

Original Article

EARLY ENTERAL NUTRITION IN ICU PATIENTS: EXPERIENCES FROM MACEDONIA

Mirjana Shosholcheva,^{1,2} Nikola Jankulovski^{1,3}¹Medical Faculty, University "Ss. Cyril and Methodius", Skopje²University Clinic of Surgery "St. Naum Ohridski", Skopje³University Clinic of Abdominal Surgery, Clinical center "Majka Teresa"

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RANA ENTERALNA ISHRANA KOD PACIJENATA U JIL: ISKUSTVA IZ MAKEDONIJE

Mirjana Shosholcheva,^{1,2} Nikola Jankulovski^{1,3}¹Medicinski fakultet Univerziteta "Sv. Ćirilo i Metodije", Skoplje²Univerzitetska hirurška klinika "Sv. Naum Ohridski", Skoplje³Univerzitetska klinika za abdominalnu hirurgiju, Klinički centar "Majka Tereza"

Summary. Early enteral nutrition starts during the first 24 to 48 hours following hospitalization, trauma or injury in hemodynamic stable patients. Either gastric or small bowel feedings are acceptable for intensive care unit patients. The benefits from early versus delayed enteral nutrition are lower incidence of infections, hospital length of stay and mortality. The aim of our investigation was to determine the benefits of early enteral nutrition compared to the concepts "nothing by mouth" in elective GI surgery with jejunal enteral nutrition and/or oral nutrition and to parenteral nutrition in patients with extensive burns, patients with polytrauma and severe acute pancreatitis. Subjects and Method: A total of 87 patients were investigated. Early enteral nutrition was started via naso-jejunal tube, gastrostomy or jejunostomy with standard isocaloric formula. Primary outcome measure was all cause mortality for 4 weeks, while secondary outcome measures were systemic and local complications, inflammatory response, length of hospital stay and adverse events. Results showed reduced hospital length of stay. There were no adverse events such as dehiscence of anastomosis, wound infection or intraabdominal abscess. There was only one fatal outcome. Clinical assessment showed promising results for better outcome in patients with burns and polytrauma. The results obtained in the severe acute pancreatic group were not significant, but enteral nutrition is preferred to "nothing by mouth concept". There was no disease exacerbation; the dynamic CT scan, levels of pancreatic enzymes, C – reactive protein, serum proteins and metabolic panel showed improvement. Conclusion: Enteral nutrition must be started whenever patients can be fed enterally since the chances for better outcome in ICU patients are increased.

Key words: early enteral nutrition, elective GI surgery, burns, polytrauma, severe acute pancreatitis, benefit

Sažetak. Rana enteralna ishrana kod hemodinamski stabilnih pacijenata započinje u prvih 24-48h hospitalizacije, traume ili povrede. Gastrična ili ishrana preko tankog creva prihvatljiva je za pacijente u jedinici intenzivnog lečenja. Prednosti rane enteralne ishrane u odnosu na odloženu su niža incidenca infekcija, kraće vreme boravka u bolnici i niži mortalitet. Cilj ovog istraživanja je odrediti prednosti rane enteralne ishrane u odnosu na koncept "ništa na usta" kod elektivne GI hirurgije sa jejunalom enteralnom nutricijom i/ili oralnom i parenteralne nutricije kod pacijenata sa opsežnim opekotinama, politraumom i teškim akutnim pankreatitisom. Materijal i metod: Ispitivano je ukupno 87 pacijenata. Rana enteralna ishrana je započeta preko nazo-jejunalne sonde, gastrostome ili jejunostome sa standardnom izokaloričnom formulom. Primarno su ispitivani svi uzroci smrtnosti u prve 4 nedelje, a potom sistemske i lokalne komplikacije, inflamatorni odgovor, dužina hospitalizacije i neželjeni efekti. Rezultati su pokazali kraću dužinu hospitalizacije. Nije bilo neželjenih događaja kao što su dehiscencija anastomoze, infekcija rane ili intraabdominalni absces. Bio je samo jedan smrtni ishod. Dobijeni su ohrabrujući rezultati za bolji ishod kod pacijenata sa opekotinama i politraumom. Rezultati dobijeni za grupu obolelih od teškog akutnog pankreatitisa nisu bili značajni ali je enteralna ishrana poželjna. Nije bilo egzacerbacije bolesti; CT pregled, nivo pankreasnih enzima, C-reaktivnog proteina, serumskih proteina i metaboličkih pokazatelja ukazivao je na poboljšanje. Zaključak: Enteralnu ishranu bolesnika u jedinici intenzivnog lečenja treba započeti kad god je to moguće jer su šanse za bolji ishod povećane.

Ključne reči: rana enteralna ishrana, elektivna GI hirurgija, opekotine, politrauma, akutni pankreatitis, benefit

Introduction

Nutrition plays an important role in general therapeutic procedures in critically ill patients as a method of treatment for prevention of malnutrition and correction of metabolic processes. Since recently, there has been a new term in use, “nutritional failure”, which means adaptive response to critical illness. Besides the evidence of the benefits of early nutritional support, time, route, mixture of the food as well as assessment of the nutritional status still remain the subject of controversies.

First of all, it is very important to distinguish between two main concepts: nutrition as a treatment/intervention and nutritional support for prevention of malnutrition. The main aspects of nutritional therapy and nutritional support differ in early versus late, enteral versus parenteral and standard versus special nutrition.

In the critically ill patients, malnutrition is thought to be common but underappreciated and insufficiently treated. It has been recognized as a contributory factor to increased healthcare costs and a potential contributor to adverse outcomes in these patients. Metabolic changes in critical illness differ from metabolism in physiological condition. In the acute response phase of catabolism insulin resistance is present with low T_3 , sick euthyroid syndrome and loss of lean body mass with different consequences (10% loss of lean body mass is considered to be significant, 20% critical and more than 30% lethal).

Patients admitted in an intensive care unit (ICU), who will stay for more than 3 days are at risk of malnutrition. The incidence varies from 0.5 to 100%. Malnutrition might be a risk factor for infections, prolonged wound repair and might increase morbidity, duration of mechanical ventilation, mortality and might contribute to prolonged stay in ICU and impaired immune function.

Recognition of malnutrition starts with a good working plan. According to the American Society of Parenteral and Enteral Nutrition (ASPEN) from 2012., a working frame is in use. Inflammation and its severity is the basis of identification of nutritional risk (compromised intake or loss of body mass). This has to be taken into consideration when differentiating whether malnutrition is a result of an acute or a chronic disease. In acute diseases severe

inflammatory response is present, while in chronic diseases mild to moderate inflammation might be present. Patients without inflammation might develop starvation because of malnutrition. Malnutrition is shown to be present in 43% of critically ill or surgical patients.¹

Identification of risk patients is important in the nutritional management. There is no uniform nutritional risk score, and the score that takes in consideration nutritional status, age and severity of disease (initial APACHE II score, initial SOFA score, interleukin-6 and comorbidities) seems to be very suitable for critically ill patients. According to the ASPEN and European Society of Parenteral and Enteral Nutrition (ESPEN) from 2003, patients in ICU with APACHE II score more than 10, have the highest score (score 3) and are high-risk patients.

The main goal of nutritional support in ICU patients is to give enough amount of calories, nitrogen and microelements: 25 - 35 kcal/kg/bw/day, 1.3-1.6 g proteins/bw/day, elements in trace and vitamins. The most important goal in the first 3 to 5 days is to have proper functioning of GI and to prevent atrophy, which might be achieved with early enteral nutrition.

Optimal nutritional management in ICU needs systematic approach, multidisciplinary management and repeated day assessment. Observational studies suggest that up to 60% of patients receive no enteral nutrition (EN) in the first 48 hours², although according to the ESPEN and ASPEN guidelines, patients even on mechanical ventilation, but hemodynamically stable, with functional gastrointestinal tract (GIT) must start with enteral nutrition 24 to 48 hours after admission in ICU.

The consensus of the nutrition experts is that the GIT is more physiologically and metabolically effective than the intravenous route for nutrient utilization. In functional GIT nutritional treatment/support goes with enteral, while in nonfunctional GIT with parenteral nutrition. The old surgical sentence: “If the gut works – use it, if not – make it to work, if you do not succeed – try again!” is still present today.³

The clinical question: Does early standard enteral nutrition confer any benefit to critically ill patients?, can be answered by different levels of evidence such as individual studies, consensus statements or reviews as well as by meta-analysis of randomised controlled trials performed in hospitalised

adult population, including critically ill, surgical and trauma patients.

By definition, early enteral nutrition is enteral nutrition that starts during the first 24-48 hours following hospitalization, trauma or injury in hemodynamic stable patients⁴. The main goal of the enteral nutrition is to maintain intestinal mucosal integrity by maintaining normal microvillus, intestinal mucosal height, intestinal barrier and intestinal mucosal immunity. Normal intestinal villi are present during feeding while deterioration of the intestinal integrity is present when the intestine is out of use.

The rationale for early feeding is derived from the fact that intestinal system may provide the "substrate" for MOF (the gut's integrity and immune function become compromised by critical illness), which leads to bacterial translocation and cytokine "storming". Enteral nutrition maintains Gut-Associated Lymphoid Tissue (GALT) system, which is responsible for the integrity of the intestinal mucosa. Layers of the GALT include intraepithelial lymphocytes, which first recognize foreign antibody. Lamina propria is the source of IgA, while Payer's patches in the mesenteric nodules modify antigens from the intestinal lumen. Intravenous feeding while the gut is at rest is related to significant suppression of the tissue and GALT functioning, with reduced secretion of IgA and increased permeability of the gut. Oral and enteral feeding maintain intestinal tissue and GALT functioning⁵.

The importance of early nutritional therapy in critically ill patients and recommendation for early aggressive therapy are provided by the guidelines for provision and assessment of nutritional support therapy in the adult critically ill patients by ASPEN and Society of Critical Care Medicine (SCCM).⁶ These guidelines with B and C level of significance recommend EN to be the preferred route of feeding over parenteral nutrition (PN) in critically ill patients who require nutritional support therapy; enteral feeding should be started early within the first 24-48 hours following admission; the feedings should continue over the next 48-72 hours; either gastric or small bowel feedings are acceptable in the ICU setting; critically ill patients should be fed via an enteral access tube placed in the small bowel if patients are at high risk of aspiration or if they show intolerance to gastric feeding and withhold of enteral feeding because repeated high gastric residual

volumes alone may be sufficient reason to switch to small bowel feeding (the definition for high gastric residual volume is likely to vary from one hospital to another, which is determined by individual institutional protocol). There is one controversy regarding this last postulate, which arises from the simple question: Which is the quantity of residual gastric volume, and what is the risk of aspiration. The latest attitude that residual volume more than 150 ml is a relative contraindication for gastric feeding because of the high risk of aspiration (even higher residual gastric volume of 250 ml or even 500 ml might be tolerated).

The other problems related to gastric feeding are gastric motility (especially gastric emptying) and absorption which might cause problems in critically ill patients, as well as Sy of "intolerance to enteral nutrition by the upper GI" (in 46% of patients).⁷

Feeding via small intestine is possible only when there is minimal length of small intestine for tolerance of enteral feeding of about 90 to 100 cm depending on whether it is jejunum or ileum.

The advantages of feeding via small intestine versus gastric feeding are: better absorptive effect, less perturbation of motility, lower gastric residual volume, lower risk of regurgitation and aspiration, and consequently lower risk of pneumonia. More distal placement of the tube (better in jejunum than in duodenum) is a better choice.⁸

Data in the literature indicate the benefits of early versus delayed EN regarding lower incidence of infections by 55%, hospital length of stay (LOS) by 2.2 d and mortality by 64%.^{9,10,11}

Having in mind the guidelines for early enteral nutrition in ICU patients we have conducted several clinical trials in order to assess the benefits of the enteral nutrition.

The hypothesis set for the first trial was that early enteral nutrition might be of benefit to surgical patients. The aim of the study was to confirm the benefit of early enteral nutrition (in the first 24 to 48 hours postoperatively) compared with the concept "nothing by mouth" in elective GI surgery with jejunal enteral nutrition and/or oral nutrition.

Subjects: Thirty-two patients from two University clinics of surgery, University Clinical Center and University City hospital, were included in the period from 1st of January till 31st of December 2013.

Method: Enteral nutrition was started in the first 24 to 48 hours via gastrostomy or jejunos-

tomy. Data on the nutritional support in patients admitted at University Clinical Center is presented in Table 1. Total gastrectomy was performed in 16 patients, naso-jejunal tube was inserted intraoperatively and feeding was started on the second day with standard isocaloric formula. Caloric intake was increased gradually till day 4 or 5. At this time, contrast radiography was performed to check the condition of the anastomosis; the tube was removed, and patients continued oral intake. Numbers of ICU and hospital days are also presented. Complications were found in three patients, but mortality was zero. Table 2 presents data obtained from the Abdominal Department of the University Clinical Center. In 16 patients with different diagnoses gastrostoma or jejunostoma was performed. Enteral nutrition was started in the first 24 hours with standard formula.

Results: Results showed a decrease in length of ICU days and hospital stay. Hospital LOS varied from 2 to 23 days. There were no adverse events such dehiscence of anastomosis, wound infection, pneumonia or intraabdominal abscess. There was only one exitus letalis of a patient with esophageal carcinoma due to the terminal stage of the disease.

Discussion: Despite the evidence that early enteral nutrition has clinical benefits, many physicians wait before starting enteral therapy. There are erroneous reports that enteral nutrition is contraindicated in absence of bowel sounds. Normal myoelectric activity has been shown to be present in the absence of bowel sounds. Therefore, the presence of bowel sounds is not necessarily an indicator of intestinal function. The approximate time in which myoelectric activity is present in the GI tract following surgery is as follows: in small intestine after 4-8 hours, in gaster after 24 hours and in colon after

3 to 5 days.¹²

This clinical trial has limitations. The evidence is insufficiently robust to drive practice (the number of patients is small). A large pragmatic randomized trial is warranted to better guide clinical practice.

The second trial that we have performed analyzed the effect of early enteral nutrition in patients with extensive burns, who were treated in the Center for burns. Table 3 presents data on the nutrition regimen in the burned patients hospitalized during the year of 2013, with very strong evidence for performing enteral nutrition in the first 24 to 48 hours. Patients with percentage of burned area are also presented.

The majority of studies for early enteral nutrition have not included polytrauma patients. Therefore, it is very difficult to obtain evidence on the benefit of early enteral nutrition in these patients since they have many risk factors that might contribute to the final outcome. Table 4 summarizes data on the nutrition in polytrauma patients but the method is inadequately described and hence the search process is not adequate. However, clinical experiences have shown promising results for better outcome in these patients.

The most challenging trial was the assessment of nutrition in pancreatic patients. First of all, it was very important to assess all different nutritional strategies in acute pancreatitis and to find out which acute pancreatitis condition best suits to EN. The biggest therapeutic benefits of EN are seen in patients with severe acute pancreatitis (SAP).

It is an ongoing trial; it is a prospective, randomized clinical trial of enteral nutrition for treatment of acute pancreatitis, which was started in 2013. The aim of the study is to find if there is any benefit from early EN in patients with SAP.

**Table 1. Early enteral nutrition in the patients with GI surgery
(Data from University Clinic of Surgery for 2013 year)**

Abdominal surgery	Number of patients	Study protocol	Formula	Day	Caloric intake (kcal) (Mean $\pm$)	ICU days	Hospital days	Mortality (28 days)
Total gastrectomy	16	SBT	Standard isocaloric	2	800 $\pm$ 100	7 (4-12)	19(13-24)	-
				3	1200 $\pm$ 100			
				4-5	1900			

SBT = small bowel tube; jejunostomy

Subjects and method: Two groups of patients were included. We complied with the ASPEN guidelines for nutrition in patients with acute pancreatitis from 2002. In the first group we included 6 patients with severe pancreatitis and we monitored them from January 2014 till December 2014. Patients were classified as “predictive severe” acute pancreatitis if they were admitted within 24 hours and fulfilled one or more of the following criteria: APACHE II score ≥ 8 , Ranson score ≥ 3 and CRP level > 150 mg/L. The second group comprised patients who did not receive anything by mouth, except intravenous fluids. Primary outcome measure was all cause mortality for 4 weeks, while secondary outcome measures were systemic complications, local complications, inflammatory response (CPR),

length of hospital stay (LOS) and adverse events.

Protocol: EN was delivered through a naso-jejunal feeding tube placed endoscopically; abdominal X-ray was performed to check the tube’s position (naso-jejunal placement was considered correct, when the tip of the tube was placed beyond Treitz’ ligament); EN was started immediately using a very strict volume regimen (20 ml/h in the first 24 hours, increased by 10 ml/h every 6 hours until 45 ml/h, between 24-48 h, 65 ml/h, between 48-72 hours and, at 72 hours and thereafter: full nutrition, defined as an energy target of 25 kcal/kg/day). Standard formula without immunosupplements and anti-oxidants was used.

Results: A small number of patients was included in this study and therefore the results are insuffi-

**Table 2. Early enteral nutrition in the patients with GI surgery
(Data from Abdominal Department of the University Clinical Center for 2013 year)**

Gender/age	Diagnosis	Surgery	First day	EN	Hospital LOS(days)
M / 54	Ca larynges. Stenosis oesophagi	Gastrostomae	< 24 h	SF	2
F / 58	Stenosis oesophagi	Gastrostomae	< 24 h	SF	23
M / 56	Ca oesophagi	Gastrostomae	< 24 h	SF	21
F / 46	Stenosis oesophagi	Gastrostomae	< 24 h	SF	4
M / 70	Stenosis oesophagi	Gastrostomae	< 24 h	SF	?
M / 46	St. post gastrectomia tot.	Jejunostomae	< 24 h	SF	6
F / 49	Ca oesophagi	Gastrostomae	< 24 h	SF	9
F / 48	Stenosis antropylorici	Jejunostomae	< 24 h	SF	9
F / 75	Ca oesophagi partis dist.	Gastrostomae	< 24 h	SF	8
M / 67	Intoxicatio cum HCL	Jejunostomae	< 24 h	SF	6
F / 77	Ca oesophagi dist. et cardiae	Jejunostomae	< 24 h	SF	Exitus let.
M / 25	Stenosis pylori.	Jejunostomae	< 24 h	SF	9
F / 62	Ca laryngis	Gastrostomae	< 24 h	SF	4
M / 30	Stenosis pylori.	Jejunostomae	< 24 h	SF	7
M / 79	Ca oesophagi	Gastrostomae	< 24 h	SF	15
F / 61	Stenosis oesophagi	Jejunostomae	< 24 h	SF	6

cient. Estimates of treatment effect are not very stable, but there is a great signal that EN is preferred to “nothing by mouth” concept in patients with SAP. The benefit from EN was evident; we found no disease exacerbation in the 6 examined patients; the dynamic CT scan with contrast showed improvement of the pathological condition as well as the level of pancreatic enzymes, C – reactive protein, serum proteins and metabolic panel. The outcome was good and they were discharged home in a good condition. These first results showed that enteral nutrition has started to be preferred nutrition in patients with severe acute pancreatitis; there is no rationale to start initial nutritional treatment with parenteral nutrition; early enteral nutrition via naso-jejunal tube might lead to better outcome. Parenteral nutrition can be used if there is no tolerance for enteral nutrition.

Discussion

Several scoring systems are used to predict SAP. Predicting SAP might be according to: Ranson criteria (RC), APACHE score, CT index (necrosis); focus on age, BMI, SIRS, BUN/creatinine, comorbidities; Atlanta classification (scores, complications, organ failure); or transient versus persistent organ failure at 48 hrs.¹³ SAP patients who benefit (improve outcome) from EN are recognized with RC more than 3, APACHE II more than 8 and CRP more than 150.

There are several studies which have investigated nutrition in SAP trying to answer questions as when to start (early, very early or delayed nutrition; the problem of pancreas rest), how to feed (parenteral, enteral; post-pyloric or gastric); which formula to use (elemental, polymeric or immune-enhancing) and finally what are the risks, complications and outcomes.

The traditional model for nutrition in SAP is parenteral nutrition, but over the last 10 to 15 years EN has been established. The guidelines with high level of evidence (B) published in the Journal of clinical nutrition from 2009, recommend EN in all patients who need nutritional support. Parenteral nutrition is indicated in nonfunctional gut or when EN is not possible (prolonged ileus, complex pancreatic fistulae)^{14,15,16}

Starting EN might be questionable for those who support maintaining pancreas in rest. There are two concepts regarding nutrition in pancreatic patients: pancreas rest and gut appliance. Avoiding pancreatic secretion to reduce inflammation has been confirmed in animal studies where the amount of pancreatic secretion is in inverse correlation with the width of pylorus. In human studies, it has been found that continuous feeding through distal jejunum does not stimulate exocrine pancreatic secretion. The benefit of EN lies in the fact that the gut is in use, maintaining intestinal integrity to prevent bacterial translocation and causative SIRS.

There is sufficient evidence for naso-jejunal en-

Table 3. Nutrition in patients with burns
(Data from Center for burns – 2013)

% of burned surface	Number of patients (total =34)	Day of starting EN and PN	EN	PN
< 10%	8	1	yes	/
	5	2	yes	/
11-21%	2	1	yes	/
	7	2	yes	/
21-30%	1	1	yes	/
	3	2	yes	/
31-40%	2	2	yes	/
	3	2	/	yes
41-50%	1	2	yes	/
	1	3	/	yes
> 51%	2	1	yes	/

EN = enteral nutrition; PN = parenteral nutrition

Table 4. Nutrition in polytrauma patients
(Data from University Clinic of Surgery for 2013 year)

Patient No.	Gender Age	Diagnosis	LOS in ICU	NG tube placement	Start of enteral nutrition
1.	F/14	Polytraumatismus, Contusio capitis, F-ra alla majoris ossis sphenoidalis	4 days	/	/
2.	M/5	Comma cerebri F-ra capitis aperta, Laceracio cerebri	6 days	First day	Second day
3.	M/9	Comma cerebri traumatica, SAH traumatica, Contusio cerebri reg. pars temporalis	6 days	First day	Third day
4.	F/16	Comma cerebri traumatica, Rinorrhagia, Otorrhagia l.dex.	5 days	/	/
5.	M/26	Commotion cerebri, Contusio capitis, Epistaxis	4 days	First day	Third day
6.	M/5	Contusio capitis, Haemathoma epiduralis reg. temporalis l. dex	4 days	First day	Second day
7.	F/41	Polytraumatismus, Contusio cerebri, Haemorrhagia itracerebralis	9 days	First day	Second day
8.	M/51	Comma-Contusio cerebri, Haemorrhagia intracerebralis	2 days	First day	Second day
9.	F/75	Comma cerebri, F-ra costae	46 days	Sixth day	Tenth day
10.	M/57	Comma cerebri, Insufitientio respiratoria, St. post. op. pp. Ca caput pancreatic	6 days	Second day	Third day
11.	M/78	F-ra basis cranii, Otorrhagia l. dex.	32 days	First day	Second day
12.	M/72	Comma cerebri, Haemorrhagia intraventricularis	8 days	First day	Second day
13.	F/69	Comma-Contusio cerebri, Mydriasis, F-ra orbitalis pars basalis	14 days	First day	Forth day
14.	M/45	Comma cerebri, Colapsus	2 days	First day	Second day
15.	M/64	Comma-contusio cerebri, Haemorrhagia itracerebrale bill.	49 days	First day	Second day

LOS = length of stay; NG tube = nasogastric tube

teral nutrition (NJ-EN) in SAP². Since 1988 several studies have compared NJ-EN with PN in a large cohort of patients with SAP and showed reduced infectious complications, inflammation, organ failure, hospital LOS and radiological changes of pancreatitis. This effect was greatest in the sickest cohort of patients (APACHE II>13). There was no detectable difference in mortality. Naso-jejunal enteral feeding was confirmed as safe when started immediately (within 6 hours). Probiotic feed supplementation was found not to be beneficial. However, it was suggested that probiotic feed supplementation may cause harm and increase mortality. Mortality in the probiotic group was 16% compared

to 6% (placebo). Some of the patients in the probiotic group developed fatal gut ischemia compared to none in the placebo group. This mortality difference was not supported by the meta-analysis. There is no evidence that supports immune-nutrition. No evidence exists to confirm the benefit of prokinetics in SAP as well as intravenous supplementation of anti-oxidants.

The physiologic benefits of providing EN in patients with SAP are: gut integrity maintenance (less bacterial challenge, endotoxemia); set tone for systemic immunity (innate, acquired responses); attenuate stress response and disease severity (CRP, glucose); faster resolution of disease process (Du-

ration SIRS, LOS). Timing for EN is an important issue. The recommendation is to start within 24-48 hrs¹⁷.

The outcome benefits of EN compared to the concept "no nutrition" regarding post-operative complications in acute pancreatitis are reduction in mortality, systemic infections, multiple organ failure and hospital LOS.¹⁸ There are some unexpected benefits of EN regarding abdominal compartment syndrome where the mechanisms are ascites, hypoalbuminemia, pancreatic or bowel edema.¹⁹ Some benefits are found in pancreatic fistulae which complicate 3 to 36% of Whipple procedures when EN is administered per NJ tube 20 cm below anastomosis.²⁰

Conclusion

There is a question that needs an answer: how to feed ICU patients? There are shortcomings of the enteral nutrition, but EN must be started whenever patients can be fed enterally or when there are no contraindications. All patients might be assessed for nutritional score. If the feeding is not possible by mouth, then other routes for EN might be used. Aggressive strategies for EN increase chances for better outcome, and reduce the need for PN in ICU patients.

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