the administration of EN in 24 critically ill (predominately post-cardiopulmonary bypass patients) patients as measured by D-xylose and 3-O methyl glucose (absorption), and lactulose and L-rhamnose (permeability) [17].

Recent Data on Timing

The 2004 EAST guidelines gave a level I recommendation to the notion that enteral nutrition support should be initiated within 72 h when feasible. Within this recommendation, the authors noted no difference between 48 and 72 h. The one caveat to this was a statement regarding the initiation of enteral support as early as possible in the setting of severe burns due to increased incidence of gastroparesis observed in delayed groups [1••]. Of note, distinction was given between three injury types: burns, blunt/penetrating abdominal/torso, and head injury again highlighting the heterogeneity of the "trauma patient." Due to the nature of the available trials for examining this question, groups are more easily broken down to involve early (<72 h) versus late (>72 h) intervention groups.

Unfortunately, the available trials examining this question in a prospective fashion specifically among trauma patients are few. Doig et al. performed meta-analysis in trauma patients, which included only three studies comprised of 126 patients, which attempted to delineate appropriate timing of enteral support. This study focused on trials where enteral nutrition was provided within 24 h of insult. The meta-analysis demonstrated a mortality improvement in patients receiving early EN within the first 24 h [18]. However, as is commonplace in the existing nutrition support literature, it should be noted that confounders were readily apparent. To illustrate this point, the most recent included trial in the meta-analysis from 2004 by Kompan et al. examined 52 multiply injured trauma patients (ISS > 20, mean 32) where one group received early EN (mean 10 h) and another received late (mean 38 h) EN with primary endpoints being pneumonia and gastrointestinal intolerance. Of note, the late EN group also received PN which confounds the results if the focus remains on the timing question. There was a statistically significant increase in pneumonia and intolerance in the late (and PN) group [19]. Supplemental parenteral nutrition is not widespread practice in the USA, somewhat limiting the applicability of these data.

More recent studies by ASPEN and SCCM provided more thorough, though less focused, evaluation of critically ill patients. The ASPEN/SCCM guidelines examined 21 trials (conducted between 1979 and 2012) that included 936 critically ill patients in a meta-analysis. This was a heterogeneous group of critically ill patients. The authors found significant reductions in mortality and infectious complications in the early enteral group when compared to delayed groups prompting the recommendation for early enteral support in critically ill patients within 24-48 h of admission to the ICU. Of note, authors noted that the quality of evidence was "very low" [2••, 3]. However, recently, at least one post hoc secondary analysis of a large recent RCT raised concerns for harm associated with the delivery of any nutrient type (parenteral or enteral) early in the setting of critical illness [20]. The EPANIC trial was designed to examine the role for early supplemental PN in critical illness versus no supplemental PN. This was a large trial comprised of 4640 critically ill patients [21]. This post hoc analysis suggested that regardless of the route of administration (PN or EN), any nutrient administered early resulted in a delayed recovery.

Finally, the question arises regarding the "dosing" of enteral nutrition. Several recent trials have suggested that "trophic" feeding strategies (set volume of EN support with caloric delivery far below traditional caloric requirement calculations) are equivalent to full feeding strategies in critically ill patients. Arabi et al. randomized 894 critically ill patients (of which 20 % were non-operative trauma patients) to permissive underfeeding (trophic targeting 40–60 % of goal) or standard enteral feeding (70–100 % targeted goal) and found

no difference in outcomes between the feeding strategies [22]. Studies in acute lung injury patients and surgical ICU patients have yielded similar results in demonstrating non-inferiority of "trophic" feeding strategies with follow-up extending to 1 year after intervention [23–25]. This notion coincides with the concept of non-nutritional EN benefits in maintaining GI barrier function and microbiome composition, as the provision of some substrate at the level of the gut early appears to be of greater importance than the amount provided.

The Enteral Versus Parenteral Question

Historical Perspective

The 2004 EAST guideline recommendation supporting the initiation of early EN was based largely on studies published in the 1980s and 1990s [6, 8]. The proposed superiority of EN support appears to manifest clinically as a reduction in infectious complications; however, mortality differences have not been consistently demonstrated. In fact, one meta-analysis demonstrated lower mortality in the PN group despite higher infectious morbidity [26]. The more recent ASPEN/SCCM guidelines, both in 2009 and 2016, recommended EN over PN in critically ill patients with a quality of evidence rated as "low to very low" [2••, 3]. The authors performed meta-analysis including nine studies comprised of 496 patients comparing EN to PN which demonstrated a significant reduction in infectious complications in the EN group [2••]. Five of these nine studies were conducted in trauma patients, one of which was in the setting of traumatic brain injury [7, 27–30]. They describe the use of EN as "practical and safe" likely highlighting the reduced cost and technical administration of EN when compared to PN [31].

EN has been evaluated in multiple scenarios common in the trauma population, including the open abdomen. Multi-institutional retrospective analysis of 597 patients with open abdomen as a result of damage control surgery demonstrated safety in patients with bowel injury as well as improved fascial closure, decreased complications, and decreased mortality in those receiving EN without bowel injury. [32]. EN has been evaluated prospectively in the setting of prone positioning (comparing nasogastric to post-pyloric placement) [33] and gastrointestinal anastomosis [34] all demonstrating safety. Absolute contraindications to EN are few, but include proximal gastrointestinal discontinuity, bowel obstruction, and concern for mesenteric ischemia. Most experts would avoid EN in the setting of active ongoing resuscitation or increasing vasopressor requirements [2••, 3].

Understandably, given the above evidence, enteral support has become the standard approach to nutrition support in the trauma patient and viewed as the superior option. However, recent trials have resulted in controversy regarding the true risk associated with PN administration. Co-interventions in the ICU have changed dramatically over the last two decades and, as can be seen, most of these trials predate many of these improvements. As an example, glycemic control has become a standard throughout ICUs in the USA and many of these trials were conducted prior to this realization which could directly impact studies regarding efficacy of PN. The advances in critical care have led physicians and surgeons to question if the administration of parenteral nutrition currently is as "risky" as shown in the earlier studies from the 1980s and 1990s.

In an attempt to examine this question, Doig et al. examined 1372 patients with relative contraindications to EN and these patients were randomized to receive either PN or standard care. The PN was given immediately upon admission to the ICU in the PN group and the standard group was supported at the discretion of the treating physician (average 2.8 days to EN or PN support). The authors found no difference in infectious complications or mortality between the groups, but did demonstrate a reduction in ventilator days (0.5 days) and less muscle wasting (as per subjective global assessment) in the early PN group [35]. This trial hinted at the potentially improved safety profile associated with current PN administration when compared to historical populations but translatability was limited by the contraindications to EN in the study population. A second study, the CALORIES trial by Harvey et al. examined the outcomes of critically ill patients receiving EN versus PN in a multi-institutional pragmatic design. The study population consisted of 2400 critically ill adult patients expected to be admitted to the ICU for greater than 72 h. Nutrition support was initiated within 36 h and continued for a period of five days. The enteral group was fed with a nasogastric or nasojejunal tube with expectation to reach goal (25 kcal/kg adjusted body weight) within 48 to 72 h. The parenteral group was given 25 kcal/kg PN through a dedicated central venous access lumen. Moderate glycemic control was maintained in both groups (<180 mg/dL). The primary endpoint was all cause mortality at 30 days and secondary endpoints included duration of organ support, infectious complications, length of stay, and mortality at ICU discharge, 90 days, and 1 year. Interestingly, both groups received equivalent calories and protein. They found no outcome difference with regard to mortality. Among secondary outcomes, vomiting and hypoglycemic episodes were found to be significantly increased in the EN group [36••]. Thus, two large recent trials contradict the majority of the findings of the earlier trials possibly indicating that due to changes in critical care, PN may now carry substantially less risk than once believed. These findings thus need to be evaluated critically in the publication of future guidelines.

Conclusion and Recommendations

Recent trials examining fundamental concepts relevant to nutrition support in the critically ill patient have altered clinical practice. While there are substantial inherent limitations in the available literature, a current reasonable recommendation in the setting of severe trauma is the provision of early EN when feasible. However, findings from the CALORIES trial certainly lower the threshold for earlier initiation of PN in patients where EN is not feasible and long-term nutrition support is indicated. Additionally, dosing strategies based on several recent trials imply that trophic feeding during the first week will likely yield similar outcome benefits to full feeding strategies. Finally, regardless of the route of administration, most of the available evidence supports ongoing nutritional support of critically ill/injured patients over the withholding of nutrition support during critical illness.

Compliance with Ethical Standards

Conflict of Interest Dr. Miller has recieved honoraria from Abbott and Nestle Nutrition. The additional authors declare they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

1.•• Jacobs DG, Jacobs DO, Kudsk KA, Moore FA, Oswanski MF, Poole GV, et al. Practice management guidelines for nutritional support of the trauma patient. J Trauma. 2004;57(3):660–78. **Management recommendations from 2004 specific to trauma patients**.
2.•• McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically Ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016;40(2):159–211. **Management guidelines for adult critically ill patients with some specific considerations in the trauma population**.
3. McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically Ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2009;33(3):277–316.
4. Villet S, Chiolero RL, Bollmann MD, Revelly JP, Cayeux RNM, Delarue J, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr. 2005;24(4):502–9.
5. 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(2):350–7.
6. Moore EE, Jones TN. Benefits of immediate jejunostomy feeding after major abdominal trauma: a prospective randomized study. J Trauma. 1986;26:874–81.
7. Peterson VM, Moore EE, Jones TN, et al. Total enteral nutrition versus total parenteral nutrition after major torso injury: attenuation of hepatic protein synthesis. Surgery. 1988;104:199–207.
8. Kudsk KA, Minard G, Wojtysiak SL, Croce M, Fabian T, Brown RO. Visceral protein response to enteral versus parenteral nutrition and sepsis in patients with trauma. Surgery. 1994;116:516–23.
9. Carrico CJ, Meakins JL, Marshall JC, Fry D, Maier RV. Multiple-organ-failure syndrome. Arch Surg. 1986;121(2):196–208.
10. Chen Z, Wang S, Yu B, Li A. A comparison study between early enteral nutrition and parenteral nutrition in severe burn patients. Burns. 2007;33(6):708–12.
11. Kaur N, Gupta MK, Minocha VR. Early enteral feeding by nasoenteric tubes in patients with perforation peritonitis. World J Surg. 2005;29(8):1023–7. discussion 1027-8.
12. Piton G, Capellier G. Biomarkers of gut barrier failure in the ICU. Curr Opin Crit Care. 2016 Jan 22.
13. Alverdy J, Zaborina O, Wu L. The impact of stress and nutrition on bacterial-host interactions at the intestinal epithelial surface. Curr Opin Clin Nutr Metab Care. 2005;8(2):205–9.
14. Groos S, Hunefeld G, Luciano L. Parenteral versus enteral nutrition: morphological changes in human adult intestinal mucosa. J Submicrosc Cytol Pathol. 1996;28(1):61–74.
15. Ikezawa F, Fukatsu K, Moriya T, Ueno C, Maeshima Y, Okamoto K, et al. Reversal of parenteral nutrition-induced gut mucosal immunity impairment with small amounts of a complex enteral diet. J Trauma. 2008;65(2):360–5. doi:10.1097/TA.0b013e31817c9711. discussion 366.
16. Aydin S, Ulusoy H, Usul H, Yulug E, Cobanoglu U, Aydin K, et al. Effects of early versus delayed nutrition on intestinal mucosal apoptosis and atrophy after traumatic brain injury. Surg Today. 2005;35(9):751–9.
17. Hadfield RJ, Sinclair DG, Houldsworth PE, Evans TW. Effects of enteral and parenteral nutrition on gut mucosal permeability. Am J Respir Crit Care Med. 1995;152:1545–8.
18. Doig GS, Heighes PT, Simpson F, Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials. Injury. 2011;42(1):50–6.
19. Kompan L, Vidmar G, Spindler-Vesel A, Pecar J. Is early enteral nutrition a risk factor for gastric intolerance and pneumonia? Clin Nutr. 2004;23:527–32.
20. Casaer MP, Wilmer A, Hermans G, Wouters PJ, Mesotten D, Van den Berghe G. Role of disease and macronutrient dose in the randomized controlled EPaNIC trial: a post hoc analysis. Am J Respir Crit Care Med. 2013;187(3):247–55.
21. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, Meyfroidt G, et al. Early versus late parenteral nutrition in critically ill adults. N Engl J Med. 2011;365:506–17.
22. Arabi YM, Haddad SH, Tamim HM, Rishu AH, Sakkijha MH, Kahoul SH, et al. Near-target caloric intake in critically ill medical-surgical patients is associated with adverse outcomes. JPEN J Parenter Enteral Nutr. 2010;34(3):280–8. Epub 2010/05/15.
23. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med. 2011;39(5):967–74.
24. Charles EJ, Petroze RT, Metzger R, Hranjec T, Rosenberger LH, Riccio LM, et al. Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care

unit: a randomized controlled trial. Am J Clin Nutr. 2014;100(5): 1337–43. doi:10.3945/ajcn.114.088609. Epub 2014/10/22.

25. Needham DM, Dinglas VD, Bienvenu OJ, Colantuoni E, Wozniak AW, Rice TW, et al. One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. BMJ. 2013;346:f1532.
26. 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(1):12–23.
27. Adams S, Dellinger EP, Wertz MJ, Oreskovich MR, Simonowitz D, Johansen K. Enteral versus parenteral nutritional support following laparotomy for trauma: a randomized prospective trial. J Trauma. 1986;26(10):882–91.
28. Young B, Ott L, Haack D, et al. Effect of total parenteral nutrition upon intracranial pressure in severe head injury. J Neurosurg. 1987;67(1):76–80.
29. Moore FA, Feliciano DV, Andrassy RJ, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications: the results of a meta-analysis. Ann Surg. 1992;216(2): 172–83.
30. Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding: effects on septic morbidity after blunt and penetrating abdominal trauma. Ann Surg. 1992;215(5):503–11.
31. Vanderheyden S, Casaer MP, Kesteloot K, Simoens S, De Rijdt T, Peers G, et al. Early versus late parenteral nutrition in ICU patients: cost analysis of the EPaNIC trial. Crit Care. 2012;16(3):R96.
32. Burlew CC, Moore EE, Cuschieri J, Jurkovich GJ, Codner P, Nirula R, et al. Who should we feed? Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. J Trauma Acute Care Surg. 2012;73(6):1380–7. discussion 1387-8
33. Sams VG, Lawson CM, Humphrey CL, Brantley SL, Schumacher LM, Karlstad MD, et al. Effect of rotational therapy on aspiration risk of enteral feeds. Nutr Clin Pract. 2012;27(6):808–11.
34. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. BMJ. 2001;323(7316): 773–6.
35. Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. JAMA. 2013;309(20):2130–8.
36.•• Harvey SE, Parrott F, Harrison DA, Bear DE, Segaran E, Beale R, et al. Trial of the route of early nutritional support in critically ill adults. N Engl J Med. 2014;371(18):1673–84. **Recent large randomized trial examining enteral versus parenteral nutrition support strategies. There was no mortality difference between the groups**.